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Title:
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Date:
2016-11-01

Citation:
Wilkins, E. J., Archibald, A. D., Sahhar, M. A. & White, S. M. (2016). “It wasn't a disaster or anything”: Parents’ experiences of their child's uncertain chromosomal microarray result. American Journal of Medical Genetics Part A, 170 (11), pp.2895-2904. https://doi.org/10.1002/ajmg.a.37838.

Persistent Link:
https://hdl.handle.net/11343/291958

**TITLE**

# "It Wasn't a Disaster or Anything": Parents' Experiences of Their Child's Uncertain Chromosomal Microarray Result

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Abstract

Chromosomal microarray is an increasingly utilized diagnostic test, particularly in the pediatric setting. However, the clinical significance of copy number variants detected by this

technology is not always understood, creating uncertainties in interpreting and communicating results. The aim of this study was to explore parents' experiences of an uncertain microarray result for their child.

This research utilized a qualitative approach with a phenomenological methodology. Semi-structured interviews were conducted with nine parents of eight children who received an uncertain microarray result for their child, either a 16p11.2 microdeletion or 15q13.3 microdeletion. Interviews were transcribed verbatim and thematic analysis was used to identify themes within the data.

Participants were unprepared for the abnormal test result. They had a complex perception of the extent of their child's condition and a mixed understanding of the clinical relevance of the result, but were accepting of the limitations of medical knowledge, and appeared to have adapted to the result. The test result was empowering for parents in terms of access to medical and educational services; however, they articulated significant unmet support needs. Participants expressed hope for the future, in particular that more information would become available over time.

This research has demonstrated that parents of children who have an uncertain microarray result appeared to adapt to uncertainty and limited availability of information and valued honesty and empathic ongoing support from health professionals. Genetic health professionals are well positioned to provide such support and aid patients' and families' adaptation to their situation as well as promote empowerment.



**KEY WORDS**

16p11.2 Deletion Syndrome

Chromosome 15q13.3 Microdeletion Syndrome

Genetic Counseling

Genetic Testing

Microarray Analysis

Parents

Pediatrics

Physician-Patient Relations

Qualitative Research

Uncertainty

## INTRODUCTION

Chromosomal microarray (CMA) testing has been relatively recently adopted into routine clinical practice in pediatric genetics clinics and it is now the recommended first cytogenetic diagnostic test for individuals with unexplained developmental delay (DD) or intellectual disability (ID), autism spectrum disorders (ASD), or multiple congenital anomalies [Gijsbers et al. 2009; Manning and Hudgins 2010; Miller et al. 2010]. The major advantage of CMA testing in this setting over other technologies is the increased diagnostic yield; 15-20% compared to 3% using conventional karyotyping [Miller et al. 2010]. However, assessments of the diagnostic utility of CMA testing are complicated because the variants identified are often difficult to interpret: disease-associated variants may be consistently associated with a definable phenotype or may be associated with a range of phenotypic expression, and penetrance and expressivity may be affected by factors such as modifier genes or epigenetic effects [Lee and Scherer 2010]. When the clinical significance

of a variant is "ambiguous, doubtful or undecided" [Vos et al. 2009] it is defined as a variant of uncertain significance (VOUS).

The value of diagnostic certainty is incontrovertible: it informs prognosis, treatment options and recurrence risk, and may improve access to services and support [Lopez-Rangel et al. 2008], particularly in the context of a well-recognized condition [Lenhard et al. 2005; Makela et al. 2009]. By contrast, identification of a VOUS in a patient has the potential to significantly complicate clinical diagnosis and medical management as well as the provision of genetic counseling [Girirajan et al. 2012].

Until recently, patient experiences of uncertainty in the context of CMA testing had to be inferred from studies of uncertainty more generally. However, several recent studies have now explored parents' experiences of uncertain CMA results in a pediatric setting, providing insight into their understanding and interpretation of the result, its perceived value, and the needs of families undergoing CMA testing [Jez et al. 2015; Kiedrowski et al. 2015; Reiff et al. 2012; Reiff et al. 2015]. Results from these studies indicate that parents' comprehension of their child's CMA result is variable and may be influenced by many factors including access to genetic counseling and written material [Jez et al. 2015; Kiedrowski et al. 2015; Reiff et al. 2012]. Parents interviewed for two of these studies reported seeking additional information about their child's test result in an effort to make meaning of it, a task often made difficult by a lack of available knowledge about rare and novel CMA results as well as challenges in navigating the abundance of information available on the Internet [Kiedrowski et al. 2015; Reiff et al. 2012]. Interestingly, whilst these parents, and those surveyed by Jez et al. appeared to understand the scientific uncertainty associated with their child's test result and discussed the prognostic uncertainty accompanying it, they tended to describe the VOUS as

the cause of their child's medical condition and expressed feelings of relief and alleviation of feelings of guilt following the disclosure of the result [Jez et al. 2015; Kiedrowski et al. 2015; Reiff et al. 2012].

The importance of investigating the effects of new genetic technologies on health professionals and patients has been previously noted [Fanos 2012]. More specifically, understanding parents' experiences and their practical and psychosocial needs in the context of uncertain CMA results for their child is critical for facilitating optimum coping and adjustment in families, and ensuring that children receive appropriate treatment and care. Previous studies have focused on parents' comprehension and interpretation of the CMA result, as well as its personal significance. A broader understanding of parents' experiences, for example their preferences regarding communication of results, the opportunity for follow-up, and access to support, is vital for the provision of genetic counseling. Thus the purpose of this exploratory qualitative study was to further understand this phenomenon in order to contribute to the ongoing evaluation of a newly introduced genetic test, inform health professionals' interactions with families, and to potentially identify unmet support needs leading to improved genetic counseling processes.



## MATERIALS AND METHODS

### *Ethics*

The study was approved by The Royal Children's Hospital (Melbourne, Victoria) Human Research Ethics Committee and registered with the University of Melbourne.

### *Design*

As little is known about experiences of uncertain CMA results an exploratory qualitative approach was chosen for this study. Qualitative research is a useful approach when researchers want to understand a complex issue via direct contact with participants and their experiences and it is essential when there is minimal knowledge of the phenomenon being studied [Liamputtong 2013]. A phenomenological methodology was used; this approach is concerned with exploring commonalities between individual experiences, and attempts to identify the "universal essence" of the phenomenon via development of a combined description of the experience [Creswell 2013].

*Participants*

Participants were recruited via Victorian Clinical Genetics Services (VCGS), an organization located in Victoria, Australia that provides clinical genetics services to families and individuals. Participants were parents of children who had CMA testing performed by the VCGS cytogenetics laboratory. A purposive sampling strategy was used to identify children who underwent CMA testing for investigation of DD/ID, ASD, and/or multiple congenital anomalies, where the family attended an appointment with a VCGS clinical geneticist to discuss the results. Potential participants were eligible for inclusion in the study if CMA testing for the child identified either a 16p11.2 microdeletion (OMIM 611913) or 15q13.3 microdeletion (OMIM 612001), both of which were reported by the testing laboratory as being of uncertain clinical significance at the time of results disclosure, and did not identify any clearly pathogenic CNVs. We excluded participants who could not provide voluntary and informed consent, and due to limited resources, those who did not speak English. Families who did not attend an appointment with a clinical geneticist at VCGS were also excluded in an effort to maximize the consistency of patient management.

Laboratory and clinical records were reviewed and information about the study and letters of invitation were posted to families that met the inclusion and exclusion criteria. Potential participants were asked to respond via an expression of interest form. A follow-up telephone call was made to those families who did not respond.

*Data collection*

Between May 2013 and August 2013, each participant was interviewed via a semi-structured interview conducted either in person or by telephone by EJW. Interviews were conducted at least six months after the appointment with the clinical geneticist to allow time for the participants to have begun to interpret and adjust to the information. Voluntary informed consent was obtained from all participants. Participants who were interviewed by telephone had their consent recorded orally using an informed consent script. Although an interview guide was used, interviews were conducted in a conversational style and questions were guided by each participant's responses to previous questions with additional topics explored when they arose during an interview. Interviews were audio-recorded and transcribed verbatim.

*Data analysis*

In accordance with the guidelines described by Braun and Clarke [Braun and Clarke 2006] thematic analysis was used to identify and report topics within the data. Interview transcripts were uploaded to NVivo10 software (QSR International Pty Ltd 2012) in order to perform preliminary coding of the interview text and a summary of each interview was written based around the preliminary topics identified. Data collection occurred simultaneously with this stage of analysis and continued until theoretical saturation occurred. Potential topics were then further reviewed and refined in an iterative process designed to

confirm their accuracy and validity in relation to the entire dataset. In order to ensure scientific rigor and identify and resolve differences in analysis, all interview transcripts were co-coded by two authors and the processes of coding and identifying topics were carried out in collaboration with all authors.

## RESULTS

Of 21 families who met study inclusion criteria and were invited to participate, eight agreed to be interviewed. Six interviews were conducted over the telephone and two were conducted face-to-face (in the participants' homes). In one face-to-face interview, both parents of the child were interviewed together at their request. For all other interviews one parent was interviewed. Demographic characteristics of participants are presented in Table I.

Of the children of the parents who participated in this study who had CMA testing, seven were male and one was female, and their ages ranged from two to 11 years at the time of testing. Five of the children had a de novo microdeletion and three had an inherited microdeletion. The children demonstrated a spectrum of phenotypes: participants reported combinations of DD/ID, speech difficulties, behavioral difficulties, ASD, spinal malformations, obesity, and epilepsy in their affected child. The time between the genetics appointment and the interview ranged from nine to 36 months.

Through the data analysis process, five broad topics emerged from the interviews: (i) preparedness for the CMA test and the accompanying result, (ii) interpretation of the result and assignment of causality, (iii) acceptance of limitations; flexibility and adaptation to the

result, (iv) disappointment with the lack of support provided by health professionals, and (v) hopes and fears for the future.

*Preparedness for the CMA test and the accompanying result*

Although not all participants recalled being informed that the CMA test was being requested, those who did reported that someone other than a clinical geneticist (most often a pediatrician) was the requesting clinician and the test tended to have been performed in conjunction with other genetic and non-genetic tests. Participants generally did not recall the information provided about the test at the time it was requested and commented on receiving very limited information upfront:

*"[The pediatrician] actually didn't tell us anything. Just that it was a genetic test."*
*Parent 6*

Furthermore, participants reported that the requesting clinician had explicitly stated that the CMA test was unlikely to find a cause for their child's difficulties and/or medical conditions:

*"We took him to a pediatrician and it was her who said, 'we'll do the range of blood tests, ..... not expecting anything, but we may as well just do all the ..... genetic testing as well, just check everything'."*
*Parent 5*

Participants articulated that because of this, they were not particularly anxious about the test during the time spent waiting for the result:

*"We weren't concerned at all because we didn't think there'd be anything there."*

*Parent 1*

Participants from five families reported that the requesting clinician disclosed the test result (either by telephone or in a face-to-face appointment), and that a referral to a clinical geneticist followed this; two participants received their child's result directly from the clinical geneticist; and one recalled receiving the result in the mail, and then having appointments with the requesting clinician and a clinical geneticist. Due to the low expectation of receiving a result set out by the requesting clinician, participants recalled feeling surprised to receive an abnormal result for their child. Furthermore, participants recalled the requesting clinicians were also surprised to have received an abnormal result for the child, and parents were left with the impression that the health professional did not have the expertise to adequately explain it to them:

*"I think he honestly thought there would be nothing that came up. So when he did call us with the result, he could tell us what the results were but he had no idea about the disorder. ….. I think when that new screening [CMA testing] came out and it was picking up lots of things, I don't think the doctors had a clue what was coming up either."*

*Parent 1*



*Interpretation of the result and assignment of causality*

Participants' discourse demonstrated a mixed understanding of the clinical relevance of their child's microdeletion. All participants indicated that they felt the microdeletion explained their child's phenotype, although some participants expressed this with more conviction than others:

*"Because of the array test we got an answer so even though it wasn't necessarily an answer we wanted, ..... we didn't feel like we had to keep looking any more."*

*Parent 1*

*"I think well from what I've read, from what it can affect with the learning and speech and everything, I think its contributed to, .... she's just who she is. ….. I think everything when it boils down to it, its all part of this deletion. ..... 'Cos everything that she seems to have had seems to be in the documentation that I've read."*

*Parent 4*

Participants' recollections suggested variation in health professionals' interpretations of the results and the advice they gave. For example, one participant recollected the way in which health professionals' opinions about the likely pathogenicity of her child's microdeletion convinced her that the search for an answer was over:

*"The geneticist said in her mind that all that we had seen with him fitted in with other kids with this deletion. Um the pediatrician said the same thing so we were happy that we could stop subjecting him to a thousand more tests, that this was the explanation."*

*Parent 5*

Despite articulating a belief that the microdeletion was causal of their child's condition, participants frequently commented that the published clinical phenotype did not accurately describe their child. Although this did not appear to challenge their belief in the pathogenic nature of the microdeletion, it appeared to trouble them from the perspective of the utility of the information:

*"Most of the stuff that was on the Internet was for kids that were more severely affected than him. There wasn't anything on kids ..... that were in the same boat as him so basically weren't that affected. ..... I've stopped looking on the Internet for any research because ..... it just didn't seem to relate to him."*

*Parent 1*

In addition, there appeared to be uncertainty about the permanence of the effects of the microdeletion:

*"I suppose, .... I'd like to know, .... can he overcome this through intervention and occupational therapy and speech and what not?..... Is he always going to have this problem where he can't really talk, he's always gonna struggle? .... Can he be trained even though he's got this deletion?"*

*Parent 3*

*Acceptance of limitations; flexibility and adaptation to the result*

Participants' comments suggested they felt positive about the CMA test despite mixed feelings about their child having a microdeletion and the lack of available information:

*"I'm glad that the test was there even though they weren't able to supply us with a lot of ongoing information. ….. I'm glad to have a name for it."*

*Parent 6*

Participants also made positive comments about the openness and honesty of clinical geneticists in acknowledging the gaps in scientific and medical knowledge and suggested that this candor had enabled them to accept the paucity of available information:

*"Because it was something new they gave us the information that they had and ..... it was very good 'cos they were very open. And saying 'we can't give you definite answers on things because it is something that's new, so we don't have the research and the documentation behind it'. ..... So that was really good. I wasn't disappointed or anything."*
*Parent 6*

However, there also appeared to be considerable ambivalence about the result. Reasons for this ambivalence included that its importance was overshadowed by other aspects of family life, it had little perceived practical value, it did not mean much to participants, or participants seemed to have a generally pragmatic approach to life and readily incorporated the result into their understanding of their child. Participants who were ambivalent about the value of the CMA result also tended to express disappointment about the lack of available information and clinical geneticists' communication of this:

*"I left kind of the same as I arrived because she didn't have any real information for me. It was not very satisfying. ….. She just kind of said it was a wait and watch, and do what we can do, kind of thing. ..… I think that was the worst part. ..… I thought when we go and see this geneticist lady she's gonna be able to tell me what to expect and ..… what other children who have the same sort of thing go through, but yeah, she couldn't so it was kind of a let down."*
*Parent 9*

However, despite feelings of ambivalence or disappointment, all participants commented that they felt very strongly that the test result was invaluable in enabling them to access specific medical interventions as well as support for their child in the education system. Several articulated that without the CMA result, they would have been unlikely to succeed in their attempts to access such resources.

Participants' discourse suggested that the CMA result encouraged them to contemplate for the first time the prospective long-term care needs of their child and the impact this may have on their own future. Additionally, the abnormal CMA result and accompanying information about the associated phenotypic spectrum had the potential to give rise to disappointment in participants about the prospect of additional health problems, such as schizophrenia and obesity, as their child grew older. Nevertheless, participants demonstrated considerable flexibility in their expectations of genetic testing and appeared able to readily adjust to the consequences of utilizing a relatively new test. In particular, participants were accepting of the fact that their child was at the forefront of clinical CMA testing and the effect this had on their experience:

*"It would have been great to have ..... a lot more information supplied but things have to start somewhere. ..... He just happens to be at the forefront of this thing starting. So that's fine."*

*Parent 6*

*Disappointment with the lack of support provided by health professionals*

Despite many positive comments about their interactions with health professionals, participants reported disappointment with some parts of the interactions. This disappointment appeared to relate to a perceived lack of guidance in accessing information and support:

*"I guess my main issue ..... was I felt like we were given the information and like I said, just said, 'oh well we don't know anything, see you later'. I mean it would have been nice for them to have said ..... 'we don't know much about it but maybe you can go and have a look here' or, 'you can go and talk to the people here' or you know, it would have been nice to have been pointed in the direction of someone who knew something."*
*Parent 9*

Participants in the current study stated that they had primarily sourced information about their child's microdeletion from the Internet. Often participants searched the Internet for information as soon as the result was disclosed and continued to do so following appointments with health professionals, although this was not ongoing for all participants and two participants deliberately chose not to access information via the Internet. Participants recalled receiving minimal guidance from health professionals regarding accessing further information from the Internet or other sources.

In terms of access to support, participants sought assistance in navigating the education system, ascertaining what resources were available to them, and identifying appropriate patient support groups. Participants described feeling lost and alone, and unsure where to turn, and there was an overall sense of frustration evident from their comments. Some were disappointed that assistance was not forthcoming from health professionals

whereas others seemed to feel it was their own responsibility to seek information and support:

*"A health professional really can't steer me in that way because they've done what they have to do, they've diagnosed the problem. I now have to try and find, and you can't find it, try and find a way that I have to live the rest of my life with [child's name]. With the way she is. ...… The doctors are just a part of it. They're the part that tells me the information of what's happened. And now I have to get everything else together."*

*Parent 4*

Participants' self-reported psychosocial support needs were variable and influenced by many factors. Similar to comments about accessing information, participants reported using the Internet to identify appropriate patient support groups. Participants' attitudes to seeking support from other affected individuals spanned the spectrum from having no desire to make contact with others, to seeking individuals with an identical microdeletion to their child. Overall participants were interested in participating in a support group of some description, but generally were not aware of any that might be appropriate to their needs. In addition, participants communicated that they felt the majority of resources were international and therefore less useful.

Two participants reported being very active in online support groups – both were happy to participate in general groups relating to a specific aspect of their child's phenotype (e.g. autism), although one had also identified several groups that were specific to her child's microdeletion. Both of these participants indicated that the goal of their participation in the

support groups was to seek other individuals who had or were having similar experiences to them in order to reassure themselves about their own situation and provide moral support:

*"There's other people out there who have it and I can talk to them and they can tell me ..... what their child ..... does and doesn't do and ..... we can compare a little bit."*
*Parent 9*

A further disappointment articulated by participants was the lack of short-term follow-up after the appointment with the clinical geneticist. Participants from the six families that had not attended a review appointment (including those who had been informed of the result by the clinical geneticist and those who knew the result in advance) felt there would have been value in having a second appointment with the clinical geneticist once they had been given time to process the information provided in the first appointment:

*"'What are your questions, what are your questions?' And we didn't have any to be honest on the day I was feeling a little bit, not shell-shocked or numb, that's too extreme, but ..... I was processing it, so I ..... wasn't able to ask. ..… I think what would have been handy would have been if we'd had a follow-up appointment in maybe a month. ..… It would have given us time to ..... digest the information and process it and look up a bit of stuff then go back with informed questions."*
*Parent 2*

*Hopes and fears for the future*

Participants' thoughts about the future were mixed. Some focused on the positives and expressed hope for what their child might achieve, whereas others expressed concerns

about challenges their child may face. One participant expressed relief at the range of abilities reported for others with the same microdeletion as her child. This knowledge gave the participant hope that her child's intellectual and behavioral development might exceed her current expectations, and provided the impetus for her to persevere with interventions aimed at enhancing her child's abilities. Another participant identified hopefulness as a tool for coping with her child's situation:

*"I guess you've got to be hopeful that things are going to turn out okay, I mean you can't raise a child thinking the worst so obviously ... I hope that he's going to grow to be able to be independent and ..... things like that but I don't stress about it a whole lot."*
*Parent 9*

For others the prognostic uncertainty inherent in their child's situation and the inability of health professionals to remove this was overwhelming:

*"I think the hard thing was, there was nowhere ..... and no one that could say where they sort of expected him to end up ..... even when we saw the geneticist ..... no one could really say 'look other kids have done this or have achieved this'."*
*Parent 1*



Participants indicated that they were very worried about their child's future and were hopeful that some certainty would be forthcoming before too long by way of improved medical knowledge:

*"That's what she [clinical geneticist] said, you know in a couple of years' time they'd have more information ..... and more research to be able to compare things with."*

*Parent 3*

In terms of accessing new information in the future, participants were not aware of the existence of a formal follow-up schedule for their child although one participant articulated that she felt she could re-contact the genetics service if she wished to, which she appreciated.

## DISCUSSION

This study contributes to a growing understanding of parents' experiences of receiving a CMA result of uncertain clinical significance for their child. The findings of this study support the findings of previous studies exploring this phenomenon and provide further insight into the information and support needs of families when a child has a VOUS detected by CMA testing. Furthermore, the acceptance, flexibility and resilience demonstrated by participants in this study as well as their capacity for hopefulness has broadened understanding of the perceived value of such results and highlighted opportunities for health professionals to aid in the adaptation and empowerment of patients and their families in this situation.



In alignment with a recent study examining the implementation of CMA technology into clinical practice, the results of this study demonstrate that it is becoming more common for non-genetic health professionals to request genetic tests such as CMA [Turbitt et al. 2013]. This increase in non-genetic health professionals requesting genetic tests such as CMA has led to concerns that patients may not receive adequate pre-test counseling and

therefore may not provide informed consent for testing [Reiff et al. 2013; Turbitt et al. 2013]; however, there is an apparent lack of formal recommendations relating to what constitutes adequate pre-test counseling for CMA testing. The current study did not set out to evaluate clinicians' provision of pre-test counseling and given that the results are based on participants' recollection of events it would be unfair to conclude that the counseling was inadequate. Nevertheless, the results do suggest that pre-test discussion was minimal. It is also worth considering the tension between what is practical and what is best practice, as has been noted previously by healthcare professionals providing CMA testing [Reiff et al. 2014]. Potential barriers to the ideal of informed decision-making with regards to CMA testing include the complexity of the information to be provided, and practical considerations such as the limits on clinicians time, both in terms of the time allocated to an appointment and the time required for education and training.

In addition to their responsibilities for pre-test information provision, the requesting clinician is also generally responsible for disclosing the test results. The guidelines of the American College of Medical Genetics state that CMA results should be disclosed by a health professional with appropriate genetics expertise [Kearney et al. 2011]. However, this is increasingly not the case in practice and participants in the present study reported that the requesting clinician often lacked the knowledge and expertise to explain the result to them. Supporting this, three recent studies of clinicians' perspectives on the use of CMA technology in pediatric settings found that non-genetic health professionals were uncomfortable explaining uncertain results [Reiff et al. 2014; Reiff et al. 2013; Turbitt et al. 2015]. Furthermore, non-genetic health professionals stated that they would discuss results of uncertain significance with a genetic health professional and/or refer the family to a genetics service [Reiff et al. 2013], as occurred for participants in this study. The results presented

here indicate that in this situation it is important that the referral is prompt and the patient is seen in a timely manner.

It has been shown that the certainty of the diagnosis is central to parents' experiences of the diagnostic process [Graungaard and Skov 2007]. For participants in this study, the appointment with the clinical geneticist served to either provide an explanation or expand on a previous explanation of the child's CMA result. Interestingly all of the participants reported (with varying degrees of certainty) that the result provided a diagnosis for their child. This supports results of previous studies that have also shown that parents may interpret a VOUS result as causal of their child's phenotype [Jez et al. 2015; Kiedrowski et al. 2015; Reiff et al. 2012]. The reasons for this cannot be known as all studies were concerned with parents' experiences and participants were not asked to justify their perception of the result, but may include the actual words used by health professionals to explain the result, participants' desires for answers, as well as parallels between the reported phenotype and their child's phenotype.

Despite the perceived diagnostic certainty reported by participants in this study, other types of uncertainty associated with the CMA result, such as prognostic uncertainty, appeared to significantly influence their experiences. Not surprisingly, the uncertainty appeared to affect participants' assessments of the effectiveness of the clinical geneticist because it limited how reassuring the geneticist could be and the amount of information they could provide. When writing about medical uncertainty, Parascandola et al. noted that when faced with uncertainty, many clinicians either avoid discussing it or oversimplify the relevant information [Parascandola et al. 2002]. Both Parascandola et al. and Lipinski et al. recommend that clinicians acknowledge uncertainty and Lipinski et al. suggest doing so may

assist parents in accepting the absence of prognostic information [Lipinski et al. 2006]. Furthermore, Parascandola et al. hypothesize that in order to preserve trust in the relationship it may be important that patients understand the source and nature of the uncertainty [Parascandola et al. 2002]. Clinicians may achieve this by explaining the reasons for the uncertainty and expressing a level of comfort with it [Parascandola et al. 2002]. Additionally, in order to assist parents in managing uncertainty, it may be beneficial to focus on what is known about the child's condition as well as the things over which parents do have control such as gathering information, advocating on behalf of the child, ensuring the child's wellbeing, and self-care [Madeo et al. 2012]. Lipinski et al. also suggest that when problem-focused approaches to coping are not available, promoting an emotion-focused approach (such as remaining positive, and seeking social support) may assist parents in increasing their perceived personal control [Lipinski et al. 2006]. It is not clear from the results of this study exactly how or to what degree uncertainty was explored by the clinical geneticists seen by participants. However, participants' positive comments about the clinical geneticists and their apparent acceptance of the absence of prognostic information may imply that the uncertainty was adequately acknowledged and discussed.

The importance of access to information and psychosocial support following an abnormal genetic test result cannot be overstated; however, the potential for parents of children with a rare genetic condition to be left without sufficient information about their child's diagnosis and prognosis is well-recognized [Gundersen 2011]. Information-seeking behavior (via the Internet) as demonstrated by participants in the current study has been previously documented [Makela et al. 2009; Roche and Skinner 2009; Skinner and Schaffer 2006; Starke and Moller 2002] and has the potential to increase scientific literacy, confidence in an individual's own expertise, and confidence in communication with health professionals

[Roche and Skinner 2009; Skinner and Schaffer 2006]. Likewise, participation in support groups has the potential to provide both practical and emotional benefits to parents of children with a medical diagnosis [Law et al. 2001; Solomon et al. 2001]. With specific reference to situations associated with uncertainty, Parascandola et al. note that utilizing psychosocial supports can reduce perceived uncertainty potentially via access to information and opportunities to increase self-confidence [Parascandola et al. 2002]. All but one participant in the current study articulated a desire for psychosocial support in some form, although specific support needs were varied. Such diversity of needs has been previously noted in a study involving parents of children with ID [Makela et al. 2009] and is an important consideration when facilitating access to support for individual patients.

Despite the lack of relevant information available to participants in the current study, evidence of the benefits of information-seeking behavior was identifiable in many of the interviews conducted. However, there are also potential pitfalls when using the Internet to search for medical information [Lewis et al. 2010; Makela et al. 2009] and participants in the current study experienced many of these. Participants lamented their inability to find answers to their questions, and admitted feeling overwhelmed by the volume of available information, and anxious when they identified contradictory information from different sources. Resources that presented a more severe phenotype than they expected for their child also distressed many parents. Similarly, participants were commonly disappointed in the lack of assistance they received from health professionals in identifying and accessing psychosocial support. Those participants who were satisfied with the level of psychosocial support they were currently receiving indicated that they had been proactive in obtaining it for themselves. Those participants who had not joined an organized support group but expressed a desire to

do so indicated that their lack of involvement was due to a lack of awareness that the opportunities existed.

Results from this study demonstrate the value of health professionals providing patients with advice regarding Internet searches. Participants in the current study and Reiff et al.'s study reported being cautioned against searching for information online; however, many did so anyway [Reiff et al. 2012]. Accordingly, Smith and Pollin suggest that the increasing access of the Internet by patients requires that genetic health professionals shift their focus from *provision* of information to *navigation* of information [Smith and Pollin 2010]. It has been recommended that useful guidance may include explaining the result in detail (e.g. to avoid inadvertently accessing information on whole chromosome deletions rather than microdeletions), warning patients about the likelihood of finding irrelevant information, and directing them to useful resources [Reiff et al. 2012].

Despite the challenges associated with caring for their child, participants in this study tended to regard the future with hope. Participants focused on short-term coping but remained optimistic that increasing medical knowledge would provide their family with more information and better opportunities in the future, an attitude identified in previous studies [Kiedrowski et al. 2015; Reiff et al. 2012]. Bernhardt et al. have shown that patients value ongoing support from genetic health professionals and the ongoing provision of information [Bernhardt et al. 2000] and it has also been shown that a concrete commitment to ongoing follow-up significantly affects parents' perceptions of their results disclosure appointment [Ashtiani et al. 2014]. Participants in the current study articulated a desire for a follow-up appointment shortly after the initial appointment with the clinical geneticist. Unfortunately, this is a well-recognized request from patients that is often difficult to facilitate due to limited

resources [McAllister et al. 2008; Skirton 2006]. Furthermore, although participants in this study were open to long-term follow-up with the genetics clinic they were unclear about the mechanism for this. This confusion has been previously noted and raises concerns about patients becoming lost to follow-up and potentially being unaware of updated information [Kiedrowski et al. 2015].

There are some limitations to the current study. The rigorous application of inclusion and exclusion criteria supported recruitment of participants likely to have had similar experiences, enhancing the potential to derive a combined description of their experiences. However, the exclusion of non-English speaking participants, parents of children over 18 years old, and families not seen by VCGS for a face-to-face post-test appointment means that the experiences of these individuals remain unknown. Importantly, whilst participants in this study appeared to adapt to uncertainty and limited availability of information associated with their child's test result, this may not be the case for families who are not referred to a clinical genetics service. Furthermore, for reasons of feasibility, this study was limited to interviewing parents about their experiences. Qualitative research often provides the foundation for larger projects using quantitative methods. In order to comprehensively explore the phenomenon of experiences of uncertain CMA results, research involving other key informants will be important.



An encouraging finding of the study was the flexibility and resilience demonstrated by parents following detection of a VOUS by CMA testing. In particular, it appears that an honest and collaborative approach by health professionals is appreciated by patients and beneficial to their adjustment to the result. Despite this, there are a number of aspects that could be improved in order to optimize patient care. The participants in this study were either

referred to a clinical geneticist for results disclosure or following results disclosure. Whilst clinical geneticists are clinicians who have undergone specialty training in genetics and are recognized to provide genetic counseling [Haan 2003] the results of the current study indicate that the inclusion of a genetic counselor in the process may be beneficial, as previously noted [Ashtiani et al. 2014; Reiff et al. 2014]. It is recognized that time constraints may make it challenging to incorporate a genetic counselor into a clinic appointment; however, a genetic counselor could provide patients with a follow-up telephone call following the appointment either to provide telephone counseling or arrange an appointment with a genetic counselor. Alternatively, the structure of the clinic may be altered to include a multidisciplinary team of specialists, as has been arranged for other conditions [Hill et al. 2003]. In addition to this broad recommendation, several specific suggestions for practice, made in response to issues arising directly from the results of this study, are presented in Table II.

## CONCLUSION

This study exploring parents' experiences of CMA testing for their child in cases where a VOUS was detected demonstrated that participants were empowered and retrospectively positive about the value of CMA testing and the potential for further tests in the future. In the absence of information and medical advice about a VOUS detected by CMA testing, individuals valued honesty about the uncertainty and empathic ongoing support from health professionals. As part of a multidisciplinary team clinical geneticists and genetic counselors are well positioned to provide such support and therefore aid in the adaptation and empowerment of patients and their families in order to promote optimum physical and mental health outcomes.

This study represents an important initial contribution to our understanding of parents' experiences of an uncertain CMA result for their child and lays the foundation for additional qualitative and quantitative research. Future research into the experiences of families who do not have contact with a clinical genetics service, as well as the experiences of the health professionals involved in requesting CMA testing and reporting the results will further enhance understanding and inform practice.

## ACKNOWLEDGEMENTS

This study was completed in partial fulfillment of the requirements for the Master of Genetic Counselling, University of Melbourne, Victoria, Australia and was supported by the Victorian Government's Operational Infrastructure Support Program. We thank the participants in this study for taking the time to share their experiences with us. We thank Dr Jan Hodgson for her valuable comments on this manuscript.

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| **Table I. Demographic Characteristics of Participants** | |
|---|---|
| | |
| **Characteristic** | **Participant** |
| Age range (years) | |
| 30-39 | 2 |
| 40-49 | 6 |
| ≥50 | 1 |
| Relationship to child | |
| Biological mother | 5 |
| Biological father | 2 |
| Adoptive mother | 2 |
| Relationship status | |
| Married / de facto | 7 |
| Divorced / separated | 2 |
| Highest level of education | |

| | |
|---|---|
| Primary school | 1 |
| Secondary school, not completed | 1 |
| Secondary school | 2 |
| Trade / technical / vocational training | 1 |
| University, not completed | 2 |
| University | 2 |

**Table II. Suggestions for Practice**

| Issue | Recommendation |
|---|---|
| The increasing involvement of non-genetic health professionals in genetic testing. | Improved education and training for non-genetic health professionals is required. Recent studies have explored the CMA-specific education and resource needs of non-genetic health professionals and have demonstrated a requirement for appropriate professional education and training amongst clinicians [Dunlop et al. 2015; Reiff et al. 2013; Saleh et al. 2013]. Recommendations from one of these studies include extended training opportunities such as graduate programs, incorporation of genetics into the existing curriculum, and additional professional development opportunities [Dunlop et al. 2015]. |
| The necessity of adequate pre-test counseling to ensure patients provide informed consent to testing. | The pre-test counseling process should be optimized within the limits of clinicians' time and knowledge, and should include a discussion of the potential for uncertain or unexpected results. To facilitate this, consensus guidelines covering pre-test counseling, interpretation and reporting of results, and post-test counseling are required [Bruno et al. 2013; De Wolf et al. 2013]. |
| The requirement for health professionals to provide patients with guidance in accessing additional information and to facilitate access to psychosocial support. | Due to increasing scientific literacy amongst the general public, health professionals should be encouraged to consider a collaborative rather than didactic approach to communication of information. In particular, it is recommended that health professionals provide guidance to patients about Internet searching, and if possible direct them to useful online resources [Roche and Skinner 2009]. Every effort should be made to facilitate psychosocial support opportunities with other individuals who have the same CMA result, the same type of CMA result (e.g. a VOUS), and/or a similar phenotype. |
| The importance of providing | Patients should be provided with clear options for follow-up |

| | |
|---|---|
| appropriate follow-up to patients. | within the limits of available public health resources. This relates to short-term follow-up, for example a telephone call following the appointment with the clinical geneticist, and long-term follow-up, for example as new information becomes available. |