Epilepsy & Behavior 90 (2019) 178–190

Contents lists available at ScienceDirect

Epilepsy & Behavior

journal homepage: www.elsevier.com/locate/yebeh

Parents of a child with epilepsy: Views and expectations on receiving genetic results from Whole Genome Sequencing

Iris Jaitovich Groisman, Thierry Hurlimann, Béatrice Godard *

Université de Montréal, PO Box 6128, Station Centre-ville, Montreal H3C 3J7, Canada

ARTICLE INFO

Article history:
Received 31 July 2018
Revised 2 November 2018
Accepted 19 November 2018
Available online 22 December 2018

Keywords:
Epilepsy
Pharmacoresistance
Whole Genome Sequencing
Personalized medicine
Return of results
Family communication

ABSTRACT

Purpose: The use of Next Generation Sequencing technologies (NGS), such as Whole Genome Sequencing (WGS), is expected to improve the often complex and protracted course of treatment of patients with epilepsy by providing an earlier and more accurate diagnosis. As part of the "Personalized medicine in the treatment of epilepsy" project, which aimed to determine whether WGS could be used as a valuable "diagnostic tool" in pharmacoresistant epilepsies, we examined parents' expectations, hopes, and concerns upon receiving results related to their child's epilepsy, comorbidities, resistance to medication, and genetic information on unrelated conditions, and how these results could impact their and their child's life.
Methods: Parents of 32 children participating in the genetic study completed either paper or online questionnaires. A descriptive analysis of responses and comments was conducted regarding parents' experience with their child's epilepsy, as well as their views on WGS, and expectations and concerns surrounding such test results.
Results: Most respondents had trouble explaining the medical causes of their child's epilepsy ($n = 27$), and a majority ($n = 26$) feared that their child may be treated unjustly because of their epilepsy, although some acknowledged that their child had never actually been treated unjustly ($n = 13$). A majority of respondents had also experienced feelings of guilt due to their child's epilepsy ($n = 23$), and some expected WGS results to have an impact on those feelings. The anticipation of benefits for their child was the parents' primary reason to get involved in a genomic research project, closely followed by altruism. A majority expressed strong intentions to receive as many WGS results as possible, considering that any could be beneficial for them and their child, even when mutations were not found. Respondents were divided as to how and when to tell their child that they might have newly discovered predispositions to develop another disease. In proportion, more parents expressed concerns about sharing unexpected results with their family members compared with sharing results linked to epilepsy, comorbidities, and pharmacoresistance.
Conclusion: Our results reinforce the importance of having clear guidelines to help parents manage their expectations and better navigate the complexities of receiving and sharing WGS results. Despite the small size of our sample, we believe that our results are meaningful to clinical practice.

1. Introduction

Epilepsy, a common neurological disorder affecting people worldwide, is characterized by recurrent and unprovoked seizures (http://www.who.int/mediacentre/factsheets/fs999/en/index.html) [1]. Individuals with epilepsy have higher rates of hospitalization/consultation compared with those with several other chronic conditions [2]. In addition, results of these studies show that epilepsy impacts negatively on individuals' social interactions, education, and employment [3]. They highlight the importance of controlling the disease's symptoms (i.e., achieving freedom from seizures), improving overall health, and decreasing stigma [4]. This information is consistent with earlier reports that largely attribute epilepsy's global burden to patients' social exclusion and stigma [5].

Neurological conditions account for an extensive portion of undiagnosed diseases [6]. As for epilepsy, there is a recognized uncertainty and complexity in its diagnosis. This is observable in the search for more linear procedures to better identify epilepsy types [7], as well as by the development of updated classification systems by the International League Against Epilepsy and the World Health Organization, reflecting scientific advances in various medical areas, including genetics [8]. Although epilepsy presents a strong genetic component, typical "monogenic" epilepsy is rare [9]. The use of Next Generation Sequencing technologies (NGS), such as Whole Genome Sequencing (WGS) and Whole Exome

* Corresponding author.
E-mail address: beatrice.godard@umontreal.ca (B. Godard).
URLs: https://www.mdsocp.umontreal.ca, https://www.santepop.qc.ca (B. Godard).

https://doi.org/10.1016/j.yebeh.2018.11.020
1525-5050/

Sequencing (WES), is expected to be a promising path towards a more accurate diagnosis of neurological conditions, including various types of epilepsy, and to reduce patients' common treatment odyssey [10]. Next Generation Sequencing technologies are currently allowing the identification of new genetic susceptibility factors associated with the disease, in particular, rare Copy Number Variants (CNVs) – deletions and duplications – which have been shown to be important risk factors for both generalized and focal epilepsies [11,12].

In 2013, Genome Canada and Génome Québec granted support to a research project entitled "Personalized medicine in the treatment of epilepsy" (http://www.genomequebec.com/152-en/project/personalized-medicine-in-the-treatment-of-epilepsy.html) [13]. This project aimed to determine whether WGS could be used to search for a genetic cause of pharmacoresistant variants and to better understand the response – or lack thereof – to medication in both adults and children. Considering the technological advances in research, we deemed it important to assess the hopes and concerns of parents of children with epilepsy. We examined their expectations on receiving or not receiving results revealing the cause of their child's epilepsy, possible comorbidities, genetic factors regarding the resistance of their child's seizures to medication, and genetic information on unrelated conditions (incidental findings (IFs)). Also explored was how parents thought such results would impact their lives, including that of the child and of the immediate family. The views of adult participants with pharmacoresistant epilepsy on these matters will be addressed in a separate publication. This article focuses on parents' perceptions.

The findings offer insight into the needs of parents whose lives are affected by a child's epilepsy and could thus, contribute to the development and implementation of resources to further assist parents and children touched by this complex condition.

2. Materials and methods

2.1. Recruitment and data collection

The "Personalized medicine in the treatment of epilepsy" study referred to in the Introduction section recruited minors and adults with pharmacoresistant epilepsy. Parents of participating children in the said project, at Sainte-Justine Hospital in Montreal and British Columbia Children's Hospital in Vancouver, were invited to complete our questionnaire once they accepted to participate in the genomic study and before obtaining any results. The study was approved by the Research Ethics Board of both institutions.

Forty-three parents of children aged less than 18 years were recruited to participate in the genetic study, and 32 completed our questionnaire. The latter were handed out by a member of the healthcare team during a medical visit and were to be taken home and completed at the respondents' convenience, thereafter to be returned using an enclosed, prestamped envelope. Seven (7/32) respondents preferred to answer online and thus, received a link to the website hosting the questionnaire. Both parents were invited to answer the questions together or independently. Among respondents, four fathers and 17 mothers from 21 different families answered the questions. In addition, eleven couples completed the questionnaires together. (Supplementary Table 1 contains demographic information of respondents).

The questionnaire was available in English and French on paper format or online using Research Electronic Data Capture (REDCap) hosted by the *Unité de Recherche Clinique Appliquée* of Sainte Justine Hospital. The questionnaires were completed between May 2016 and the end of March 2017. The time to complete the questionnaire was between 30 and 45 min. The questionnaire contained questions addressing the following: (1) respondents' experience in dealing with their child's epilepsy, (2) knowledge of the cause(s) of that epilepsy, and (3) parent(s)' decision to allow their child to participate in the research project on the genetics of epilepsy. Also examined were perceptions and expectations about (4) results that could explain the cause of the child's epilepsy, (5) results related to possible comorbid conditions, (6) responses to medication, and (7) unexpected results. Respondents were presented with a table summarizing all possible genetic results they might receive, specifying that all results would be scientifically and clinically validated and actionable (Supplementary Table 2). Participants were allowed to skip any question they did not want to answer and were provided with ample possibilities to add comments and their own thoughts at various points of the questionnaire. The questionnaire was based on current

Table 1
Your experience and concerns surrounding your child's epilepsy.

1.1. Apart from physicians and other health professionals, who else did you tell that your child has epilepsy? (Check one or more answers)

	Most	Some	None
Family members (parents, grandparents, brothers, sisters, uncles, aunts and cousins)	28	2	1
Friends	21	10	1
Colleagues at work[a]	20	7	0

1.2. Your experience with epilepsy

	Often	A few times	Never	I don't know/I am not sure
a) Have you ever had problems obtaining access to appropriate healthcare and a medical specialist for your child?	4	12	16	0
b) Have you ever had problems obtaining access to social services that could help you and your child cope with epilepsy? (For instance: financial assistance programs, respite services, school/learning support, other social service support)	5	12	14	1
c) Have you ever experienced feelings of guilt because of your child's epilepsy? (For instance, some parents feel guilty, believing their child's epilepsy is their fault, or they may think they did something wrong, for example, by not reacting appropriately before, during, or after their child's seizures)	6	17	9	0
d) Have you ever had trouble explaining the medical causes of your child's epilepsy?	14	13	4	1
e) Have you ever feared that people may treat your family members (your other children, your parents, siblings, cousins, nephews, etc.) unjustly because of your child's epilepsy?	3	7	19	3
f) Have family members ever told you that they had been treated unjustly by others because of your child's epilepsy?	2	3	25	2
g) Have you ever feared that your child may be treated unjustly, because of his/her epilepsy? (For instance, a fear that people may frown at your child; leave him/her out, criticize him/her, or a fear that teachers, future employers, insurance companies, or other institutions/people may treat him/her differently than other people)	13	13	5	2
h) Has your child ever been treated unjustly because of his/her epilepsy?	1	12	15	3
i) Have you ever been afraid of being treated unjustly, because of your child's epilepsy? (For instance, a fear that people may frown at you or your child; leave you out, criticize you, or a fear that employers, insurance companies, or other institutions may treat you differently than other people)	4	10	15	2
j) Have you ever been treated unjustly because of your child's epilepsy?	3	8	17	4

[a] The question was not applicable to 7 respondents.

literature about ethical issues surrounding the return of WGS results, parents' expectations about research endeavors related to the medical condition of their offspring, and epilepsy [14–28]. A pretest to evaluate language difficulties and appropriateness of subjects was conducted in Montreal during 2015. A total of nine participants were recruited for pretesting the questionnaire, four at St. Justine Hospital and five at the association *Épilepsie Montréal Métropolitain*, following approval by St. Justine Hospital's Research Ethics Board. The results of the pretest helped optimize the layout of the questionnaire, improve the clarity and readability of questions, thus diminishing the time required for completion.

2.2. Data analysis

Research Electronic Data Capture (REDCap) was also used for data management. Information from the completed questionnaires was transferred to an Excel database. Descriptive statistics were used to depict sample characteristics. A descriptive analysis of responses and comments was conducted regarding parents' experience with their child's epilepsy, as well as their views on WGS and expectations and concerns surrounding such test results. The text that appears on the tables, including subtitles, contain the exact text presented to participants. Participating parents completed the questionnaires alone or together with the other parent of the child (Supplementary Table 1). We refer to participants to the present study as "respondents" and/or "parents" without further discrimination.

Box 1
Parents' comments and thoughts on stigma*

Have you ever feared that your child may be treated unjustly, because of his/her epilepsy? (For instance, a fear that people may frown at your child; leave him/her out, criticize him/her, or a fear that teachers, future employers, insurance companies or other institutions/people may treat him/her differently than other people) If so, who do you fear could treat your child unjustly and why?
Yes: [by] neighbours, friends, kids, [at] school.
Yes: being refused in sport activities, daycare. School will start next year.
Yes: we are afraid of [such] situations in the future, although nothing happened so far.
Yes: [by] schoolmates.
Yes: [by] daycare services, insurance, bank.
Yes: [because] my daughter has a developmental delay because of spasms.
Yes: I would not like my daughter to be looked at with fear or aversion in the presence of her sisters; this would make them sad.
Yes: [by] sport team (fear that one will limit his level of activity); [by] teachers, employers (fear they will mistake his memory problems with a lower intelligence).
Yes: [fear that people] do not accept his difference, given that he does not speak and does not understand anymore… he goes into fits of anger. Fear of the look of others because of [their] lack of understanding, fear that they actually put him aside because of fear, lack of resources.
Yes: [by] daycare services (like us, they were not used to deal with this kind of disease)
Yes: I fear the day my daughter will go to school (fear of rejection, bullying)
Yes: [in] school settings, [by] friends, friends' parents. Fear they put him aside, they avoid him
Yes: [fear that] future friends at school put him aside.
Yes: I still fear my child is treated differently because we are living in a society in which difference is poorly looked upon
Yes: [by the] general public
Yes: [by] classmates at school, teachers' aids, people at church
Yes: In the school, [by] people that are not aware of medical condition
Sometimes I feel he is not chosen for participating in some activities because of his illness.

* The comments that were originally written in French have been translated into English for the purposes of the present publication.

3. Results

3.1. Experiences with epilepsy

As shown in Table 1, one respondent in two considered that their access to appropriate healthcare and medical specialists for their child, as well as to social services such as offering respite or school/learning support, had been problematic. Parents were also asked whether they knew about the cause(s) of their child's epilepsy: eighteen of them reported that they were told the cause was unknown. Except for four respondents, all other parents had trouble explaining the medical causes of their child's epilepsy. At the same time, results provided on Table 1 show that the majority of parents enrolled in this study talked about their child's health condition to relatives, teachers, most friends, and work colleagues. Some parents explicitly mentioned that they had shared this information with other parents, sitters, educators, or health professionals, such as a dentists or optometrists. A few of them explained that they did so for safety reasons.

Box 2
Examples of unjust treatment*

Has your child ever been treated unjustly because of his/her epilepsy? If so, by whom and why?
Yes: [swimming] instructor's refusal, [who] feared [my child] could drown
Yes: [by] daycare services, insurance
Yes: [by] friend's parents, [who] withdrew their invitation for fear of epilepsy
Yes: At school, the teacher found him burdensome and the class was not adapted for him. It was a language course, but [my child] does not talk and does not understand anymore. His friends put him aside because he was going into fits of anger or cannot make himself understood. [Some] take pity on his condition and then give him more chances, spoil him more, treat him like a baby.
Yes: [at] the school and respite services for ASD [autism spectrum disorders] [they] refuse to take care of him as long as epilepsy is not controlled.
Yes: [by] staff in school settings, [my kid] is not allowed to participate in extracurricular activities if one of the parents is not accompanying him.
Yes: [by] a family friend [who] tends to shut my son out of activities, because, according to her, he is not capable
Yes: [by] a woman at [the grocery] because I put my son on the changing table and she wanted to use it [during a seizure]
Yes: [by] [Name of a cruise company] and [by] a friend's mother
Yes: At school, needed help with homework but very hard to get any help. Home based daycares all said 'no space'; drivers license, he has one, but when we told them that he has epilepsy, they had no idea what to do, first they said no to the driver's license. Applying for grants or scholarships for going to post-secondary school, epilepsy is not enough of an issue; have to prove why it is affecting him still, lots of running around to prove it. Part time job, he does not put down epilepsy, he has not had a seizure for over 8 years.
Public staring, assuming she is typical
Mostly his friends do not want him in their group.

* The comments that were originally written in French have been translated into English for the purposes of the present publication.

Table 2
Questions about your decision to allow your child to participate in the research project on the genetics of epilepsy.

What is/are the main reason(s) that led you to consent to your child's participation in the research project on the genetics of epilepsy? (Check one or more answers)	N
Help develop better treatments for people with epilepsy	24
Help treat my child's epilepsy	23
Help find one or more genetic mutations that cause my child's epilepsy	23
Help better understand epilepsy in general	17
Help decrease the stigma attached to epilepsy (being frowned at, left out, criticized, etc.)	11
Other reasons? Please specify:	6
- Advancement of science for future generations	
- Help other children	
- Maybe it could also contribute to treat his developmental delay and improve his future quality of life	
- To be able to be in close contact with experts in the field and let them evaluate my child	
- To do everything on my power to help my child and other children that suffer from the same disease	
- So that siblings can know whether the disease is genetic and they will decide by themselves whether they will have children in the future	
- To help in any way possible, to help other families from suffering	
- I want him to be good	

A vast majority of the respondents feared that their child might be treated unjustly because of his/her epilepsy. As shown in Box 1, some parents explicitly expressed their concerns of seeing their child being left out of daycare, sport activities, and/or social interactions with classmates. Yet, almost half of the parents acknowledged that, despite their fears, their child had never actually been treated unjustly because of their epilepsy (Table 1). This leaves an almost equivalent number of parents who reported that their child had already been treated unjustly by various people, notably by being excluded from various activities and/or social interactions (see Box 2).

Almost half of the parents had already feared being treated unjustly themselves because of their child's epilepsy (Table 1). Most of them had concerns of being treated unfairly by their employer, as a result of the need to take time from work to take care of their child. Eleven respondents reported having experienced actual unjust treatment at work (Table 1) (for instance, one employer questioning the rationale behind work absences) or in their social lives, mainly by people – including friends – who did not want to witness seizures, who were annoyed by the child's behavior or by the measures that had to be implemented for the child's safety.

The majority of respondents had also experienced feelings of guilt because of their child's epilepsy (Table 1). For instance, some parents believed that the child's epilepsy was their fault or that they had done something wrong, for example, by not reacting appropriately before, during, or after their child's seizures.

3.2. Reasons that led parents to agree with their child's participation

Respondents were asked to explain the reasons that led them to allow their child to participate in the prospective genetic research study using WGS. Among a list of nonexclusive reasons (Table 2), parents agreed with their child's participation to help develop better treatments for people with epilepsy, to help treat their child's epilepsy, to help find one or more genetic mutations that caused their child's epilepsy, to help better understand epilepsy in general, or to help decrease the stigma attached to epilepsy (i.e., being frowned at, left out, criticized, etc.).

For almost half of the respondents, the use of WGS in the research protocol did not influence their decision to agree with their child's participation. Conversely, nine respondents acknowledged that the use of WGS had an influence on their decision: most of them explicitly expressed their hope that WGS could help find the cause(s) of their child's epilepsy. For instance, some parents were interested in having their child participate because "until now, no cause – biological, genetic or metabolic – for my daughter's epilepsy could be found", "[WGS could] identify other mutations or problems", or because "my child did not respond well to medication at the beginning and these tests could help, anything that can help is welcome". Lastly, three respondents stated that the use of WGS made them hesitate to agree about their child's recruitment, because of "fear of having the results whether positive or negative", "fear of receiving other results that are not linked with epilepsy", and "fear for the confidentiality of information". One respondent had concerns that their child "did not understand well enough the impact of [his/her] consent".

3.3. Receiving results about the cause(s) of epilepsy — results showing a mutation

What would parents think if WGS showed a mutation explaining their child's epilepsy? As shown in Table 3, the majority of participants to our study felt this would help them manage their child's situation, whether to explain the medical causes of the condition to others, to improve treatment, or to plan the future of their child. However, respondents had divided opinions when asked if they would be concerned if such results could mean that there is no specific treatment for their child's epilepsy, as shown on Table 3, question e. But, most respondents did not foresee any concerns sharing such results with their family members nor did they expect to fear people's reactions about such results. Among the few that had concerns, one explained they would find it hard to share this information with their other children and another respondent with other family members. As for the risk that their child be treated unjustly by others, the majority of participants thought that a result showing a mutation would not increase this risk.

The impact of such results on the respondents' feelings of guilt was considered. One out of two expected that they would not feel guilty if

Table 3
Results about the cause of your child's epilepsy — a mutation is found.

What would you think if the results of your child's Whole Genome Sequencing showed that he/she has a mutation that explains his/her epilepsy?	Yes	No	I don't know/I'm not sure
a) Such results could improve my child's treatment	23	0	6
b) Such results could help me get a better access to healthcare and social services for my child	10	7	13
c) Such results could help me and my child to plan his/her future	23	1	6
d) Such results would make it easier for me to explain to others the medical causes of my child's condition	26	0	4
e) I would be concerned such results could mean that there is no specific treatment for my child's epilepsy	13	12	5
f) I would feel guilty if such results meant that I may have passed on this mutation to my child	6	16	8
g) I would have concerns about deciding when and how to tell my child about such results	7	18	5
h) I would fear people's reactions if I told them about such results	4	23	3
i) I would be concerned such results could increase the risk that my child be treated unjustly by others	4	20	5
j) Such results could make me feel less guilty (For instance, such results could mean that I did nothing wrong to cause my child's epilepsy)	8	15	6
k) I would have concerns about sharing such results with my family members	2	27	1

Table 4
Results about the cause of your child's epilepsy — no mutation is found.

What would you think if the results of your child's Whole Genome Sequencing showed that he/she has no mutation that explains his/her epilepsy?			
	Yes	No	I don't know/I'm not sure
a) Just knowing such results would be good, even if they are not useful for my child's treatment	28	0	3
b) I would be relieved to know that researchers could not find such a mutation in my child's genes	13	9	10
c) I would be disappointed because such results would not help explain my child's condition	15	12	5
d) I would still wonder if my child has one or more mutations that researchers could not find	11	13	7
e) I would be concerned such results could mean that there is no specific treatment for my child's epilepsy	17	13	3
f) Such results could make me feel guilty, because if no genetic cause is found, it could lead me to think that I did something that could explain why my child has epilepsy	2	26	4
g) Such results could make me feel less guilty, because they could mean that I didn't pass on a mutation to my child	4	20	8
h) I would have concerns about sharing such results with my family members	1	30	1
If yes, why? No comments			

such results meant that they may have passed on this mutation to their child. An almost equal number answered they would feel guilty or they did not know how they would feel. Parents were also asked whether such results could make them feel less guilty, as this genetic information could mean, for instance, that they did nothing wrong to cause their child's epilepsy. Fifteen parents did not think that such results could make them feel less guilty, with some stressing that they never thought they were responsible for their child's condition and thus, had never had feelings of guilt. The discovery of a mutation that could contribute to explain epilepsy would have reduced the feelings of guilt of eight

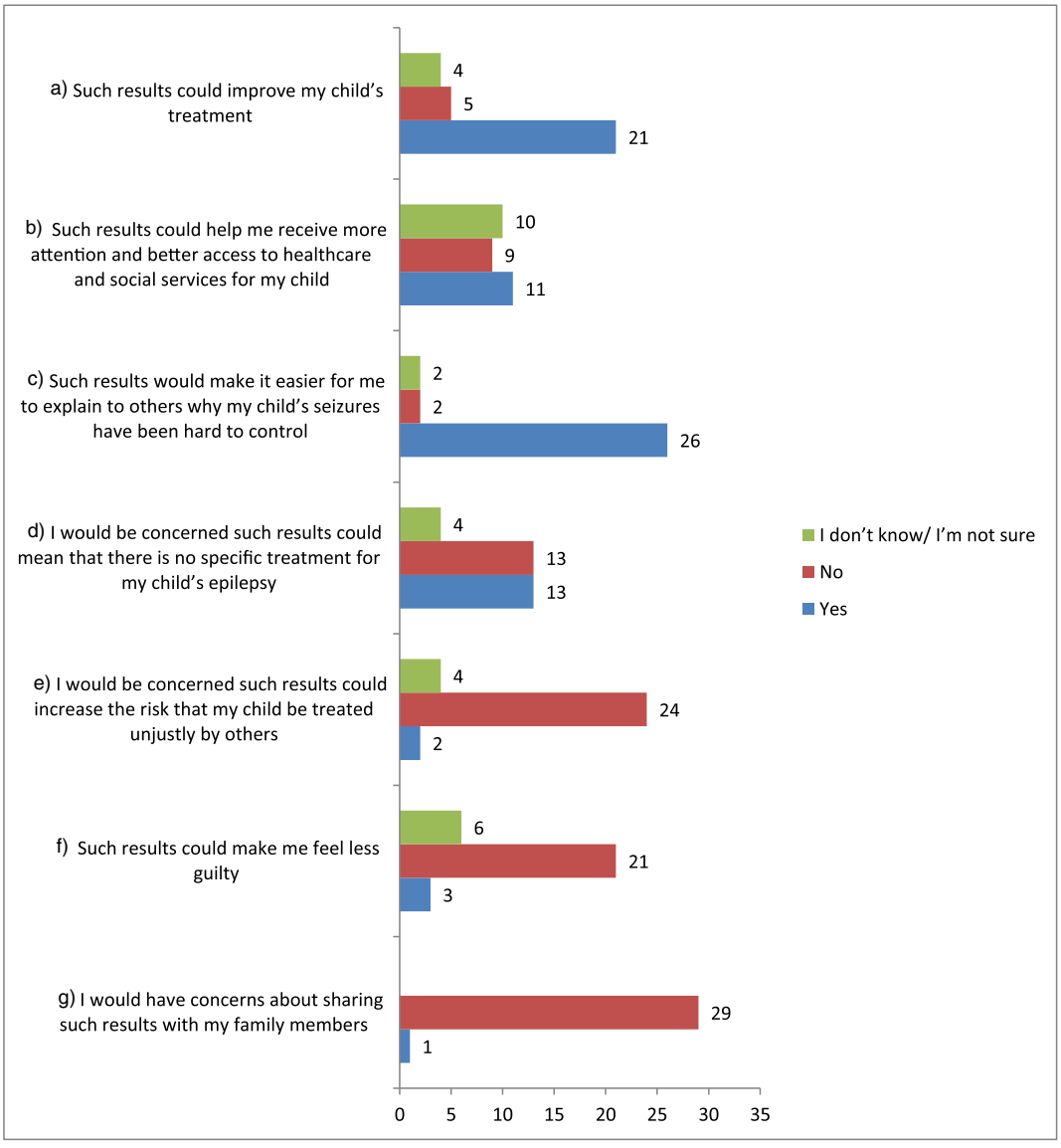

Fig. 1. What would you think if the results of your child's Whole Genome Sequencing showed that he/she has a mutation that explains why seizures have been hard to control with antiepileptic drugs? (Number of respondents by question).

respondents. For instance, one of them explicitly stated that such results would confirm she did nothing wrong during her pregnancy. Six participants did not know whether finding a mutation that could explain the cause of epilepsy – and thus, the appearance of this condition is out of their control as explained on Table 3, point J – would impact their feelings of guilt.

3.4. Receiving results about the cause(s) of epilepsy — results showing no mutation

Respondents' opinions if WGS were to show no mutation are presented in Table 4. Almost half of the respondents would be relieved to know that researchers could not find a mutation in their child's genes while other respondents would not feel relieved or could not predict their feelings. The vast majority of respondents thought that just knowing such a result would be good, even if it was not useful for their child's treatment, and they would have no concerns about sharing such information with family members. Opinions were divided regarding concerns that such results could mean there was no specific treatment for their child's epilepsy and possible disappointment if results would not help explain their child's condition (Table 4, questions e and c respectively).

For most respondents, knowing that no mutation could be found would not impact their potential feelings of guilt, because if no genetic cause was found, it could lead them to think that they did something that would explain why their child had epilepsy. It also appears that for several respondents, such results would not make them feel less guilty, even if it meant they did not pass on a mutation to their child.

3.5. Receiving results about response to antiepileptic drugs

We asked participants about their thoughts on possible WGS results showing their child had a mutation explaining why seizures had been resistant to antiepileptic drugs. The majority considered that such results would make it easier for them to explain to others why their child's seizures had been hard to control (Fig. 1). In addition, they would not have concerns about sharing such results with family members and would not be concerned that such results might increase the risk of

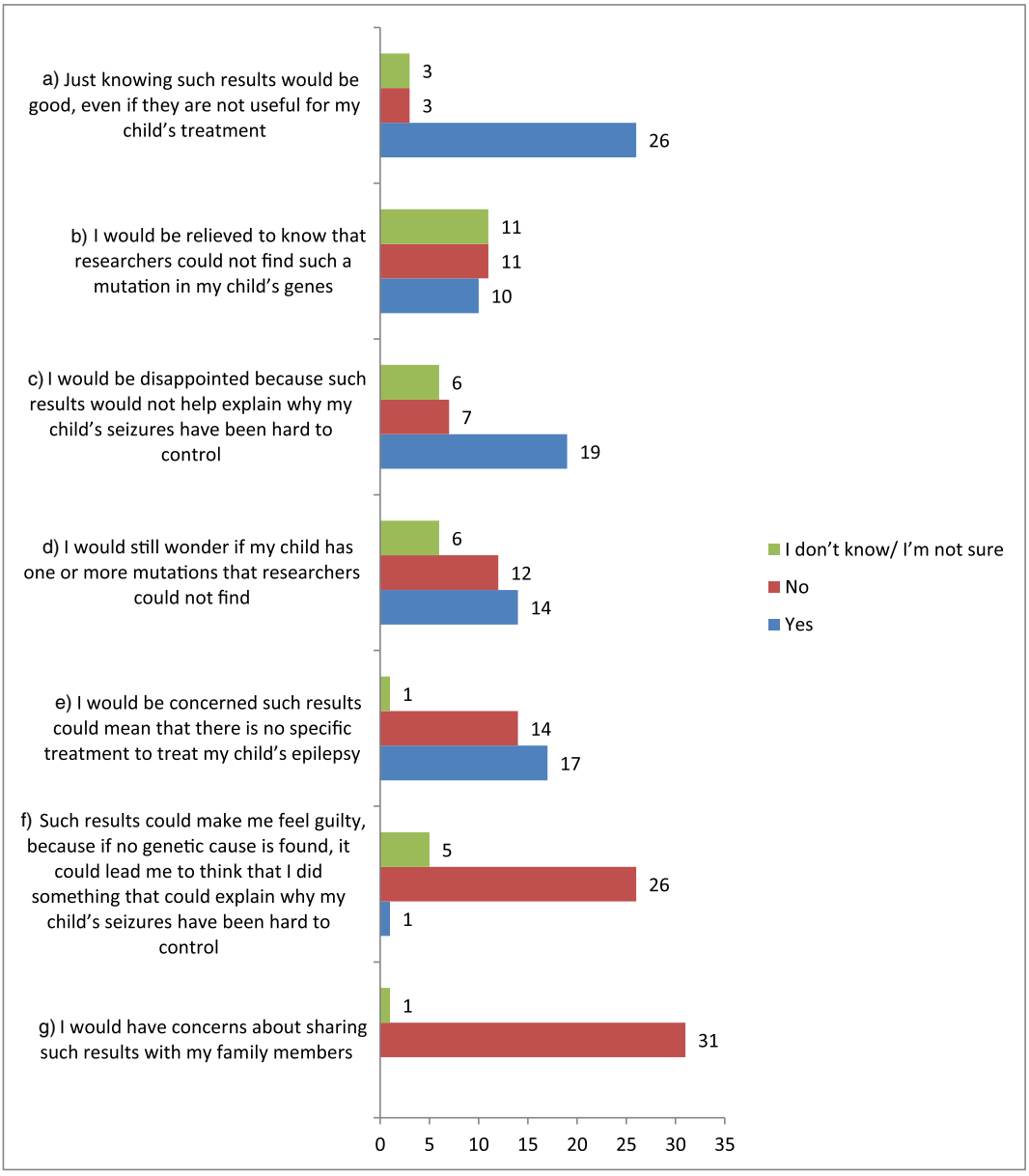

Fig. 2. What would you think if the results of your child's Whole Genome Sequencing showed that he/she has no mutation that explains why seizures have been hard to control with antiepileptic drugs? (Number of respondents by question).

their child being treated unjustly by others. Parents also thought that such information could improve their child's treatment. For several respondents, it would not alleviate their feelings of guilt. Some parents were concerned that such results could mean that there was no specific treatment for their child's epilepsy while this was not a concern for others. Similarly, parents had divided opinions when it came to determining whether such results could help them receive more attention and better access to healthcare and social services for their child.

If the results of the WGS showed that a child had *no mutation* explaining why seizures had been drug-resistant, just knowing such results would be good, even if they were not useful for treatment (Fig. 2). Still, more than half of respondents would be disappointed because such results would not help explain why their child's seizures had been hard to control. Opinions were more divided to the effect that such results could mean that there was no specific treatment for their child's epilepsy. Some parents would still wonder if their child had one or more mutations that researchers could not find. About respondents' relief if no mutation explaining drug resistance was found, respondents' opinions were equally divided as shown on responses to question b on Fig. 2. Finally, except for one respondent, no one would have concerns about sharing such results with family members. Absence of mutations related to drug-resistance would not alleviate respondents' feelings of guilt.

3.6. Receiving results related to comorbidities

Most respondents were in favor of receiving results revealing a mutation explaining why their child had a medical condition that sometimes came with epilepsy, such as one causing intellectual difficulties (Fig. 3). Such results would help them understand their child's condition, take action in support of their development, or bring better access to healthcare and social services. For instance, a parent wrote that they could "better draw a future for [their] daughter as a person with a deficiency and perhaps know the degree of intellectual deficiency she might have". Parents also thought that these results would make it easier for them to explain to others why their child had health problems besides epilepsy. Except for one respondent who feared that such results would stress family members even more and/or not be understood, most parents did not have concerns about sharing such results with family members, and many did not think that these results could increase the risk that their child be treated unjustly by others.

More than half of respondents would not feel guilty if such results meant that they may have passed on this mutation to their child. At the same time, half of them stated that such results would not make them feel less guilty, because it could mean that their child's intellectual development may have been partly beyond their control, despite their efforts. One of the respondents explicitly stated that such results could

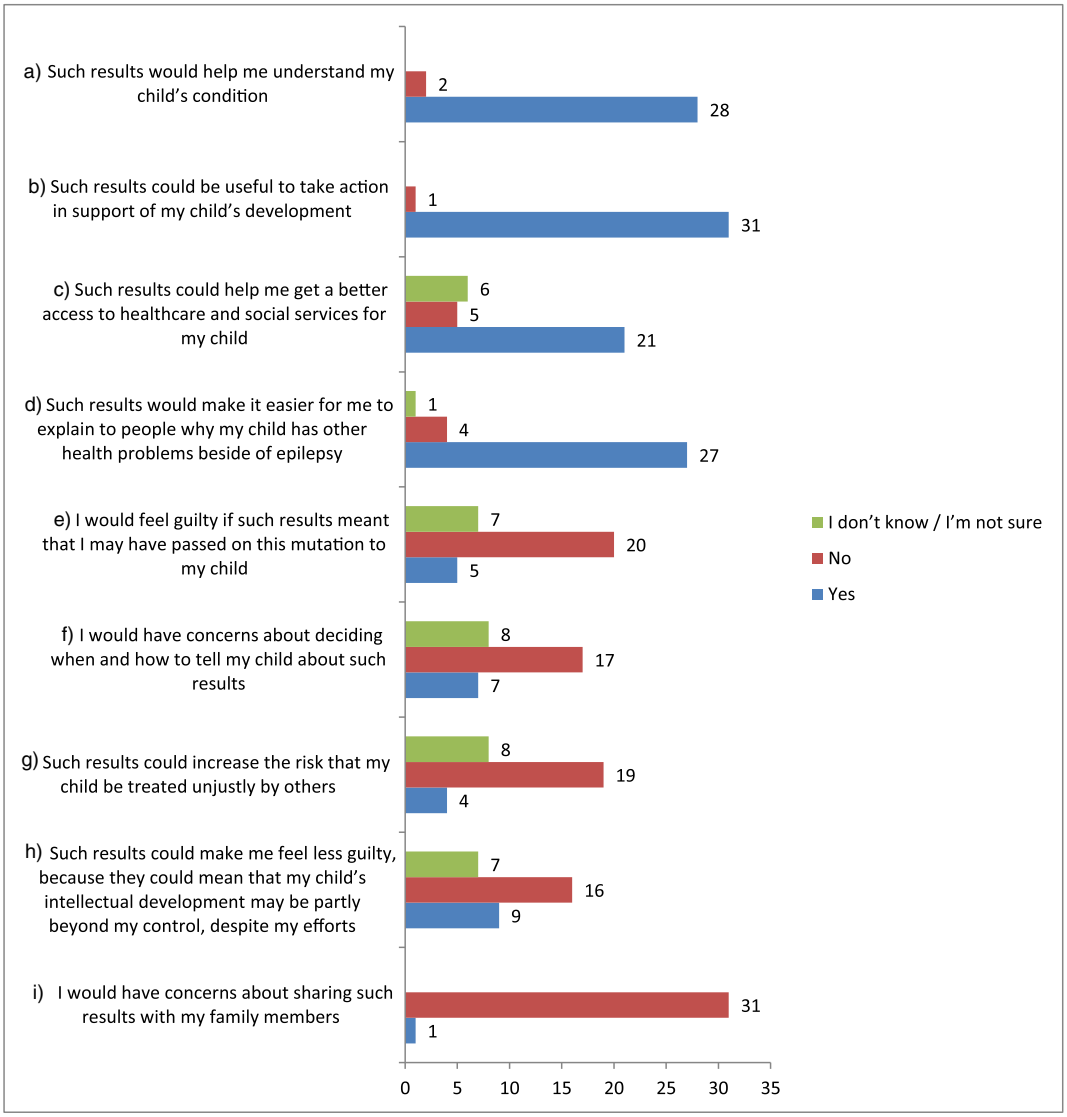

Fig. 3. Results indicating mutations that explain comorbidities (number of respondents by question).

ease the pressure on them while other respondents stressed that this information could help them draw a future for their child, by knowing more about the level of his/her deficiency.

3.7. Receiving unexpected results

Respondents were presented with a table of all possible results that could be obtained from a WGS, including IFs. Fig. 4 shows that most participants wanted to know about health conditions unrelated to epilepsy, even for conditions that would be life-threatening and could not be prevented or treated, or for conditions that would have a negative impact on quality of life and could neither be prevented nor treated. Many parents, although worried by potential unexpected results, explicitly stressed that such genetic results could help them better anticipate their child's future and plan for measures that could contribute to their quality of life (see Box 3).

As shown on Fig. 5, the simple fact of knowing any unexpected results from their child's WGS would be good, even if the scientists are not sure that the results could be useful for their child's current or future health. Also, many respondents would not have concerns about being uselessly worried if they were to receive unexpected results that only indicated that there was a probability but no certainty that their child could develop another disease. Indeed, more than half of respondents wanted to know about their child's risks of developing a disease if it was known that this disease would only appear late in their adult life.

When asked whether they would have concerns about sharing unexpected results with family members, in proportion, more parents expressed concerns about sharing unexpected results with their family members compared with sharing results linked to epilepsy, comorbidities, and pharmacoresistance. More than half likewise had no concerns that unexpected results could increase the risk that their child be treated unjustly by others. However, respondents were more divided as to when and how to tell their child that they might develop another disease as shown on the answers to question c, Fig. 5.

Finally, with the exception of one person, all respondents ($n = 31$) wanted to be informed of results showing that their child had a mutation that might cause adverse reactions to certain medications or affect the effectiveness of medications that they were not currently taking, even if it was not known if they would have to take them in the future. As shown in Box 4, parents considered that this information could help in choosing an alternative treatment.

4. Discussion

4.1. Medical well-being of children

Our results show that the anticipation of medical benefits is parents' primary reason to involve their child in a research project on personalized medicine in the treatment of epilepsy, shortly followed by altruism, so as to benefit others affected by epilepsy. Whether to help develop better treatments or find genetic mutations, better understand the condition in general or decrease the stigma attached to epilepsy, these are all reasons leading parents to agree to their child's participation in such a research project. The balance between altruism and personal gain in our respondents is concordant with results from earlier studies on research participants' motivations to receive information from WGS [29]. Interestingly, for most parents in our study, the use of WGS was viewed as an additional tool that motivated parents to have their child participate, and not a determinant. Only nine respondents said that it was one of the reasons why they wanted their child to participate. This does not mean that all parents saw no potential benefit resulting from their child's WGS, but this was not their primary motivation. Respondents' children were diagnosed with a pharmacoresistant epilepsy and, as a result, parents had had to cope with many attempts to control their child's seizures and/or adverse reactions to antiepileptic drugs, with more or less success, and their quest for answers had been protracted and complex. In such circumstances, while they all seemed to understand the general research goals of the project and were aware of the uncertainty of receiving actionable WGS results, their hopes in terms of answers and medical benefits for their child's condition were significant. We believe that parents "actively reframed" their child's participation in the genomic project "as an opportunity to

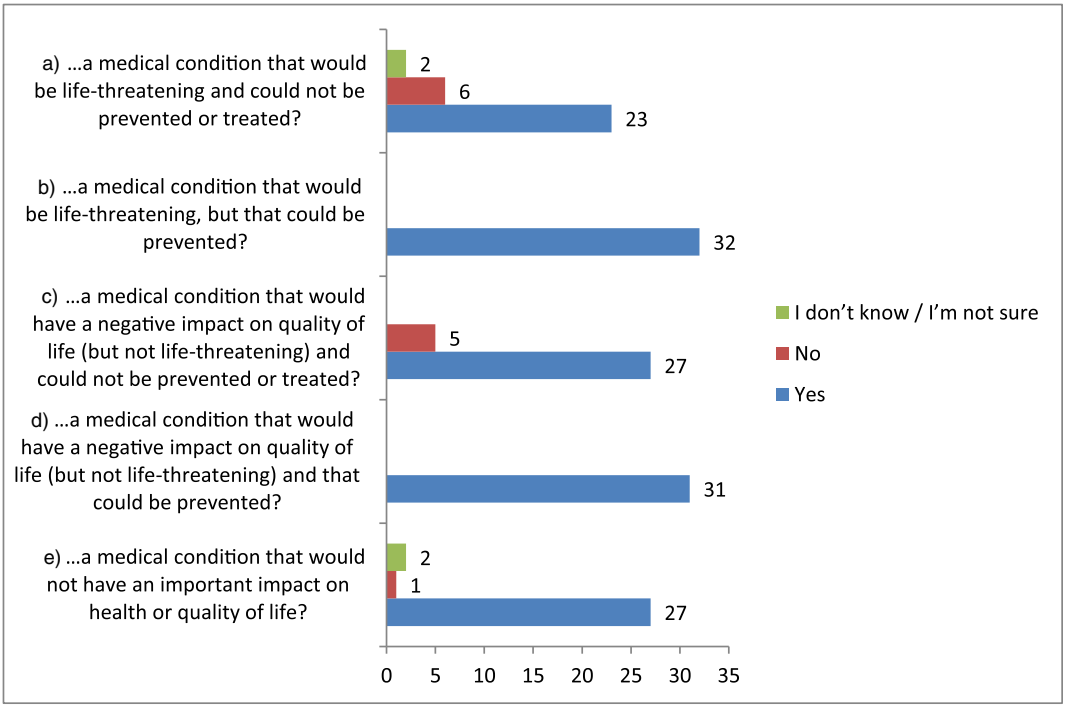

Fig. 4. Unexpected results: If you were given the choice to receive results about your child's risk(s) of developing a medical condition that is not associated with epilepsy, would you want to know about… (Number of respondents by question).

Box 3
Reasons for choosing the types of unexpected results*

Could you tell us more on your thoughts when choosing the types of unexpected results you would like to know about?
[We want to know about] all results because we never got results or causes [that explain] his/her health status and his/her global developmental delay. We would have a [better] idea of what to expect in the long term and have [a] prognosis for our future.
We would like to have a better idea of his/her genetic background in order to help us to plan for the future [and] know what to expect.
Everything that can be discovered about our child's health is very important for us, for his/her development or [the] treatments that could help him/her.
We want to know everything.
Since our son is 8 months old, we've been doing everything to offer him an exceptional quality of life, to allow him [to have] an optimal development… whatever the unexpected discovery(ies), we will do everything in our power to help our son.
Whatever the unexpected results will show, just knowing about certain realities will lead me to adapt the way I understand my child and to adapt my interventions
I hope my child has no other diseases
Fear of never knowing why my daughter is sick. Fear that there will never be any treatment to stop the seizures and improve her quality of life.
When you have a sick kid, it comes with its share of surprises… if we could eliminate some of them
Even if the news are not good, we would like to know all the same about his/her condition
We are moderately optimistic people. We believe that getting as much information as possible can only be a benefit. Who knows, with scientific progress, and the lightning speed of new scientific discoveries, where we will be in the future?
We have thought long and hard on this section [of the questionnaire]. It scared us to receive an unexpected result: it is frightening and very "anxiogenic", thus we would not like to know about something that cannot be prevented nor cured… living in anxiety is not enticing.
In my opinion, it is preferable to know about all positive or negative results about our child's current and future health from the very start. This would allow us to better organize ourselves for our child's current and future quality of life. It is better to have a result – whatever the result – than living in uncertainty and ask oneself everyday what is the cause of the disease and what is the disease that my child has.
It is important to know in order to plan for his/her future
For sure, it would be a shock. But my goal is to enjoy as much as possible every moment with my child. If we don't know [a result], there might be things that we could have missed. But at the same time, I would prefer to think that this will not happen.
Everybody is at risk to develop some diseases in their lives. If these diseases cannot be cured, then it is not needed to know it because this would too much influence the way we envision the rest of our lives. If we are informed that our child has a medical condition that would threaten his/her life and that could be treated, I would feel privileged to be able to prevent it. Knowing such information is rare.
If the medical conditions can be prevented or treated, I want to know it so that I can give him the best chance and offer him a better quality of life. I would feel guilty if he had such conditions, but at least something could be done. I could also have his sister tested and treat her if needed. On the contrary, I don't want to know about medical conditions that cannot be prevented nor treated. This would cause too many worries and too much anxiety for me. I would also feel guilty to have given birth to a child with such conditions and I would be afraid that his sister could have the same conditions. However, because science is progressing, what cannot be treated today could be treated in the future, so nothing will prevent my child from asking for his results, when he is adult.
[With results] we could plan for a better organisation (environmental, monetary, etc.), so that his/her future could be adapted to his/her condition and thus improve his/her quality of life.
The more information the better. Good or bad we roll with the punches and live each day to the fullest but to be able to watch for things to ensure our child the best life possible.
Knowing does feel better than not knowing, in that case. In any circumstance. There would be a chance, that if come with hope does the best.

* The comments that were originally written in French have been translated into English for the purposes of the present publication.

enhance [his/her] clinical care" and in particular, to get answers "while simultaneously acknowledging the general research aims". Such expectations may be described as "therapeutic appropriation" by McDougall and colleagues [30]. In this respect, it is worth noting that respondents had divided opinions when it came to expect whether the discovery of a mutation that could explain epilepsy or drug resistance would help them receive more attention and better access to healthcare and social services for their child. Yet, a majority of them believed that this would be the case if they got results indicating mutations that explained comorbidities, such as conditions causing intellectual difficulties, for instance. However, parents' expectations about potential clinical benefits for their child can also result from incomplete understanding of the research scope and goals, in which case, the thoughts expressed by respondents would not be attributable to therapeutic appropriation.

As discussed in detail in the next paragraphs, parents participating in our study understood the types of information that WGS can produce (about the cause of their child's epilepsy, the resistance of their child's seizures to antiepileptic drugs, comorbidities linked to epilepsy or, still, predispositions to other health conditions); and they expressed strong intentions to receive them all, considering that any result could be beneficial for them and their child, and agreeing in many cases that "just knowing would be good". Our results are in accordance with those from large longitudinal projects such as ClinSeq, in which the evaluation of participants' preferences on receiving results from WGS was one of the goals of the study [31].

Regarding the result of their child's WGS showing a mutation explaining their epilepsy or resistance to antiepileptic drugs, the vast majority of parents thought that knowing such a result would be beneficial. For instance, parents saw potential benefits in the management of their child's condition, whether for improving their child's treatment, better planning their future, or to make it easier to explain to others what the medical causes of their child's condition were or why their child's seizures had been hard to control.

In cases where no mutation explaining epilepsy or drug resistance was found, parents considered that just knowing such results "would be good", even if they were not useful for their child's treatment. Yet, more or less half of the respondents had concerns that such results could mean there was no specific treatment for their child's epilepsy or seizures. Almost half of respondents would be disappointed because such results would not offer them any answer about their child's condition.

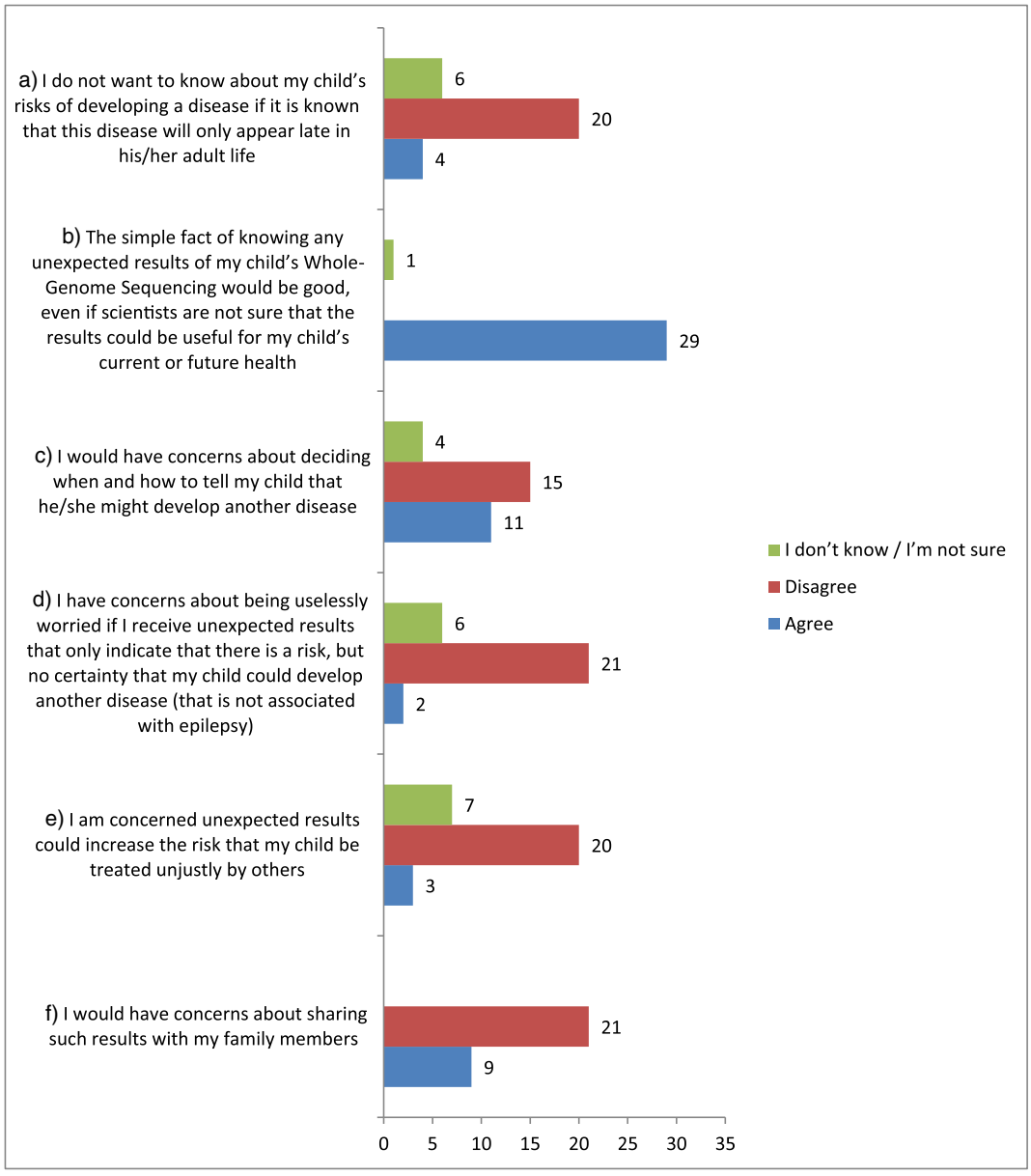

Fig. 5. Do you agree with the following statements about unexpected results? (Number of respondents by question).

A major goal of genetic studies with patients with epilepsy is to obtain a clear diagnosis that could end or altogether avoid multiple, successive treatment attempts, clarify prognosis, allow for reproductive decisions, and lead to better social support [32]. Another equally important goal is to identify drug targets, thus, providing a "precision medicine" approach to the treatment of such a complex condition in which mutations in different genes may cause clinically indistinguishable syndromes while mutations in a single gene can cause a wide range of phenotypes [32]. Freedom from seizures impacts patients' overall health and quality of life from a clinical and social perspective [4]. It comes as no surprise that while almost all results were seen as welcome by respondents, including information on drug response not linked to epilepsy, not receiving a clear answer as to why seizures were hard to control, or why their child had epilepsy came as a disappointment or raised concerns that such results could mean that there was no specific treatment for their child. In this regard, we deem it necessary to address such potential fears and feelings while communicating results, as they are likely not grounded in scientific evidence and could arouse preventable anxiety.

Seizures and intellectual disabilities have already been linked [33], as were epilepsy with autism and Tourette syndrome, among others [34]. Receiving results related to comorbidities would also help parents understand their child's condition and allow them to take action in support of their development or of a better access to healthcare and social services. Not surprisingly, parents also thought that these results would make it easier for them to explain to people why their child had other health problems, besides epilepsy.

Parents' perceptions on WGS results relating to late-onset diseases that could affect their child must be underlined. More than half of them wanted to know about their child's risks of developing such diseases. Such a stance raises specific ethical issues about children's future autonomy [17,18] and is at odds with many current recommendations: for instance, the Consolidated Statement of Principles of the Quebec Network of Applied Genetic Medicine in its provision 10.3.2 states that "individual results or incidental findings that have implications for the future health of a minor should not be returned" [35]. While further research in this topic with a larger sample size is needed, we believe our results could be informative to the development, revision, and/or update of guidelines.

Box 4
General response to medications*

If you were given the choice, would you like to be informed of results showing that your child has a mutation that might cause adverse reactions to certain medications or affect the effectiveness of medications that he/she is not currently taking, even if it is not known if he/she will have to take them in the future?
This could help in the choice of an alternative treatment, if applicable
Especially since my child does not speak I have this worry
Yes all results are necessary to be known in order to provide the best care to our child
He did not respond well to a medication at the beginning of his treatment and it was not funny at all
This would prevent potentially unpleasant or even dangerous situations
It's always useful to know to avoid aggravating situations
Knowing could protect him from a potentially adverse reaction, and could guide a physician's treatment choices in the future.
My son went through 18 different meds, plus experimental medication out of France, none worked to fully control. Knowing could protect him from a potentially adverse reaction, and could guide a physician's treatment choices in the future

* The comments that were originally written in French have been translated into English for the purposes of the present publication.

4.2. Sharing WGS results

Most respondents had no concerns about sharing results revealing a mutation that could explain their child's epilepsy or pharmacoresistance with family members nor did they anticipate fearing people's reactions to such results. The same was true for results about a mutation explaining comorbidities, such as intellectual disorders. However, and in proportion, more parents expressed concerns about sharing unexpected results with their family members compared with sharing with them the results linked to epilepsy, comorbidities, and pharmacoresistance. Facio et al. reported that a third of participants in their study on intentions to receive genetic information from WGS wished to know the results specifically to inform their children and family members [31]. According to Poduri et al. [36], while many people affected by epilepsy have no affected relatives, the risk of epilepsy is increased in first-degree relatives of individuals with epilepsy. Thus, sharing genetic information may have implications for passive participants, that is, family members whose DNA was not sequenced. In this regard, it has been recommended that familial implications of sharing genetic information should be made clear in clinical and research settings before consent to any genetic test commences [37,38].

4.3. Social well-being of children and parents

Living with epilepsy can often be experienced as a lengthy and arduous obstacle course, due as much to varying degrees of access to healthcare as to diagnostic difficulties. Thus, parents who have never had issues explaining the medical causes of their child's epilepsy are few and far between, in particular, outside the family circle. One in two parents had difficulties obtaining access to services that could help them and their child cope with epilepsy, such as financial assistance programs, respite services, school/learning support, or other social service support. Almost the same proportion mentioned that their child had been treated unjustly by various individuals because of their epilepsy, whether at daycare, school, or during holidays, by family friends or by strangers, in private or public places, and respondents were even more likely to harbor this fear than to experience unjust treatment, as some parents stated clearly. Our results are concordant with Bandstra's description on existing and perceived stigma as two separate conditions affecting patients with epilepsy, with the latter possibly more prevalent than the former [20]. The data presented herein correlate with other studies showing how stigma influences the affected individual yet also the parents of a child with epilepsy [5,20,39]. Interestingly, sharing WGS results about the cause(s) of their child's epilepsy, their seizures' response to antiepileptic drugs, related comorbidities, or unexpected results would not increase the risk that their child be treated unjustly by others, according to most respondents. Does this result indicate that parents manifest a high level of resilience and inner strength, implying that "my child has already been treated unjustly, so his/her WGS result would not change anything…"? At the same time, it is worth noting that for a third of respondents, genomic research could help decrease the stigma attached to epilepsy. Further research would be required to consolidate such findings.

4.4. Parents' sense of guilt

The results showed that majority of parents had experienced feelings of guilt because of their child's epilepsy. Our results indicate that the use of diagnostic tools – such as WGS – does not mitigate such feelings. If one parent out of two did not foresee feeling guilty if the result of their child's WGS showed that they may have passed on this mutation, an almost equal number would not feel less guilty if the results of their child's WGS could mean that they did nothing wrong to cause their child's epilepsy. Even in the case of a WGS showing that their child had a mutation explaining why seizures had been hard to control with antiepileptic drugs, two parents out of three expected they would feel just as guilty.

Similarly, to learn that no mutation could be found would not impact their potential feelings of guilt for the majority of parents – because if no genetic cause was to be found, it could lead them to think that they had somehow caused or contributed to their child's epilepsy – nor make many of them feel less guilty, even if it could mean that they did not pass on a mutation to their child. We found that feelings of guilt were common among parents of a child with epilepsy and should deserve special attention in order to provide sufficient social support.

5. Limitations

Are our data representative? It is not, at least not in the general, statistical sense. Because of the number of respondents, we could not discount any bias introduced by equally considering responses that were originated by couples answering together and those from parents that responded individually nor we could not control responses that might be influenced by gender. The main genomic study was originally designed to recruit a higher number of children with pharmacoresistant epilepsy, and thus, our methodology to explore parents' views would have likely been different if changes in the genomic project management could have been predicted. Nevertheless, we think our results genuinely describe valid and relevant experiences and issues helpful to understand the long, difficult, and winding road of parents of a child living with pharmacoresistant epilepsy. They illustrate various parental perceptions and thus, yield a good starting point for tailored interventions such as the development of clinical consultations well suited to the practical requirements and needs of families affected by epilepsy. It must be noted that since the designing of our questionnaire, synonyms for the term "incidental findings" have appeared in numerous publications. Throughout this work, we have referred to IFs as genetic information unrelated to epilepsy and/or conditions that are sometimes diagnosed in conjunction with epilepsy.

6. Conclusion

Sharing WGS results either related to epilepsy, response to medication, and even comorbidities and unexpected results was not perceived by respondents as increasing the risk that their children be treated

unjustly. This is an interesting outcome from our work considering the stigma attached to epilepsy.

It seems that the use of WGS would not be a tool that could alleviate parents' feelings of guilt. Parents were more likely to say they felt guilty than not guilty, whether the results showed they had passed on a mutation to their child or that there was an apparent absence of a genetic cause.

As it has been shown in other studies, most parents are in favor of receiving any result, whatever the type. This reinforces the importance of having clear guidelines to help them navigate the complexities of conveying information that will impact the present and future life of numerous individuals simultaneously.

Despite the small size of our sample, we believe that our results could be meaningful and actionable for practitioners. They constitute relevant contributions to problem analysis, are suggestive of solutions, including for those confronted with daily practical challenges, i.e., making parents partners in the decision process on the basis of their experience and feedback. Taking into account the experiences of parents of a child with epilepsy and engaging them as partners in planning and decision-making can only lead to improved quality of parental and affected child life.

Supplementary data to this article can be found online at https://doi.org/10.1016/j.yebeh.2018.11.020.

Acknowledgments

We thank Mr. John Bisping for helpful discussion, and personnel from the Unité de Recherche Clinique Appliquée at Sainte Justine Hospital for the technical support on the use of REDCap electronic data capture tools. We are indebted to the parents of children with epilepsy that took time from their busy lives to participate in this study, including those that helped with pretesting the questionnaires. We gratefully acknowledge the support of the Canadian Institutes of Health Research (CIHR), Génome Québec and Genome Canada.

Dedication

Iris J. Groisman dedicates this work to the memory of Jessica Yudcovitch, a beautiful soul, forever loved.

Funding

This work was supported by the Canadian Institutes of Health Research (CIHR grant number EOG-126775) and Génome Québec and Genome Canada (grant number LSP 2012-4507).

Conflict of interest

Iris Jaitovich Groisman is a consultant of public and private Institutional Review Boards. B.G. and T.H. declare no conflict of interest.

References

[1] World Health Organization. Epilepsy. http://www.who.int/mediacentre/factsheets/fs999/en/index.html; February 2018, Accessed date: 24 April 2018.
[2] Reid AY, Metcalfe Y, Patten SB, Wiebe S, Macrodimitris S, Jette N. Epilepsy is associated with unmet health care needs compared to the general population despite higher health resource utilization—a Canadian population-based study. Epilepsia 2012;53:291–300.
[3] Gilmour H, Ramage-Morin P, Wong SL. Epilepsy in Canada: prevalence and impact. Health Rep 2016;27:24–30.
[4] Josephson CB, Patten SB, Bulloch A, Williams JVA, Lavorato D, Fiest KM, et al. The impact of seizures on epilepsy outcomes: a national, community-based survey. Epilepsia 2017;58:764–71.
[5] Baulac M, de Boer H, Elger C, Glynn M, Kalvikainen R, Little A, et al. Epilepsy priorities in Europe: a report of the ILAE-IBE Epilepsy Advocacy Europe Task Force. Epilepsia 2015;56:1687–95.
[6] Gahl WA, Markello TC, Toro C, Fajardo KF, Sincan M, Gill F, et al. The national institutes of health undiagnosed diseases program: insights into rare diseases. Genet Med 2012;14:51–59.7.
[7] Gaggero R, Pistorio A, Pignatelli S, Rossi A, Mancardi MM, Baglietto MG, et al. Early classification of childhood focal idiopathic epilepsies: is it possible at the first seizure? Eur J Paediatr Neurol 2014;18:376–80.
[8] Jette N, Beghi E, Hesdorffer D, Mosh SL, Zuberi SM, Medina MT, et al. ICD coding for epilepsy: past, present, and future—a report by the International League Against Epilepsy Task Force on ICD codes in epilepsy. Epilepsia 2015;56:348–55.
[9] Poduri A, Lowenstein D. Epilepsy genetics—past, present, and future. Curr Opin Genet Dev 2011;21:325–32.
[10] Le Pichon J-B, Saunders CJ, Soden SE. The future of next-generation sequencingin neurology. JAMA Neurol 2015;72:971–2.
[11] Mefford HC, Yendle SC, Hsu C, Cook J, Geraghty E, McMahon JM, et al. Rare copy number variants are an important cause of epileptic encephalopathies. Ann Neurol 2011;70:974–85.
[12] Monlong J, Girard SL, Meloche C, Cadieux-Dion M, Andrade DM, Lafreniere RG, et al. Global characterization of copy number variants in epilepsy patients from whole genome sequencing. bioRxiv; 1992; 24. https://doi.org/10.1101/199224.
[13] Génome Québec. Personalized medicine in the treatment of epilepsy. http://www.genomequebec.com/152-en/project/personalized-medicine-in-the-treatment-of-epilepsy.html, Accessed date: April 2018.
[14] Abdul-Karim R, Berkman BE, Wendler D, Rid A, Khan J, Badgett T, et al. Disclosure of incidental findings from next-generation sequencing in pediatric genomic research. Pediatrics 2013;131:564–71.
[15] Baret L, Godard B. Opinions and intentions of parents of an autistic child toward genetic research results: two typical profiles. Eur J Hum Genet 2011;19:1127–32.
[16] Bennette CS, Trinidad SB, Fullerton SM, Patrick D, Amendola L, Burke W, et al. Return of incidental findings in genomic medicine: measuring what patients value—development of an instrument to measure preferences for information from next-generation testing (IMPRINT). Genet Med 2013;15:873–81.
[17] Bredenoord AL, Onland-Moret NC, Van Delden JJ. Feedback of individual genetic results to research participants: in favor of a qualified disclosure policy. Hum Mutat 2011;32:861–7.
[18] Fernandez CV, Strahlendorf C, Avard D, Knoppers BM, O'Connell C, Bouffet E, et al. Attitudes of Canadian researchers toward the return to participants of incidental and targeted genomic findings obtained in a pediatric research setting. Genet Med 2013;15:558–64.
[19] Jackson L, Goldsmith L, O'Connor A, Skirton H. Incidental findings in genetic research and clinical diagnostic tests: a systematic review. Am J Med Genet A 2012;158A:3159–67.
[20] Bandstra NF, Camfield CS, Camfield PR. Stigma of epilepsy. Can J Neurol Sci 2008;35:436–40.
[21] Fisher RS, Vickrey BG, Gibson P, Hermann B, Penovich P, Scherer A, et al. The impact of epilepsy from the patient's perspective II: views about therapy and health care. Epilepsy Res 2000;41:53–61.
[22] Godard B, Cardinal G. Ethical implications in genetic counseling and family studies of the epilepsies. Epilepsy Behav 2004;5:621–6.
[23] Hammond CL, Thomas RH, Rees MI, Kerr MP, Rapport F. Implications for families of advances in understanding the genetic basis of epilepsy. Seizure 2010;19:675–9.
[24] Helbig KL, Bernhardt BA, Conway LJ, Valverde KD, Helbig I, Sperling MR. Genetic risk perception and reproductive decision making among people with epilepsy. Epilepsia 2010;51:1874–7.
[25] Paschal AM, Hawley SR, St Romain T, Liow K, Molgaard CA, Sly J, et al. Epilepsy patients' perceptions about stigma, education, and awareness: preliminary responses based on a community participatory approach. Epilepsy Behav 2007;11:329–37.
[26] Shostak S, Ottman R. Ethical, legal, and social dimensions of epilepsy genetics. Epilepsia 2006;47:1595–602.
[27] Shostak S, Zarhin D, Ottman R. What's at stake? Genetic information from the perspective of people with epilepsy and their family members. Soc Sci Med 2011;73:645–54.
[28] Namey EE, Beskow LM. Epilepsy patient-participants and genetic research results as "answers". J Empir Res Hum Res Ethics 2011;6:21–9.
[29] Facio FM, Brooks S, Loewenstein J, Green S, Biesecker LG, Biesecker BB. Motivators for participation in a whole-genome sequencing study: implications for translational genomics research. Eur J Hum Genet 2011;19:1213–7.
[30] McDougall R, Martin D, Gillam L, Hallowell N, Brookes A, Guillemin M. Therapeutic appropriation: a new concept in the ethics of clinical research. J Med Ethics 2016;0:1–4.
[31] Facio FM, Eidem H, Fisher T, Brooks S, Linn A, Kaphingst KA, et al. Intentions to receive individual results from whole-genome sequencing among participants in the ClinSeq study. Eur J Hum Genet 2013;21:261–5.
[32] Myers CT, Mefford HC. Advancing epilepsy genetics in the genomic era. Genome Med 2015;7:91.
[33] Gandomi SK, Farwell Gonzalez KD, Parra M, Shahmirzadi L, Mancuso J, Pichurin P, et al. Diagnostic exome sequencing identifies two novel IQSEC2 mutations associated with X-linked intellectual disability with seizures: implications for genetic counseling and clinical diagnosis. J Genet Couns 2014;23:289–98.
[34] Cukier HN, Dueker ND, Slifer SH, Lee JM, Whitehead PI, Lalanne E, et al. Exome sequencing of extended families with autism reveals genes shared across neurodevelopmental and neuropsychiatric disorders. Mol Autism 2014;5(1).
[35] Sénécal K, Thorogood A, Parry D, Yoly Y, Knoppers BM. The 2016 Quebec Network of Applied Genetic Medicine consolidated statement of principles. https://www.rmga.qc.ca/en/documents/Enonceconsolide_ENprint.pdf, Accessed date: October 2018.

[36] Poduri A, Sheidley BR, Shostak S, Ottman R. Genetic testing in the epilepsies—developments and dilemmas. Nat Rev Neurol 2014;10:293–9.
[37] Dheensa S, Fenwick A, Lucassen A. 'Is this knowledge mine and nobody else's? I don't feel that.' Patient views about consent, confidentiality and information-sharing in genetic medicine. J Med Ethics 2016;42.
[38] Wright CF, Middleton A, Barrett JC, Firth HV, FitzPatrick DR, Hurles M, et al. Returning genome sequences to research participants: policy and practice. Wellcome Open Res 2017;2:15. https://doi.org/10.12688/wellcomeopenres.10942.1.
[39] Nabi Amjad R, Nikbakht Nasrabadi A, Navab E. Family stigma associated with epilepsy: a qualitative study. J Caring Sci 2017;6:59–67.