University of Cincinnati

Date: 3/25/2016

I, Hayley Grandine, hereby submit this original work as part of the requirements for the degree of Master of Science in Genetic Counseling.

It is entitled:
Patient and Parent Experiences of Dual Genetic Diagnoses: Neurofibromatosis Type 1 and an Additional Genetic Disease

Student’s name: Hayley Grandine

This work and its defense approved by:

Committee chair: Elizabeth Schorry, M.D.
Committee member: Carrie Atzinger, M.S., C.G.C.
Committee member: Martha Walker, M.S., C.G.C.
Patient and Parent Experiences of Dual Genetic Diagnoses:
Neurofibromatosis Type 1 and an Additional Genetic Disease

A thesis submitted to the
Graduate School
of the University of Cincinnati
in partial fulfillment of the
requirements for the degree of

Master of Science
in the Department of Pediatrics
of the College of Medicine

By

Hayley Grandine
B.A. Whitman College
May 2014

Committee Chair: Elizabeth Schorry, MD
Committee Members: Martha Walker, MS, LGC, Carrie Atzinger, MS, CGC
Abstract

Dual or multiple genetic diagnoses, although uncommon, are anecdotally evident from clinical geneticists and genetic counselors, and are found in 1% of individuals who undergo whole exome sequencing. Currently, there is no published research on the impact on families and patients of having a dual genetic diagnosis. This qualitative, exploratory study involved open-ended interviews with adult patients and parents of children affected by Neurofibromatosis Type 1 and another genetic disease. The goal was to develop an initial understanding of how having a second genetic diagnosis affects this population. A total of nine individuals participated in the study: six parents who had a child with a dual diagnosis and three adults with a dual diagnosis themselves. Thematic analysis was used to identify common themes in participant responses. Results indicated that the parents were strongly emotionally impacted by the diagnoses and often felt isolated. However, the affected adults did not report these negative impacts and considered themselves to be only mildly affected by their conditions. Both findings are consistent with previous research on individuals with one genetic condition. Although the difficulties of complex medical management and navigating the healthcare system also exist for families dealing with one genetic diagnosis, these challenges may be more severe for families dealing with two. Future research can be guided by these initial findings to further explore the needs of this population.

Key words: Neurofibromatosis Type 1, Dual Diagnosis, Genetic Disease, Emotional Impact, Life Experiences
Acknowledgements

Acknowledgments

This project was supported by a Research Award from the Division of Human Genetics at Cincinnati Children’s Hospital Medical Center. We would like to thank Sarah Collier for transcript coding and data analysis efforts. We would also like to thank Dr. Ann Olney, Dr. Bruce Korf, and Dr. Ashley Cannon for their help in recruiting participants for the study.
# Table of Contents

Introduction ................................................................................................................................. 1  
Methods ........................................................................................................................................ 5  
Results ......................................................................................................................................... 8  
Discussion ..................................................................................................................................... 13  
Tables .......................................................................................................................................... 18  
References .................................................................................................................................... 21  
Appendix 1 – Adult Interview Guide ............................................................................................... 23  
Appendix 2 – Parent Interview Guide ............................................................................................. 27  
Appendix 3 – Codebook .................................................................................................................. 31
List of Tables and Figures

**Table 1** – Studies in which two or more genetic diagnoses were identified

**Table 2** – Profile of participants

**Table 3** – Perception of relative disease severity
Introduction

The diagnosis of a genetic disorder affects many aspects of the lives of patients and families. These include medical care, psychosocial wellbeing, reproductive planning, and others. Little is known about the impact of being diagnosed with more than one genetic disorder. Dual or multiple genetic diagnoses, although uncommon, are anecdotally evident from practicing clinical geneticists and genetic counselors who can often readily provide a handful of examples in their patients. On a broader scale, ascertainment of dual genetic diagnoses seems to be increasing with the availability of hundreds of genetic diagnostic tests through the advent of whole exome sequencing (WES), next generation sequencing (NGS), and other laboratory technologies.

Among the first 250 patients on whom WES was performed at Baylor College of Medicine, dual diagnoses were identified in 4 people (Yang et al., 2013). In this same cohort, 30 patients received a medically actionable incidental finding in a gene unrelated to the symptoms for which the patient underwent WES. Twenty-three patients received a dual diagnosis when WES was performed on the next 2000 consecutive patients at Baylor, and 92 received a medically actionable incidental finding (Yang et al., 2014). In a study of 3,040 consecutive patients who had WES performed at the GeneDx commercial laboratory (www.genedx.com), 25 patients were found to have two distinct genetic diagnoses, three patients had three distinct genetic diagnoses, and 129 patients out of 2,091 had a medically actionable incidental finding (Retterer et al., 2015). Table 1 summarizes all three studies. These data suggest that dual genetic diagnoses occur in at least 1% of individuals undergoing WES. To view these findings in perspective, it is important to note that patients who undergo WES make up only a small proportion of individuals receiving genetic evaluation, and there are many other patients who receive genetic diagnoses through clinical genetic evaluation without WES.
Common knowledge indicates that a genetic diagnosis has significant impact on individuals and families. Indeed, public and private organizations started forming decades ago for the specific purpose of sharing emotional support and reducing feelings of isolation in families with a genetic disorder. The Genetic Alliance, created in 1986, is today a network of more than 1,200 disease-specific advocacy organizations plus universities, private companies, government agencies, and public policy organizations (http://www.geneticalliance.org). The Alliance, does not, however, include any support groups dedicated to individuals who have two or more genetic diagnoses (Alyson Krokosky, personal communication, January 24, 2016).

Many research studies have documented the impact of genetic diagnoses on individuals and families. McAllister et al. (2007) identified common emotional and societal effects for patients who have any genetic disease. The emotional effects included worry about risks to children, anger, anxiety, uncertainty, guilt, sadness and grief, depression, and redemptive adjustment. Societal effects included family conflict and communication difficulties, isolation, stigma, reduced life choices, financial burden, misinformation, and secrecy. Hildenbrand et al. studied disease-related stressors on families who have a child with sickle cell disease. These stressors included medical complications, treatment, disruption in daily routine, emotional reactions, social challenges, and concerns about the future. (Hildenbrand, Barakat, Alderfer, & Marsac, 2015).

There is also information available on how families deal with the emotional and societal impact of genetic disease. Hildenbrand et al. (2015) studied stressors and coping strategies in families who have children with sickle cell disease and found that the patients used strategies of seeking social support, maintaining normalcy, emotional expression, relaxation, distraction, and cognitive avoidance. Their parents’ strategies included social support, expressing emotions,
maintaining normalcy, educating others, fostering child autonomy, engaging in spirituality and self-care, and promoting acceptance. A 2014 study of caregivers for children with cystic fibrosis found two main categories of coping strategies: (1) “Proactive,” which included strategies such as planning, positive reframing, and acceptance, and (2) “Avoidant,” which included self-distraction, substance use, and self-blame (Sheehan, Hiscock, Massie, Jaffe, & Hay, 2014.) Increased use of “avoidant” strategies was associated with increased problem behaviors in the caregiver’s child and poorer mental health of the caregiver.

Parental perception of disease severity is another factor contributing to adjustment and coping. Adolescents affected by a genetic disease may not have the same perception of the severity of their disease as their parents do. One study found that adolescents with neurofibromatosis type 1 (NF1) viewed their condition as being less severe than their parents perceived it to be (Sebold, Lovell, Hopkin, Noll, & Schorry, 2004). However, this same group found that parents did have an accurate perception of their child’s disease severity, correlating with the degree of medical severity assessed by a clinician. Males with Duchenne muscular dystrophy (DMD) and their parents have also been studied: Boys with DMD did not score lower than a control group of healthy peers on a health-related quality of life questionnaire, though their parents significantly underestimated their sons’ moods and emotions, self-perception, and social acceptance in comparison to what the children themselves reported (Houwen-van Opstal, Jansen, van Alfen, & de Groot, 2014). The majority of research has involved patients and families who are dealing with a single genetic disease. Searches of Pub Med (www.pubmed.com) and Journal of Genetic Counseling revealed only one study on the impacts of dual genetic diagnoses: Nassab et al (2015) described the experiences and challenges of five parents whose children had any two genetic diagnoses. Novel experiences faced by these families that differ from families dealing
with just one genetic disease included frustration toward health care providers who are
dismissive of parental input on medical management, delay in second diagnosis due to
misattribution of symptoms to the first diagnosis, and difficulty balancing medical management
of two conditions.

With better ascertainment of genetic diagnoses through technological advancement and lowered
costs of testing, the number of dual genetic diagnoses is likely to increase. There is a need for
research to identify the psychosocial and genetic counseling needs of people with dual genetic
diagnoses, define how their clinical and personal experiences may differ from the experiences of
people with single genetic diagnoses, and learn how health professionals can better support
patients and families.

This study focused on adults and children who have NF1 and at least one other genetic diagnosis.
NF1 is a relatively common genetic disorder affecting 1 in 3000 individuals (Jett & Friedman,
2010). NF1 is characterized by multiple café-au-lait spots, axillary and inguinal freckling,
multiple cutaneous neurofibromas, and iris Lisch nodules. About one-half of affected individuals
also have learning disabilities. Less common symptoms include plexiform neurofibromas, optic
nerve or other central nervous system gliomas, malignant peripheral nerve sheath tumors,
scoliosis, tibial dysplasia, and vasculopathy. Inheritance is autosomal dominant and de novo
mutations account for about one-half of cases (Jett & Friedman, 2010).

There has been much research on how NF1 as a sole diagnosis affects families. Overall, NF1
causes highly variable phenotypes and highly variable levels of quality of life and functional
disability dependent on that phenotype (Garwood et al., 2012). Scores on the Pediatric Quality of
Life Inventory, which looks at physical, emotional, social, and school functioning, are lower
among children with NF1 than among children without NF1 in a control group. Lower scores are specifically related to short stature, neurofibromas, bone lesions, and psychiatric problems (Saltık & Başgül, 2013). Parents of children with NF1 tend to have higher levels of stress than parents of typically developing children (Esposito et al., 2014). Mothers of children with NF1 whose children have greater levels of neurological impairment than other children with NF1 were found to have higher levels of distress and family conflict, and lower levels of social support (Reiter-Purtill et al., 2008). There have been case reports of individuals who have a dual diagnosis of NF1 and another genetic disorder. The second diagnoses reported include Tuberous Sclerosis Complex, Multiple Endocrine Neoplasia Type 2, Huntington’s disease, and Down syndrome. (Bosanko et al., 2016, Ercolino et al., 2014, Kawakami et al, 2014, Schaffer et al. 2014).

This research study used qualitative analysis to address the following question: What is the experience of patients and families who have a dual diagnosis of NF1 and another genetic condition? By comparing the experiences of these families to what is already reported in the literature on those with just NF1 or other single genetic diseases, a starting point was created for understanding how the addition of a second diagnosis affects the experiences, coping strategies, and unique needs of this population.

**Methods**

This qualitative research study involved analysis of data collected in semi-structured telephone interviews using an interview guide which was created specifically for this study. This study was
determined to be exempt from review by the Cincinnati Children’s Hospital Medical Center (CCHMC) Institutional Review Board (Study # 2015-2855).

Participants

Eligible participants included adults age 18 or older who had NF1 and another serious genetic condition and parents who have a child under age 18 diagnosed with NF1 and another serious genetic condition. Exclusion criteria were: being non-English speaking, having a second diagnosis caused by multifactorial inheritance, or having a second diagnosis determined to be non-serious by the research team. In this study, “serious” was defined as affecting health, affecting medical care, or causing intellectual disability.

NF1 was chosen as the common genetic diagnosis of participants because of available data on its effect on quality of life and because of its prevalence and the large pool of potential research participants in the NF clinic at CCHMC.

Recruitment methods:

- Query of the electronic medical records and NF1 clinical database maintained at CCHMC and sending invitation letters by US Mail to eligible adult patients and parents
- Solicitation of potential participants via an information table at the July 2015 NF family conference at CCHMC
- Posting of announcements of the study in the Children’s Tumor Foundation NF Registry and on the website www.ctf.org
- Sending of emails to members of the NF Clinical Consortium and the National Society of Genetic Counselors, asking that they inform eligible patients and families about the study and have them contact the PI if interested
Data Collection

Data were collected using semi-structured telephone interviews. All interviews were conducted by the PI, using one of two interview guides which were created by the PI specifically for the current study and designed to take 15-45 minutes to complete (Appendix A and B). One interview guide (Appendix A) was used for participants who were interviewed about their experiences as a parent of a child with NF and another genetic condition, and the other interview guide (Appendix B) was used for participants who were interviewed about their experiences as an adult who has NF and another genetic condition. Consent for participation was obtained verbally over the telephone, immediately prior to the interview being conducted. The interview guide included demographics questions on participants’ ages, level of education, and family history. Open-ended questions related to how participants’ feelings have changed over time, effects of the diagnoses on daily life, support systems, severity and medical management of the two diseases, access to genetic counseling, and views on genetic counseling. Interviews were audio-taped and their content was transcribed by the PI using Microsoft Word. A $10 gift card was mailed to each participant after the interview as compensation for their time.

Data Analysis

Thematic analysis was used to identify common themes in participant responses. Data were analyzed by the interviewer and a second coder with the computer program Atlas.ti Version 7.5.2. Codes developed from the interview data were sorted into categories based on relatedness. To address inter-coder variability, the PI and second coder met purposely to discuss discrepancies in coding and reach a consensus for each discrepancy; this was done for all interviews.
Results

Participants

There were eleven children and six adults with dual diagnoses of NF1 and another genetic disease ascertained from the medical record search and NF1 database search at CCHMC. One child was excluded from the study because his family was not English speaking, and one adult had already been solicited from the NF family conference. The other potential participants were sent informational letters about the study, and only one parent replied to the letter. After being contacted via phone, two affected adults and two additional parents of affected children also agreed to participate.

Thirty-six additional individuals expressed interest in the study after learning about it online from the CTF and NF Facebook groups (where the study was shared by others who had seen it on CTF), but none of these individuals met inclusion criteria of having a second, serious genetic diagnosis or an affected child under age 18, or they did not respond to email replies from the PI. Two individuals contacted the PI after learning about the study from a member of NSFC or the NF Consortium.

In total, nine people participated in this study. Three were adults who had NF1 and another genetic diagnosis themselves, and six were parents of children with NF1 and another genetic diagnosis. See Table 2 for full details. Participants ranged in age from 24 to 60 years old. Ages of the children ranged from to 3 to 11 years old. The interviews ranged in length from 12 minutes to 43 minutes, with a mean length of 24 minutes.
Emergent Themes

Themes which emerged from the data analysis were emotions, actions, and experiences of participants. These themes are detailed below.

*Emotions about the diagnoses*

Participants were asked about their feelings and emotions at the time of diagnosis, currently, and how things have changed over time. There was a wide variety of responses to all three of these questions. Participants recalled a wide range of emotions immediately after receiving a diagnosis. The most common emotion described by participants was fear, which four parents expressed. Other common emotions that were related by three parents each were devastation, sadness, and a feeling of “why me”. The two co-parents who had a child who inherited both genetic conditions from a parent expressed guilt, although the four participants who had a child who inherited one genetic condition from a parent did not express this. Two affected adults and one parent said that they felt that the second diagnosis was “just another medical thing going on”, and that it wasn’t a very emotional experience.

Regarding how their emotions have changed since the time of diagnosis, participants again gave many different responses. Three commonalities, shared by three participants each, were the following: 1) They try to just deal with day-to-day management of the conditions and not dwell on feelings, 2) The diagnoses mean different things to them at different life stages, and 3) Their feelings about the diagnoses have not changed at all over time. Participants also contributed thoughts about their own condition or their child’s diagnoses at the time of the interview. Three participants, two adults and one parent, shared that the diagnoses are part of the affected person’s self-identity. The most prevalent comment, which was expressed by two affected adults and two
parents, was that the diagnoses are not completely negative, and are something unique about the person.

“[My feelings about the diagnosis haven’t] changed too much…you either have it or you don’t have it, if I have it [my life is] still the same as it was before.” – Adult with NF and a 2nd diagnosis

*Actions taken by participants*

Participants reported that they had taken action in the areas of medical management, ways of seeking support, coping strategies, and lifestyle changes. Nearly every participant had put time and effort into managing a complex medication situation. Six had frequent doctor appointments, five had frequent appointments for therapies, two had many required medications, and another two participants reported that the travel required to see different specialists is frequent and time-consuming.

The PI also probed participants regarding their family support and use of support groups. Five parents expressed feelings of isolation. Some felt isolated because they are not geographically close to other people with the same diagnosis, while others felt isolated because one or both of the diagnoses were so rare. Five participants did have friends, from a support group or otherwise, who had themselves or had children who had health problems or genetic conditions who were a source of support. Emotional support from family members was received by four participants. Two parents talked about using online support groups, such as Facebook groups. Two adults and one parent said that they did not have anyone that they talked to about the diagnoses. Besides obtaining support from other people and online, all six parents used information-seeking as a method of coping.
“But, you know I’m sort of a type A personality so I immediately started doing research, and forums and parent support groups, and, I just started learning the best I can…” – Parent of a child with NF1 and a 2nd diagnosis

Other methods, mentioned by one parent each, were religious faith, appreciating the small things, living in the moment, avoiding information, and involvement in advocacy groups. One method, reflecting that the situation could be worse than it is, was noted by three parents. The three affected adults talked about obtaining support through family and friends but no other methods of coping.

The main lifestyle changes mentioned throughout the interviews had to do with employment or financial problems. Two adults and two parents expressed being affected financially by the diagnoses, and two parents had to quit their job or cut down on hours as a result of the diagnoses.

Experiences relating to the diagnoses

Participants reported on many different types of experiences they have had, such as the experience of receiving both diagnoses, how much information they were given at that time, perception of how serious the diseases are, experiences with the healthcare system, and experiences with and thoughts regarding genetic counseling.

When asked to recall the time of either diagnosis, the most prevalent experience, shared by five parents and one adult, was that the information and resources given about the condition were insufficient or non-existent.
“They didn’t have anybody that really sat down and talked to us… I can’t believe that in this day and age that the hospitals don’t offer that for families as they are getting ready to leave the hospital.” – Parent of a child with NF1 and a 2nd diagnosis

Two parents felt that the resources they were given at the time of diagnosis were adequate. There was a mix of expected and unexpected diagnoses. Four parents and one adult said that one or both of the diagnoses had been suspected for a while, and five parents and one adult said that at least one of the diagnoses was completely unexpected.

Perception of disease and correlation with medical doctors’ viewpoints was also explored. Four participants (three adults and one parent) considered at least one of the diagnoses to be mild. Five considered at least one diagnosis to have variable severity depending on the day or year, and seven participants considered one diagnosis to be more severe than the other. NF1 was considered to be the more severe diagnosis in five of the nine cases. See Table 3 for details. Six participants said that their doctor agrees about which diagnosis was more severe (if either), and one parent and one affected adult said that their doctor does not agree.

A problem that was mentioned by three parents was a feeling that they or their child looks healthier than they are, which causes others to not understand the problems they face.

“She looks ok… we allow her to be as much as a child as she possibly can be and I think that it has maybe fooled some people, like you know they’re fine, they’ve got it together when really we are falling apart…” – Parent of a child with NF1 and a 2nd diagnosis

There were several viewpoints related to the healthcare system. One adult and two parents thought that their doctors didn’t understand the diagnoses or combination of them, and that they had to be the one explaining the problem to the doctor. Two parents and one adult mentioned
experiencing problems with their insurance company. Three parents didn’t have appropriate medical facilities close to their home. The most common experience, related by four parents, was that they have to be their child’s advocate in order to get the care that their child needs.

Participants were asked about their experiences with genetic counseling and thoughts about wanting or not wanting genetic counseling in the future. Five participants had previously had genetic counseling, and found the experience helpful. Main reasons for wanting to see a genetic counselor included family planning purposes and finding resources, which were identified by three participants each, and helping a partner or family member understand the diagnoses and simplifying genetic information; each of these was identified by two participants.

Discussion

In this study, a qualitative approach was used to explore nine individuals’ experiences of how a dual genetic diagnosis of NF1 and a second genetic disorder affects their lives.

Discussion of Themes

There was a large variety of feelings identified about the diagnoses, both with emotions regarding the initial diagnosis and how things have changed over time. Although some emotions such as fear were identified by multiple participants, overall each participant shared a different combination of emotions. Feelings reported included anger, uncertainty, guilt, and sadness, which overlap with those reported by McAllister et al (2007) in patients with genetic disease.

A unique aspect of this study was learning that three, or one third of participants, felt a lack of emotion after receiving the second genetic diagnosis. Two of the participants who felt this way
were affected adults themselves. As a set, they seemed to be less emotionally affected by the diagnoses compared to the parents. The only adult who did not report feeling this way was not old enough to remember the time of her diagnosis. The idea that individuals who have one or more genetic diagnoses themselves feel less emotional about the diagnosis is supported by the work of Sebold et al (2004) and Houwen-van Opstal (2014), which showed that children and adolescents affected with a genetic disease considered themselves to be less severely affected than their parents consider them to be. For example, Sebold et al (2004) gave the Perception of Severity of Chronic Illness questionnaire to a group of adolescents with NF1 and their parents, and as a group the adolescents’ scores were significantly lower than the parents’. Qualitative analysis revealed that compared to the parents, the adolescents were less worried about both current medical complications and the uncertainty of potential future complications.

Many participants expressed that finding support was difficult, often due to geographical factors or rarity of the diagnoses, although most participants (six out of nine) did report some form of social support. Reiter-Purtill et al (2008) found that among mothers of children who have NF1, social support was significantly correlated to the child’s level of neurological impairment, with mothers of children who had more impairment having lower levels of support. Due to the phenotypic diversity of NF1 and the second diagnoses, and this study’s low sample size, it is difficult to hypothesize whether this reported difficulty finding support is greater than for those dealing with a single genetic diagnosis. It is possible that having a more medically complex child would similarly lead to lower levels of support.

Among other methods of coping with the diagnoses, information seeking was by far the most frequently used strategy. Interestingly, this method was used by all six parents who were interviewed and none of the three affected adults. This suggests that information seeking is a
useful tactic for parents trying to learn about an unfamiliar diagnosis. Affected adults may be less likely to seek information either due to a level of comfort with their condition, or to a learning disability that prevents them from seeking medical information. The only coping mechanism reported by the three affected adults was talking with others who have the same diagnosis or other health problems.

The largest area in which study participants reported having had problems was with the healthcare system, with the major concern being that not enough information was given to them at the time of diagnosis. Of interest, all of the participants were seen in a major medical center with an established NF clinic for at least part of their medical care, and extensive information would have been available through these resources. The lack of information was likely a driving factor in why every parent interviewed reported seeking information as one of the first things they did to help cope with the diagnosis. It is unknown how much information was truly reported to participants – the fact that many participants felt scared, angry, overwhelmed, or other strong emotions at the time of diagnosis may have impacted how much information they were able to take in at the time, leading them to process less information that what was actually presented. However, regardless of the reasons behind it, many participants reported that they felt that they were on their own in learning about the diagnoses and they would have liked to have been given more information by their healthcare provider. This is an important point to keep in mind for all providers who are responsible for giving these kinds of diagnoses to patients and families.

The feeling of being “on their own” may be increased for individuals and families who are dealing with not one, but two or more rare diagnoses. While many families of patients with a single genetic diagnosis deal with many of these same problems, including lack of information, insurance and employment issues, these issues may be amplified by having more than one rare
disease. For example, when participants reported needing to educate their doctors about their diagnoses, it is more likely with two diagnoses that a doctor won’t be familiar with one of them, or that a doctor may never have seen a patient with the same combination of conditions and be unsure how to manage the patient. These problems could result in parents feeling a need to be their child’s advocate in order to receive the best care for their child, as they may be the only one familiar with their child’s unique medical situation. As Nassab et al (2015) reported, parents feel frustrated with providers who are dismissive of their input, and parents in our study felt that they had no choice but to advocate for their child.

**Study Limitations**

There are several limitations to this study which must be acknowledged. The small sample size, although intended due to the exploratory nature of the study, limits the generalizability of the findings. The fact that all patients had NF1 as a common diagnosis also limits the generalizability of the findings to other genetic conditions. In addition, participants were self-selecting, so the opinions and experiences of those who participated may differ from those who did not participate in the study.

**Research Recommendations**

Further qualitative research with a larger sample size and wider variety of diagnoses would be helpful in confirming and expanding the findings of this study.

**Conclusions**

This is one of the first studies with the goal of examining the patient and parent experience of having dual genetic diagnoses, and there are several key findings which will be helpful in
informing future research. One major finding is the sense of isolation noted by parents, and the
difficulty in finding social support when a child has multiple complex conditions. In our small
sample, adults with NF1 and second genetic disease appeared to be less emotionally impacted
and often perceived that they were only mildly affected by the condition, in contrast to the more
intense emotions and large impacts reported by parents. Finally, while participants were affected
in similar ways as expected in families dealing with one genetic diagnosis, this impact may be
exacerbated by the need to manage two conditions and navigate the healthcare system with this
rare combination. Lack of familiarity by healthcare providers adds to the challenge for these
families.
# Tables

<table>
<thead>
<tr>
<th>Reference</th>
<th>Sample Description</th>
<th>N</th>
<th># of patients with dual/triple diagnosis (%)</th>
<th># of patients with incidental finding (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yang et al 2013</td>
<td>Primarily pediatric patients seen at Baylor College of Medicine</td>
<td>250</td>
<td>4 (1.6%)</td>
<td>30 (12%)</td>
</tr>
<tr>
<td>Yang et al 2014</td>
<td>Primarily pediatric patients seen at Baylor College of Medicine</td>
<td>2000</td>
<td>23 (1.15%)</td>
<td>92 (4.6%)</td>
</tr>
<tr>
<td>Retterer et al 2015</td>
<td>Patients who had exome sequencing through GeneDX</td>
<td>3040</td>
<td>28 (.92%)</td>
<td>129 (6.2% out of 2091)</td>
</tr>
</tbody>
</table>

Table 1. Studies in which two or more genetic diagnoses were identified
<table>
<thead>
<tr>
<th>Interview Type</th>
<th>Participant Number</th>
<th>Age range and sex of participant</th>
<th>Genetic disorder status of participant</th>
<th>2nd diagnosis</th>
<th>Age range and sex of affected child</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adult</td>
<td>1</td>
<td>Female, 21-25</td>
<td>Dual diagnosis</td>
<td>Leri-Weill dyschondrosteosis</td>
<td>N/A</td>
</tr>
<tr>
<td>Adult</td>
<td>2</td>
<td>Male, 31-35</td>
<td>Dual diagnosis</td>
<td>Charcot-Marie-Tooth disease</td>
<td>Male, 1-5 (see footnote)</td>
</tr>
<tr>
<td>Adult</td>
<td>3</td>
<td>Female, 21-25</td>
<td>Dual diagnosis</td>
<td>Sickle cell disease</td>
<td>N/A</td>
</tr>
<tr>
<td>Parent</td>
<td>4</td>
<td>Female, 36-40</td>
<td>Single diagnosis (Long QT)</td>
<td>Long QT &amp; Common variable immunodeficiency</td>
<td>Female, 6-10</td>
</tr>
<tr>
<td>Parent</td>
<td>5</td>
<td>Female, 46-50</td>
<td>Unaffected</td>
<td>Prader-Willi syndrome</td>
<td>Male, 1-5</td>
</tr>
<tr>
<td>Parent</td>
<td>6</td>
<td>Male, 41-45</td>
<td>Unaffected (Carrier of ectodermal dysplasia)</td>
<td>Ectodermal dysplasia, unspecified type</td>
<td>Female, 1-5</td>
</tr>
<tr>
<td>Parent</td>
<td>7</td>
<td>Female, 21-25</td>
<td>Unaffected</td>
<td>Charcot-Marie-Tooth disease</td>
<td>Male, 1-5</td>
</tr>
<tr>
<td>Parent</td>
<td>8</td>
<td>Male, 56-60</td>
<td>Unaffected</td>
<td>Partial trisomy 15q</td>
<td>Female, 6-10</td>
</tr>
<tr>
<td>Parent</td>
<td>9</td>
<td>Female, 31-35</td>
<td>Single diagnosis (NF1)</td>
<td>Klinefelter syndrome</td>
<td>Male, 11-15</td>
</tr>
</tbody>
</table>

*Table 2* Profile of Participants. Adult participants have a diagnosis of NF1 and the specified second diagnosis, and parent participants have a child who has a diagnosis of NF1 and the specified second diagnosis. Details on how individual participants were recruited is omitted in the interest of confidentiality and anonymity.

1 Participants 2 and 7 are co-parents. Participant 2 was interviewed regarding having a dual diagnosis himself, and not specifically regarding his son.

2 The wife of participant 8 was involved in parts of the interview and answered some of the questions as well.
NF is more mild than second diagnosis | NF is more severe than second diagnosis | The diagnoses are equal in severity
---|---|---
Parents | 2 | 4 | 0
Adults | 1 | 1 | 1

*Table 3* Perception of Relative Disease Severity
References


Appendix 1 – Adult Interview Guide

Introduction: Hello, I am calling for (name). My name is Hayley Grandine and I am a genetic counseling graduate student at the University of Cincinnati and Cincinnati Children’s Hospital. I am working on the research study “Exploring Dual Diagnoses of Neurofibromatosis Type-1 and an Additional Genetic Disease.” We are talking with adults who have both NF1 and another genetic disease. We hope that learning about your and others’ experiences will help health care providers better serve these individuals with more than one genetic diagnosis. It is completely your choice whether or not you want to participate in the study. There are no right or wrong answers or feelings in response to these questions. If you don’t want to answer any of the questions, we can skip them, and you can end the interview at any time. Also, the conversation will be tape recorded.

*Can you tell me why you want to do the study?*

Do you still want to have the interview today?

I will first ask some basic questions about you, and then we will move on to some more personal questions about your experiences. Are you ready to get started?

**Demographics**

1. How old are you?
2. Are you male or female?
3. How far did you go in school?
4. Our records show that you have NF1 and *(other disease)* – is this correct?
5. Does anyone else in your family have NF1?
6. Does anyone else in your family have *other disease*?
Thanks for answering those questions for me! Now, I am going to ask about when you got diagnosed and what that was like, if you were old enough to remember.

**Diagnosis**

7. When were you diagnosed with NF1?

8. When were you diagnosed with other disease?

9. *If they were old enough to remember* - Can you describe what it was like when you were diagnosed with *the first diagnosis*? What happened, and how did you feel?

   **Follow up questions, depending on what he/she says:**

   a. *Who gave you the diagnosis?*

   b. *How much information were you given about the diagnosis (genetics, prognosis, management, recurrence risk, etc)*

   c. *How did you feel after getting the diagnosis?* *(how you felt right then, how you felt when you got home, what you did after the appointment, conversations you had with family or friends)*

   d. *Was the diagnosis expected or a surprise?*

10. *If they were old enough to remember* - Now, can you describe what it was like when you were diagnosed with *the second diagnosis*? Again, what happened, and how did you feel?

   **Same follow up questions as #11**

**Perception of Disease Severity**

11. In what ways do the two diagnoses affect your daily life?

   **Follow up questions**
a. How does NF affect daily life?

b. How does the other diagnosis affect daily life?

c. How does your doctor describe your disease severity?

d. What is the medical management for NF1?

e. What is the medical management for the other disease?

f. How do you feel about the fact that you have both diseases?

12. Which of the two diseases do you think is more serious?

a. Is there one diagnosis that you focus on more?

b. And why?

c. Is there one diagnosis that gets focused more by your doctors?

Coping

13. Are you involved in any support groups?

a. Do you have people that you can talk to about your medical situation?

14. How have your feelings about having NF and other disease changed since the time that you first received the diagnoses?

Thanks again for answering all of these! We are almost done. The last part of our discussion is about genetic counseling.

Genetic Counseling Needs

Genetic counseling is the process of helping people understand and adapt to the medical, emotional, and family effects of the genetic parts of diseases. Often this process involves looking at family and medical histories to assess the chance of whether someone can get or pass on a
disease, teaching about inheritance, testing, management, and providing resources and counseling to help families deal with their risk or condition (Resta et al., 2006)\(^1\).

15. Have you ever talked to a genetic counselor?

- **a. If yes - How was that experience? Who provided the genetic counseling to you?**
  
  Did you meet with a genetic counselor, genetics doctor, and/or genetics nurse?

- **b. If yes – Did you find it helpful? Were there ways that it could have been more helpful?**

- **c. If not – Do you think that this is something you would be interested in? Why or why not?**

Appendix 2 – Parent Interview Guide

Introduction: Hello, I am calling for (name). My name is Hayley Grandine and I am a genetic counseling graduate student at the University of Cincinnati and Cincinnati Children’s Hospital. I am working on the research study “Exploring Dual Diagnoses of Neurofibromatosis Type-1 and an Additional Genetic Disease.” We are talking with parents of children who have both NF1 and another genetic disease. We hope that learning about your and others’ experiences will help health care providers better serve the families of individuals with more than one genetic diagnosis. It is completely your choice whether or not you want to participate in the study. There are no right or wrong answers or feelings in response to these questions. If you don’t want to answer any of the questions, we can skip them, and you can end the interview at any time. Also, the conversation will be tape recorded.

Can you tell me why you want to do the study?

Do you still want to have the interview today?

I will first ask some basic questions about you and your child, and then we will move on to some more personal questions about your experiences. Are you ready to get started?

Demographics

1. What is your age?
2. Are you male or female?
3. How far did you go in school?
4. Our records show that one of your children has NF1 and (other disease) – is this correct?
5. What is the name of your child who has NF1 and name of other disease? How old is he/she?
6. Do you have any other children? What ages are they?
   
   a. *If other children* – do any of your other children have NF1?
   
   b. *If other children* – do any of your other children have *other disease*?
   
   c. *If other children* - do any of your other children have NF1 and *other disease*?

7. Do either you or *name of child’s* father/mother have NF1?

8. Do either you or *name of child’s* father/mother have *other disease*?

Thanks for answering those questions for me! Now, I am going to ask about *name of child’s* diagnosis and what that was like.

**Diagnosis**

9. When was *name of child* diagnosed with NF1?

10. When was he/she diagnosed with *other disease*?

11. Can you describe what it was like when *name of child* was diagnosed with the first diagnosis? What happened, and how did you feel?

   **Follow up questions, depending on what he/she says:**

   a. *Who gave you the diagnosis?*

   b. *How much information were you given about the diagnosis (genetics, prognosis, management, recurrence risk, etc)*

   c. *How did you feel after getting the diagnosis? (how you felt right then, how you felt when you got home, what you did after the appointment, conversations you had with family or friends)*

   d. *Was the diagnosis expected or a surprise?*
12. Now, can you describe what it was like when name of child was diagnosed with the second diagnosis? Again, what happened, and how did you feel?

Same follow up questions as #11

Perception of Disease Severity

13. In what ways do the two diagnoses affect (name of child’s) daily life?

Follow up questions

a. How does NF affect daily life?

b. How does the other diagnosis affect daily life?

c. How does your doctor describe name of child’s diseases severity?

d. How severely affected would you say (name of child) is by his diseases?

e. What is the medical management for NF1?

f. What is the medical management for the other disease?

14. Which of the two diseases do you think is more serious?

a. Is there one diagnosis that you focus on more?

b. And why?

c. Is there one diagnosis that gets focused more by name of child’s doctors?

Coping

15. In what ways do name of child’s diagnoses affect YOUR daily life?

a. How do you feel about name of child having both NF1 and other disease?

16. Are you involved in any parent support groups?

a. Do you have people that you can talk to about your child’s medical situation?
17. How have your feelings about *name of child* having NF and *other disease* changed since the time that you first received the diagnoses?

Thanks again for answering all of these! We are almost done. The last part of our discussion is about genetic counseling.

**Genetic Counseling Needs**

Genetic counseling is the process of helping people understand and adapt to the medical, emotional, and family effects of the genetic parts of diseases. Often this process involves looking at family and medical histories to assess the chance of disease for family members, teaching about inheritance, genetic testing, management, resources, or research, and counseling to help families adapt to the condition (Resta et al., 2006).  

18. Have you ever talked to a genetic counselor?

   a. *If yes - How was that experience? Who provided the genetic counseling to you? Did you meet with a genetic counselor, genetics doctor, and/or genetics nurse?*

   b. *If yes – Did you find it helpful? Were there ways that it could have been more helpful?*

   c. *If not – Do you think that this is something you would be interested in? Why or why not?*

---

Appendix 3 – Codebook

Themes/Codes

1. **Emotions** – This theme focuses on emotional reactions/consequences of having/having a child with two or more genetic diseases
   a. After/during diagnosis – This theme focuses on participant’s feelings immediately after receiving a diagnosis
      1. Used to it – Use this code if the participant felt that the diagnosis was just one more medical thing going on
      2. Devastating – Use this code if the participant was very upset after receiving the diagnosis
      3. Want to fix – Use this code if the participant wanted to make the diagnosis go away or fix it
      4. Scared – Use this code if the participant felt scared during the process of receiving the diagnosis
      5. Why me – Use this code if the participant felt like they needed to know how/why this had happened
      6. Overwhelming – Use this code if the participant felt overwhelmed after the diagnosis
      7. Different world – Use this code if the participant felt like they were entering a different world from what they’d experienced so far in life
      8. Worst case scenario – Use this code if the participant immediately started worrying about the worst thing that could happen with the diagnosis
      9. Sad – Use this code if the participant felt sad after receiving the diagnosis
     x. Angry – Use this code if the participant felt angry after receiving the diagnosis
    xi. No different – Use this code if the participant didn’t feel any different than before after receiving the diagnosis
    xii. Guilt – Use this code if the participant felt guilty after receiving the diagnosis
   b. Now – This theme focuses on feelings the participant has about the diagnoses now (if it has been more than a year since the diagnosis)
      1. Relationships – Use this code if the diagnoses affect how the participant thinks about romantic relationships
      2. Reproductive issues – Use this code if having the diagnoses affect how the participant thinks about the possibility of having children or grandchildren
      3. Self-identity – Use this code if the participant considers the diagnoses to be a part of who the affected person is
4. No limits – Use this code if the participant feels that the affected person is capable of anything he/she wants to do despite the diagnoses
5. Just different – Use this code if the participant now feels that the diagnosis is not a completely bad thing
6. Bigger purpose/plan – Use this code if the participant feels that the diagnoses happened for a reason
7. Still, why me – Use this code if the participant still feels like they need to know why this happened to him/her
8. Fear of the future – Use this code if the participant is apprehensive about what the future might hold as a result of the diagnoses

   c. Changes – This theme focuses on how the participant’s feelings about the diagnoses have changed over time
      1. Come to terms – Use this code if the participant feels more at peace about the diagnoses now than immediately after diagnosis
      2. Overcoming a challenge – Use this code if the participant felt that coming to terms with the diagnosis was a challenge they had to overcome
      3. Less fear – Use this code if the participant’s fear about the condition has lessened with time
      4. Different at different life stages – Use this code if the participant’s feelings about the diagnoses change depending on where in life the affected person is
      5. Understanding – Use this code if the participant now understands much more about the diagnoses
      6. Moving forward – Use this code if the participant expresses they have to just deal with day-to-day management of the diagnoses and not focus about feelings about them
      7. No change – Use this code if the participant doesn’t think their feelings about the diagnoses have changed over time
      8. More difficult – Use this code if the participant expresses that the diagnoses have been more difficult to deal with than he/she initially thought they would be

2. **Actions** – This theme focuses on actions the participant has taken as a result of having/having a child with two or more genetic diseases
   a. Medical management – This theme focuses on the medical management of the diagnoses
      1. Frequent doctor visits – Use this code if the patient has to spend a lot of time going to medical appointments
      2. None – Use this code if at least one of the diagnoses requires no medical management
      3. Lots of medications – Use this code if the affected person takes many different medications
4. Frequent therapies – Use this code if the affected person has frequent therapy appointments
5. Travel – Use this code if the participant has to travel frequently to see different specialists
b. Finding support – This theme focuses on the participant’s experience with support groups
   1. Isolated – Use this code if the participant doesn’t live near any/many other people with the same diagnoses
   2. Friends with health problems/genetic conditions – Use this code if the participant has friends who also have/ have children with health problems who serve as a source of support
   3. Rely on family – Use this code if the participant uses their family as a source of support to talk about the diagnoses
   4. Others don’t understand – Use this code if the participant finds that people who don’t deal with similar problems can’t understand his/her problems
   5. Internet – Use this code if the participant uses the internet to connect with others about one or both diagnoses
   6. Started a group – Use this code if the participant started their own support group since they couldn’t find one
   7. No time/effort – Use this code if the participant doesn’t have enough time or want to put in the effort to find or participate in a support group
   8. No support – Use this code if the participant doesn’t have anyone that they talk to about their/their child’s medical condition
c. Coping strategies – This theme focuses on strategies the participant used/uses to cope with the diagnoses
   1. Religion – Use this code if the participant uses their faith as a way to deal with the diagnoses
   2. Appreciate small things – Use this code if the participant makes time to appreciate smaller things in life as a result of the diagnoses
   3. Live in the moment – Use this code if the participant makes the decision to live in the moment and not worry about the future
   4. Information seeking – Use this code if the participant researched the condition on his/her own
   5. Avoiding information – Use this code if the participant decided to stop looking for information because it was overwhelming or scary
   6. Advocacy/fundraising – Use this code if the participant volunteers with advocacy groups or organizes fundraisers for one or both of the conditions
   7. Could be worse – Use this code if the participants feels that the diagnoses could be something worse
d. Lifestyle changes – This theme focuses on changes the participant has had to make to his/her lifestyle as a result of the diagnoses
1. Employment – Use this code if the participant has had to quit his/her job, change jobs, or cut down on hours as a result of the diagnoses
2. Financial – Use this code if the participant has been affected due to financial issues

3. **Experiences** – This theme focuses on the experiences that participants have had as a result of having/having a child with two or more genetic diseases
   a. Diagnosis – This theme focuses on participant’s experiences at the time of diagnosis
      1. Minimal/no resources – Use this code if the participant wasn’t given any/many specific resources (such as handbooks, support groups, etc.)
      2. Expected – Use this code if the diagnosis was expected based on the patient’s phenotype and did not come as a surprise
      3. Unexpected – Use this code if the diagnosis came as a complete surprise
      4. Long process – Use this code if it was a long process in order to finally get one or both of the diagnoses
      5. Resources – Use this code if the participant was given lots of resources about the diagnosis
   b. Daily living – This theme focuses on how the diagnoses affect the daily life of the individual who has them
      1. Daily activities – Use this code if the diagnoses affect daily living activities
      2. Pain/fatigue – Use this code if the diagnoses cause pain or fatigue
      3. Different than peers – Use this code if the person affected feels that they are different than their peers because of the diagnoses
      4. Hospitalizations – Use this code if the diagnoses cause frequent hospitalizations
      5. Learning – Use this code if the diagnoses affect learning
      6. Behavior issues – Use this code if the diagnoses cause behavioral problems
      7. Developmental delay – Use this code if the diagnoses cause developmental delay
   c. Perception of severity – This theme focuses on how severe the participant considers the diagnoses
      1. Mild – Use this code if the participant describes one of the diagnoses as mild
      2. Variable – Use this code if the participant describes one of the diagnoses as having variable severity depending on the day/year/etc.
      3. One more severe – Use this code if the participant considers one diagnosis to be more severe than the other
      4. Equal focus – Use this code if both conditions are receiving equal focus from healthcare professionals
      5. Doctors agree – Use this code if the disease the participant thinks is more severe also receives more medical attention
6. Doctors don’t agree – Use this code if the disease the participant thinks is more severe doesn’t receive the most medical attention
7. Both the same – Use this code if the participant considers both diagnoses are equal in severity
d. Society – This theme focuses on how the participant feels that the diagnoses fit into society as a whole
   1. Help others – Use this code if the participant feels that their experiences are able to help others
   2. Looks deceiving – Use this code if the participant feels that they/their child looks healthier than they truly are and that this fools people into thinking they don’t need help
e. Healthcare system – This theme focuses on the participant’s experience with the healthcare system
   1. Doctors don’t know – Use this code if the participant has to explain their diagnosis or diagnoses to their doctors
   2. No direction – Use this code if the participant hasn’t received guidance on how to find specialists or which specialists to seek out
   3. Lack of care coordination – Use this code if the participant has experienced trouble due to a problem of care coordination between medical professionals
   4. Care coordination – Use this code if the participant has experience with medical professionals who have given consideration to the fact that the individual has more than one genetic disorder
   5. Insurance issues – Use this code if the participant has dealt with frustration related to dealing with insurance companies
   6. Lack of facilities – Use this code if the participant doesn’t have medical specialists geographically close to his/her home
   7. Parent/self-advocate – Use this code if the participant feels that they constantly need to advocate for themselves/their child to get the care he/she needs
   8. Doctors assume – Use this code if the participant has experienced that doctors assume that they know more than they actually do
f. Genetic counseling – This theme focuses on the participant’s experience with genetic counseling
   1. Family planning/Inheritance – Use this code if the participant would like to talk to a genetic counselor about inheritance pattern or family planning purposes
   2. Helping someone else – Use this code if the participant would like to see a genetic counselor with a partner for the purposes of helping a partner or family member understand the genetic conditions
   3. Resources – Use this code if the participant would like to see a genetic counselor to help find resources about a condition
4. Coping – Use this code if the participant would like to see a genetic counselor for support with coping with a condition
5. Call us – Use this code if the participant would like for genetic counselors to call and follow up or schedule another appointment months or years after the initial diagnosis without the family requesting it
6. Simplify – Use this code if the participants would like for genetic counselors to explain things in a more easily understandable way, since genetics and genetic conditions are so complicated
7. Helpful – Use this code if the participant has had genetic counseling and it has been extremely helpful
8. Go-to person – Use this code if the participant feels that his/her genetic counselor is his/her go-to person when he/she has questions about one or both of the conditions

g. School system – This theme focuses on the participant’s experience with the school system
   1. Problems – Use this code if the participant has experienced problems with the school system