DECODE

THE IMPACT STUDY

IDENTIFYING THE PERSPECTIVES OF PATIENTS DIAGNOSED WITH PRIMARY MEMBRANOPROLIFERATIVE GLOMERULONEPHRITIS AND PARENTS OF PATIENTS REGARDING POTENTIAL PARTICIPATION IN FUTURE CLINICAL TRIALS

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TO REFERENCE THIS REPORT

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INTRODUCTION

What is MPGN?

MPGN stands for “Primary membranoproliferative glomerulonephritis” and represents a group of rare kidney disorders associated with complement activation [1]. In MPGN, there is an abnormal thickening of the glomerular basement membrane, which leads to impaired kidney function. The symptoms of MPGN can include blood or protein in the urine, high blood pressure, swelling in the legs or feet, decreased urine output, fatigue, edema, loss of appetite, anxiety and depression [2]. MPGN is severe and the prognosis is unfavorable: about half of all patients, mostly children, develop end-stage renal disease and need dialysis within 10 years of onset.

Treating MPGN is challenging because of its heterogeneity. Patients have abnormal activation at different levels of the complement system. Historically, MPGN has been classified as type I, II and III based on light microscopy and glomerular ultrastructure. More recently, MPGN has been divided into different types of sub-diseases including IC-MPGN, C3 glomerulopathy (C3G), Dense deposit disease (DDD) and C3 glomerulonephritis (C3GN). However, this current classification brings challenges and does not fully reflect the disease etiology.

Treatment for MPGN depends on the type and severity of the disease, and may include medications to control blood pressure, reduce inflammation, and suppress the immune system. In severe cases, kidney transplant may be necessary. It remains often unclear which patients are most likely to respond to a treatment [3].

Several drugs targeting the complement have been already approved or are investigated in trials for other conditions. Conducting clinical trials for MPGN patients is essential to identify new and more efficient treatment pathways. However, very little is known about what motivates or prevents MPGN patients from participating in clinical trials. Developing clinical trials for small patient groups, and recruiting enough participants, is often expensive and demanding. Participation may be influenced by considerations such as the number of biopsies that have to be taken [4], where the trial takes place and for how long, how data are used and shared with patients and researchers [5] [6], and whether access to treatment is secured, also after trial closure [2]. Exploring the views of patients regarding diverse aspects of participation in clinical trials is useful to support the design and development of future clinical trials and facilitate recruitment.

The DECODE project

DECODE (*Defining stratification of patients with C3 Glomerulopathies/immune complex-mediated glomerular diseases for better diagnosis and tailored treatment*) is a 3-year European research project) funded by ERAPerMed. The project aims to improve the diagnosis and treatment of patients with C3 Glomerulopathies and other immune complex-mediated glomerular diseases. By combining the use of omics technologies and clustering analysis, the project develops a more precise and accurate method for diagnosing and classifying patients with these diseases based on their individual disease mechanisms. This involves identifying specific biomarkers, genetic mutations, and other factors that may contribute to the disease. Developing new methods for diagnosing and classifying patients may contribute to identify more tailored and personalized treatments for the patients.

A primary outcome of the project will be the design of protocols for future clinical trials to evaluate the effect of selected complement inhibitors in patients stratified according to clusters. It is hoped that future

clinical trials will offer patients a larger chance of recovery. The DECODE project (March 2021- February 2024) is led by professor Ariela Benigni at the Mario Negri Institute for Pharmacological Research in Bergamo, Italy, and involves partner research institutions from Italy, Greece, Germany and Norway as well as patient organizations in Italy and the Netherlands.

The IMPACT study

The IMPACT study is part of the DECODE project. IMPACT stands for *"Identifying the perspectives of patients diagnosed with primary Membranoproliferative glomerulonephritis and/or parents of patients regarding potential PArticipation in future Clinical Trials."*

The overall objective of this study was to investigate the views and perspectives of an international sample of patients diagnosed with MPGN and parents of children diagnosed with MPGN regarding any potential future participation in clinical trials. More specifically, the study investigated:

- Participant views regarding life with the disease
- Willingness to participate in future clinical trials
- Views regarding data sharing with researchers
- Help and support needed to live with the disease
- Future expectations regarding research.

Results from the IMPACT study can provide directions for the design of future clinical trials and information to patients regarding treatment options, consequences of participating in a clinical trial, data sharing practices, and potential follow-up post clinical trial.

The IMPACT study was conducted in two steps:

- An international anonymous online survey. Results from the survey are provided in this report.
- Digital individual interviews with MPGN patients and parents of patients. Results from the interviews will be reported elsewhere.

METHODS

An anonymous online survey was developed in collaboration with researchers and representatives from patient organizations in Italy, Germany, and the Netherlands. The survey was posted on the DECODE website in September 2022 and the survey link was shared with the patient organizations, which promoted it in their networks including organization members and social media platforms. The link was also shared with research groups collaborating with DECODE and that could disseminate it among their patients. The survey closed in February 2023.

An IMPACT study flyer (Appendix 1) was developed to provide general information about the survey. The flyer was shared with patient organizations and research groups in the network of DECODE.

The survey consisted of two questionnaires:

- A questionnaire to patients aged 16 years or older (29 questions)
- A questionnaire to parents of patients below 16 years of age (30 questions)

Completing each questionnaire was estimated to take approximately 15-20 minutes. The questionnaires are provided in Appendix 2 (To patients) and Appendix 3 (To parents of patients).

Some questions in the survey were based on a previous questionnaire used in connection with the organization of a patient meeting by the National Kidney Foundation in the United States [2].

Only the five first questions in the questionnaires were mandatory as they collected demographic data and basic information. Patients or parents interested in completing the survey were asked to consent to the use of their data for research at the start of the questionnaire.

The survey was available in 6 languages (English, Italian, Dutch, German, French, Norwegian) on the DECODE website.

The survey protocol received an ethics waiver from the Regional Committees for Medical and Health Research Ethics (REK Sør-Øst 479358) in Norway.

The survey data were processed in Excel and simple descriptive statistics were produced. The free-text responses were analyzed qualitatively by translating responses in the different languages using Google translate and summarizing them according to recurrent response categories.

KEY FINDINGS

- Overall, survey respondents described their or their child's quality of life and living conditions with the disease as good or average. Living with MPGN, however, brings several important physical limitations and mental burdens and has an impact on family life and family planning.

- Most respondents trusted that their doctor could help manage the disease, but experienced that current treatments do not fully address their needs.

- Patients and parents of patients were largely willing to participate or let their child participate in potential future clinical trials. The main motivating factor for entering a clinical trial was hope that the new treatment will improve kidney function.

- Most important factors influencing a decision to participate or not in a clinical trial include the types of expected side effects and the number of biopsies to undergo. Practical considerations regarding participation such as trial duration and location, and frequency of visits, were likely to be given less weight in the decision-making process.

- Respondents saw the severity and number of side effects as a playing a very important role in the selection of a treatment, more so than how and how often the treatment must be taken.

- Survey respondents wanted to be informed about general trial results and their or their child's individual results. They also found important to have the possibility to continue treatment for free after trial end.

- Survey respondents largely supported the sharing of their data for research on other diseases, much less for research outside of the health sector. Main perceived benefits of data sharing included contributing to the development of new treatments and helping to improve the diagnosis of future patients. Main perceived drawbacks of data sharing included the risk that the data may be used for purposes the respondents disagreed with. About a third of respondents did not see any drawback with sharing their data.

- Survey respondents gathered information about their or their child's kidney disease through their general practitioner or their nephrologist. They also used internet and the media and consulted patient organizations to collect information. They wanted to receive more information about their own or their child's prognosis, kidney-friendly diets, and strategies to reduce symptoms.

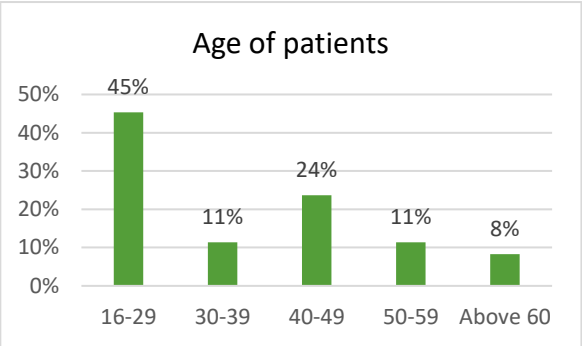
- Survey responses were largely similar between patients aged 16 years or above and parents of patients below the age of 16.

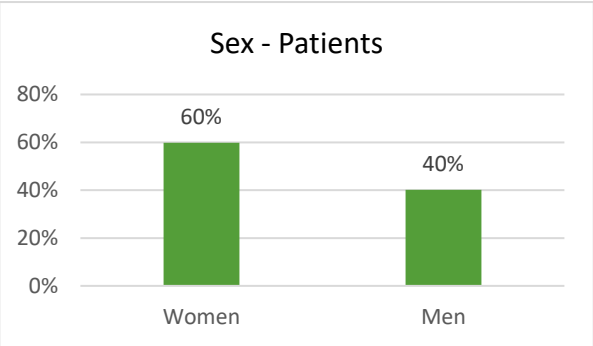
RESULTS

Results from survey questionnaire to patients aged 16 years or older

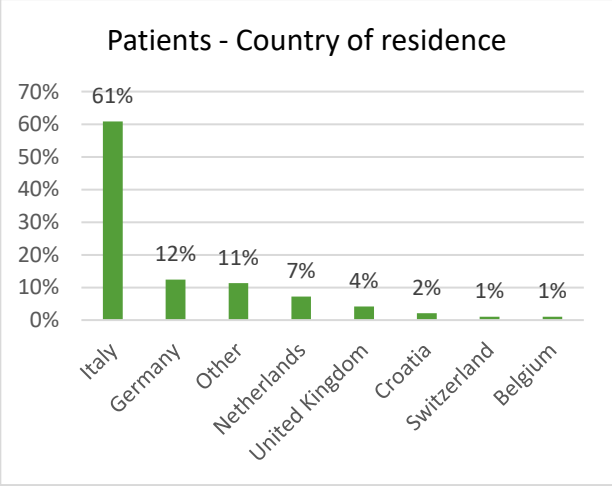
Respondents' demographics

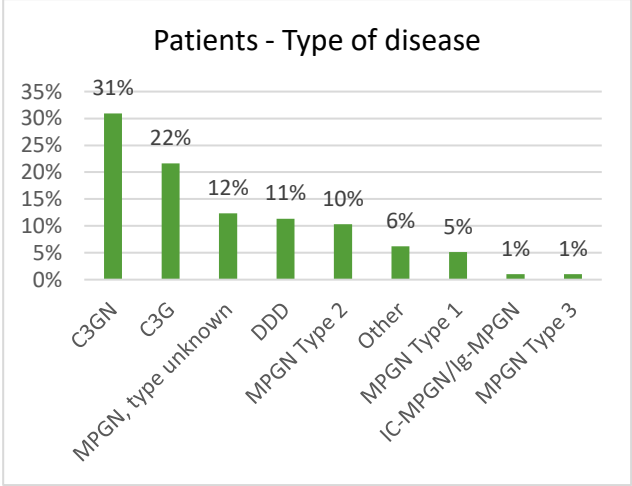
This survey questionnaire collected responses from 97 people aged 16 or older. Most respondents were young adults (45%, N=44 aged 16-29) or middle aged (24%, N=23 aged 40-49) and were women (60%, N=58).





The respondents were primarily geographically located in Italy (61%, N=59), Germany (12%, N=12) and the Netherlands (7%, N=7). 11 respondents (11%) were in countries outside of the European Union.

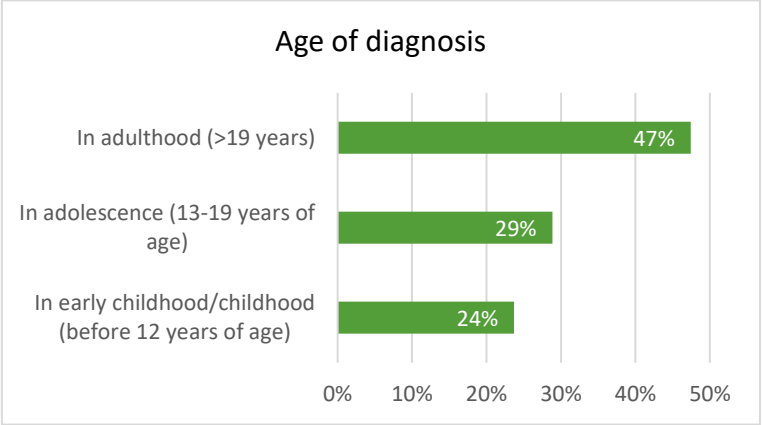




Most respondents reported to have been diagnosed with C3GN (31%, N=30) or C3G (22%, N=21).

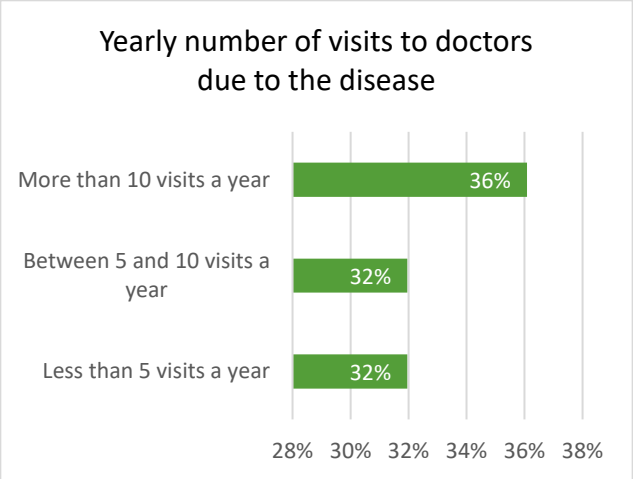
12 respondents had been diagnosed with MPGN but did not know which type. 11 had been diagnosed with DDD and 16 with MPGN, either type 1, 2 or 3.

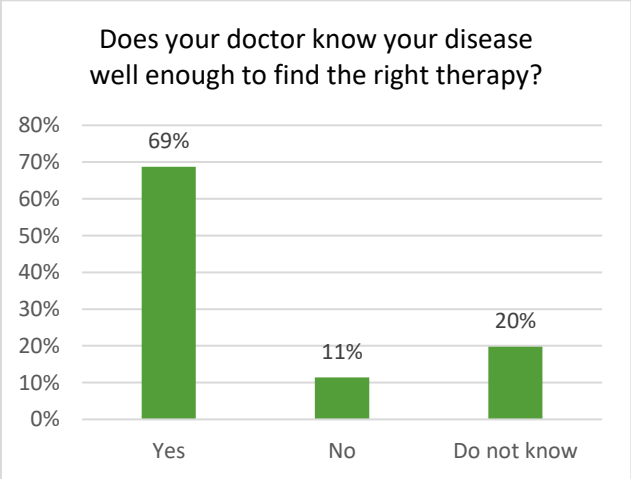
Most respondents have been diagnosed in adulthood (47%, N=46) or in adolescence (29%, N=28).



Interaction with doctors

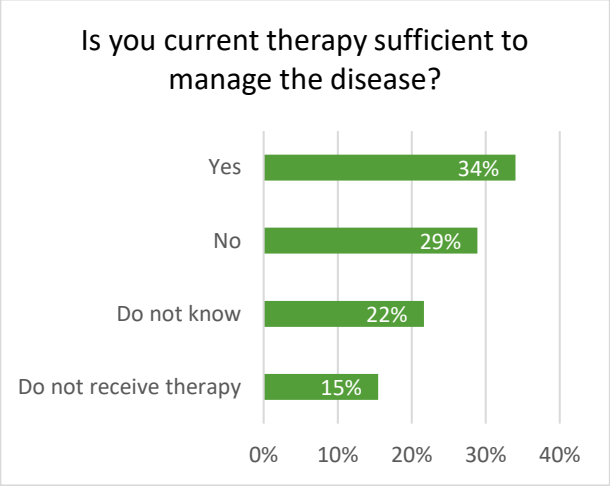
Most respondents (36%, N=35) reported to have visits to doctors, for instance nephrologists, dermatologists, or eye specialists, due to their disease, more than ten times a year.

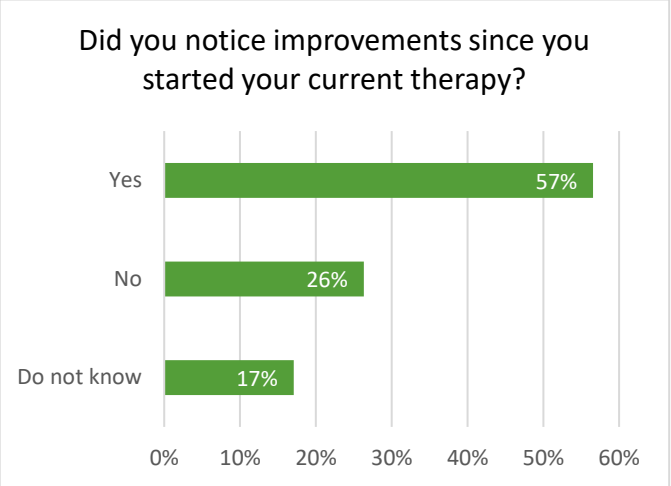




69% (N=66) of respondents believed that their doctor knows their disease well enough to be able to find the right therapy for them. 20% (N=19) did not know and 11% (N=11) thought that it was not the case.

Views on current treatment

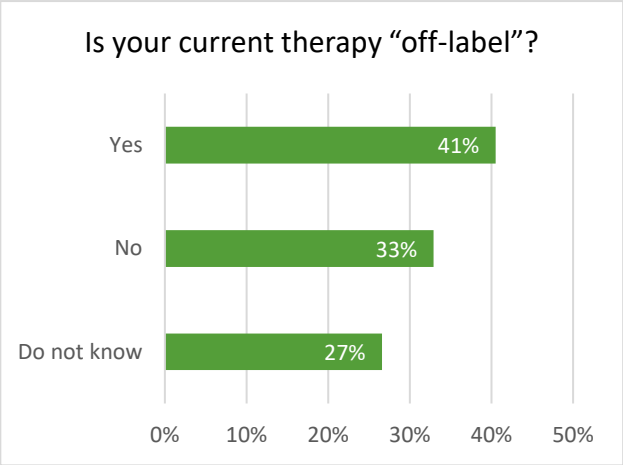


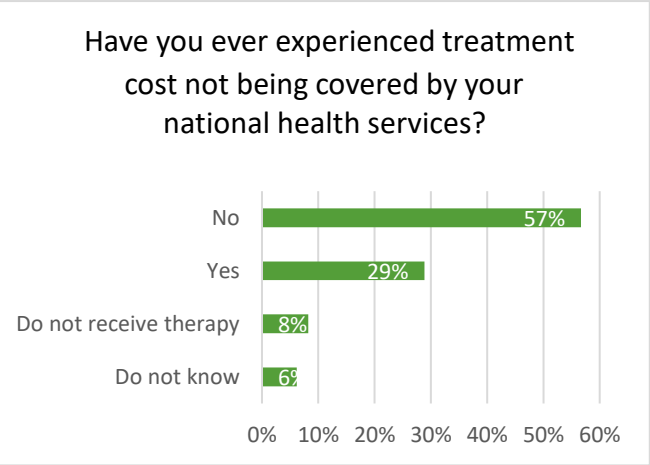


A slight majority of respondents (34%, N=33) thought their current therapy is sufficient to treat their disease while 29% (N=28) did not think so and 22% (N=21) did not know. 15% of respondents (N=15) reported not to receive any therapy for their disease.

57% of respondents (N=43)[1] experienced some improvements after they started their current therapy while 26% (N=20) did not and 17% (N=13) did not know.

Access to treatment



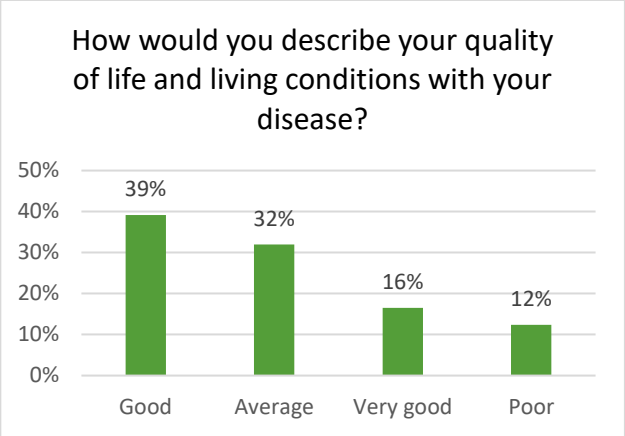


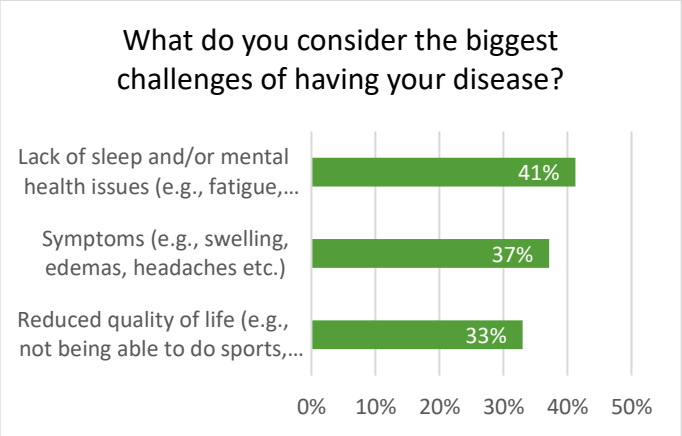
41% (N=32)[1] of respondents reported their current therapy to be “off-label”, which was defined in the survey questionnaire as being “A drug approved by the European Medical Agency for another disease, not for your diagnosis.” 33% (N=26) did not receive off-label therapy whereas 27% (N=21) did not know whether their current therapy is off-label or not.

57% (N=55) of respondents had never experienced that the cost of their treatment was not covered by their national health service whereas 29% (N=28) had made such experience.

[1] Answers from respondents indicating they did not receive treatment were excluded.

Living with the disease



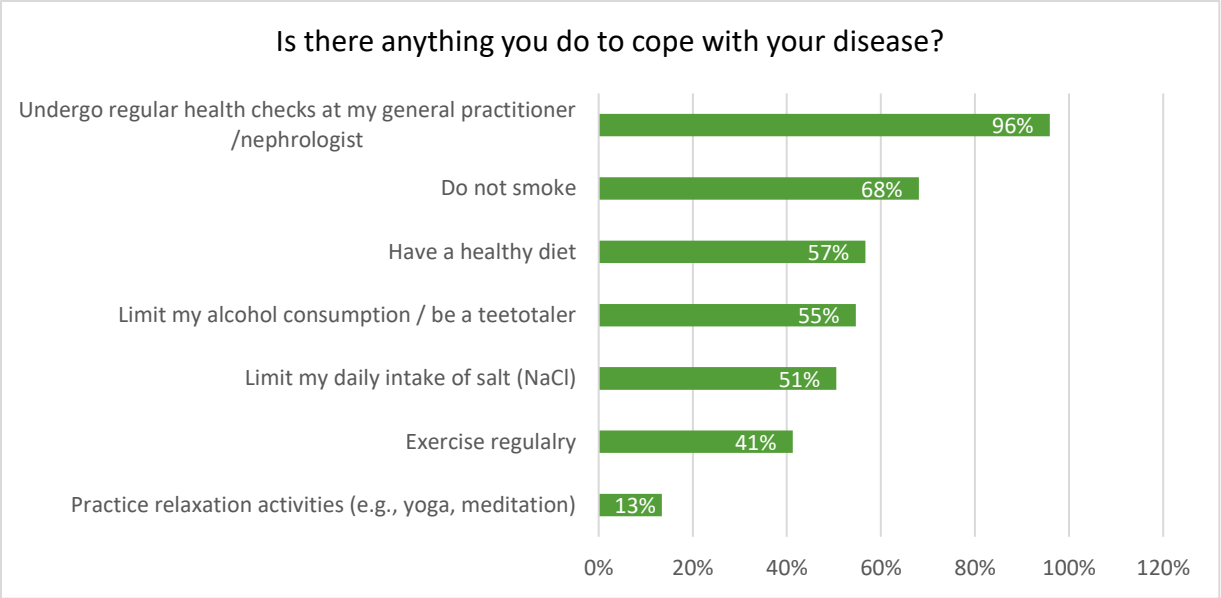


Most respondents described their quality of life and living conditions with the disease as good (39%, N=38) or average (32%, N=31).

The respondents could select two out of three types of challenges living with the disease. 41% of respondents (N=40) considered lack of sleep and/or mental health issues (e.g., fatigue, anxiety, depression, fears etc.) as being the biggest challenge. 37% reported (N=36) reported symptoms (e.g., swelling, edemas, headaches etc.) to be challenging whereas 33% (N=32) saw their quality of life reduced (e.g., not being able to do sports, pursue an education, maintain a job etc.).

The respondents had the possibility to provide some written feedback about experienced challenges. These included:

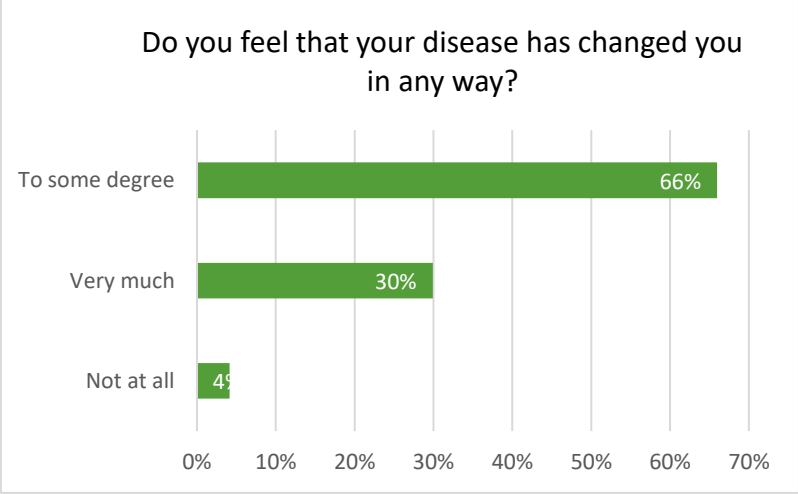
- Disease progression: Having to manage the disease and limit its progression, having to undergo several kidney transplant and experiencing disease recurrence on the transplants, and not knowing what the future will bring.
- Concerns related to having an increased risk of developing other diseases, like Covid-19, and having to manage these diseases and undergo treatment for them.
- Having to live with symptoms such as energy shortage and tiredness, always being cold, often sick, prone to develop infections, falling suddenly asleep, experiencing muscle aches, headaches, light oedemas, and hypertension.
- Reduced quality of life: Having to follow a low-salt diet, weight gain due to cortisone therapy, not being able to take sports supplements, experiencing limited performance, having to avoid over-exertion or not being able to go on a trip.
- Impact on pregnancy: Difficulty of carrying on a pregnancy without problems.
- Limited access to drugs due to bureaucracy.



The respondents could select two out of seven types of activities to cope with the disease. Most respondents (96%, N=93) underwent regular health checks with their general practitioner or nephrologist. Not smoking was selected by 68% (N=66) of respondents, followed by having a healthy diet (57%, N=55), limiting alcohol consumption or not consuming alcohol (55%, N=53), limiting daily intake of salt (51%, N=49), exercising regularly (41%, N=40) and practicing relaxing activities (13%, N=13).

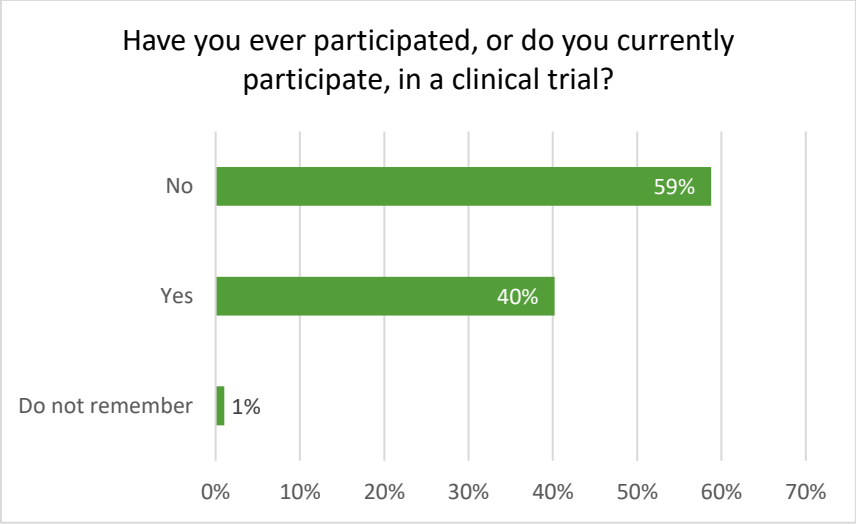
The respondents had the possibility to provide some written feedback about activities. These included:

- Taking transplant medication
- Enjoying life
- Not thinking of oneself as a sick person
- Vaping
- Trying to sleep more
- Taking extra vitamins.

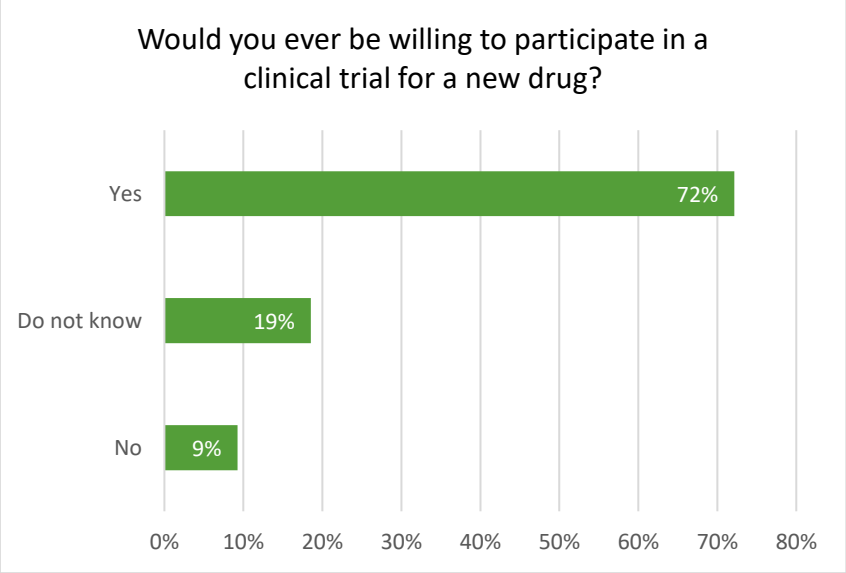


Most respondents felt that the disease had changed them to some degree (66%, N=64%) or very much (30%, N=29).

Participation in clinical trials

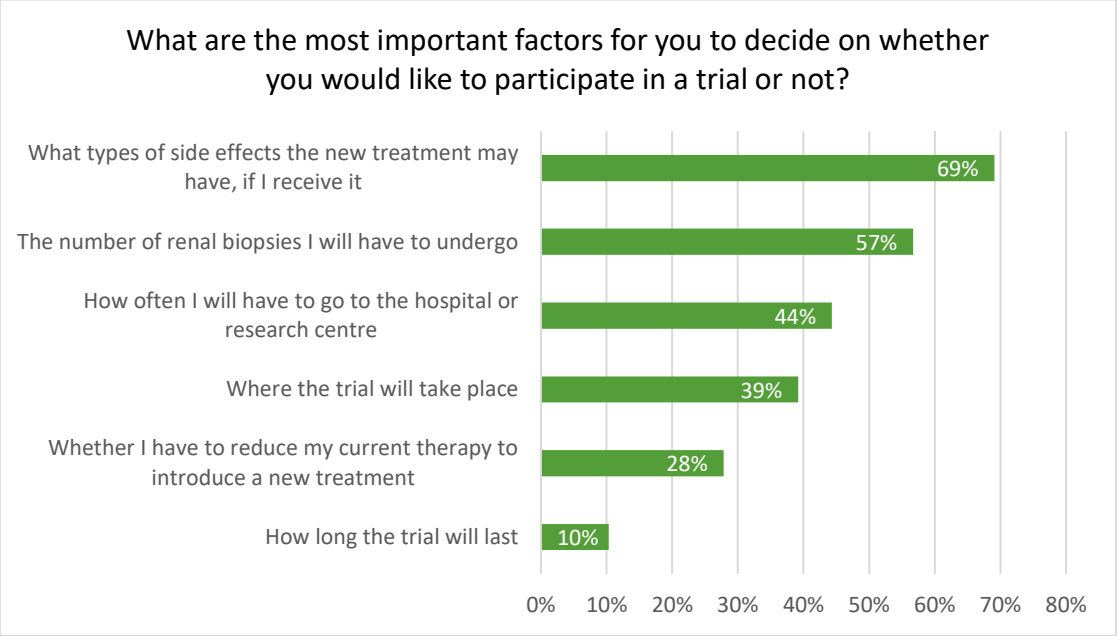


Most respondents (59%, N=57) had never participated and did not participate in a clinical trial at the time they completed the questionnaire whereas 40% (N=39) have had some experience of clinical trials.



A large majority of respondents (72%, N=70) reported to be willing to participate in clinical trials for a new drug whereas 19% (N=18) did not know whether they would be willing and 9% (N=9) were not willing to participate in a trial.

Factors influencing decision to participate in a clinical trial

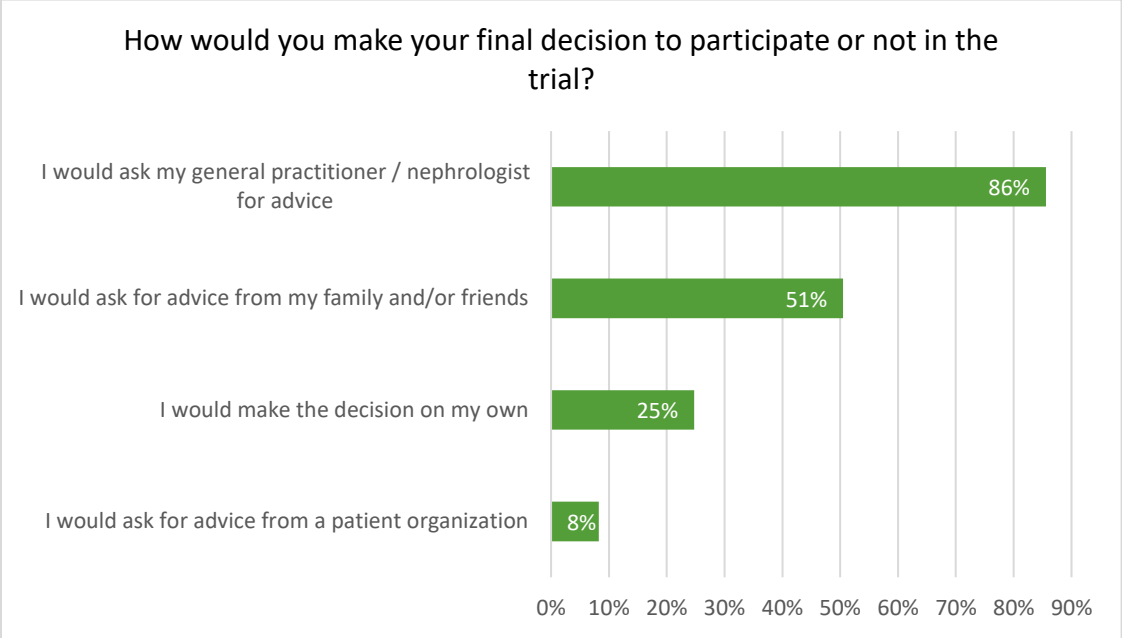


The respondents could select the three most important factors that may influence their decision to participate in a clinical trial. Most respondents (69%, N=67) selected the types of side effects the new treatment may have as the most influential factor followed by the number of biopsies they would have to undergo (57%, N=55). Other factors included how often participation in the clinical trial requires going to the hospital or research centre (44%, N=43), where the trial will take place (39%, N=38), whether participation in the clinical trial will require reducing current therapy (28%, N=27) and how long the trial will last (10%, N=10).

The respondents had the possibility to indicate other factors in writing. These included:

- Results from Phase I and II clinical trials
- Scientific data on mechanism of action and preclinical predictors of likely efficacy
- Disease progress, if placed in a placebo group
- If the trial is open to transplant recipients
- If guarantee is provided that the transplanted kidney will not be damaged
- Logistics related to the working obligations
- Size of the placebo arm.

Decision to participate in a clinical trial



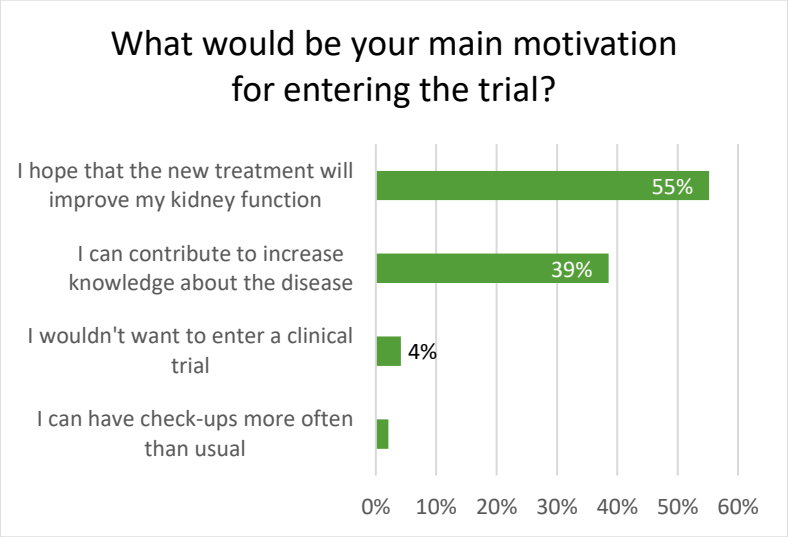
The respondents could select all options that applied to make their final decision regarding participation in a clinical trial. Most respondents (86%, N=83) would involve their practitioner or nephrologist in the decision-making process regarding their participation in a clinical trial. 51% of respondents (N=49) would ask for advice from family and friends whereas 25% (N=24) would make the decision on their own and 8% (N=8) would ask for advice from a patient organization.

The respondents had the possibility to indicate other ways of making their decision in writing.

These included:

- Asking a doctor specialized in the disease
- Asking the partner instead of family.

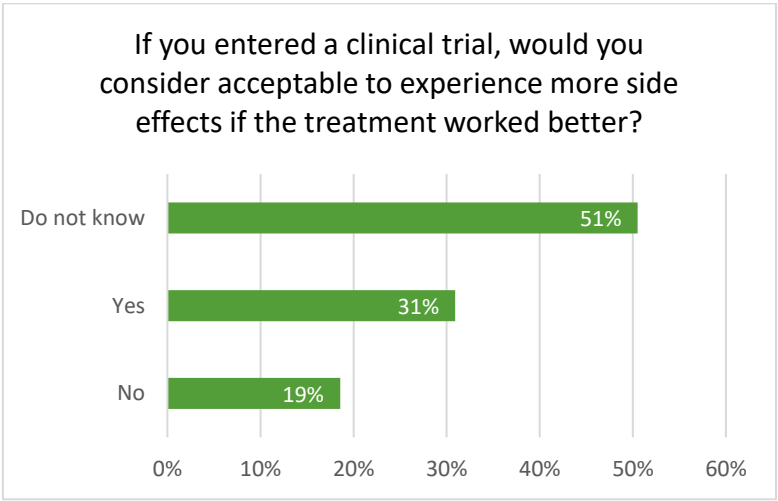
Motivations for entering a clinical trial



The respondents could select only one factor motivating participation in a clinical trial. 55% of respondents (N=53%) reported that any hope that the new treatment will improve kidney function was the main motivating factor. 39% (N=37) of respondents saw as motivating being able to increase knowledge about the disease.

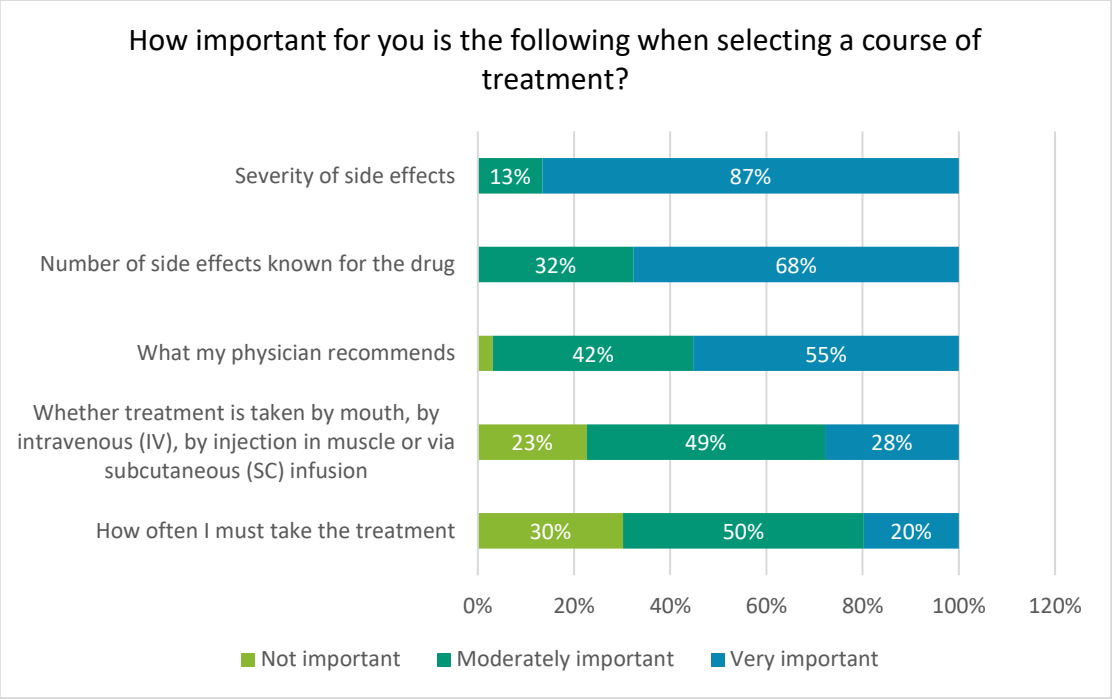
The respondents had the possibility to indicate other motivating factors. These included:

- Contributing to finding a treatment that works for transplanted patients
- The possibility of improving the quality of life of those who will eventually benefit from the drug in the future.

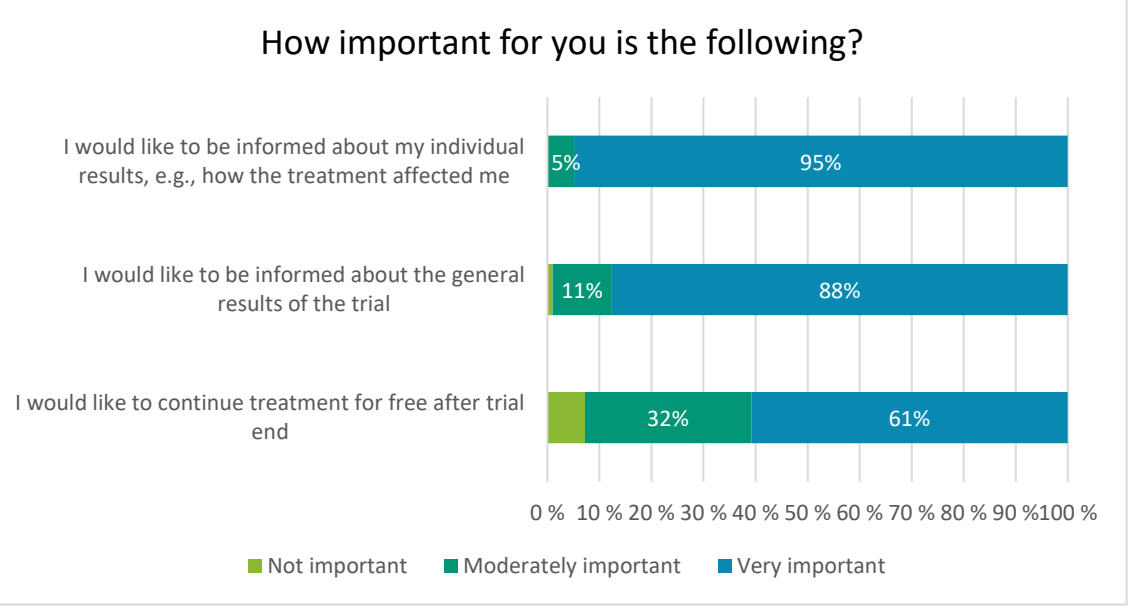


Most respondents (51%, N=49) did not know whether experiencing more side effects would be acceptable if the treatment worked better whereas 31% (N=30) thought it would be acceptable and 19% (N=18) did not think so.

Factors influencing treatment selection

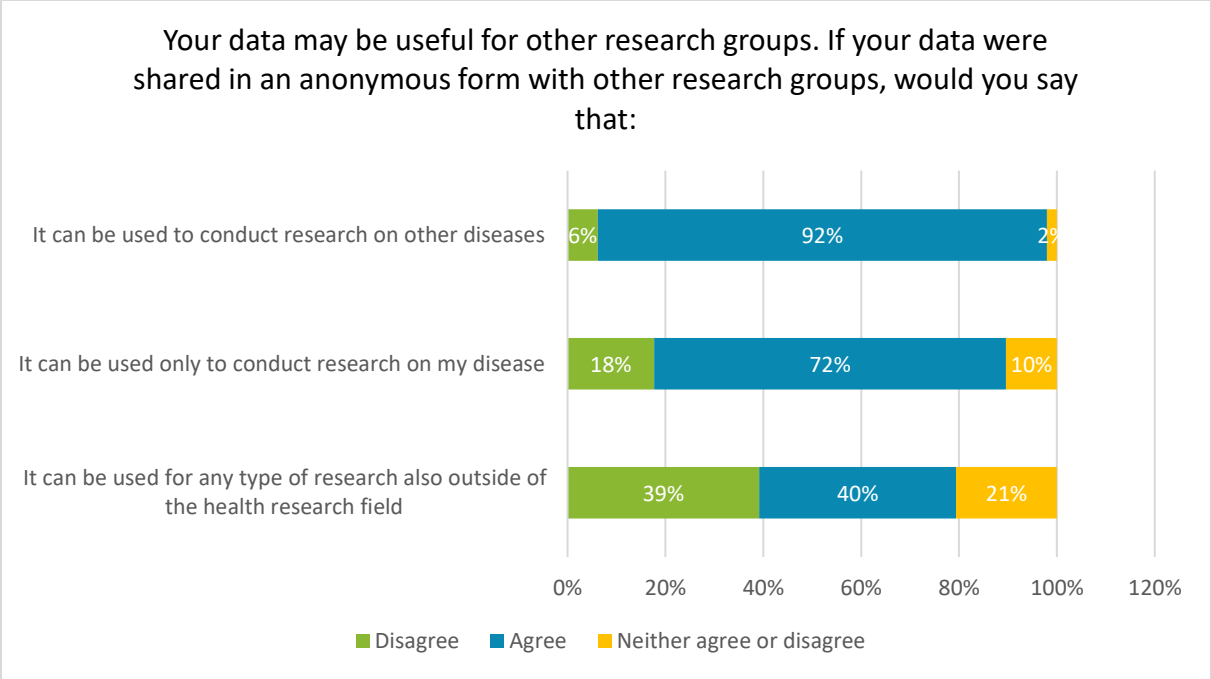


Most respondents (87%, N=84) reported the severity of side effects as a very important factor playing a role in the selection of a treatment followed by the number of side effects known to the drug (68%, N=65) and what the physician recommends (55%, N=53). How the treatment is taken was considered moderately important by 49% of respondents (N=48). Similarly, how often the treatment must be taken was seen as moderately important by 50% of respondents (N=48).



95% of respondents (N=92) saw as very important to be informed about their individual results from a clinical trial, and 88% (N=85) would like to be informed about general trial results. Having the possibility to continue treatment for free after trial end was considered very important by 61% of respondents (N=59).

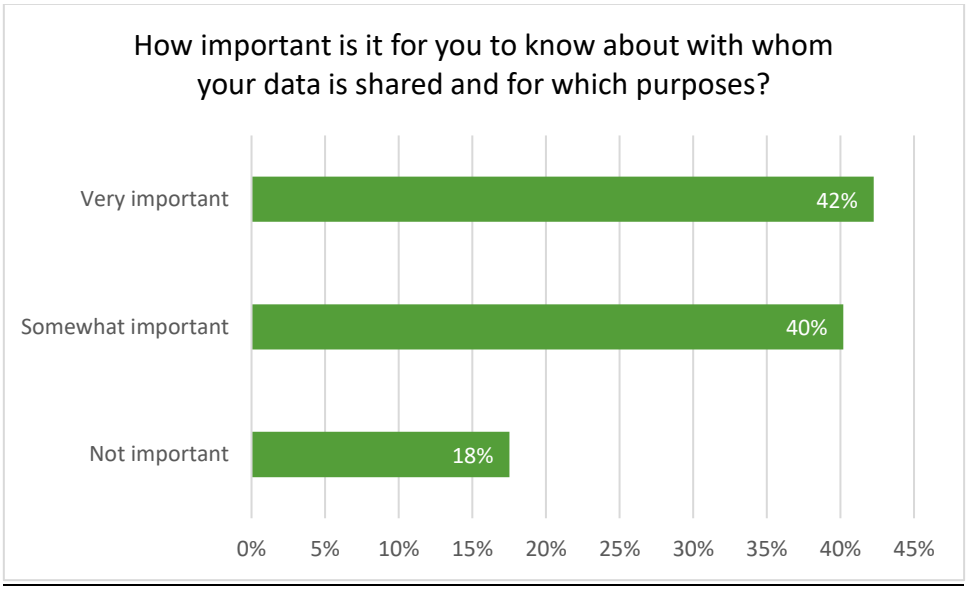
Perspectives on data sharing



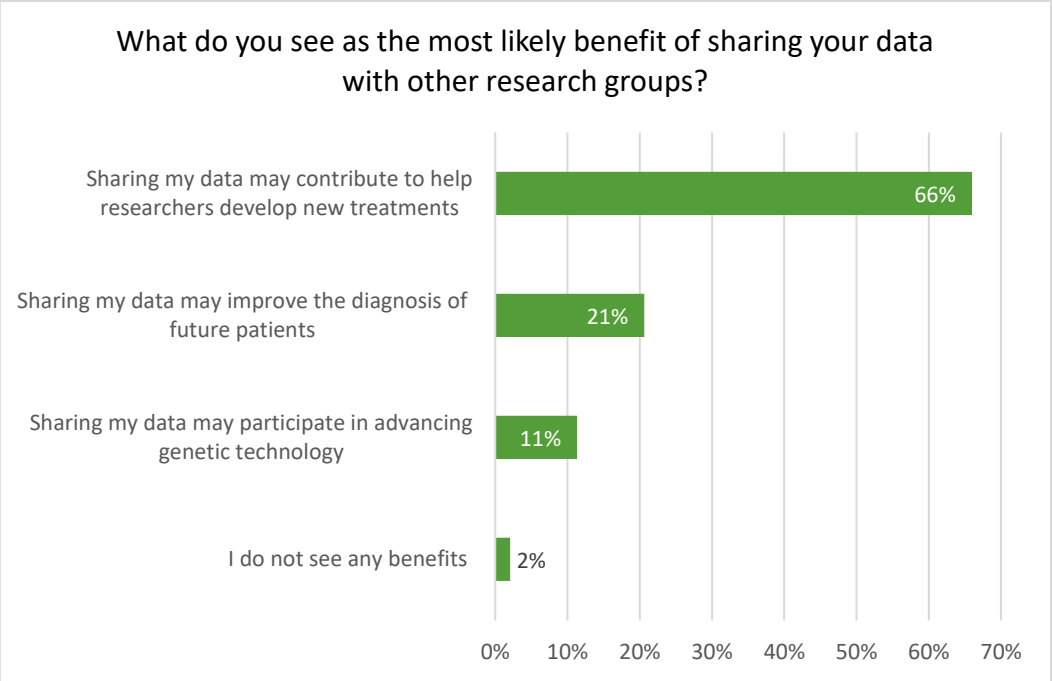
92% of respondents (N=89) reported to support the sharing of their data to conduct research on other diseases. 40% of respondents (N=39) support the use of their data to conduct research outside of the health research field whereas 39% do not (N=38).

The respondents had the possibility to make additional comments. These included:

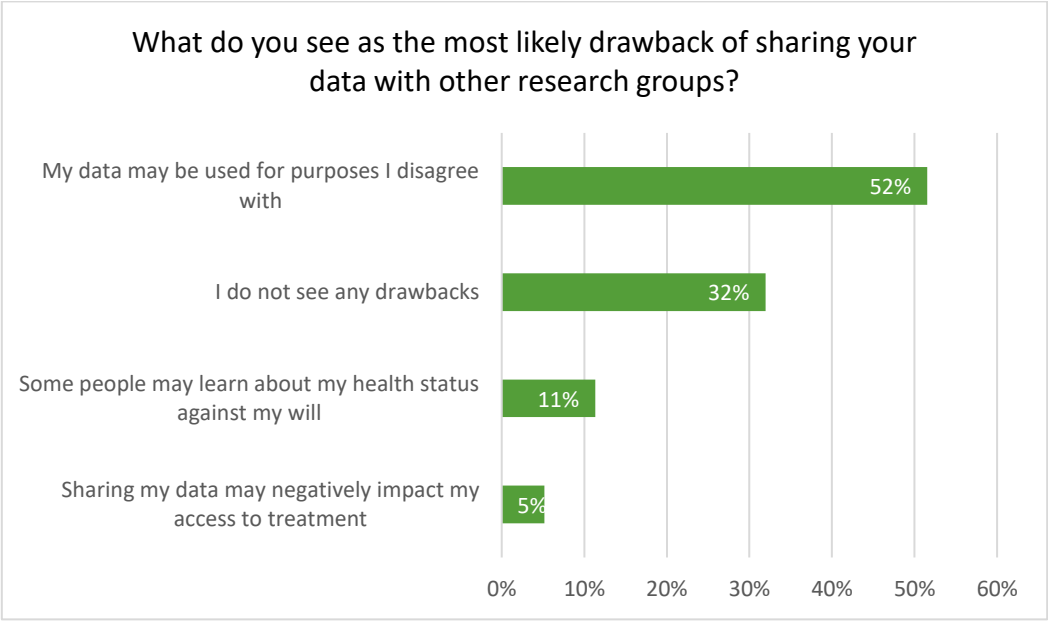
- Depends on the research
- OK if the data sharing is anonymous



82% (N=80) of respondents saw as important or somewhat important to know with whom their data is shared and for which purposes.

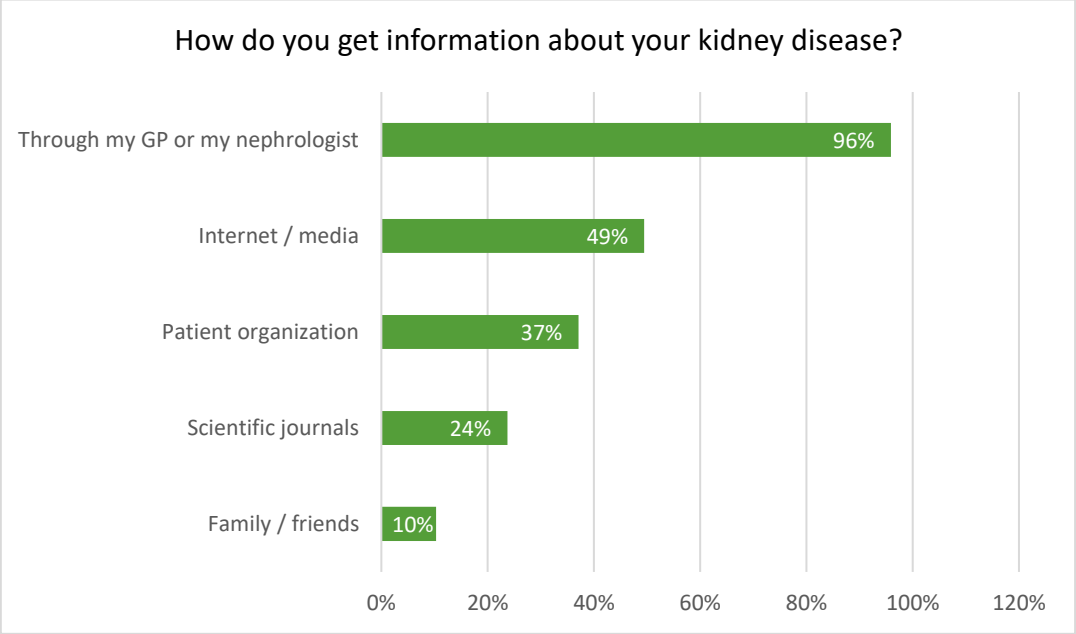


Respondents were asked to select what they saw as the most likely benefit of sharing their data with other research groups and could select only one benefit. Most respondents (66%, N=64) believed that sharing their data may contribute to help researchers develop new treatments whereas 21% (N=20) thought it may help improve the diagnosis of future patients. 11% (N=11) believed sharing their data may contribute to advancing genetic technology.

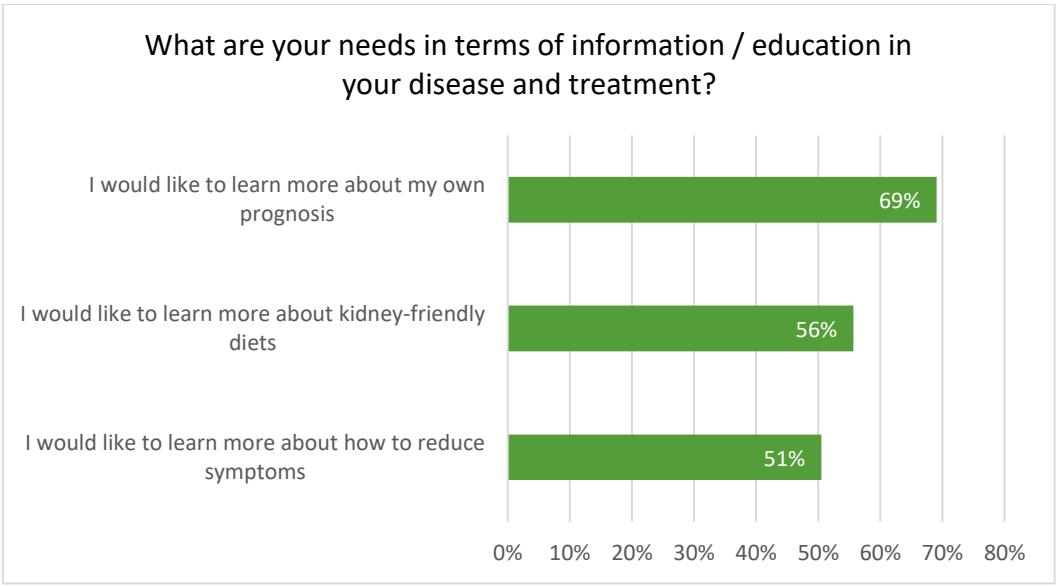


Respondents were asked to select what they saw as the most likely drawback of sharing their data with other research groups and could select only one drawback. Most respondents (52%, N=50) saw as a likely drawback that their data may be used for purposes they disagree with, whereas 32% (N=31) did not see any drawback. 11% (N=11) feared that some people may learn about their health status against their will and 5% (N=5) feared that data sharing may negatively impact access to treatment.

Information sources and needs



The respondents were asked to select sources of information about the disease and could select as many as they wanted. Most respondents (96%, N=93) get information about their kidney disease through their general practitioner of their nephrologist. Other sources of information include internet and the media used by 49% of respondents (N=48), information through patient organizations (37%, N=36) and scientific journals (24%, N=23) and family and friends (10%, N=10).



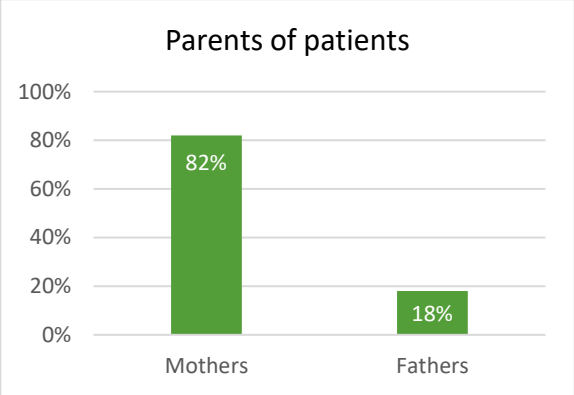
Most respondents (69%, N=67) would like to know more about own prognosis whereas 56% (N=54) would like to know more about kidney-friendly diets and 51% (N=49) would like to know more about how to reduce symptoms. Other needs expressed in writing include:

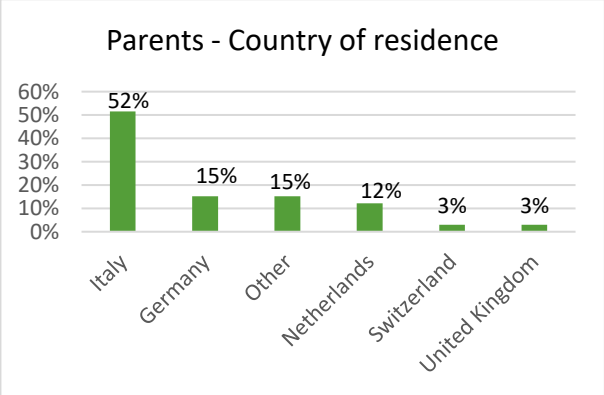
- Physicians across specialties to be more knowledgeable about the disease and comorbidities
- Knowing more about new diets.

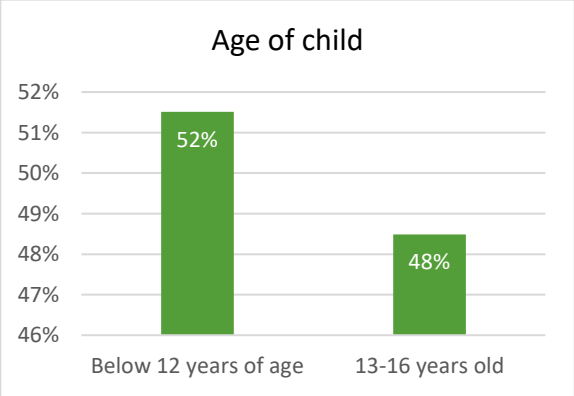
Results from survey questionnaire to parents of C3G/IC-MPGN patients aged below 16 years of age

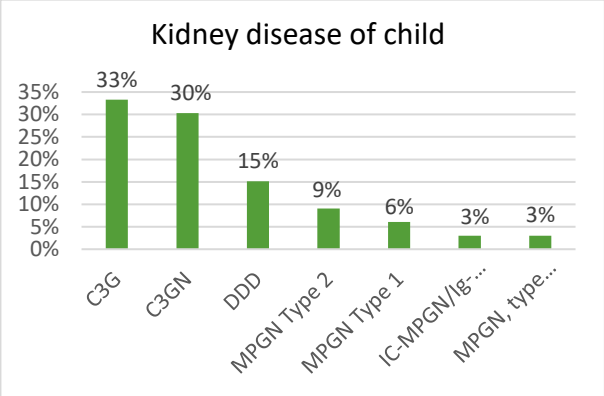
Respondents' demographics

This survey questionnaire collected responses from 33 people. Most respondents were mothers (82%, N=27) residing in Italy (52%, N=17), Germany (15%, N=5) and the Netherlands (12%, N=4). 5 respondents (15%) were in countries outside of the European Union.



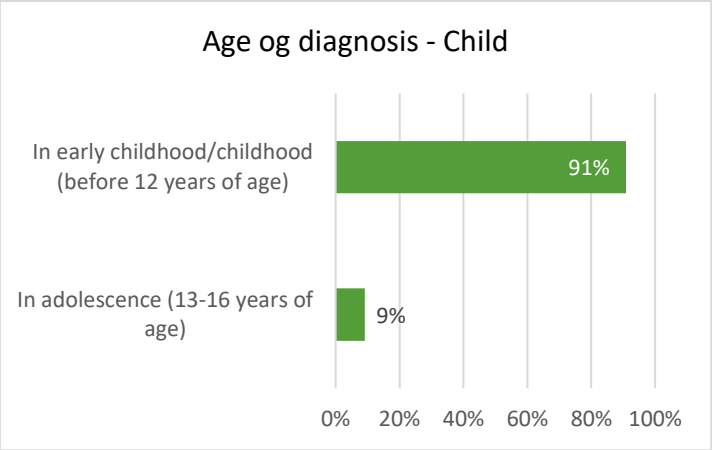






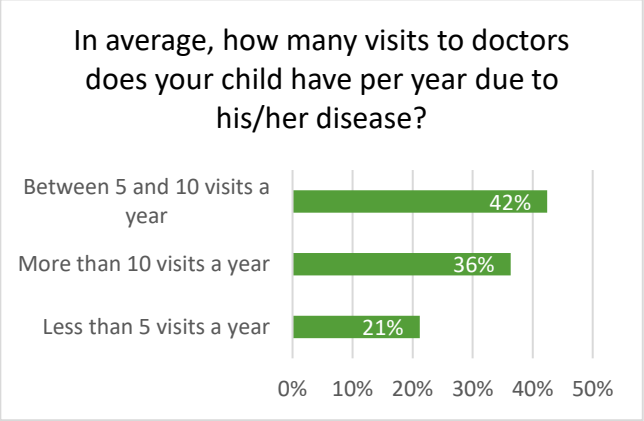
52% of parents (N=17) reported their child to be below 12 years of age whereas 48% (N=16) had a child in adolescence.

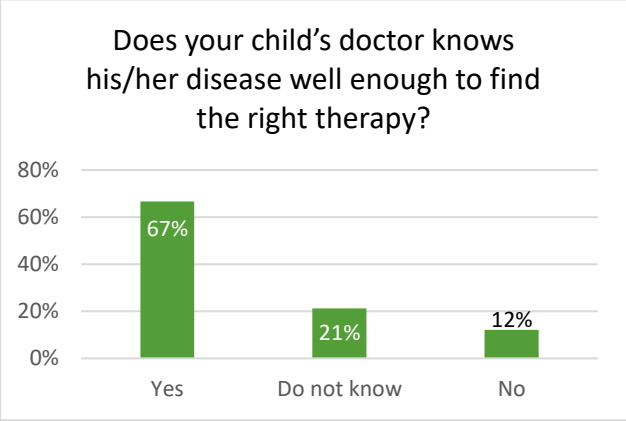
Most parents reported their child to have been diagnosed with C3G (33%, N=11) or C3GN (30%, N=10). The children of 5 respondents (15%) had been diagnosed with DDD whereas 6 had been diagnosed with MPGN, either type 1, 2 or unknown.



Most children (91%, N=30) had been diagnosed in early childhood or in childhood.

Interaction with doctors

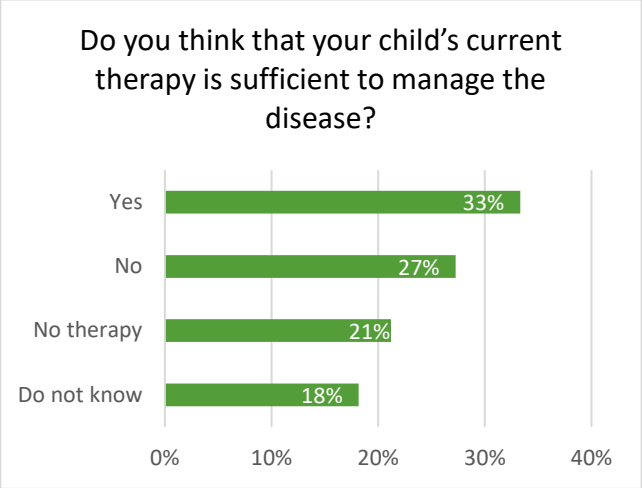


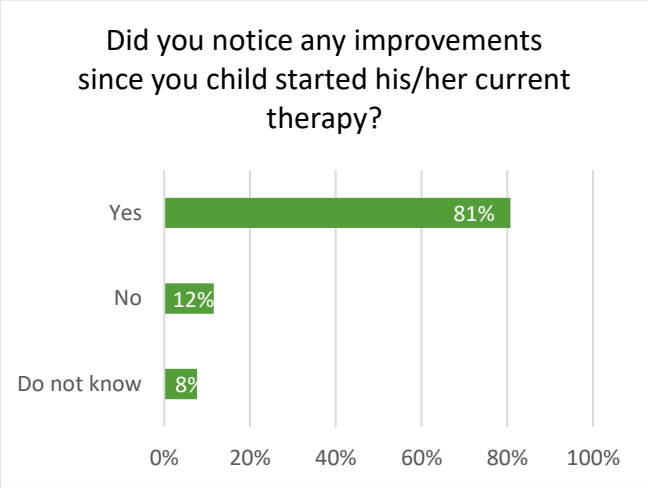


Most parents (42%, N=14) reported their child to have visits to doctors, for instance nephrologists, dermatologists, or eye specialists, due to their disease, between five to ten times a year.

67% (N=22) of parents believed that their child's doctor knows the disease well enough to be able to find the right therapy for the child. 21% (N=7) did not know and 12% (N=4) thought that it was not the case.

Views on current treatment

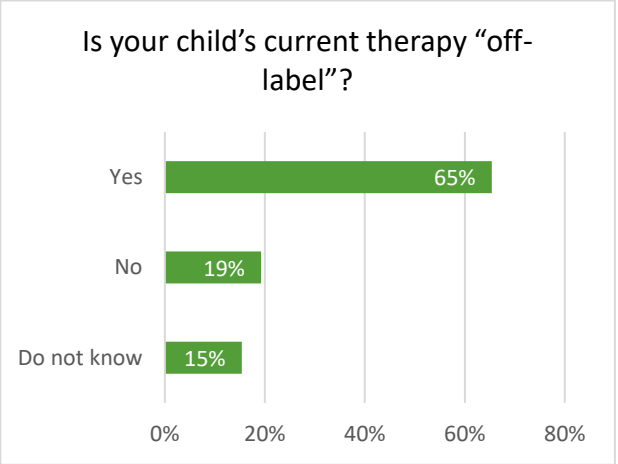


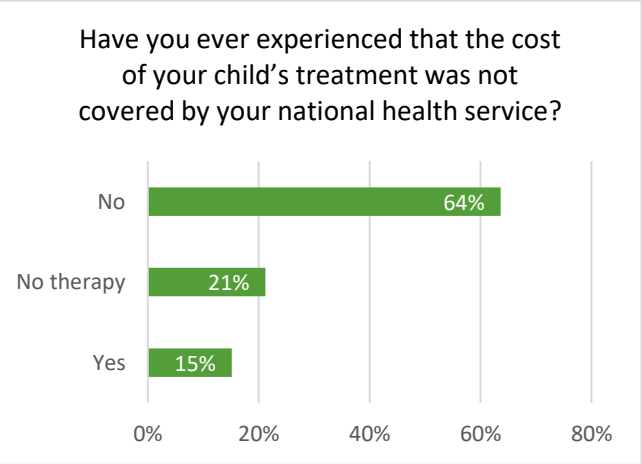


A slight majority of parents (33%, N=11) believed their child's current therapy to be sufficient to treat the disease whereas 27% (N=9) did not think so and 18% (N=6) did not know. 21% of parents (N=7) reported that their child did not receive any therapy for their disease.

81% of parents (N=21)[2] experienced some improvements after their child started his/her current therapy while 12% (N=3) did not and 8% (N=2) did not know.

Access to treatment



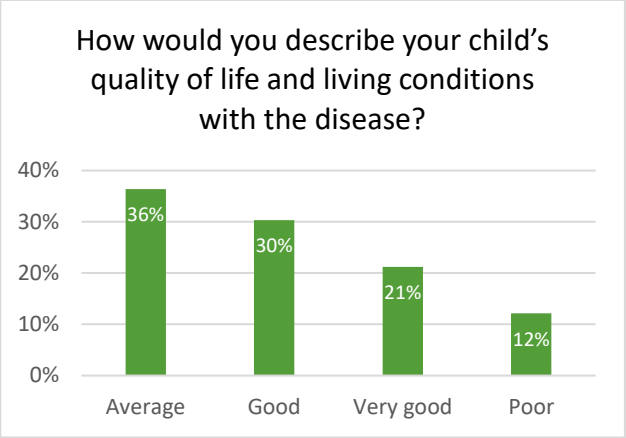


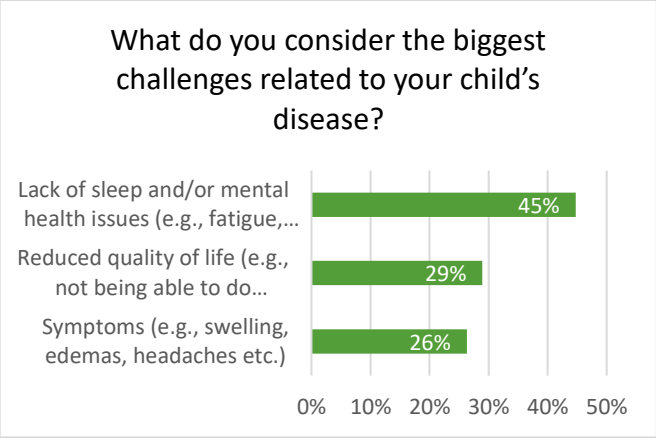
65% (N=17)[2] of parents reported their child's current therapy to be "off-label", which was defined in the survey questionnaire as being "A drug approved by the European Medical Agency for another disease, not for your diagnosis." 19% (N=5) did not receive off-label therapy whereas 15% (N=4) did not know whether their current therapy is off-label or not.

64% (N=21) of parents had never experienced that the cost of their child's treatment was not covered by their national health service whereas 15% (N=5) had made such experience.

[2] Answers from respondents indicating their child did not receive treatment were excluded.

Living with the disease



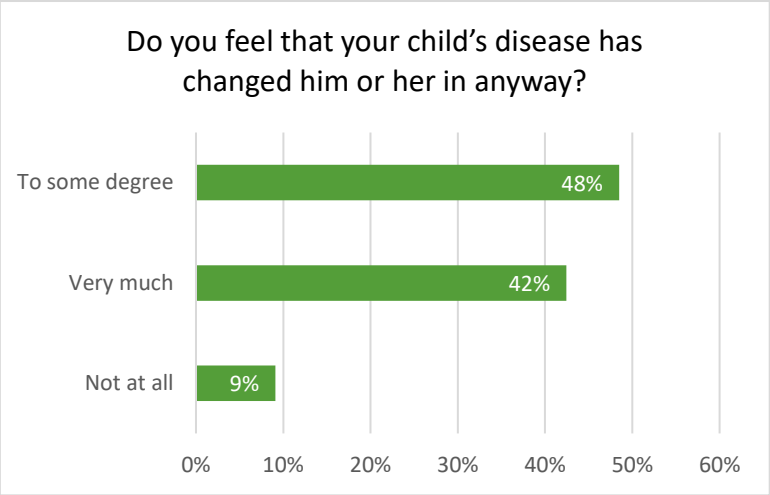


Most parents described their child's quality of life and living conditions with the disease as average (36%, N=12) or good (30%, N=10) whereas 21% (N=7) considered it as very good and 12% (N=4) as poor.

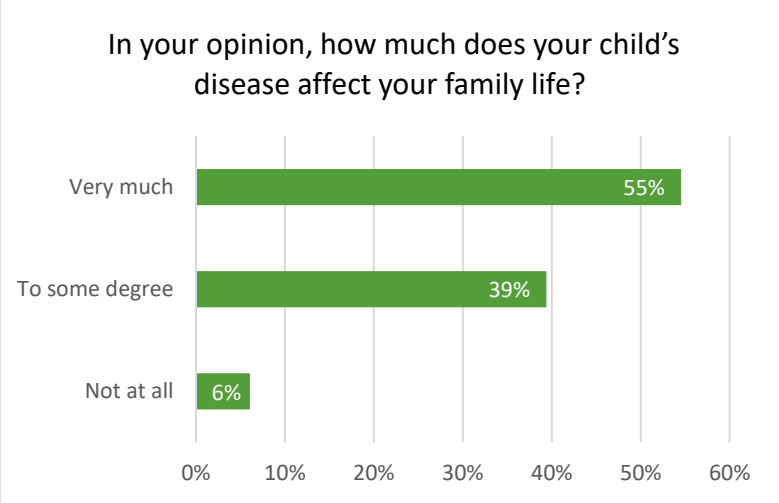
The respondents could select 2 types of challenges out of 3, that their child encountered by living with the disease. 45% of parents (N=17) reported lack of sleep and/or mental health issues (e.g., fatigue, anxiety, depression, fears etc.) as being the biggest challenge. 29% (N=11) saw their child's quality of life reduced (e.g., not being able to do sports, pursue an education, maintain a job etc.) whereas 26% (N=10) reported their child's symptoms (e.g., swelling, edemas, headaches etc.) to be challenging.

The parents had the possibility to provide some written feedback about challenges. These included:

- Psychological consequences such as phobia and anxiety, fear about the future and about being very sick again
- Tiredness and mood swings
- Frequent visits to hospitals for treatment, inability to make long, distant journeys
- Dependence on the supplier of the drug (insurance will not reimburse treatment)
- Having to follow a low sodium diet.

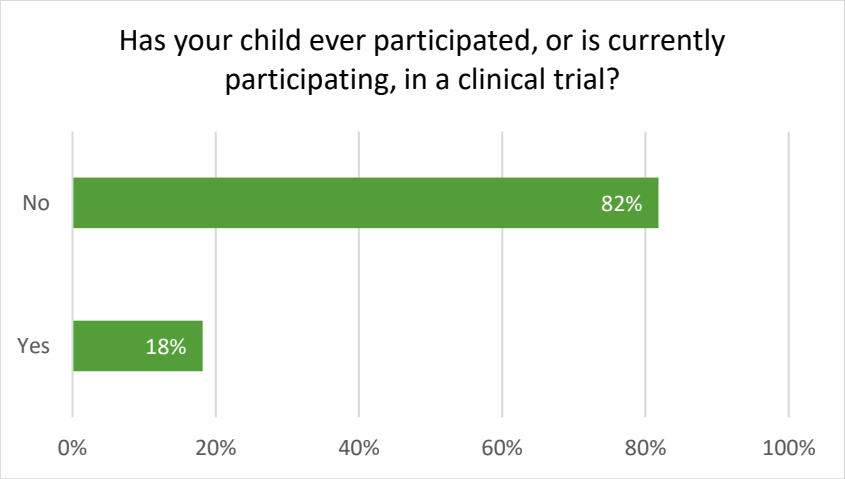


Most parents experienced that the disease had changed their child to some degree (48%, N=16) or very much (42%, N=14).

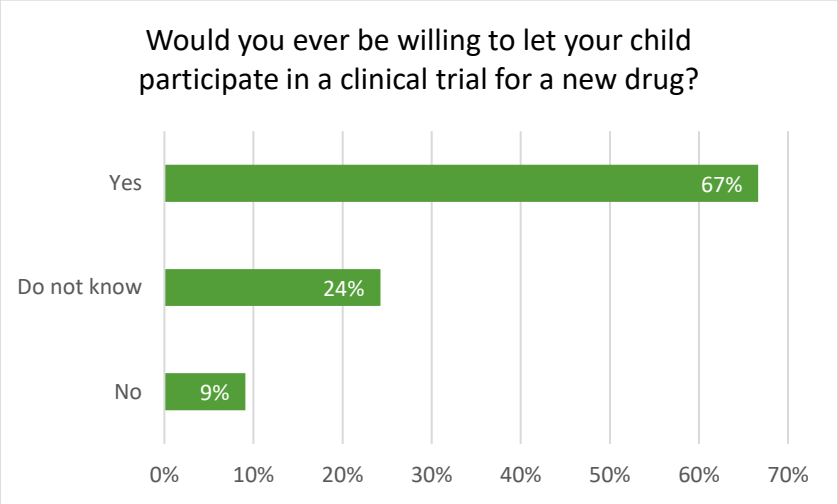


Most parents experienced that their child's disease affected their family life very much (55%, N=18) or to some degree (39%, N=13).

Participation in clinical trials

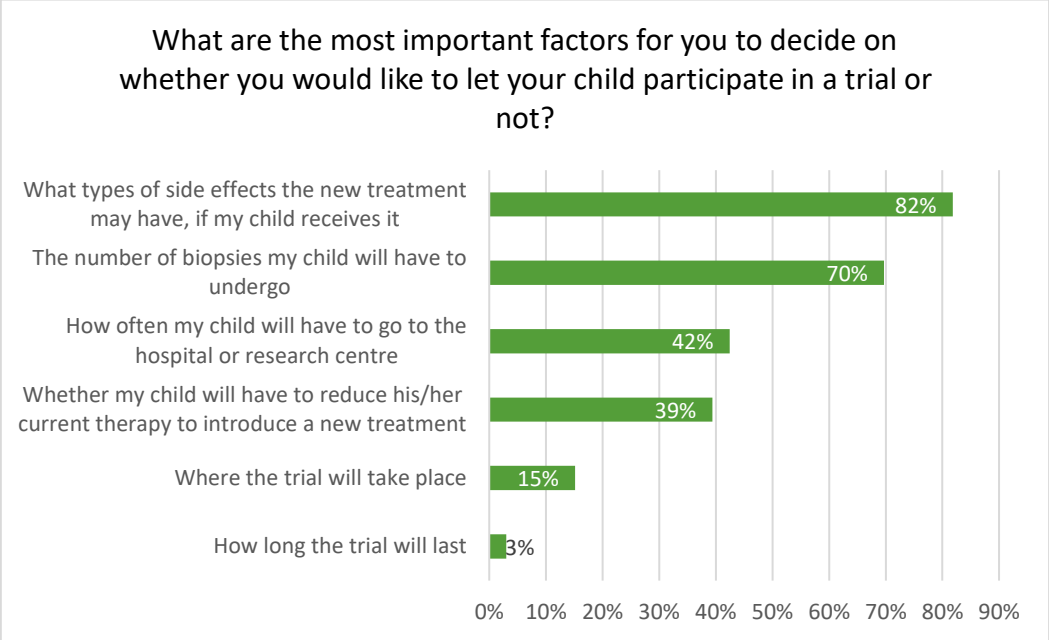


According to the parents, most children (82%, N=27) have never participated and do not currently participate in a clinical trial whereas 18% (N=6) have some experience of clinical trials.



Most parents (67%, N=22) reported to be willing to let their child participate in clinical trials for a new drug whereas 24% (N=8) did not know whether they would be willing and 9% (N=3) were not willing to let their child participate in a trial.

Factors influencing decision to let own child participate in a clinical trial

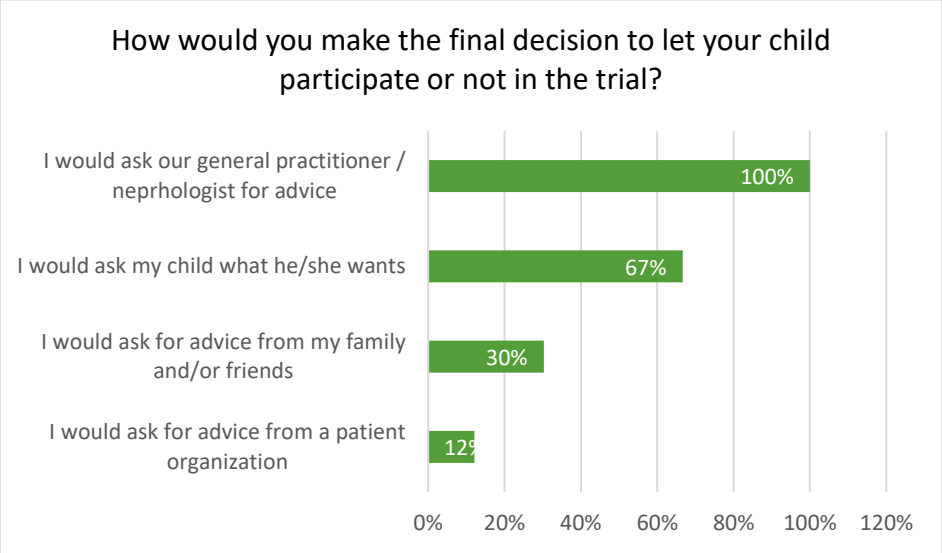


The respondents could select the three most important factors that may influence their decision to let their child participate in a clinical trial. Most parents (82%, N=27) selected the types of side effects the new treatment may have as the most influential factor followed by the number of biopsies their child would have to undergo (70%, N=23). Other factors included how often participation in the clinical trial requires going to the hospital or research centre (42%, N=14), whether participation in the clinical trial will require reducing the child's current therapy (39%, N=13), where the trial will take place (15%, N=5), and how long the trial will last (3%, N=1).

The parents had the possibility to indicate other factors in writing. These included:

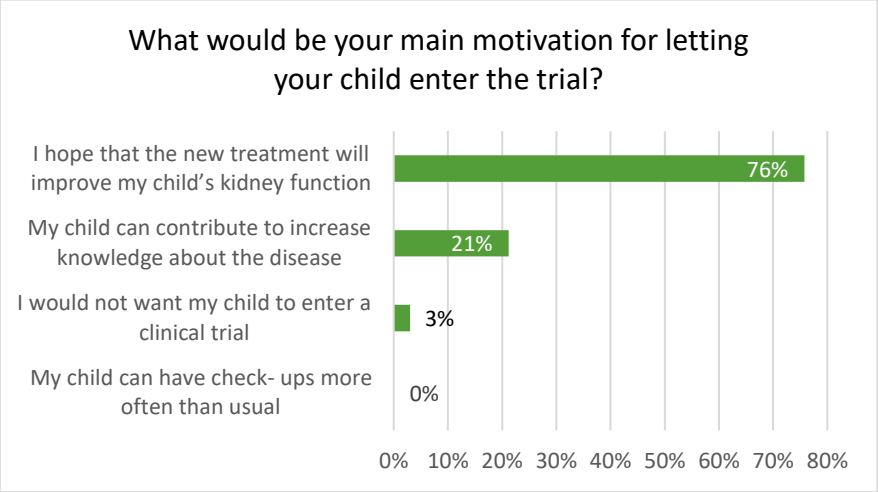
- What the doctor thinks
- Not willing to let the child participate in the placebo arm of a study.

Decision to participate in a clinical trial

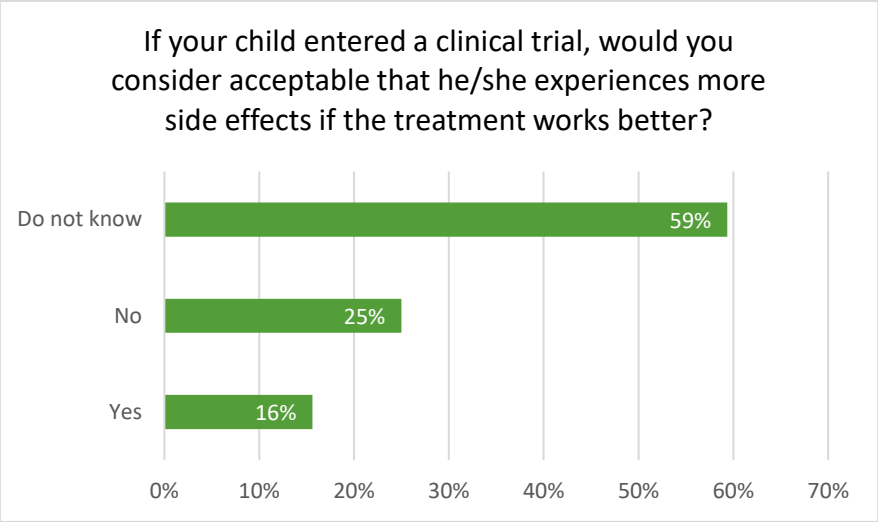


The respondents could select one or several ways to make their final decision regarding participation in a clinical trial. All parents (100%, N=33) would involve their practitioner or nephrologist in the decision-making process regarding their child's participation in a clinical trial. 67% of parents (N=22) would ask their child what he/she wants whereas 30% (N=10) would ask for advice from family and friends. 12% (N=4) would ask for advice from a patient organization.

Motivations for letting own child entering a clinical trial

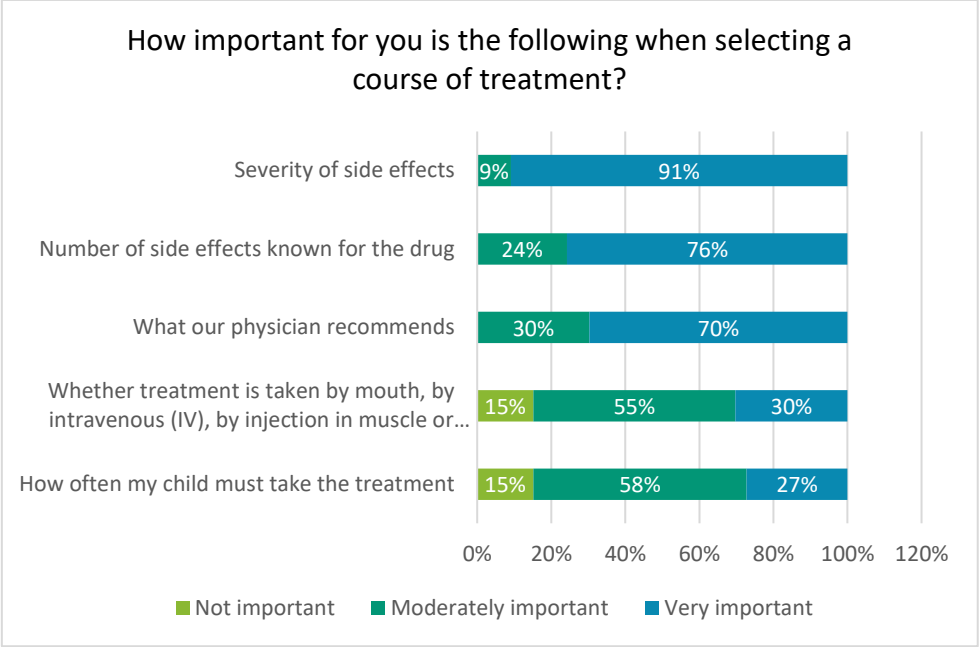


The respondents could select only one factor motivating participation in a clinical trial. 76% of parents (N=25%) reported that any hope that the new treatment will improve kidney function was the main motivating factor. Being able to increase knowledge about the disease was selected by 21% of the parents (N=7).

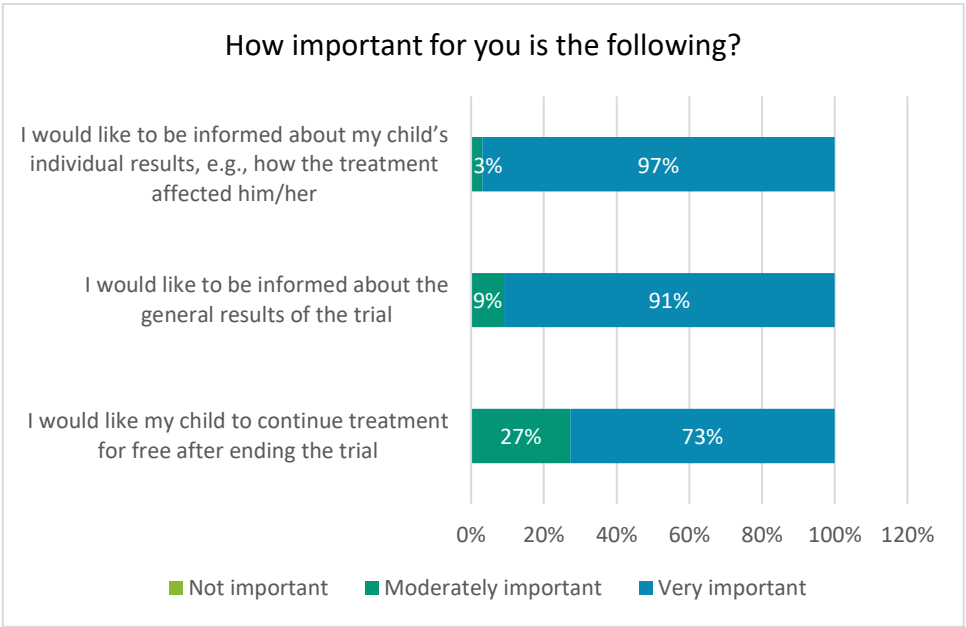


Most parents (59%, N=19) did not know whether it would be acceptable to let their child experience more side effects if the treatment worked better whereas 25% (N=8) thought it would be not acceptable and 16% (N=5) thought it would be acceptable.

Factors influencing treatment selection

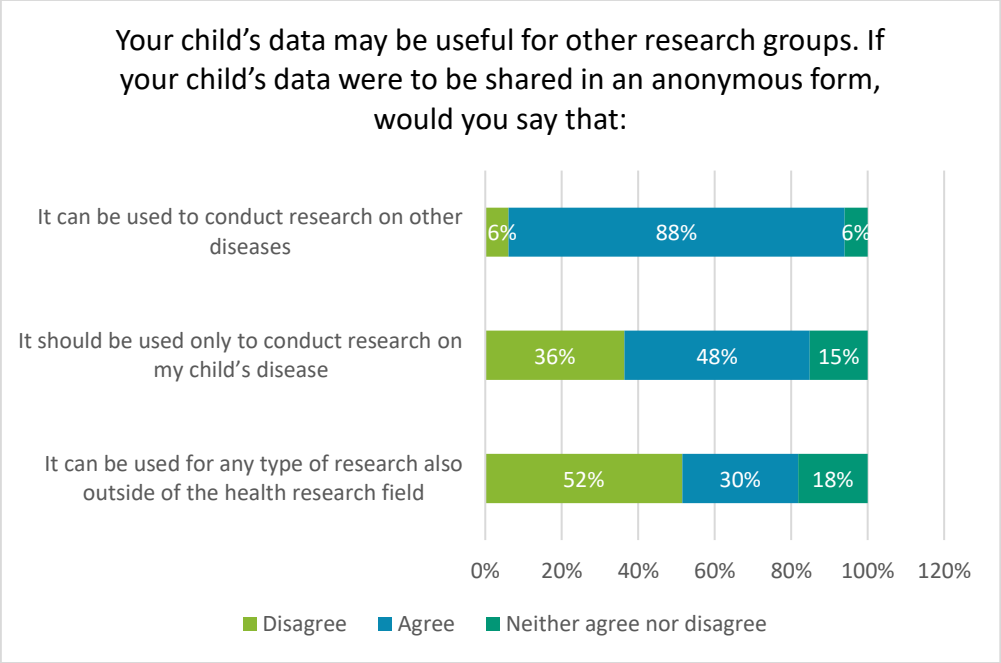


Most parents (91%, N=30) reported the severity of side effects as a very important factor playing a role in the selection of a treatment for their child, followed by the number of side effects known to the drug (76%, N=25) and what the physician recommends (70%, N=23). How the treatment is taken (by mouth, by intravenous (IV), by injection in muscle or via subcutaneous (SC) infusion) was considered moderately important by 55% of parents (N=18) whereas how often the treatment must be taken was seen as moderately important by 58% of respondents (N=19).

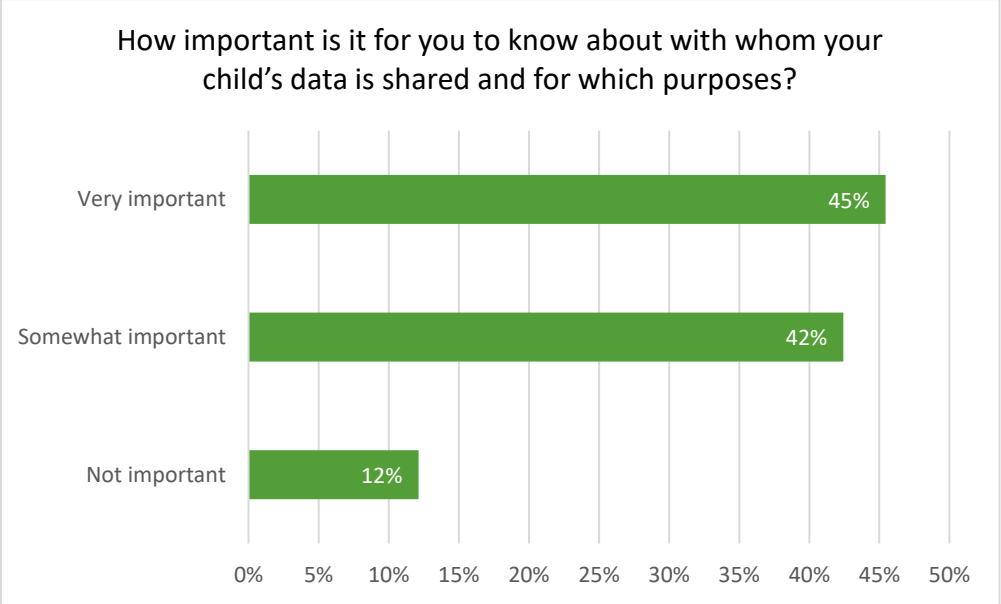


97% of parents (N=32) saw as very important to be informed about their child's individual results from a clinical trial, and 91% (N=30) would like to be informed about general trial results. Having the possibility for their child to continue treatment for free after trial end was considered very important by 73% of parents (N=24).

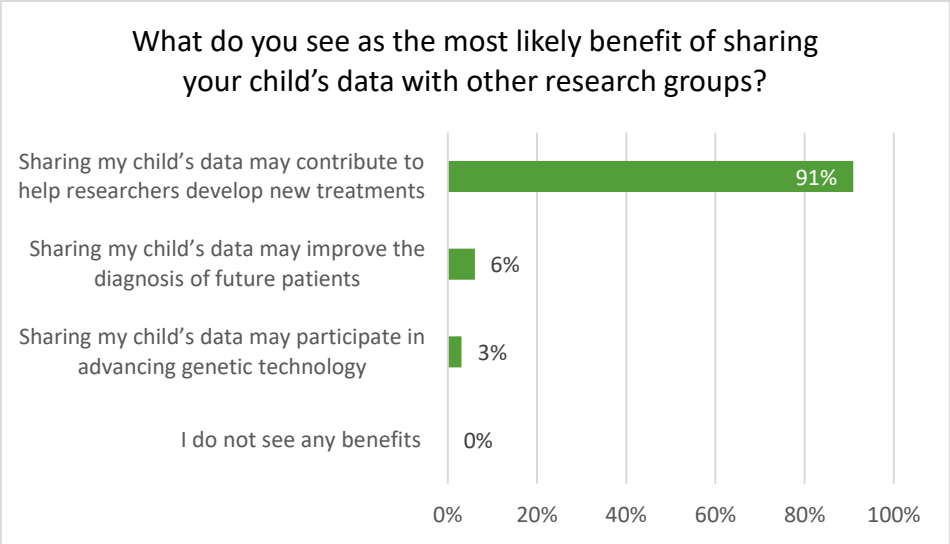
Perspectives on data sharing



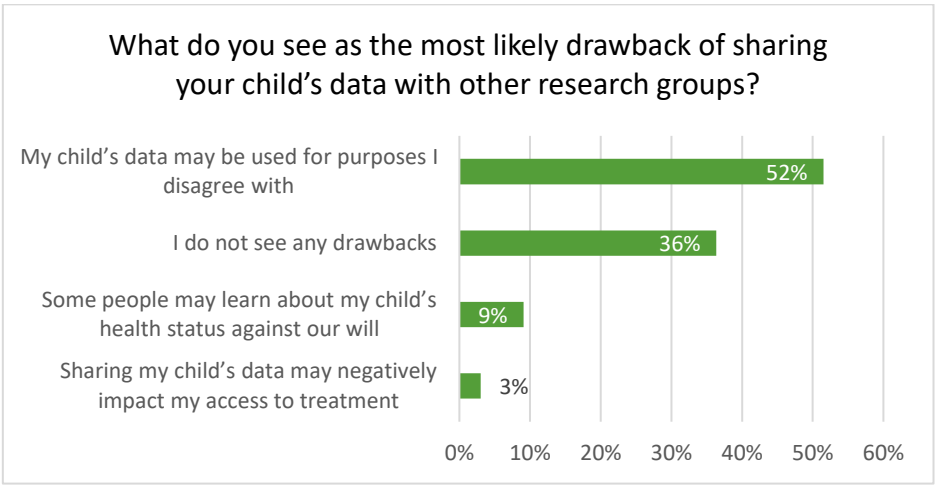
88% of respondents (N=29) supported the sharing of their data to conduct research on other diseases. A majority of parents (52%, N=17) do not support the use of their data to conduct research outside of the health research.



87% (N=29) of parents found it important to know with whom their child's data is shared and for which purposes.

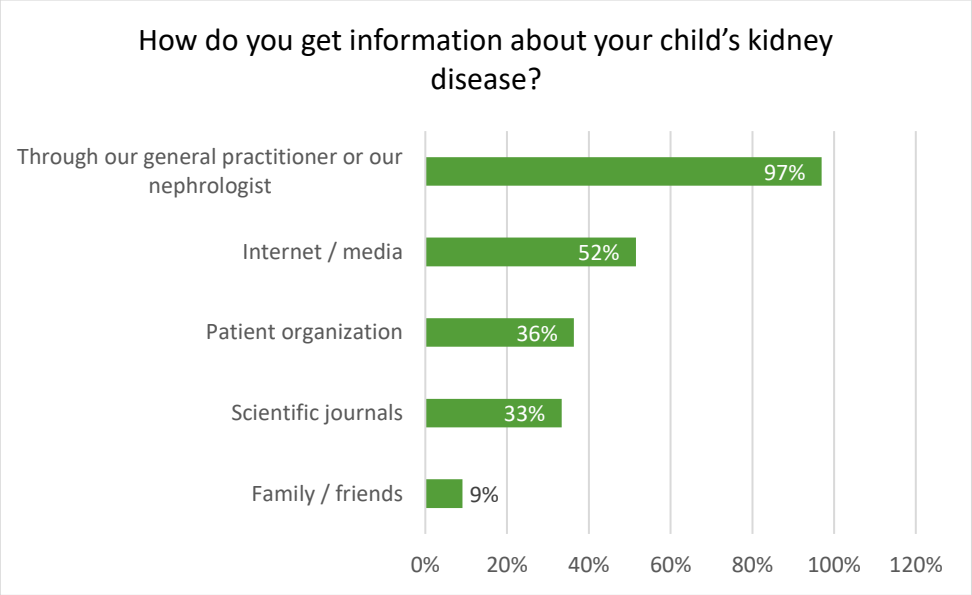


Respondents were asked to select what they saw as the most likely benefit of sharing their child's data with other research groups and could select only one benefit. Most parents (91%, N=30) believed that sharing their data may contribute to help researchers develop new treatments whereas only 6% (N=2) thought it may help improve the diagnosis of future patients.

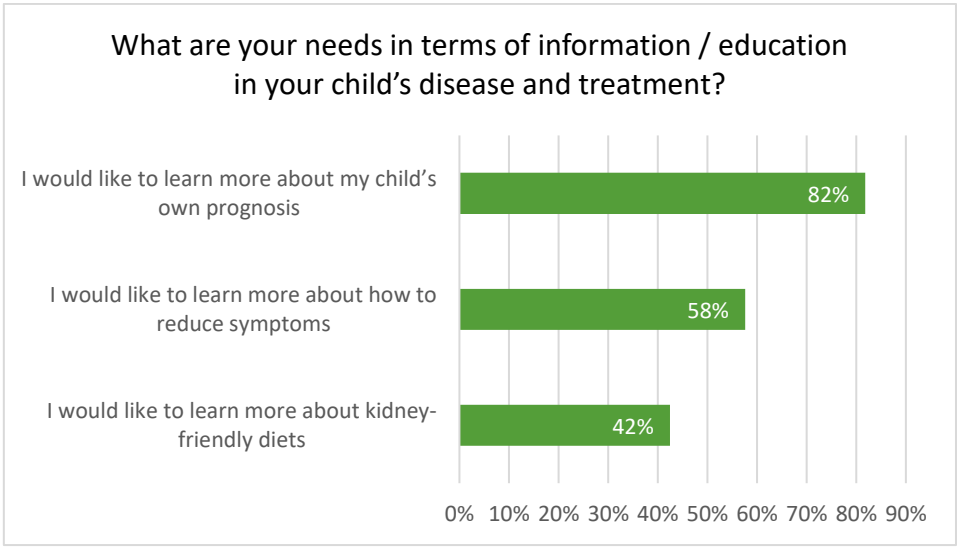


Respondents were asked to select what they saw as the most likely drawback of sharing their data with other research groups and could select only one drawback. Most parents (52%, N=17) saw as a likely drawback that their data may be used for purposes they disagree with, whereas 36% (N=12) did not see any drawback. 9% (N=3) feared that some people may learn about their child's health status against their will and 3% (N=1) feared that data sharing may negatively impact access to treatment.

Information sources and needs



The parents were asked to select sources of information about the disease and could select as many as they wanted. Most respondents (97%, N=32) get information about their kidney disease through their general practitioner or their nephrologist. Other sources of information include internet and the media used by 52% of respondents (N=17), information through patient organizations (36%, N=12) and scientific journals (33%, N=11) and family and friends (9%, N=3).



Most respondents (82%, N=27) would like to know more about their child's prognosis and 58% (N=19) would like to know more about how to reduce symptoms. 42% (N=14) would like to learn more about kidney-friendly diets.

DISCUSSION

The IMPACT study aimed to investigate the views and perspectives of an international sample of patients diagnosed with MPGN and parents of children diagnosed with MPGN regarding any potential future participation in clinical trials. Such perspectives are useful to guide the design and development of future clinical trials.

Strong interest in participating in future clinical trials

Living with MPGN is physically and mentally challenging. Overall, the survey respondents described quality of life and living conditions with MPGN as good or average (71% of patients, 66% of parents) despite physical and mental constraints. Only about a third (34% of patients, 33% of parents) experienced that their – or their child's - therapy was sufficient to treat the disease, thus suggesting that this patient group is in need for better treatments.

Although most survey respondents had no experience of participation in clinical trials (59% of patients, 82% of children, according to parents), they were largely willing to participate or let their child participate in a clinical trial for a new drug (72% of patients, 67% of parents). Previous studies have shown similar levels of interest in clinical trial participation [2]. For the IMPACT survey respondents, the main motivating factor for participation was the hope that new treatments will improve kidney function. Other studies have shown that maintaining kidney function is of great importance for patients [7].

For a long time, access to clinical trials for MPGN has been scarce. Conducting research on a very rare disease that affects a very small number of individuals is often not prioritized by pharmaceutical companies in search of high market returns. When MPGN trials are conducted, the inclusion criteria are often strict, making the trials hardly accessible to transplant recipients and young patients despite disease occurrence in early age [2]. In recent years, more interventional trials have been launched or are under planning[3]. The DECODE project aims to support the design of protocols for clinical trials of smaller size such as single arm studies, based on a precise diagnostic re-classification of patients. In such trials, all participants will ideally be exposed to potentially effective treatment, which should increase trial acceptability and facilitate patient enrollment.

Participation in clinical trials is conditioned by several factors

Willingness to participate in clinical trials is not unconditional. Our results show that the factors having greatest influence on any decision to participate or not in clinical trials are 1) the severity of side effects the new treatment may have (87% of patients, 82% of parents), 2) the number of side effects (68% of patients, 70% of parents) and 3) the number of biopsies to undergo (57% of patients, 70% of parents). Contrary to results from a previous study among C3G patients [2], most of our respondents did not know whether they would find acceptable to experience more side effects of the new treatment offered in a clinical trial if the treatment worked better (51% of patients, 59% of parents). This suggests the need for providing patients and families with comprehensive information about potential sides effects and what they may mean for the trial participant's quality of life. Other practical factors regarding participation such as the frequency of required visits to the hospital or research centre, trial location and duration, and how treatment is administered, were seen as less important when considering participation in a clinical trial.

As new clinical trials are under way, it will be important to address the concerns of patients and parents by providing clear and comprehensive information about the risks and benefits of participation as well as alternatives to participation. Examples of the type of information to provide in informed consent forms have been recently proposed [8] and the DECODE project is outlining a guideline for informed consent specifically tailored for MPGN patients, that will be available on the DECODE website in 2024. Research

[3] See ClinicalTrials.gov

groups may also consider involving patients and patient advocacy groups in the design of trial protocols and information material to ensure that the specific needs and concerns of the patients are addressed, and potential burdens related to participation are reduced to the extent possible [9].

Interest in clinical trial results

Survey respondents clearly indicated that they wanted to be informed about general clinical trial results (88% of patients, 91% of parents) and about their - or their child's - individual results (95% of patients, 97% of parents). Providing information to participants about trial results is a basic ethical requirement that is still insufficiently fulfilled [10]. General results can for instance be provided through the trial's website, direct communication to participants, or by using platforms such as ClinicalTrials.gov. The return of individual trial results, including results from genetic analysis, is also encouraged given that such return is carefully planned, participants are informed that the results will be provided and have consented to such feedback, resources are available to communicate results in a clear and appropriate manner, and medical follow-up can be organized [11]. Providing concise and understandable information is particularly important when trial participants are young children and adolescents. Access to individual results can enable patients to make more informed decisions about their ongoing care and potential treatment options and contribute to building trust and confidence in the research process.

Strong willingness to support data sharing for research purposes

Our results show that patients and parents largely support the sharing of their - or their child's - data for health research both on MPGN and on other diseases (92% of patients, 88% of parents). They were much less supportive of the sharing of their data to conduct research outside of the health research field (39% of patients and 52% of parents did not support such data sharing). The respondents were aware of the potential benefits of data sharing for health research and had few concerns regarding such sharing. About a third of respondents (32% of patients, 36% of parents) did not see any drawback with data sharing.

The respondents' willingness to share data is likely motivated by the understanding that health data can contribute to scientific knowledge and lead to improved treatment for their disease. Previous research has shown that rare disease patients largely support data sharing and, in some cases, even initiate data sharing through patient communities [12]. Our results, however, show that any support of data sharing practices is conditioned by a requirement to inform patients about how the data are being used, and for which purposes (very or somewhat important for 82% of patients and 87% of parents). Researchers planning for future clinical trials will have to clearly communicate their data sharing plans and explain to patients how privacy and data security will be protected to maintain patient trust and engagement in research endeavors.

Need for additional information and support

Our respondents used a variety of information channels to learn about their – or their child's - disease. However, general practitioners and nephrologists remain the main trusted source of information for most respondents (96% of patients, 97% of parents). Health care professionals have a critical role to play to inform patients and families about diagnosis and ways to manage the disease, kidney-friendly diets, and approaches to reduce symptoms as pinpointed by survey respondents. As shown by our results, patients and parents would make the final decision to participate in a clinical trial in collaboration with their practitioner or nephrologist (86% of patients, 100% of parents). In the future, more efforts can be done to ensure that health care professionals are aware of, and can inform patients and families, about clinical trials. Health care professionals are well placed to collaborate with patients and help them make informed choices based on a discussion of the risks and benefits of participation and available evidence [13]. Support

information and clinical trial material should also be made more easily available, for instance, through digital platforms, to increase patient and health care professional awareness about clinical trials.

Equity in access to treatment

A significant share of survey respondents (41% of patients, 65% of parents) reported to have access to "off-label" therapy, i.e., drugs approved by the European Medical Agency for another disease, not for their – or their child's – diagnosis. Some respondents had experienced that the cost of the treatment was not covered by their national health service (29% of patients, 15% of parents). Treatment for MPGN can be very expensive if patients receive drugs such as Eculizumab, which is one of the most expensive drugs on the market to treat orphan diseases [14]. Expensive treatments are usually covered by health care services in Europe, but this could change as financial resources may be restricted in the future due to stringent budget limitations. It is also unclear for how long treatments such as Eculizumab should be administered to patients. Outside of Europe, patients experience to be denied access to treatment if they cannot pay for it themselves in the absence of a universal social welfare system [15]. Preventing MPGN patients from becoming so ill that they need dialysis, or a transplant, is the most humane and cost-efficient approach and should be the greatest priority. This can only be achieved by ensuring fair and equitable access to clinical trials and treatment for all [16].

STUDY LIMITATIONS

The IMPACT survey was made publicly available on the DECODE website and shared with patient organizations and research groups in the project's network, which primarily encompasses Europe. The survey respondents were likely patients and parents who are engaged and interested in issues related to MPGN. The survey results are not representative of the views of MPGN patients worldwide, but rather provide an indication of which perspectives MPGN patients and families have regarding participation in clinical trials for MPGN.

CONCLUSION

Still a lot is unknown regarding how to best treat MPGN and maintain kidney function in MPGN patients. More clinical trials are highly needed to evaluate the effects of new drugs, offer patients a greater chance of recovery, and reduce costs for health care systems. Patients and parents of patients are willing to participate in clinical trials and trust their physicians that they can provide them with good guidance. The number of patients participating in clinical trials could potentially be significantly higher given that clear and concise information is provided to patients and is easily accessible, and physicians are well-informed about the trials and know how to discuss the pros and cons of participation with their patients.

REFERENCES

1. Cook HT, Pickering MC. Histopathology of MPGN and C3 glomerulopathies. Nat Rev Nephrol. 2015;11(1):14-22. doi:10.1038/nrneph.2014.217.
2. Feldman DL BA, Nester C. Voice of the patient. Report of Externally-led Patient-Focused Drug Development Meeting on: Complement 3 Glomerulopathy (C3G)2018.
3. Smith RJH, Appel GB, Blom AM, Cook HT, D'Agati VD, Fakhouri F et al. C3 glomerulopathy - understanding a rare complement-driven renal disease. Nat Rev Nephrol. 2019;15(3):129-43. doi:10.1038/s41581-018-0107-2.
4. Olson EM, Lin NU, Krop IE, Winer EP. The ethical use of mandatory research biopsies. Nat Rev Clin Oncol. 2011;8(10):620-5. doi:10.1038/nrclinonc.2011.114.
5. McCormack P, Kole A, Gainotti S, Mascalzoni D, Molster C, Lochmuller H et al. 'You should at least ask'. The expectations, hopes and fears of rare disease patients on large-scale data and biomaterial sharing for genomics research. Eur J Hum Genet. 2016;24(10):1403-8. doi:10.1038/ejhg.2016.30.
6. Kalkman S, van Delden J, Banerjee A, Tyl B, Mostert M, van Thiel G. Patients' and public views and attitudes towards the sharing of health data for research: a narrative review of the empirical evidence. J Med Ethics. 2022;48(1):3-13. doi:10.1136/medethics-2019-105651.
7. Carter SA, Gutman T, Logeman C, Cattran D, Lightstone L, Bagga A et al. Identifying Outcomes Important to Patients with Glomerular Disease and Their Caregivers. Clin J Am Soc Nephrol. 2020;15(5):673-84. doi:10.2215/CJN.13101019.
8. Nguyen MT, Goldblatt J, Isasi R, Jagut M, Jonker AH, Kaufmann P et al. Model consent clauses for rare disease research. BMC Med Ethics. 2019;20(1):55. doi:10.1186/s12910-019-0390-x.
9. Tong A, Scholes-Robertson N, Hawley C, Viecelli AK, Carter SA, Levin A et al. Patient-centred clinical trial design. Nat Rev Nephrol. 2022;18(8):514-23. doi:10.1038/s41581-022-00585-w.
10. Emanuel EJ, Wendler D, Grady C. What makes clinical research ethical? JAMA. 2000;283(20):2701-11. doi:10.1001/jama.283.20.2701.
11. Vears DF, Hallowell N, Bentzen HB, Ellul B, Nøst TH, Kerasidou A et al. A practical checklist for return of results from genomic research in the European context. European Journal of Human Genetics. 2023. doi:10.1038/s41431-023-01328-6.
12. Courbier S, Dimond R, Bros-Facer V. Share and protect our health data: an evidence based approach to rare disease patients' perspectives on data sharing and data protection - quantitative survey and recommendations. Orphanet J Rare Dis. 2019;14(1):175. doi:10.1186/s13023-019-1123-4.
13. Babac A, von Friedrichs V, Litzkendorf S, Zeidler J, Damm K, Graf von der Schulenburg JM. Integrating patient perspectives in medical decision-making: a qualitative interview study examining potentials within the rare disease information exchange process in practice. BMC Med Inform Decis Mak. 2019;19(1):188. doi:10.1186/s12911-019-0911-z.

14. Luzzatto L, Hyry HI, Schieppati A, Costa E, Simoens S, Schaefer F et al. Outrageous prices of orphan drugs: a call for collaboration. Lancet. 2018;392(10149):791-4. doi:10.1016/S0140-6736(18)31069-9.
15. Roberti J, Cummings A, Myall M, Harvey J, Lippiett K, Hunt K et al. Work of being an adult patient with chronic kidney disease: a systematic review of qualitative studies. BMJ Open. 2018;8(9):e023507. doi:10.1136/bmjopen-2018-023507.
16. Martin DE, Harris DCH, Jha V, Segantini L, Demme RA, Le TH et al. Ethical challenges in nephrology: a call for action. Nat Rev Nephrol. 2020;16(10):603-13. doi:10.1038/s41581-020-0295-4.

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- The MPGN registry, Italy
- The Progetto DDD Onlus , Italy
- Nierpatiënten Vereniging Nederland (NVN), The Netherlands
- Landsforeningen for Nyrepasienter og Transplanterte (LNT), Norway
- Selbsthilfegruppe für komplementvermittelte Erkrankungen, Germany

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APPENDIX

Appendix 1 – The IMPACT Study flyer

The IMPACT survey: Identifying the perspectives of patients diagnosed with primary membranoproliferative glomerulonephritis and/or parents of patients regarding potential participation in future clinical trials

Currently, there is no approved treatment for primary membranoproliferative glomerulonephritis diseases like MPGN, IC-MPGN, C3G, C3GN or DDD. Clinical trials are often the only opportunity for patients to access new drugs. Understanding how to design future clinical trials in ways that take into consideration the needs of patients and caregivers is important and can help improve trial outcomes.

Are you diagnosed with a primary membranoproliferative glomerulonephritis disease or are you a parent of a child with membranoproliferative glomerulonephritis? Take our online survey to let us know:

- What is it like to live with a primary membranoproliferative glomerulonephritis disease?
- What is important for you when considering participation in a clinical trial for you or your child?
- What kind of support do you need from researchers and health care professionals?

The survey is anonymous, available in 6 languages (English, Italian, Dutch, German, French, Norwegian), and takes approximately 20 minutes to complete:

hiip://www.era -decode.eu/survey.html

After taking the survey, you can also volunteer to a digital interview with our research team to discuss survey questions in more detail, if you so wish. Your responses will help researchers design future clinical trials for MPGN. General results will be available on the DECODE website in 2023.

DECODE is a project aiming to identify new strategies to improve diagnosis, prognosis, and treatment of MPGN patients. The project is led by Professor Ariela Benigni at the Mario Negri Institute, Italy. The survey is organized in collaboration with Progetto DDD Onlus, the Dutch Kidney Patients Association, and the German association for rare complement-mediated diseases.

To know more about DECODE: hiip://www.era -decode.eu/index.html

For any questions regarding the survey, please contact decode@fhi.no

Selbsthilfegruppe für komplementvermittelte Erkrankungen

Appendix 2 - Survey questionnaire to patients aged 16 years and older

INFORMED CONSENT

Please tick the box.

- I am above 16 years of age and I consent to the use of these data for research

Please tell us a little bit about yourself

1. What is your age? (Mandatory question)

- 16-29
- 30-39
- 40-49
- 50-59
- >60

2. Do you identify as: (mandatory question)

- Male
- Female
- Other/Prefer not to tell

3. In which country do you reside? (Mandatory question)

'List of countries'

4. What is your kidney disease? (Mandatory question)

- MPGN Type 1
- MPGN Type 2
- MPGN Type 3
- IC-MPGN/Ig-MPGN
- MPGN, but I don't know the type
- C3G glomerulopathy (C3G)
- Dense Deposit Disease (DDD)
- C3 glomerulonephritis (C3GN)
- Other, please specify:

5. When were you diagnosed? (Mandatory question)

- In early childhood/childhood (before 12 years of age)
- In adolescence (13-19 years of age)
- In adulthood (>19 years of age)
- Do not know

6. In average, how many visits to doctors do you have per year due to your disease? E.g., nephrologist, dermatologist, eye specialist

I) Less than 5 visits a year

II) Between 5 and 10 visits a year

III) More than 10 visits a year

7. Do you think that your doctor knows your disease well enough to be able to find the right therapy for you?

I) Yes

II) No

III) I do not know

8. Do you think that your current therapy is sufficient to treat your disease?

I) Yes

II) No

III) I do not know

IV) I currently do not receive any therapy

9. Did you notice any improvements since you started your current therapy?

I) Yes

II) No

III) I do not know

IV) I currently do not receive any therapy

10. Is your current therapy “off-label”? (Off-label means, that the drug you get is approved by the European Medical Agency for another disease, not for your diagnosis)

I) Yes

II) No

III) I do not know

IV) I currently do not receive any therapy

11. Have you ever experienced that the cost of your treatment was not covered by your national health service?

I) Yes

II) No

III) I do not know

IV) I currently do not receive any therapy

12. How would you describe your quality of life and living conditions with your disease?

I) Poor

II) Average

III) Good

IV) Very good

13. What do you consider the biggest challenges of having your disease (please select maximum 2 challenges)?

I) Reduced quality of life (e.g., not being able to; do sports, pursue an education etc.)

II) Lack of sleep and/or mental health issues (e.g., fatigue, anxiety, depression, fears etc.)

III) Symptoms (e.g., swelling, edemas, headaches etc.)

IV) Other: [Free text]

14. Is there anything you do to cope with your disease? (Select all that apply)

I) Undergo regular health checks at my general practitioner

II) Have a healthy diet

III) Exercise regularly

IV) Do not smoke

V) Limit my alcohol consumption / be a teetotaler

VI) Limit my daily intake of salt (NaCl)

VII) Practice relaxation activities (e.g., yoga, meditation)

VIII) Other: [Free text]

15. Do you feel that your disease has changed you in anyway?

I) Not at all

II) To some degree

III) Very much

Participation in a clinical trial

16. Have you ever participated, or do you currently participate, in a clinical trial, e.g., to test a new drug for your disease?

I) Yes

II) No

III) I do not remember

17. Would you ever be willing to participate in a clinical trial for a new drug?

I) Yes

II) No

III) I do not know

18. What are the most important factors for you to decide on whether you would like to participate in a trial or not? Please select the three most important factors

I) The number of renal biopsies* I will have to undergo

II) Whether I have to reduce my current therapy to introduce a new treatment**

III) How long the trial will last

IV) Where the trial will take place

V) How often I will have to go to the hospital or research centre

VI) What types of side effects the new treatment may have, if I receive it

VII) Other: [Free text]

** Renal biopsy is performed by inserting a thin needle through the skin and into the kidney after local anesthesia is performed. It is generally considered to be a safe procedure and serious complications are uncommon. Less serious complications can occur and include pain, bleeding and development of an abnormal connection (fistula) between two blood vessels.*

*** This transition period between different treatments could last over several weeks or months.*

19. How would you make your final decision to participate or not in the trial? (Select all that apply)

I) I would ask my general practitioner / nephrologist for advice

II) I would make the decision on my own

III) I would ask for advice from my family and/or friends

IV) I would ask for advice from a patient organization

V) Other: [Free text]

20. What would be your main motivation for entering the trial (please select one)?

I) I can contribute to increase knowledge about the disease

II) I can have check-ups more often than usual

III) I hope that the new treatment will improve my kidney function

V) Other: [Free text]

21. If you entered a clinical trial, would you consider acceptable to experience more side effects if the treatment worked better?

I) Yes

II) No

III) I do not know

22. How important for you is the following when selecting a course of treatment (Not important, moderately important, very important)?

I) Whether treatment is taken by mouth, by intravenous (IV), by injection in muscle or via subcutaneous (SC) infusion

II) How often I must take the treatment

III) Number of side effects known for the drug

IV) Severity of side effects

V) What my physician recommends

VI) Other: [Free text]

23. How important for you is the following? (Not important, moderately important, very important)?

I) I would like to be informed about the general results of the trial

II) I would like to be informed about my individual results, e.g., how the treatment affected me

III) I would like to continue treatment for free after ending the trial

IV) Anything else you think is important regarding clinical trials, please specify: [Free text]

Use and sharing of health data, including genetic data

If you should participate in a clinical trial, the researchers will likely collect health data about you. This may include genetic data.

24. Your data may be useful for other research groups wanting to develop treatments for your disease. If your data were shared in an anonymous form (i.e., the researchers will not be able to re-identify you) with other research groups, would you say that (agree, disagree, neither agree nor disagree):

I) It can be used only to conduct research on my disease

II) It can be used to conduct research on other diseases than C3G/IC-MPGN

III) It can be used for any type of research also outside of the health research field

IV) Other: [Free text]

25. How important is it for you to know about with whom your data is shared and for which purposes?

I) Not important

II) Somewhat important

III) Very important

26. What do you see as the most likely benefit of sharing your data with other research groups (please select only one)?

II) Sharing my data may improve the diagnosis of future patients

I) Sharing my data may contribute to help researchers develop new treatments

III) Sharing my data may participate in advancing genetic technology

IV) I do not see any benefits

V) Other: [Text box]

27. What do you see as the most likely drawback of sharing your data with other research groups (please select only one)?

I) My data may be used for purposes I disagree with

II) Sharing my data may negatively impact my access to treatment

III) Some people may learn about my health status against my will

IV) I do not see any drawbacks

V) Other: [Text box]

Further information

28. How do you get information about your kidney disease? (Select all that apply)

I) Through my GP or my nephrologist

II) Internet / media

III) Patient organization

IV) Scientific journals

V) Family / friends

VI) Other: [Free text]

29. What are your needs in terms of information / education in your disease and treatment? (Select all that apply)

I) I would like to learn more about how to reduce symptoms

II) I would like to learn more about kidney-friendly diets

III) I would like to learn more about my own prognosis

IV) Other: [Free text]

Appendix 3 - survey questionnaire to parents of C3G/IC-MPGN patients aged below 16 years of age

INFORMED CONSENT

Please tick the box.

- I am above 16 years of age and I consent to the use of these data for research

Please tell us a little bit about yourself as a parent

1. Are you a mother or father? (Mandatory question)

- Mother
- Father

2. In which country do you reside? (Mandatory question)

'List of countries'

3. What is your child's age? (Mandatory question)

- Below 12 years of age
- 13-16 years old

4. What kidney disease does your child have? (Mandatory question)

- MPGN Type 1
- MPGN Type 2
- MPGN Type 3
- IC-MPGN/Ig-MPGN
- MPGN, but I don't know the type
- C3G glomerulopathy (C3G)
- Dense Deposit Disease (DDD)
- C3 glomerulonephritis (C3GN)
- Other, please specify:

5. When was your child diagnosed? (Mandatory question)

- In early childhood/childhood (before 12 years of age)
- In adolescence (13-19 years of age)

6. How would you describe your child's quality of life and living conditions with the disease?

I) Poor

II) Average

III) Good

IV) Very good

7. In average, how many visits to doctors does your child have per year due to his/her disease? E.g., nephrologist, dermatologist, eye specialist

I) Less than 5 visits a year

II) Between 5 and 10 visits a year

III) More than 10 visits a year

8. Do you think that your child's doctor knows your child's disease well enough to be able to find the right therapy for him/her?

I) Yes

II) No

III) I do not know

9. Do you think that your child's current therapy is sufficient to manage the disease?

I) Yes

II) No

III) I do not know

IV) My child currently does not receive any therapy

10. Did you notice any improvements since you child started his/her current therapy?

I) Yes

II) No

III) I do not know

IV) My child currently does not receive any therapy

11. Is your child's current therapy "off-label"? (Off-label means, that the drug is approved by the European Medical Agency for another disease, not for your child's diagnosis)

I) Yes

II) No

III) I do not know

IV) My child currently does not receive any therapy

12. Have you ever experienced that the cost of your child's treatment was not covered by your national health service?

I) Yes

II) No

III) I do not know

IV) My child currently does not receive any therapy

13. How would you describe your child's quality of life and living conditions with the disease?

I) Poor

II) Average

III) Good

IV) Very good

14. What do you consider the biggest challenges related to your child's disease (please select maximum 3 challenges)?

I) Various side effects of the treatment (e.g., nausea, shortness of breath, allergic reactions etc.)

II) Reduced quality of life (e.g., not being able to; do sports, pursue an education etc.)

III) Restrictions due to nutrition/diet

IV) Lack of sleep and/or mental health issues (e.g., fatigue, anxiety, depression, fears etc.)

V) Symptoms (e.g., swelling, edemas, headaches etc.)

VI) Other: [Free text]

15. Do you feel that your child's disease has changed him or her in anyway?

I) Not at all

II) To some degree

III) Very much

16. In your opinion, how much does your child's disease affect your family life?

I) Not at all

2) To some degree

3) Very much

Participation in phase II clinical trials

17. Has your child ever participated, or is currently participating, in a clinical trial, e.g., to test a new drug for your disease?

I) Yes

II) No

III) I do not remember

18. Would you ever be willing to let your child participate in a clinical trial for a new MPGN drug?

I) Yes

II) No

III) I do not know

19. What are the most important factors for you to decide on whether you would like to let your child participate in a trial or not? Please select the three most important factors

I) The number of biopsies* my child will have to undergo

II) Whether my child will have to reduce my current therapy to introduce a new treatment**

III) How long the trial will last

IV) Where the trial will take place

V) How often my child will have to go to the hospital or research centre

VI) What types of side effects the new treatment may have, if my child receives it

VII) Other: [Free text]

** Renal biopsy is performed by inserting a thin needle through the skin and into the kidney after local anesthesia is performed. It is generally considered to be a safe procedure and serious complications are*

uncommon. Less serious complications can occur and include pain, bleeding and development of an abnormal connection (fistula) between two blood vessels.

*** This transition period between different treatments could last over several weeks or months.*

20. How would you make the final decision to let your child participate or not in the trial? (Select all that apply)

I) I would ask my child what he/she wants

II) I would ask our general practitioner for advice

III) I would ask for advice from my family and/or friends

IV) I would ask for advice from a patient organization

V) Other: [Free text]

21. What would be your main motivation for letting your child enter the trial (please select one)?

I) My child can contribute to increase knowledge about the disease

II) My child can have check- ups more often than usual

III) I hope that the new treatment will improve my child's kidney function

IV) Other: [Free text]

22. If your child entered a clinical trial, would you consider acceptable that he/she experiences more side effects if the treatment works better?

I) Yes

II) No

III) I do not know

23. How important for you is the following when selecting a course of treatment (Not important, moderately important, very important)?

I) Whether treatment is taken by mouth, by intravenous (IV), by injection in muscle or via subcutaneous (SC) infusion

II) How often my child must take the treatment

III) Number of side effects known for the drug

IV) Severity of side effects

V) What our physician recommends

VI) Other: [Free text]

24. How important for you is the following? (Not important, moderately important, very important)?

I) I would like to be informed about the general results of the trial

II) I would like to be informed about my child's individual results, e.g., how the treatment affected him/her

III) I would like my child to continue treatment for free after ending the trial

IV) Anything else you think is important regarding clinical trials, please specify: [Free text]

Use and sharing of health data, including genetic data

If your child were to participate in a clinical trial, the researchers will likely collect large amounts of health data about him/her. This may include genetic data.

25. Your child's data may be useful for other research groups wanting to develop treatments for your disease. If your child's data were to be shared in an anonymous form (i.e., the researchers will not be able to re-identify your child) with other research groups, would you say that (agree, disagree, neither agree nor disagree):

I) It should be used only to conduct research on my child's disease

II) It can be used to conduct research on other diseases than C3G/IC-MPGN

III) It can be used for any type of research also outside of the health research field

IV) I do not have any opinion on how it should be used

V) Other: [Free text]

26. How important is it for you to know about with whom your child's data is shared and for which purposes?

I) Not important

II) Somewhat important

III) Very important

27. What do you see as the most likely benefit of sharing your child's data with other research groups (please select one)?

II) Sharing my child's data may improve the diagnosis of future C3G/IC-MPGN cases

I) Sharing my child's data may contribute to help researchers develop new treatments

III) Sharing my child's data may participate in advancing genetic technology

IV) I do not see any benefits

V) Other: [Text box]

28. What do you see as the most likely drawback of sharing your child's data with other research groups (please select one)?

I) My child's data may be used for purposes I disagree with

II) Sharing my child's data may negatively impact my access to treatment

III) Some people may learn about my child's health status against our will

IV) I do not see any drawbacks

V) Other: [Text box]

Further information

29. How do you get information about your child's kidney disease? (select all that apply)

I) Through our general practitioner or our nephrologist

II) Internet / media

III) Patient organization

IV) Scientific journals

V) Family / friends

VI) Other: [Free text]

30. What are your needs in terms of information / education in your child's disease and treatment? (Select all that apply)

I) I would like to learn more about how to reduce symptoms

II) I would like to learn more about kidney-friendly diets

III) I would like to learn more about my child's own prognosis

IV) Other: [Free text]