Caregiver Adaptation in Disorders of Sex Development

Tanenbaum, Rachel

University of Michigan

Mentors: Dr. David Sandberg, Dr. Jennifer Cummings

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Abstract

Adaptation among caregivers of children (ages 0 to 7) born with a disorder of sex development (DSD) was examined in this cross-sectional study. Caregivers (N = 130; n = 85 mothers; n = 45 fathers) of children born with a DSD, recruited through 12 pediatric specialty clinics around the United States, completed questionnaires assessing stress, emotional distress, health-related quality of life, decisional regret, and perception or experienced stigma related to their child's medical condition. Direct relationships between stigma and decisional regret to caregiver adaptation were hypothesized. It was predicted that the relationship between child characteristics that include age, atypicality of genitalia, and number of surgeries and caregiver adaptation will be moderated by both child and caregiver gender. Direct correlation analyses revealed a statistically significant relationships between stigma and caregiver adaptation. Regression analyses revealed the number of surgeries and degree of genital atypicality were statistically significantly related with caregiver stress as moderated by child gender. Caregivers of children with DSD may be at increased risk for distress and negative adaptation, which can affect the adaptation of their children.

Keywords: disorders of sex development, caregiver, distress, adaptation, atypical genitalia, surgery

Caregiver Adaptation in Disorders of Sex Development

Chronic illnesses have the potential to drastically impact the lives of affected individuals and their loved ones, especially their families. Managing the physical, mental, and emotional effects a chronic illness can be especially difficult for caregivers of children. The literature across various pediatric conditions suggests that caregivers of children with chronic conditions are at increased risk for psychological stress, including depression and anxiety. Caregivers of children who have chronic medical conditions have reported significantly higher levels of stress than caregivers of healthy children (Cousino & Hazen, 2013). They are responsible for helping their children cope with physical and emotional demands of the condition, which can be stressful (Silver, Westbrook, & Stein, 1998). Additionally, increased depression and anxiety have been reported in caregivers of children with asthma (Leão, Zhang, & Sosua, 2009) and cancer (Patiño-Fernandez et al., 2008). Managing a child's chronic condition can be challenging and induce stress and depression in caregivers. The increased risk for caregivers to experience stress, depression, anxiety, and distress has potential to shape how they adapt to having a child with a chronic illness (Popp, Robinson, Britner, & Blank, 2014).

Caregivers' perceptions about their children with a chronic illness affect how they treat their children. Caregivers tend to perceive their children as more vulnerable due to the illness, which correlates with a higher tendency to employ maladaptive caregiving practices, and potential for the children to have a poorer ability to adapt positively (Houtzager, Möller, Maurice-Stam, Last, & Gootenhuis, 2014). When coping with the difficulties of caring for children with a chronic illness, problems in caregivers' adaptation can be a factor of a disruption to the existing, well-established perceptions about attachment and caregiving (Pianta & Marvin, 1993). It can be difficult for parents to come to accept the child in the context of their condition

and adapt to the diagnosis. Resolution is when parents incorporate new information with their emotional state in a manner of adapting to the diagnosis, reorganizing their existing perceptions about attachment and caregiving (Pianta & Marvin, 1993). Resolution is important for positive adaptation of both caregivers and their children.

Furthermore, female versus male caregivers have a tendency to respond differently when caring for children with chronic illness. Most studies focusing on family adaptation to child illness focus on maternal functioning, as mothers are seen to be at the greatest risk for distress (Wallander et al., 1989). However, fathers can also experience distress and substantially influence the child's ability to adapt. Research has shown that more paternal involvement in disease management was associated with increased treatment adherence and quality of life (Wysocki & Gavin, 2006).

Additionally, gender differences in a child with a chronic illness can impact caregiver adaptation. Along with individual variation in stress response and coping, gender differences are present in an array of biological and psychological responses to stress. The gender of the child has been seen to affect parental responses and stress levels. Hughes, Deater-Deckard, and Cutting (2001) showed that compared with parents of boys, parents of girls showed less negative affect, overall, and stricter disciplinary tactics. Parents can also perceive their child's traits more or less favorably, depending on child gender. For example, parents show negative responses to shyness in boys, but positive responses to shyness in girls (Hughes, 2001). Gender differences in children can affect how parents respond and care for their child, and this may affect both caregiver and child adaptation in chronic illness.

Disorders of Sex Development

Disorders of sex development (DSD) is an umbrella term for congenital conditions in which chromosomal, gonadal, or anatomic sex development is atypical (Lee, Houk, Ahmed, & Hughes, 2006). DSD are rare conditions, and caregivers' reactions, experiences of distress, and ability to adapt have been less explored than in other chronic conditions.

Biologically, typical sex development depends on chromosomal sex, gonad determination, and sex differentiation. Chromosomal sex refers to the complement of parental chromosomes at fertilization. Somatic cells of a typical male fetus contain one X and one Y chromosome, while cells of a typical female fetus contain two X chromosomes (Achermann, Domenice, Bachega, Nishia, & Mendonca, 2015). Gonad determination refers to the indifferent gonad developing into either a testis or an ovary, which is programmed by genetics and critically timed (Hughes, 2001). Sex differentiation refers to the differential formation of internal and external genitalia, which is driven by sex hormones secreted from the gonads resulting in anatomic sex development (Achermann et al., 2015).

Due to the complexity of DSD, caregivers can face difficult clinical management decisions regarding children's gender of rearing or early surgery of the medical condition which are potential stressors on families (Hullmann, Fedele, Wolfe-Christensen, Mullins, & Wisniewski, 2011). These stressors can have adverse impacts on their own psychosocial adaptation (Wisniewski, 2017). Caregivers of children with DSD can experience increased anxiety, depression, and distress in relation to their child's illness (Wisniewski, 2015). Caregivers of children with DSD who have higher levels of anxiety, depression, and distress are at risk for negative parenting practices that can affect the long-term adaptation their child (Kirk et al., 2011).

Stigma

DSD are present from birth, and can have profound, life-long impacts on the individual with the DSD as well as their family members. Due to the sensitive nature of DSD and lack of knowledge from the general public, stigma is a significant challenge associated with these conditions (Lisdonk & Callens, 2017). Research has shown that caregivers who feel stigmatized by their children's condition are at increased risk for experiencing emotional distress. For example, research on caregivers of children with developmental disabilities report adverse effects on their own psychological well-being. Further, parental experiences of stigma were negatively linked to child adjustment (Li, Lam, Chung, & Leung, 2019). Caregivers' perceptions and experiences of stigma can affect how their children adapt to the world.

Decision Regret

Because caregivers of children with DSD commonly have to make many important decisions regarding their child's condition under times of high-stress or with limited information, some caregivers may experience post-decision regret (Sandberg & Mazur, 2013). Regretting a past decision is seen to be associated with stress, depression, and anxiety (Sheehan, Sherman, Lam, & Boyages, 2006). There is little research on how decision regret in caregivers of DSD affects their overall adaptation.

Genital Atypicality

In regards to medical complications that can accompany DSD, some children are born with atypical genital appearance. This event can induce confusion and feelings of helplessness in caregivers (Sanders, Carter, & Goodacre, 2008). Caregivers worry about how their children will socially, sexually, and emotionally navigate, whether and how to share information about the condition to others, and stigma (Fedele et al., 2010; Lev, 2008). For children born with atypical genitalia, a delay in assigning gender may be necessary until a diagnosis has been reached. This

postponement in gender assignment can cause stress for caregivers (Dessens et al., 2017). Caring for a child with atypical genitalia puts caregivers at increased risk for depression, anxiety, and stress about how this will affect their children in the future. Commonly, parents of children with genital atypicality even go through the stages of grief (Oliveira, Paiva-e-Silva, Guerra-Junior, & Maciel-Guerra, 2015).

Surgery

Another complex issue that accompanies having a child with DSD and atypical genitalia includes decisions regarding surgery. Types of DSD surgery include those affecting gonads, internal reproductive anatomy, and external genitalia. Gonadal surgery is performed when there is risk of a gonadal tumor and to avoid the occurrence of pubertal hormones working in opposition with the affected individual's gender identity (Gardner & Sandberg, 2018). Genital surgery refers to procedures on external genitalia or internal reproductive structures, which is commonly performed to facilitate complete sexual function and to deliver an appearance that matches gender of rearing (Mouriquand et al., 2016). Gonadal, internal reproductive, and external genitalia surgeries all come with the risk of complication and experiences of dissatisfaction by some individuals with DSD and caregivers (Crouch, Liao, Woodhouse, Conway, & Creighton, 2007).

Historically, it has been common to perform early surgery in order to make the infant's genitals more typical for the sex of rearing (Karkazis, Tamar-Mattis, & Kon, 2010). However, early surgical intervention in DSD has brought about much controversy. The factors in favor of early surgery on the clinical management side include satisfactory cosmetic appearance and functionality for sexual intercourse with sensitivity for adequate responsiveness (Lee, Schober, Nordenström, Hoebeke, Houk, & Looijenga, 2012). The factors in favor of caregivers choosing

early surgery may include anxiety, shame, stigma and desire for secrecy concerning the child's sexual anatomy (Ernst, Liao, Baratz, & Sandberg, 2018). Research shows that early surgery can alleviate levels of stress and anxiety for caregivers as seen in mothers reporting more stress if their child with atypical genitalia has not received genitoplasty (Fedele, Kirk, Wolfe-Chistensen, Phillips, & Mazur et al., 2010) and both mothers and fathers have reported less stress 6 months following their child's genitoplasty performed with the goal of "normalizing" the genital appearance (Wolfe-Christensen et al., 2017).

Some factors against early surgery include concerns residing in patient autonomy and caregivers electing for surgery to "normalize" their children's genital appearance before knowing all the risks and benefits (Crissman, et al. 2011). Other areas of concern regarding early surgery include timing of surgery, irreversibility of surgery, the effects of anesthesia when administered early in life, and long-term follow up care (Gardner & Sandberg, 2018; U.S. Food and Drug Administration, 2016). While some adults have reported satisfaction in regard to their genital surgery early in life (Migeon et al., 2002); other adults have reported discontent and harm (Köhler et al., 2012). In light of these discrepant results, there is not conclusive evidence about impacts of either surgically treating or non-surgically treating children with a DSD on the individual and their caregivers (Lee, Nordenström, Houk, Ahmed, & Auchus, 2016).

Age of Child

As children get older, their needs, desires, and communication patterns can change, as well as the caregivers' relationship with and decisions regarding their child. For example, in DSD, caregivers may have to make a decision regarding sex of rearing children, while children are still young; however, decisions regarding genital surgery may need to be made further into childhood or adolescence (Hughes et al., 2006). It has been seen that caregivers of children with

DSD may have different psychosocial needs based upon their child's stage in development (Hullmann et al., 2011). Additionally, for those whose DSD was identified at or near birth, age serves as a proxy of how long caregivers have been managing their children's condition and adapting to both the diagnosis and its clinical management. Hoekstra-Weebers, Jaspers, Kamps, and Klip (1998) found that parents of children with cancer experienced less distress and more positive adaptation over time. The relationship between the age of the child with DSD and caregiver adaptation needs more exploration in order to understand how parents adapt to having a child with a DSD over time.

Study Objectives

There is limited research about how DSD affects the daily life of children and their caregivers (Alpern, Gardner, Kogan, Sandberg, & Quittner, 2017). As with other chronic illnesses, research about caregivers with children with a DSD has focused on maternal factors with one notable exception: Wolfe-Christensen, Fedele, Mullins, Lakshmanan, and Wisniewski's (2014) research which includes data from male caregivers as well as female caregivers. Overall, fathers have been historically underrepresented in pediatric psychological research (Phares, Lopez, Fields, Kamboukos, & Duhig, 2005). Female and male caregivers are commonly differentially affected by the children's diagnosis, and more research for these differences in regards to DSD is necessary. There is evidence suggesting that people born with genital atypicality associated with DSD have increased risk of psychological distress; however, there is limited information on how this affects the mental health of caregivers (Wisniewski & Sandberg, 2015). There is little research concerning if and a how caregivers' levels of adaptation change over time.

Recognizing the importance of both patient and parent health related quality of life (HRQoL), a study was conducted to develop HRQoL measures that are specific to DSD (Alpern et al., 2017). This study generated a large dataset that includes information that addresses caregiver HRQoL with specific focus on experiences of parents and the impact on daily functioning. It can provide insight to questions raised about the relationship of caregiver adaptation of children with a DSD. The purpose of the current study is to examine how caregivers' of children with DSD experiences (stigmatization related to the child's diagnosis, and decision regret) and several characteristics of the child (age, atypicality of genital appearance, and number of genital or gonadal surgeries) are related to overall caregiver adaptation, as seen in Figures 1 to 5. Based on prior research, it is hypothesized that increased stigma and decision regret will inversely correlate with caregiver adaptation (Figure 1). Additionally, it is predicted that the relationship between child characteristics and caregiver adaptation will be moderated by both child and caregiver gender (Figure 2).

Method

Participants

Participants included 130 caregivers (n = 85; 65.4% female) of 94 young children (0-6 years at time of recruitment) who had been cared for at one of 12 US medical centers representing an array of geographic regions. Index cases included 94 children ages 0.67 to 7.32 years (M=4.0, SD=1.8) with a DSD, including 4 (4.3%) children with a sex chromosome DSD, 59 (62.8%) with a 46, XY DSD, and 31 (33.0%) with a 46, XX DSD (Table 2). The majority (n=54, 57.4%) were reared as boys; 40 (42.6%) were reared as girls.

Caregiver age ranged from 21 to 57 years old (M = 34.82, SD = 6.72). The majority reported being married (81.4%). Median household income level was $70,000 to $79,999, with

income levels ranging from under $5,000 to $100,000 or more. Most of the participants identified as Caucasian (*n*=104, 80.6%), followed by Asian or Pacific Islander (*n*=14, 10.9%), African American (*n*=6, 4.6%), then American Indian or Alaska Native (*n*=4, 3.1%), Middle Eastern (*n*=2, 1.6%), and "other" (*n*=3, 2.3%); a minority also identified as having a Hispanic ethnicity (*n*=11, 8.5%) (Table 1).

Measures

Medical chart excerpts. Research staff at each site excerpted detailed medical information from patient charts including gender of rearing, genital appearance, and the number of genital, DSD category, and/or gonadal surgeries performed. Excerpt forms were reviewed by a senior-level pediatric urologist and pediatric endocrinologist to reliably assign scores for degree of atypicality and validate diagnoses based on the Consensus Statement on Management of Intersex Disorders (Lee et al., 2006).

Genital atypicality was rated relative to the gender of rearing before reconstructive surgery (Alpern et al., 2017). The Quigley scale (scores ranging from 1 to 6 for newborns; *1=typical male appearance, 6=typical female appearance*) was applied to children reared as boys (Quigley, De Bellis, Marschke, el-Awady, Wison, & French, 1995). The Prader scale was utilized for children reared as girls with scores ranging from 0 to 5 (*0= typical female, 5= typical male*), see Figure 5 (Acherman & Hughes, 2011). To create comparability for boys and girls, DSD genital atypicality scores were transformed into 0 to 100 scale, with higher scores indicating more atypicality of appearance in relation to gender of rearing. For boys, the score on the 6-point scale ranging from 1 to 6 was subtracted by 1, then divided by 5 and multiplied by 100; for girls, the 6-point scale ranging from 0 to 5 was divided by 5 and multiplied by 100.

Experiences and reactions questionnaire (ERQ). (Rolston, Gardner, Vilain, & Sandberg, 2015). The Experiences and Reactions Questionnaire inquires about caregivers' perceptions of and experiences with stigma. It comprises two subscales in addition to a total score. The first subscale represents experiences related to other peoples' reactions to the caregivers regarding their children's condition. The second subscale represents caregivers' personal feelings about their children's urogenital condition. Participants rated each item on a 5-point Likert scale when judging comments related to other people's reactions *(1= "Strongly Agree" to 5 = "Strongly Disagree")* and when rating personal feelings about their child's DSD *(1 = "never true" to 5 = "always true")*. Higher scores represent more stigma. The internal consistency for the scales in a DSD sample ranged from 0.78-0.79 (Alpern et al., 2017).

Decision regret (DR). (Brehaut et al., 2003). The Decision Regret scale asks caregivers to reflect on a medical management decision they had made on behalf of their children and rate the confidence in their decision on a 5-point Likert scale *(1= "Strongly Agree," 5 = "Strongly Disagree")*. Higher scores represent greater caregiver regret. A DSD study sample reported an internal consistency of 0.90 for this measure (Alpern et al., 2017). Other researchers have published score categories for decision regret that assign a scale of 0= "none," 1 to 25 = "mild," and 26 to 100 = "moderate to severe" in patients who underwent distal hypospadias repair (Ghidini, Sekulovic, & Castagnetti, 2016).

Parenting stress index (PSI). (Abidin, 1995). Stress in the caregiver-child relationship was measured with the PSI, designed for parents of children from 1 month to 12 years of age. Two subscales were selected for administration: Parenting Competence and Role Restriction. The PSI asks the caregiver to rate whether each statement is descriptive of their relationship with their child, using a 5-point Likert scale *(1="strongly agree," 5="strongly disagree")*. The

Parenting Competence subscale asks caregivers to rate how they think about themselves as a caregiver, including enjoyment, and feelings of either capability or incapability. The role restriction subscale asks if they "feel trapped by their responsibilities as a parent" and "how often the child's needs control their own life." Higher scores are correlated with more negative outcomes, including feeling less competent and having more restriction. The validity of the PSI has been established in a range of populations of parents with children who have chronic illnesses (Hullman et al., 2011). The PSI has a high internal consistency (0.79 to 0.84) in a DSD sample (Alpern et al., 2017).

Hopkins symptom checklist (HSCL). (Derogatis, Lipman, Rickels, Uhlenhuth, & Covi, 1974)**.** The HSCL is a self-report symptom inventory that includes a list of physical, mental, and emotional symptoms and asks responders to rate the distress that they have felt in the past seven days, including the day they answer the survey. The HSCL utilizes 58 items and asks for ratings of distress *(1= feeling "not at all" distressed, 4= feeling "extreme" distress)* (Derogatis et al., 1974). Higher scores represent more symptoms of distress. The measure includes five symptom dimensions including somatization, obsessive-compulsive, interpersonal sensitivity, depression, and anxiety. The HSCL internal consistency ranged from 0.79-0.90 for a DSD study sample (Alpern et al, 2017).

SF36v2 mental component summary (SF36v2). (Ware, 2009**).** The SF36v2 is widely known as a practical, reliable, and valid measure of physical and mental health (Ware, 2009). The questionnaire contains 36 items measuring functional health and well-being, yielding several subscale and component scale scores. Given the focus on parental adaptation, analysis of scores were restricted to the mental component summary score.

Institutional Review Board (IRB) approval and caregiver informed consent were sought and granted prior to participation.

Data Analysis

Descriptive statistics (range, mean, standard deviation) were calculated to characterize sample demographics, predictor, and dependent variables. To compare caregiver adaptation in DSD to caregiver adaptation of children with other chronic conditions, we examined studies using the same measures in the present study that measure caregiver distress when his or her child has a chronic condition performing independent 2-sample t-tests for each comparison. Caregiver adaptation was measured by the PSI, HSCL, and SF36v2 mental component summary.

Correlational analyses were calculated to examine relationships between the total stigma score (ERQ) and each measure of caregiver adaptation and the decisional regret score (DR) and each measure of caregiver adaptation. Linear mixed effects regression analyses were used to assess associations between the child's age, atypicality of genital appearance, and number of surgeries and measures of caregiver adaptation. These exposures' effects were tested for moderation by gender of caregiver and gender of child. Total scale scores were used when available. Random intercepts were included in each model to account for child-specific effects on parental adaptation. This controlled for potential similarity in results between two parents reporting for the same child. *P* values less than 0.05 were considered significant. In order to reduce the likelihood of type 1 errors, the number of correlations and regression analyses were purposefully limited.

Results

Descriptive Statistics

Predictors. The mean of the ERQ measure, which has items asking about the reactions of others, personal reactions, and a total score concerning stigma in relation to the child's urogenital condition has a mean score is 1.81 (*SD*=0.58), with subscale scores reported in Table 3. The DR score invites caregivers of children with a DSD to reflect on a decision made about their child's condition, with higher scores representing more decisional regret. The sample mean was 12.9 out of a score of 100 (*SD*=15.76).

Adaptation. The results of the PSI for the caregivers in the present study have a mean parenting competence domain scale score of 29.4 (*SD*=7.57). The caregivers had a parenting role restriction subscale mean score of 17.47 (*SD*=5.89). Typical scores range in between 15 and 80, putting the caregivers in the sample within normal limits (Abidin, 1990). The mean HSCL total score was 1.35 (*SD*=0.36). Table 3 depicts mean scores from each individual subscale including somatization, obsessive compulsive, interpersonal sensitivity, depression, and anxiety subscales. The scores for the mental component summary of the SF36v2 yielded a mean of 47.84 (*SD*= 9.93).

Comparison to Other Conditions

When comparing adaptation in caregivers of children with DSD to caregivers of children who have other chronic conditions, using the same measures, all the comparisons were seen to have statistically significant differences with $p < 0.05$ (Table 4). Although each condition has different qualities and characteristics than DSD, the significant differences show that that the instruments used in the current study seem to be functioning as expected in the specific population.

First-Order Correlations

Concerning direct effects between stigma (ERQ) and caregiver adaptation, numerous statistically significant relationships were detected. Statistically significant correlations were detected between the SF36V2 mental component summary and total stigma scale score, $r(127) = -.33$, $p < .001$ (Table 5). The analyses demonstrated statistically significant correlations between the parenting competence domain scale score and the total stigma score, which includes personal experience and related to others' reactions, $r(129) = .48$, $p < .001$ (Table 5).

Furthermore, analysis of the PSI parenting role restriction scale score showed a statistically significant correlation with stigma, $r(129) = -.528$, $p < .001$ (Table 5). The total HSCL score had a statistically significant correlation with total stigma score, $r(129) = -.336$, $p < .001$ (Table 5). Concerning the relationship between decision regret and caregiver adaptation, the PSI parenting role restriction scale score had a statistically significant correlation with decision regret. No other measures of parental adaptation showed a statistically significant correlation with decision regret (Table 5).

Moderation

Of all regression analyses conducted, three rose to the level of statistical significance including the PSI competence in respect to atypicality moderated by child gender ($p < .008$) PSI role restriction in respect to atypicality moderated by child gender ($p < .005$), as well as the number of surgeries as moderated by child gender in respect to the PSI role restriction scale ($p < .019$) (Table 6).

Girls were coded as 1 and boys were coded as a 2. For a one unit increase in child gender, the scale score of the PSI role restriction scale score decreased by 9.02 units. Parents of boys had an overall decrease in PSI role restriction scale score of 9.02 units less than girls in respect to genital atypicality moderated by child gender. Parents of boys had a decrease in PSI competence

scale score of 8.9 units less than parents of girls in regards to genital atypicality moderated by child gender. Parents of boys had a decrease in PSI role restriction scale score of 10.11 units less than parents of girls in respect to number of surgeries experienced modified by child gender.

Discussion

Stigma

Results indicated a statistically significant correlation between the total stigma score of the ERQ, which encompasses experienced and perceived stigma, and caregiver adaptation. As stigma increases, overall caregiver adaptation significantly decreases, supporting the expected hypothesis. This parallels the finding of high levels of caregiver stress associated with perceived stigma in DSD (Crissman et al., 2011). Increased stigma experiences can lead parents to be more resistant to seek help and support from friends and family (Wisniewski, 2017). These studies support the significant relationship between higher stigma score for caregivers' correlating with less caregiver adaptation.

Decision Regret

Most of the measures of caregiver adaptation were not found to have significant correlations with decision regret, with the exception of the PSI role restriction scale score (Table 5). A study examines parents' decisional regret after genital restoration surgery in females with congenital adrenal hyperplasia (CAH), finding that parents reported low levels of decision regret in infancy and toddlerhood (Syzmanski et al., 2017). Overall low levels (ie, a floor effect) may limit the ability to examine relationships between caregiver adaptation and decision regret in the current study. In contrast, a study had mothers and fathers of children with DSD report decision regret 1 year after their child underwent a genitoplasty. They found that about a quarter of the

parents (27.9%) reported decision regret 12 months after genitoplasty, with an increased risk for regret if parents have illness uncertainty prior to the initial surgery (Ellens et al., 2017).

In the future, it may be important to examine baseline levels of illness uncertainty in caregivers before quantifying decision regret. The decision regret measure asked broad questions without evaluating the specific decisions in which the caregivers were reporting. More sensitive measures of decision regret may be necessary to identify the relationship between decision regret and caregiver adaptation.

Child characteristics and Parental adaptation; Moderation by Parent and Child Gender

The relationship between the child's age, atypicality of genital appearance, and number of genital surgeries underwent and the caregiver's adaptation were expected to be moderated by the caregiver's gender and by the child's gender. Overall, the moderation model was not supported; however, results of several analyses rose to statistically significant levels. Specifically, between PSI competence in respect to atypicality moderated by child gender, the PSI role restriction scale in respect to atypicality moderated by child gender, as well as the number of surgeries as moderated by child gender in respect to the PSI role restriction scale. It is possible that the hypothesized model may be valid; however, more sensitive measures may be necessary in order to detect these relationships. However, this finding corresponds to the Duguid, Morrison, Robertson, Chalmers, Youngson, and Ahmed (2007) study in which parents did not display abnormal levels of stress when having a child with a genital anomaly. Hullmann and colleagues (2011) found no significant differences between parenting stress levels across parents of infants/toddlers, preschool-age children, and school-age children with DSD. These results are consistent with the lack of significance in correlations between the child's age and overall caregiver adaptation.

The moderated correlations which were significant all included the PSI scales as the dependent factor and child gender as a moderator, signifying that the patient's gender may affect the amount of stress the parents experience. More research on how the gender of a DSD patient affects overall parental adaptation and parental stress differently is necessary. Studies looking at gender differences in children with a DSD find female children to be at a particular risk for problem behaviors than males (Wiskniewski, Hullman, & Mullins, 2012), which may affect parental adaptation. More studies analyzing differences in behavior and adaptation of parents and children with DSD's would be useful in looking further into how having a male or female child affects caregiver adaptation in DSD.

When looking at the direct relationships between the proposed moderators (caregiver gender and child gender) and each measure of caregiver adaptation, statistically significant differences were found between female and male caregivers in respect to the SF36v2 mental component summary, the HSCL total score, the HSCL interpersonal sensitivity score, the HSCL depression score, and the decision regret score (see Table 7 and Table 8). The significant differences between female versus male caregivers shows that caregivers may have different perspectives when raising a child with DSD in respect to the caregivers' gender. These findings reflect Wolfe-Christensen et al.'s findings of different levels of parental stress between mothers and fathers of children with DSD who have ambiguous genitalia (Wolfe-Christensen, Fedele, Mullins, Lakshmanan, & Wisniewski, 2014). It is important for providers to understand and address differences between male and female caregivers' experiences of distress.

Limitations

A retrospective cross-sectional designed was utilized; because of the cross-sectional design, data for the long-term follow up of patients and caregivers is not available. Furthermore,

causal relationships for the temporal ordering of variables cannot be assumed. Additionally, the study uses moderators that were expected to affect the direction or strength of the relation between the variables; however, different moderators can also affect the correlations including past familial events that may cause stress and distress, baseline levels of distress, quality of care received from healthcare professionals, and religious/spiritual beliefs.

Given the sample demographics, generalizability may be limited. Per the 2010 US Census, 72.% of Americans were Caucasian; most participants were Caucasian (80.6%). As such, this study could potentially benefit from a more diverse patient population in race and ethnicity. Most people included in the study were married (80.8%); according to the 2016 U.S. Census, 69% of parents of children with one or more children under 18 were married. Since the majority of participants were married, the results may not be generalizable to unmarried couples. The study may benefit from including survey responses from more unmarried couples. It is important to continue to explore the differential effects of DSD on children and their caregivers who are unmarried or single parents with an adequate sample size.

The majority of caregivers included have a high level of education (55.9%, bachelor's degree or higher), which can affect the presence of stressors and their level of understanding of the DSD. The study would benefit from including more people with lower socioeconomic status and with less formal education in order to further understand levels of caregiver adaptation in a more representative sample of caregivers with a child with a DSD. According to the 2016 U.S. Census, 33.4% of the adult population has a bachelor's degree or higher. Over half of the participants in the sample population have a bachelor's degree or higher, as opposed to just about one-third of the entire U.S. population, which has potential to impact to the generalizability of the results.

The children included range from ages 0 to 7 years-old at the time their caregivers participated. Because of this age range, it is not possible to conclude how levels of caregiver adaptation would be affected over time for older children and adolescents with a DSD. Due to the nature of the measures used, there may be bias in that the caregivers self-reported their answers to the questionnaires concerning stigma, levels of depression and anxiety, decisional regret, and levels of stress. Situational events near the time of the survey, previous life events, or their general personalities can impact their answers to the questionnaires and bring the element of subjectivity to the data.

The study would benefit from having a larger number of caregivers, with more variability in educational background, race, ethnicity, and socioeconomic status. Because the study includes children aged 0 to 7 years old. It would be of benefit to look at more children at a wider age range, including how the caregiver adaptation changes as the children reach adolescence.

Strengths of Study

The strengths of the study include identifying relationships stigma, decisional regret, and DSD characteristics moderated by caregiver and children's gender affecting overall caregiver adaptation. More DSD research would be helpful in order to better understand its specific effects on caregivers. All the questionnaires utilized had high levels of internal consistency, meaning item homogeneity where the items accurately measure the same construct, and the overall scores can reflect all the test's items (Robin, 2001). Participants were recruited from a variety of medical centers from all across the United States to increase sample variability. The study included children with an array of different types of DSD diagnoses.

Clinical Practice

Clinicians should acknowledge the increased risk of caregivers of children with a DSD to experience distress and be extremely perceptive and sensitive to the caregivers' actions, feelings, and remarks. Providers should recognize the potential for baseline differences between male and female caregivers. The significant differences between male and female caregivers' reported levels of decision regret, interpersonal sensitivity, mental health, and depression should be noted in clinical practice. This would help clinicians better identify risk factors for negative caregiver adaptation that may tend to differ between males and females. Caregivers who experience negative adaptation, stress, depression, or anxiety may benefit from support groups or mental health services targeted at alleviating some of their stressors and providing early education about their children's conditions. To cope with increased stigma in regards to having a child with a DSD, clinicians should assess whether the caregivers' stigma experiences are affecting decision making and children's adaptation. Caregivers' mental health and overall adaptation levels should be assessed and addressed by clinicians.

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Tables

Table 1
Participant Demographics

Participant Demographics	Caregivers		Children	
	n	%	*n*	%
Index Cases	130		94	
Mothers	85	65.4		
Fathers	45	46.4		
Race				
White	104	80.6	101	78.3
Asian/Pacific Islander	14	10.9	18	13.8
American Indian/Alaska Native	4	3.1	3	2.3
Middle Eastern	2	1.6	2	1.5
African American	6	4.6	7	5.4
Other/Mixed Race	3	2.3	9	7.0
Ethnicity: Hispanic	11	8.5	17	13.1
Caregiver education				
Less than high school	3	2.4		
High school or equivalent	20	15.7		
Some college	33	26.0		
Bachelor's degree or equivalent	31	24.4		
Graduate or professional degree	40	31.5		
Did not answer	3	2.3		

Table 2
DSD Child Characteristics

Child Characteristics	Children	
	n	%
Child Gender of Rearing		
Boy	54	57.4
Girl	40	42.6
Child age (Mean, *SD*)	4.0 (1.8)	
Child DSD category & diagnosis		
Sex chromosome	4	4.3
46, XY	59	62.8
Disorder of gonadal (testicular) development	7	7.4
Androgen excess	12	12.8
Other 46, XY DSD	40	42.6
46, XX	31	33.0
Disorder of gonadal (ovarian) development	1	1.1
Androgen excess	26	27.7
Other 46, XX DSD	4	4.3
Genital atypicality rating (Mean, *SD*)	41.3 (20.6)	
Range	0-80	
Number of surgical procedures		
Mean (*SD*)	2.1 (1.7)	
Range	0-8	

Table 3
Measure Scores

Measure	*n*	Mean	Standard Deviation	Minimum	Maximum
ERQ	130				
Related to others	130	2.20	0.91	1.00	5.00
Personal feelings	130	1.70	0.58	1.00	3.80
Total Score	130	1.81	0.58	1.00	3.92
DR score	130	12.9	15.76	0.00	65.00
SF36v2					
Mental component summary	127	47.84	9.93	19.03	64.09
PSI subscales					
Parenting competence	129	29.40	7.57	15.17	53.00
Parenting role restriction	129	17.47	5.89	7.00	35.00
HSCL (domain scores)	129				
Somatization	129	1.34	0.35	1.00	2.45
Obsessive compulsive	129	1.43	0.47	1.00	3.25
Interpersonal sensitivity	129	1.47	0.48	1.00	3.43
Depression	129	1.40	0.49	1.00	3.09
Anxiety	129	1.20	0.33	1.00	2.67
Total score	129	1.35	0.36	1.00	2.90

Table 4

Comparisons between Caregiver Distress in DSD to Other Chronic Illnesses

Measure	*n* (DSD)	Mean	Standard Deviation	Other Condition	*n*	Mean	Standard Deviation	*t*	*p*
ERQ[1]				Epilepsy					
Total score	130	1.81	0.58		173	2.58	0.81	9.63	<0.001*
DR score[2]	130	12.92	15.76	IBD or JIA	201	18.3	17.7	2.89	0.004*
SF36v2[3]				Rett's Syndrome					
Mental component summary	127	47.84	9.93		727	44.5	12.1	3.34	0.001*
PSI[4]				Intractable Epilepsy					
Parenting competence	129	29.4	7.57		52	55.7	30.5	6.14	<0.001*
Parenting role restriction	129	17.4	5.89		52	71.4	24.5	15.69	<0.001*
HSCL[5]				ADHD					
Total score	129	1.35	0.36		264	18.24	5.61	48.6	<0.001*

Note: t = t test statistic, *$p < 0.05$

[1]Higher scores correlate with more stigma.
[2]0-100 scale. Higher score indicates more decision regret
[3]Scores standardized on a 0 to 100 scale. Higher scores indicate more favorable health.
[4]Higher scores indicate worse outcomes: less parenting competence and more parenting role restriction.
[5]Higher scores mean worse outcomes.

Table 5
Direct Effect Correlations between Stigma & Decisional Regret and Caregiver Adaptation

Measure	Stigma (total)			Decision Regret		
	n	*r*	*p*	*n*	*r*	*p*
SF36v2						
Mental component summary	127	-0.33	0.001	127	-0.097	*ns*
PSI subscales						
Parenting competence	129	0.481	0.001	129	0.093	*ns*
Parenting role restriction	129	0.528	0.001	129	-0.196	0.026*
HSCL (domain scores)						
Somatization	129	0.242	0.006	129	0.04	*ns*
Obsessive compulsive	129	0.279	0.001	129	0.126	*ns*
Interpersonal sensitivity	129	0.387	0.001	129	0.103	*ns*
Depression	129	0.328	0.001	129	0.122	*ns*
Anxiety	129	0.198	0.025	129	0.136	*ns*
Total score	129	0.336	0.001	129	0.121	*ns*

Note: *$p < 0.05$

Table 6
Significant Fixed Effects from Moderation Analyses

Measure	Interaction Estimate	*t*	*p*
PSI subscales			
Parenting competence			
Atypical*child gender	0.219	2.708	0.008
Parenting role restriction			
Atypical*child gender	0.178	2.893	0.005
Number of surgeries * child gender	1.823	2.397	0.019

Note: t = t test statistic, *$p < 0.05$

-

Table 7
Direct Effect Correlations between Caregiver Gender and Caregiver Adaptation

Measure	*n*	Mean	Standard Deviation	Mean Difference	*t*	*p*
ERQ						
Total Score						
Female	85	1.88	0.62	0.196	2.984	*ns*
Male	45	1.69	0.48			
DR score						
Female	85	14.94	16.81	5.830	2.201	0.03*
Male	45	9.11	12.89			
SF36v2						
Mental component summary						
Female	84	45.98	10.86	-5.942	-2.969	0.004*
Male	43	51.47	9.32			
PSI subscales						
Parenting competence						
Female	84	29.92	7.67	1.513	1.098	*ns*
Male	45	28.41	7.37			
Parenting role restriction						
Female	84	18.09	6.18	1.784	1.739	*ns*
Male	45	16.31	5.19			

Note: *t* = t test statistic, *$p<0.05$

Table 8
HSCL Direct Effect Correlations between Caregiver Gender

Measure	*n*	Mean	Standard Deviation	*p*	Mean Difference	*t*	p
HSCL (domain scores)							
Somatization							
Female	85	1.37	0.35	*ns*	0.107	1.736	*ns*
Male	44	1.27	0.32				
Obsessive compulsive							
Female	85	1.47	0.50	*ns*	0.127	1.559	*ns*
Male	44	1.34	0.40				
Interpersonal sensitivity							
Female	85	1.55	0.48	0.017	0.212	2.434	0.017*
Male	44	1.33	0.46				
Depression							
Female	85	1.49	0.51	0.005	0.239	2.879	0.005*
Male	44	1.25	0.41				
Anxiety							
Female	85	1.23	0.35	*ns*	0.104	1.868	*ns*
Male	44	1.13	0.27				
Total Score							
Female	85	1.41	0.62	0.017	0.156	2.434	0.017*
Male	44	1.25	0.33				

Note: t = t test statistic, *$p<0.05$

Figures

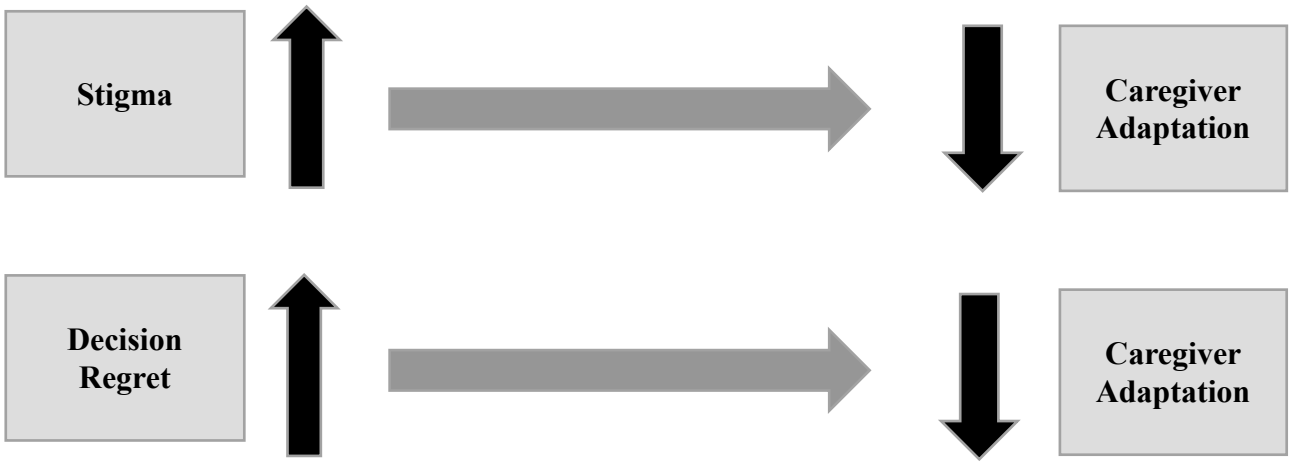

Figure 1. *Hypothesized Direct Correlations*. This figure illustrates the hypothesized direct correlations between stigma and decision regret to caregiver adaptation.

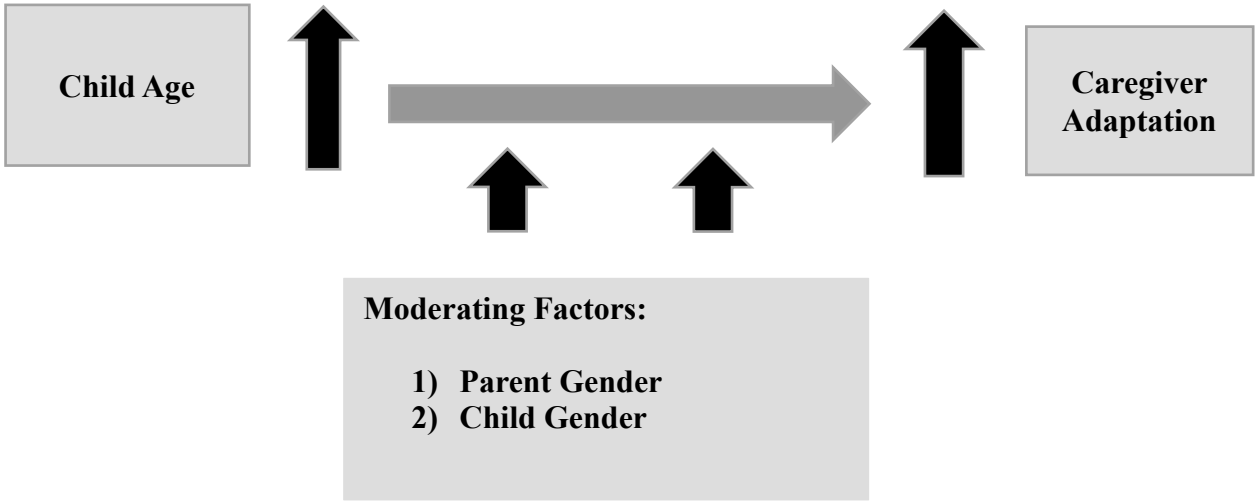

Figure 2. Hypothesized Modified Correlations between Child Age and Caregiver Adaptation. This figure illustrates the hypothesized moderated correlations between child age and caregiver adaptation.

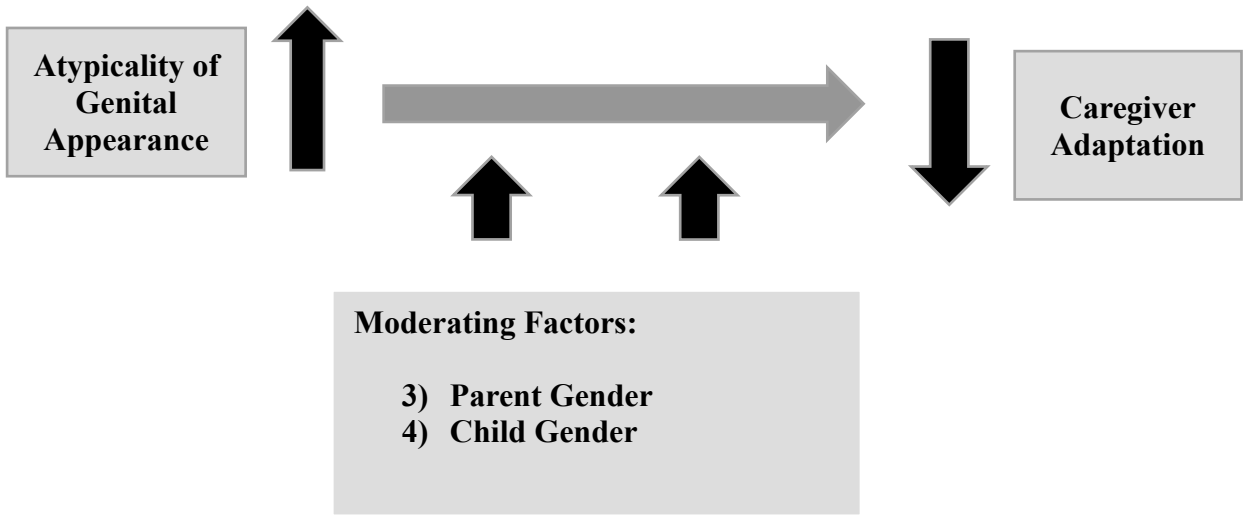

Figure 3. *Hypothesized Modified Correlations between Atypicality of Genitalia and Caregiver Adaptation*. This figure illustrates the hypothesized moderated correlations between atypicality of genitalia and caregiver adaptation.

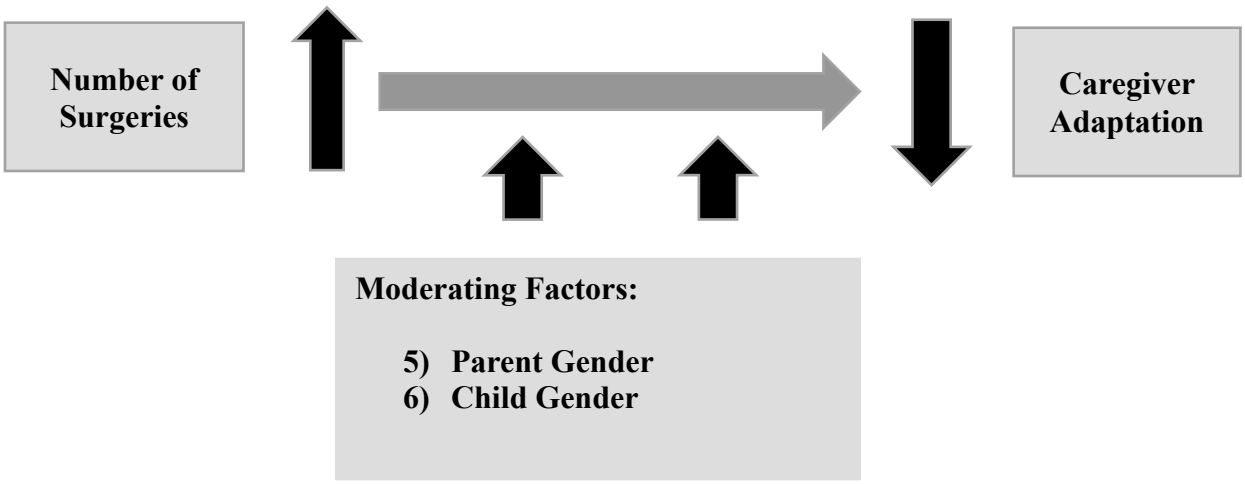

Figure 4. *Hypothesized Modified Correlations between Number of Surgeries and Caregiver Adaptation*. This figure illustrates the hypothesized moderated correlations between atypicality of genitalia and caregiver adaptation.

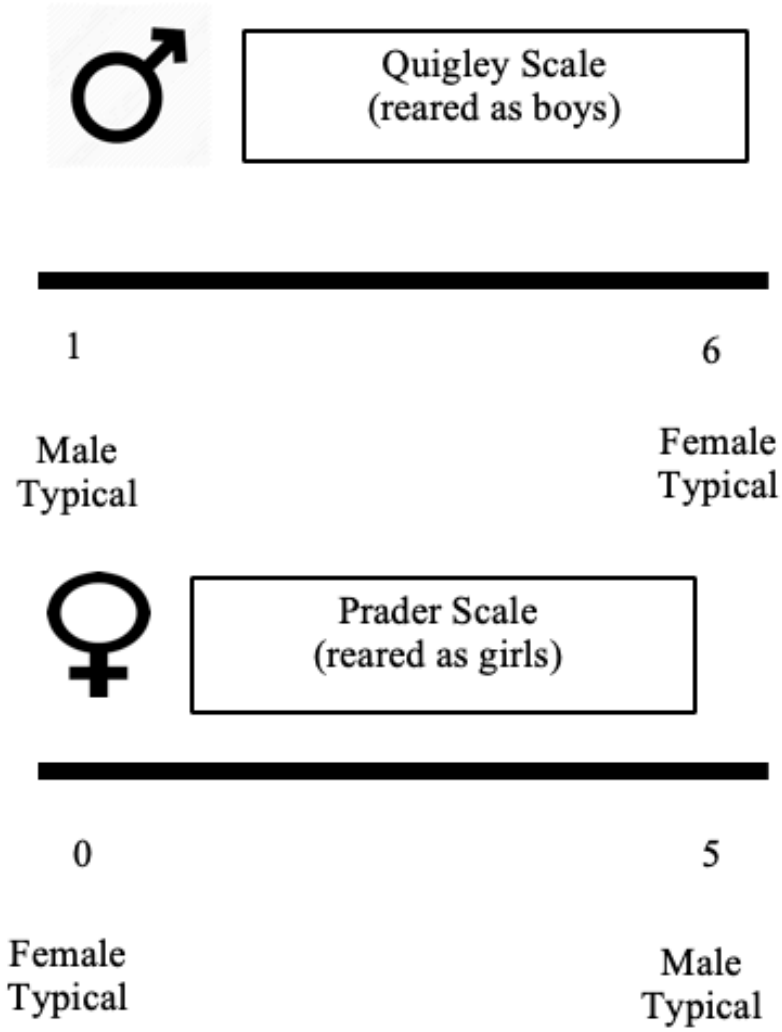

Figure 5. DSD Severity Scale for Boys and Girls. This figure illustrates the maximum and minimum severity on the scales for boys and girls, respectively.