

"It's probably nothing, but..." Couples' experiences of pregnancy following a uncertain prenatal genetic result

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CONFLICT OF INTEREST

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ABSTRACT

Introduction: A common concern regarding the introduction of Chromosomal Micro-Array in prenatal testing is the concomitant identification of an uncertain copy number variant (CNV) where significance and clinical implication for the unborn child can be difficult or impossible to predict. Following the identification of an uncertain CNV, prospective parents may decide to continue the pregnancy. The aim of this study was to explore how prospective parents manage uncertainty and experience pregnancy in light of an uncertain CNV result.

Material and methods: Qualitative interviews with 16 women and 10 partners who had received a prenatally diagnosed, uncertain CNV. Participants were recruited from the Aarhus University Hospital, Denmark and most were interviewed in their homes 1-14 weeks after birth. Data were analyzed using thematic analysis.

Results: Following the CNV diagnosis, some couples focused on the severe syndromes ruled out by the result, while others were more concerned with the new potential risks, e.g. learning disabilities. Most couples did not remember the actual diagnosis, but all described a number of attention points generated by the CNV result. During pregnancy, the couples used various strategies to limit worry and enjoy their pregnancy such as limiting information seeking, reducing talk of the CNV and deferring thoughts of potential consequences. Furthermore, ultrasound was considered a valuable resource for reducing worry as it provided reassurance about the development of the baby. Inherited CNVs caused relief on one hand, but also feelings of responsibility for the child's potential challenges. After birth, worry decreased considerably, but all couples paid some extra attention to the child's development, while also being alert to the risk wrongfully interpreting the child's development in terms of the CNV. Eleven couples expressed satisfaction with knowing about the child's CNV, whereas five couples would rather not have known.

Conclusions: The results indicate that health professionals should be mindful of terminology, remember to point out what has been ruled out by the CNV result, and discuss potential coping strategies with the couple. Furthermore, these couples may have a higher need for ultrasound during pregnancy to help reduce worry. More research is needed on the families' long-term coping.

Keywords (5-8): Chromosomal microarray analysis, copy number variants, experiences, parents, penetrance, pregnancy, uncertain significance

Abbreviations: CMA, chromosomal micro-array; CNV, copy number variant; SL, susceptibility loci; VUS, variant of uncertain significance

Key Message: Couples receiving uncertain prenatal genetic results manage uncertainty by deferring the potential risks and by focusing on enjoying pregnancy. These couples benefit from receiving useable terminology from health professionals and understanding all the conditions that the results have ruled out.

INTRODUCTION

Chromosomal Micro-Array (CMA) detects micro-deletions and -duplications associated with a variety of cognitive disorders, congenital anomalies and predispositions to neurodevelopmental conditions.¹ A common concern regarding the introduction of CMA in prenatal testing is the concomitant identification of copy number variants (CNV) of uncertain significance (VUS), or variants of incomplete penetrance and/or variable expressivity (susceptibility loci (SL)). If the pregnancy is without malformations then the risk of finding a VUS or SL is less than 1 %.^{2,3} In both cases the prognosis for the specific child can be difficult or impossible to predict. For example, an SL such as 22q11 duplication may cause intellectual disability, autism, heart malformation and schizophrenia,⁴ but the majority will have neither of these symptoms.⁵ Consequently, such CNV results can be particularly challenging both to communicate and understand.^{6,7}

Studies have shown that pregnant women who enter into prenatal screening and testing often request maximum information about their unborn child, including uncertain CNV results.⁷⁻¹⁰ However, they may be unprepared for the scope and complexity of such information,^{11,12} and for the reproductive decisions, that the new situation entails. Following the identification of a CNV, parents may decide to continue the pregnancy.¹³ However, carrying a child without knowing the potential implications of a VUS or SL result may be a source of stress and concern. The current evidence regarding how parents deal with such a situation is limited and ambiguous,^{11,13,15} and little is known about how this information about an uncertain CNV is managed by pregnant couples and how it affects their experience of pregnancy. Such knowledge is particularly relevant for the health care professionals who see the couple during pregnancy, and who must be alert to the increased risk of specific conditions and malformations while also supporting parental coping.

The aim of this study was to explore how prospective parents experience pregnancy following a prenatal diagnosis of uncertain significance or variable penetrance.

MATERIAL AND METHODS

Design

An explorative research design was chosen¹⁶ and a qualitative interview study was conducted.^{17,18}

Setting

Denmark has comprehensive and free-of-charge prenatal care available to all pregnant women including a combined first trimester screening and a second trimester malformation scan.¹⁹ In case of a high-risk screening result, women are offered a choice between non-invasive prenatal testing and invasive diagnostics and the majority chooses the latter.⁸ In case of detected or suspected fetal anomaly, women are offered invasive diagnostics. All invasive tests are analyzed using CMA. Pre-test counseling is performed by sonographers or fetal medicine specialists. In case of a VUS or SL result, the post-test counseling is performed by consultant clinical geneticists. The geneticist can refer patients to further counseling or to further ultrasound examinations to monitor the progress of the baby, or the geneticist can assist the couple in applying for termination of pregnancy. In Denmark, termination of pregnancy is legal without application < 12+0 gestational weeks, and allowed on approval by a specialist board < 23+0 gestational weeks in the case of serious fetal anomalies.

Study participants

Prospective parents with prenatally diagnosed copy number variant (CNV) of uncertain significance or variable penetrance in an ongoing or very recent pregnancy were recruited from the Department of Clinical Genetics, Aarhus University Hospital (January 2017 to March 2018). Only cases that consultant clinical geneticists deemed to be particularly challenging due to lower penetrance or limited evidence were included. When a case was identified, potential participants were contacted by the first author before or after their first genetic counseling session where the CNV was presented to them. They received written and oral information about the aim and methods of the study and 20 couples consented to being contacted by the first author 3-4 months later (none declined). However, at time of re-contact one couple withdrew consent and three couples could not be reached by phone or txt. Consequently, a sample of sixteen couples participated in the study. Participant characteristics are presented in Table 1. The different CNVs and interpretations are presented in Table 2.

Data collection

By participant choice, ten joint interviews (woman and partner) and six individual interviews (woman only) were conducted in the couples' homes (n=15) or by phone (n=1). Information about the study was repeated prior to all interviews and written consent was obtained. It was clearly stated

that participation was voluntary, and that consent could be withdrawn at any time. The semi-structured interview guide was designed to explore the couples' experiences of the diagnostic process and the meaning of the CNV in their subsequent everyday lives (Table 3). The present analysis describes the couples' post-counseling experiences. All interviews were performed by the first author, who is an experienced interviewer and during joint interviews she was careful to elicit the views of both woman and partner.

At the time of recruitment, 12 couples had ongoing pregnancies, while two couples had genetic testing due to intrauterine deaths and two couples had recently terminated pregnancy prior to the genetic counseling. Interviews were performed from June 2017 to September 2018. At the time of interview, two couples were still trying to conceive, two couples were still pregnant and 12 couples had given birth. These 12 interviews were conducted 1-16 weeks (median 6 weeks) after birth. Originally, all interviews were planned to be conducted 3-4 months after recruitment, but after conducting two interviews with couples still pregnant, this procedure was changed to interviewing couples after birth due to concerns about generating unnecessary worry. Despite differences in pregnancy-status at time of interview, all interviews were included in the analysis as they shared many similarities in content and concerns revealed. All interviews were digitally recorded, transcribed verbatim and rendered anonymous, e.g. through exclusion of personal identifiers.

Data analyses

Thematic analysis²⁰ was used to identify patterns in the transcribed data. The material was thoroughly read, initial codes were generated by the first author and a research assistant, and discussed with the co-authors. Both inductive codes (e.g. 'stop talking about it') and deductive codes (e.g. 'social support') were used. Following test-coding of three selected transcripts, the codes were discussed and further refined (e.g., to minimize overlap in content). All material was then coded by the first author and a research assistant using NVivo 10 software (QSR International, Melbourne, Australia). The coded material was read and sorted into main and sub-themes, which were discussed among all authors. For example, the above mentioned examples of codes were merged in the preliminary subtheme 'Sharing or not' which was then combined with other preliminary subthemes to form the theme of 'Managing Worry'. The analyses resulted in a total of four themes each with 3-5 subthemes (see Figure 1)

Ethical approval

The study was approved by the Danish Data Protection Agency (J. No. 1-16-02-62-17).

RESULTS

All participating couples were ethnically Danish, in heterosexual relationships, and all had participated in the national, prenatal care program. As such, they constituted a relatively homogeneous sample. However, they also represented variance in terms of personal background and current situation. Not only did they differ in age, education and parity, they also had various experiences with pregnancy and different everyday concerns. Nevertheless, despite this diversity, their experiences of receiving and managing a CNV result shared many similarities.

Personal interpretation of the result

Focus on the known or the unknown

Following the genetic counseling, the various couples interpreted the CNV differently. In interviews, the couples generally explained that something was found in the fetus that might cause some problems or challenges, but that it might be nothing. However, the couples focused on different aspects of the results. Some couples focused on what was now known and expressed relief that the finding was less severe than expected (Table 4, quote 1) and that known disorders such as Down syndrome was ruled out (Table 4, quote 2). Other couples focused more on the unknown and the uncertainties generated by the result, e.g. the risk of learning disabilities or structural malformations (Table 4, quote 3, 4). However, couples in both groups considered the result ambiguous and all described how they actively sought to come to terms with it.

Everyday terminology

At the time of the interview, only very few couples could precisely recall the specific CNV and most explained it like '*something extra on chromosome 16*' or '*one book missing in her library*' (Table 4, quote 5). During the interview, the couples used different terminology such as '*diagnosis*' or a '*genetic mutation*'. Notably, nine couples spoke of the CNV in terms of a '*chromosomal error*' [kromosomfejl in Danish]. This colloquial term is sometimes heard in everyday language when addressing serious disorders, such as Down syndrome. Thus, the use of it here was in contrast to the couples' explanation that the CNV was '*probably nothing*'. When the interviewer inquired about this terminology, many couples agreed that the term '*error*' was inappropriate, but that they did not

know what else to call it (Table 4, quote 6). One couple had deliberately decided to refer to the paternally inherited VUS as a '*genetic twist*' to convey its relative insignificance (Table 4, quote 7).

A list of attention points

Though the couples did not necessarily remember the specific CNV result, they all remembered the specific, potential consequences that had been addressed during the genetic counseling. All described a list of potential attention points regarding the child's development, e.g. risk of delayed learning, obesity and kidney problems (for another example see Table 4, quote 8). During pregnancy, many of the potential risks regarding structural malformations had been ruled out through ongoing ultrasound testing, whereas risk of obesity or learning disabilities still lingered after birth as described in more detail later. In two cases, a fetal structural anomaly was unexplained by the CNV result, and both couples reported that worry about the anomaly by far overshadowed all other CNV-related attention points, such as increased risk of attention disorders.

Managing worry during pregnancy

Worry wax and wane

The analysis showed that the couples had very different levels of worry following the result, and that worry was not a constant but something that waxed and waned during the pregnancy. For example, couples who described themselves as '*not very worried*' still reported incidences where worry over the CNV result was higher (e.g. prior to an ultrasound scan), and the four women who described themselves as '*very worried*' also expressed variations over time. For example, one woman was haunted by the mention of a slightly increased risk of psychiatric disorders (Table 4, quote 9) to the point where she had to go on sick leave. However, continuous, normal ultrasound results somewhat calmed her over time. Another woman described herself as an '*over-thinker*' and felt extremely worried throughout the pregnancy, but also reported a waning of worry mid-pregnancy, and that she – as did all other couples in the sample – used different strategies that helped them stem worry and regain control. These are described below.

Information seeking

Whereas many couples had sought information on the internet prior to the genetic counseling, only very few did so afterwards, and none sought information in other places. Rather they relied on the

information from the geneticist and expressed that it fulfilled their information needs – particularly in the light of not much detailed information available anyway (Table 4, quote 10). Several couples described bad experiences with Internet searches prior to the counseling, which made them cautious with exposing themselves to wrong and potentially worrying information. These searches had often let the couples to think that the CNV was much more serious than later realized. For example, one couple with an inherited 22q11 duplication had read information online about 22q11 deletion which is much more severe. This had caused a lot of pre-counseling anxiety.

A conscious decision to not worry

Only one couple expressed an immediate and authentic feeling that the inherited VUS was just normal variation and not something that would impact the child. Most couples expressed satisfaction with the information and care received at the post-test counseling, but all experienced some subsequent worry and concern. A common coping strategy was - after a few days or weeks – to make a conscious decision to suppress worry and rather focus on enjoying their pregnancy (Table 4, quote 11, 12). For some this was more straightforward than for others, but all expressed determination to have faith in a healthy child and most considered themselves to have had a good pregnancy.

Sharing with others or not

Around the time of testing and diagnosis, all couples described turning to family and friends for comfort and support (Table 4, quote 13). However, as the pregnancy progressed and the CNV result settled in, many couples reported talking less about it. In their experience it was demanding to explain to outsiders about the result's potential but uncertain implications (Table 4, quote 14). One couple deliberately censored information and told only of the risk of heart disease, but not about the CNV. Another reason for limiting talk of the diagnosis was that sometimes social network responded in ways that the couples found unfortunate or insensitive, e.g. suggesting that the pregnancy be terminated (Table 4, quote 15, 16). In hindsight, a few couples regretted having shared the CNV result with work colleagues or extended family.

Finally, several couples used silence as a coping strategy to control worry and focus on the normal pregnancy. They explained how they deliberately deferred the diagnosis by speaking less and less of it during pregnancy. They stopped telling new people about it, limited how they spoke about it

to family and friends who already knew and stopped talking much about the CNV between them. They denoted how this allowed them to enjoy pregnancy more (Table 4, quote 17).

Ultrasound helps

The four women who described themselves as 'very worried' during pregnancy all mentioned extra ultrasound examinations as '*a lifesaver*' (Table 4, quote 18). Also, ultrasound was valuable when it dismissed increased risk for malformations. Though several women described increase in worry prior to ultrasound, it was also highlighted as a valuable tool that re-established trust in a healthy child and thus helped couples to manage worry.

Managing an inherited CNV

The most apparent difference in the couples' responses to the CNV was its status as inherited or de novo. For couples with an inherited CNV, the heredity provided a sounding board for interpretation of the result.

Normalizing CNVs

In 13 cases, the CNV was inherited from one of the parents. For some parent carriers the inheritance was a relief, since they considered themselves normal and thus understood the CNV as an expression of human diversity (Table 4, quote 19). Also, several partners of CNV carriers emphasized that they were quite happy to be expecting a child with the partner's genetic uniqueness (Table 4, quote 20).

Cause for reflection

However, the inherited CNV was also a cause for reflection and several parent carriers mentioned feeling responsible for passing 'deviant genes' on to their unborn child. Some considered that it would be '*my fault*' if the child would later show to have learning difficulties. One father expressed concern that maybe he was a particularly subtly affected phenotype and that his son would be more severely affected. For some, the inherited CNV also caused them to reflect on their own childhood and how the CNV might have impacted their own experiences, e.g. if it could explain obesity, reading difficulties or a sensitive personality (Table 4, quote 21).

Future meaning of the CNV result

Birth changes everything

All couples that were interviewed after birth reported feeling much less worried than they had been prior to the birth (Table 4, quote 22).

Special attention

However, the attention points still lingered and several couples revealed how they paid extra attention to the child's development (Table 4, quote 23), e.g. by doing motor skill exercises with the baby to prevent risk of poor balance or by monitoring weight due to risk of future obesity. Many couples recounted how they had felt particularly proud when the child met its' milestones undeterred by the CNV. When asked to evaluate the overall impact of receiving an uncertain CNV result, eleven couples were positive and emphasized how this knowledge allowed them to support their child appropriately including early intervention in cases where of potential future challenges might arise.

The right to be imperfect

At the same time, all couples emphasized the importance of seeing the child in its own right and all addressed the risk of wrongfully interpreting the child's future development in light of the CNV (Table 4, quote 24). Also, all recognized that this intention could be difficult to execute (Table 4, quote 25) as knowledge of the CNV would always be in the back of their minds.

Most couples volunteered concern over potential stigma and fear that outsiders would judge the child due to its '*chromosome error*'. A few had shared information about the child's CNV with the maternity health visitor and a few had not (yet) discussed who (if any) should be informed in the future. However, the majority had explicitly decided not to mention the CNV to the health visitor or to future daycare staff or teachers unless '*something comes up*'. Those who had discussed the matter of disclosing the CNV result to the child, all agreed that the child had the right to know '*at some point*', e.g. if developmental issues manifested or when the child was older and able to manage the information.

In hindsight, five couples (three de novo, two inherited) would rather have been without the CNV result, as they considered the information futile and causing unnecessary worry and an unhealthy focus on the child's development. However, they also recognized that the job of the clinical

geneticist was difficult, and they conceded that it's tricky to decide what information to disclose and what to withhold from prospective parents.

DISCUSSION

Our study adds to growing body of literature looking at parental experiences of receiving an uncertain CNV result during pregnancy. In particular, our study expands our understanding of how couples managed the uncertainty, e.g. by focusing on the severe syndromes *ruled out* by the result. However, all described how the CNV result generated some concern about the child's health and development. During pregnancy, the couples used various strategies to manage worry such as limiting information seeking, reducing talk of the CNV and making a conscious decision to defer diagnosis and enjoy pregnancy. Furthermore, ultrasound was considered a valuable resource for reducing worry. After birth, worry decreased considerably, but all couples still paid some extra attention to the child's development. Eleven couples expressed satisfaction with knowing about the child's CNV, whereas five couples would rather have been without.

Our findings resonate with other research showing that parents of children with an abnormal genetic result engage in 'watchful waiting' and 'active monitoring' of the child's development.^{11, 21} Similarly, the children in the present study may become 'patients in the waiting'²² – their development may be viewed and evaluated through their *potentiality* for learning disabilities, delayed development or obesity. When the couples in our study engaged in training the baby's motor skills or monitoring food intake, they simultaneously reproduced and sought to prevent this potentiality. They were caught in a schism between being alert to the risk of medicalization, while simultaneously wanting to be proactive in supporting their child's development. However, all couples also stressed the potentiality of 'a normal life' unaffected by the CNV and the likelihood that the CNV was *'probably nothing'*. Thus, the term potentiality articulates both worries and hopeful prospects²³ and as such it can be a useful partner to 'risk' in clinical communication when addressing uncertain futures. The study by Desai et al.¹⁵ provides some insight into how parents may navigate this schism risk and normality. They found that parents who received a prenatal VUS result rated their child less competent compared to the control group at 12 months. Interestingly, at 36 months this difference was not present, but the parents were significantly less satisfied with their decision to undergo genetic testing. The authors suggest that the parents by this time rated their children to be developing normally and thus regretted having gone through a period of enhanced

surveillance and medicalization of their child.¹⁵ However, more knowledge on the long-term effects and coping strategies is needed.

We have investigated cases identified as most difficult by consultant clinical geneticists, and only cases where couples chose to continue the pregnancy or to forego pre-implantation genetic therapy in the coming pregnancy. Our results represent the couple's lived experiences and interpretations - not an accurate description of what was said or done in the genetic consultation. Ambiguous CNV results are a challenge for *both* patients and for the genetic counselors. In interview studies, genetic counselors have identified the lack of numerical probability, uncertainty of phenotype, lack of information on prognosis, and perceived distress for patients as main challenges.^{24,25} An uncertain CNV result involves a number of non-reducible uncertainties, such as the absence of scientific data or uncertainty related to probability. Thus, there is a limit to how scientific information alone can assist the couple's understanding, decision-making and management. Consequently, as suggested by Werner-Lin and colleagues,²⁶ genetic counselors must help families create pathways through uncertainty by helping them to articulate values, interpreting information, identifying options and support coping. Below, we suggest how the results from our study may be useful in such a context.

First, it was surprising to discover the couples' unfortunate use of the old-fashioned concept of 'chromosome error' which may make the parents and their social network perceive the CNV as more severe than is likely the case. We speculate that this is probably a unique Danish problem, however, parents' lack of everyday terminology or common language for CNVs has been illustrated in other studies.²⁷ Based on our results we suggest that clinical geneticist be very mindful with the terminology they use and discuss the importance of language with the couple. The clinical geneticist can even actively suggest the use of 'genetic variation', 'genetic twist' or simply 'a copy number variant' in everyday language and provide a suggestion for how the CNV can be shortly explained to others. Also, as our results include examples of regret of disclosure, health professionals can encourage couples to be conscious of what information to share and with whom.

Second, we found that in everyday life, it was the potential and uncertain consequences of the CNV that most couples struggled with. Based on our results, we suggest that it may be valuable for patients if the genetic professionals also emphasize all that is known and certain, e.g. that many syndromes and severe disorders have been ruled out by the CNV result. Furthermore, our results

point to specific coping strategies such as choosing who to share with, deferral of potential consequences and the use of ultrasound. Based on our findings, we consider it valuable to present and discuss some of these during the genetic consultation.

Third, our results indicate that some couples could benefit from an additional contact with the department of clinical genetics to maybe sort out or prioritize the list of attention points. All patients at the department are given a contact card and encouraged to call the consultant clinical geneticist if any questions should arise, but in our experience they rarely do. Other research has also described that patients benefit from having easy access to their health professionals.²⁸ Based on these results we now consider having a genetics nurse call the couple the after a few weeks. We do not have many uncertain CNV results, so that would be feasible.

Finally, when pregnant couples have ultrasound after the CNV has been identified, health professionals can take extra care to also point out what is structurally normal. Our results show that such knowledge is very valued – even for couples whose main attention point is something that does not show on ultrasound, e.g. risk of cognitive impairment. In line with other research, the couples in our study were very willing to interpret information in ways that relieve anxiety and re-establish normality in pregnancy,^{21,27} e.g. a normal ultrasound as indication of a (structurally) healthy child.

When evaluating the results, the strengths and limitations of the study must be considered. First, all participants were interviewed relatively shortly after receiving the diagnosis, which limits the risk of recall bias. Furthermore, all interviews were conducted by an experienced interviewer which is important as a skilled interviewer may elicit more nuanced responses from participants.^{16,29} Finally, researcher triangulation in all processes of analysis supported a critical and reflexive analytical process. However, the study is relatively small and would benefit from a larger sample size including multiple recruitment sites and participants with more diverse backgrounds, e.g., ethnic minorities. However, within this relatively narrow sample, we estimated that sufficient information power was obtained.²⁹ Of course, qualitative studies must always be understood within their specific context and are not generalizable in the quantitative sense of the concept; they are not intended to be. However, our results may be used as a lens through which genetic consultations in other contexts can be viewed, compared and reflected upon.

CONCLUSION

Uncertain CNV results are a main clinical challenge and concern in CMA testing. Our results show that prospective parents often manage the uncertainty by deferring the potential risks related to the CNV and focus on having a good pregnancy, but that attention to these risks continue to linger for many, also after birth. The majority appreciated the information, particularly due to the opportunity for early intervention, but one third found the information futile. Based on the results, we suggest that health professionals should be mindful of terminology, present also what has been ruled out by the CNV result, and discuss potential coping strategies. Furthermore, ultrasound was considered a valuable resource for controlling worry, and health professionals can support coping by pointing out the structurally normal. More research is needed on the families' long-term coping.

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TWEETABLE ABSTRACT

Uncertain genetic results cause worry in prospective parents. Coping strategies include focus on the normal, deferring potential risks and use of ultrasound.

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FIGURE 1 Thematic map

TABLE 1 Participant characteristics (16 couples, N = 32)

Age	
Maternal age average	30 (range: 24–40) years
Paternal age average	31 (range 25–41) years
Educational level*	
High	10
Medium	18
Low	4
Parity	
0	9
1	3
2	2
3	2
Indication for testing	
High risk screening result	12
Suspected malformation	2
Previous miscarriage	2
CNV result	
Inherited SL	9
De novo SL	1
Inherited VUS	2
De novo VUS	2
Inherited SL, de novo VUS	1
Normal	1
Ethnicity	
Danish	32
Other	0
Duration of interview	
Average duration	62 minutes
Range	45-82 minutes

CNV copy number variant, SL susceptibility loci, VUS variant of unknown significance

* Using the education nomenclature (ISCED) from Statistics Denmark, educational level was grouped into three categories; low (1–10 years), medium (11–14 years) and high (>15 years). Students are categorized by their next educational level.

TABLE 2 Copy number variants and interpretations

Array findings [hg19], Agilent oligoarray 180k	Interpretation
1q21.1(145388355-145747269)x1 mat	SL
1q21.1q21.2(146506310-147824207)x3 pat	SL
1q41(222694279-224070013)x1 dn	VUS
3p25.1(15597969-16372299)x1 pat	Normal
4p15.1-p14(34657625-36189206)x1 dn	VUS
14q12(31903863-33256210)x3 pat, (7)x2~3	VUS, Mosaicism
15q11.2(22765628-23662568)x1 mat	SL
15q13.2q13.3(30943903-32510863)x3 mat	SL
16p13.11(14968855-16267306)x3 mat, 1q31.1(186156501-188391452)x3 dn	SL,VUS
16p11.2(28824794-29109228)x1 mat	SL
16p11.2(29652999-30197341)x1 dn	SL
16p11.2(29652999-30198600)x3 mat	SL
16p13.11(14968855-16267306)x3 pat	SL
16p13.11(14968855-16292235)x3 pat, (X)x2~3	SL, Mosaicism
19p13.3p13.2(6441689-8617755)x3 mat, (Y)x1~2	VUS, Mosaicism
22q11.21(18919942-21798755)x3 pat	SL

dn, de novo; mat, maternally inherited; pat, paternally inherited; SL, susceptibility loci; VUS, variant of uncertain significance

TABLE 3 Themes in interview guide*

Theme	Examples of questions
The diagnostic process	<ul style="list-style-type: none"> • In your own words, can you describe the diagnostic process leading up to the consultation at the genetics department? (Prompt: reason for testing, communication with staff, information seeking, use of social network etc.) • What were your thoughts and concerns prior the genetic consultation?
The genetic consultation	<ul style="list-style-type: none"> • How did you experience the genetic consultation? (Prompt: preparations, expectations, understanding of result, unanswered questions) • What can you tell me about the finding / what was it that they found? • Did you discuss the possibility of termination of pregnancy • In hindsight, what (if any) should have been different about that consultation?
After the counseling	<ul style="list-style-type: none"> • How did you feel in the weeks following the consultation? (Prompt: worry/grief, use of network, additional testing of fetus/parent, information seeking, understanding of result, terminology etc.) • How did you manage worry (if worried)? • Did the genetic finding impact how you felt about the baby? • Did the genetic finding impact how you felt about yourself/your partner? • All in all, would you say that you had a good pregnancy?
After birth	<ul style="list-style-type: none"> • Now that [baby's name] has arrived, does that change how you feel about this whole situation? • In what situations do you think about the genetic finding? • Since birth, have you told anyone about the genetic finding?
The future	<ul style="list-style-type: none"> • Do you think this experience will impact you in the future? • Do you think this genetic knowledge will impact you in the future? • What are the positive/negative sides to having this genetic information about [baby's name]? • Do you expect to undergo genetic testing in a future pregnancy?
Advice	<ul style="list-style-type: none"> • What is your advice to couples in a similar situation? • Any advice for health professionals?

* The full interview guide (in Danish) can be obtained from the first author upon reasonable request.

Table 4 Illustrative quotes representative of themes

Themes		
Subtheme	#	Quotes (Interview #, finding)
Theme 1: Personal interpretation of the result		
Known or unknown?	1	<i>It was such a weight off my shoulders! I was like: 'OK, risk of mild learning disability!?' And it's not that it's nothing, of course we have to face that risk, but hey, compared to all the other stuff that... we were so relieved and happy when we left that room! (Interview 5, de novo SL)</i>
	2	<i>Really, we know a lot more about this baby then we did with Jenny (older sister). We have more certainty that this is a normal baby compared to what you have in a normal pregnancy (without CMA testing) (Interview 12, paternal VUS)</i>
	3	<i>You can say that we don't have the whole story yet. For a layperson like me it's a very confusing diagnosis – maybe it is for professionals too – because one doesn't know how it develops. If it develops... (Interview 8, paternal SL)</i>
	4	<i>I was still worried when we left the hospital [following genetic counseling]. Because what was this going to mean for her... for us? (Interview 16, maternal SL)</i>
Everyday terminology	5	<i>It was something on chromosome 16... where he had some extra copies. I don't have the exact name, but I can find it for you, if you're interested? (Interview 1, maternal SL)</i>
	6	<i>Honestly, I think chromosome error [kromosomfejl] sounds like... there's something awfully wrong. It's not a good word. But I don't know what other word to use for it (Interview 3, de novo VUS)</i>
	7	<i>We call it a genetic twist. Because it doesn't have to be an error or something bad, so I like genetic twist a lot better (Interview 10, paternal SL)</i>
List of attention points	8	<i>I was especially worried ... or I was worried about all three thing, but the short forearms... because the heart, that could be fixed and the hearing ... well, hearing aids have come a long way. But if she has any malformations in her forearms, how can you do something about that? So there I was just really aware of the scans to see if she had five fingers and if they looked nice, those forearms ... (Interview 16, maternal SL)</i>
Theme 2: Managing worry during pregnancy		
Worry wax and wane	9	<i>Oh, how I wish she had responded differently to my question! Well, I know she couldn't and she kept saying that the increase in risk was ever so small, but just the word!! Schizophrenia. I got this sinking feeling and my mind wouldn't stop' (Interview 2, de novo VUS)</i>
Information seeking	10	<i>[we haven't sought information online] since we spoke to xx [geneticist] ... Because you can't find anything anyway. And if you just google 'chromosome 1' you'll find all sorts of horrible stuff. I think it was 280 known diseases. And that's <u>not</u> what he [baby boy] has. (Interview 2, de novo VUS)</i>
A decision not to worry	11	<i>I decided – and that's what I told Jesper that day in IKEA – if we're doing this, then we have to stop thinking about it. We are not going to talk about it or about what it</i>

		<i>means. This is just how it is and we are expecting a normal, healthy boy and that's the end of it. (Interview 15, maternal SL)</i>
	12	<i>It took a lot of attention (fyldte meget), and we needed to close it down... to say, now we know this and we need to re-focus and to enjoy this pregnancy. At some point you just got to move on. Get out of the bubble and look ahead and say we'll take it as it comes. If it comes. (Interview 16, maternal SL)</i>
Sharing or not?	13	<i>It's good to have someone to open up to. Share your feelings. There's not a whole lot they can say, besides hoping that things turn out good. They can't fix it, but the support is nice (Interview 3, de novo VUS)</i>
	14	<i>If people asked about it, I was like, well, there may be an increased risk of ADD and maybe obesity and something with the kidneys, I don't know. How do you explain something you don't know yourself? (Interview 5, de novo SL)</i>
	15	<i>My parents-in-law don't really get it. It hasn't been a very good experience telling them, because they've had a lot of like... they think it's good advice. But they have never been in the situation, so they can't... (Interview 13, maternal VUS)</i>
	16	<i>I told one of my buddies and he was like, 'So, are you going to keep her?' And I was like 'Well, YES!' But that made me really angry and just tired with the world. (Interview 14, paternal SL)</i>
	17	<i>I just really think we needed to put it behind us and just enjoy the pregnancy and look forward to meeting him. And we just stopped talking about it, we 'parked it', because it's probably nothing. (Interview 14, paternal SL)</i>
Ultrasound helps	18	<i>I hold the hospital very dear (guld værd) because they gave us those extra scans. So I could get evidence that he was developing, no deformities, just everything just like it should be. And I could relax for a while. (Interview 11, normal)</i>
Theme 3: Managing an inherited CNV		
Normalising CNV's	19	<i>There must be many chromosome errors out there, I think. Which we just don't discover. That are not necessarily that serious, but just how people are. I'm not worried, but on an intellectual level, I'm intrigued. (Interview 12, paternal VUS)</i>
	20	<i>I remember when they told us that it was inherited from you [partner]... It was such a relief! You know, I chose to have children with Morten because I think he's a wonderful person with all the right qualities. I'd love to have a mini-him running around the house. So in that moment I stopped worrying and just looked forward to meeting our baby. (Interview 8, paternal SL)</i>
Cause for reflection	21	<i>I worry about a lot of things... I'm very sensitive and vulnerable... and I thought: is that because of that error, or is it just because that's who I am? Would I still be like this, if I didn't have that error? (Interview 15, maternal SL)</i>
Theme 4: Future meaning of the CNV result		
Birth changes everything	22	<i>The pregnancy was a struggle, one day at a time. But after birth... when I had him in my arms... wow, all that disappeared. I mean, physically holding him, seeing him... that he was alive and functioning and absolutely beautiful. (Interview 2, de novo VUS)</i>
Special attention	23	<i>Woman: Yes. And we really do a lot to get him off to a good start. We train a lot with him. We do a lot of motor skill games and he is very advanced already. Partner: We might be training a little bit more. I think my focus is greater than or would have been... (interview 8, paternal SL)</i>
The right to be imperfect	24	<i>He's allowed to be imperfect. He's allowed to be Emil of Lönneberga and get into trouble without it being because of his chromosome error. He's allowed to find</i>

school difficult – as all boys do – [...] And if he struggles too much, then maybe we can have that talk, but it's his right to have to struggle because life is like that.
(Interview 15, maternal SL)

25 *But if something sticks out slightly with him... I think automatically we will think: It that it? So I think we need to really pull ourselves together and not... you know, it could also just be a boy thing.* (Interview 5, de novo SL)

26 *We are not going to tell everybody. Because I don't want it to be like... when he's three and there is an issue, that people will say 'oh, well, that's because he has that chromosome error. Nobody needs to know. My parents know and my siblings know, but I've made it very clear that it's not their story to tell. I don't want it to be a stigma for him to carry* (interview 14, paternal SL)

SL, susceptibility loci; VUS, variant of uncertain significance