

## ORIGINAL ARTICLE

# Prenatal detection and evaluation of differences of sex development: A qualitative interview study of parental perspectives and unmet needs

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## Abstract

**Objectives:** Prenatal diagnoses of differences of sex development (DSD) are increasing due to availability of cell-free DNA screening (cell-free DNA screening (cfDNA)). This study explores first-hand experiences of parents whose children had prenatal findings of DSD.

**Methods:** Eligible parents were identified through chart review at a pediatric center and interviewed about their prenatal evaluation, decision making, informational sources, and support systems. Interviews were coded using a combined inductive and deductive thematic analysis. Parents also completed quantitative measures of decisional regret.

**Results:** Seventeen parents (13 mothers; 4 fathers) of 13 children (with 7 DSD diagnoses) were recruited. Four children had discordance between sex predicted by cfDNA versus prenatal ultrasound, and 2 had non-binary appearing (atypical) genitalia on prenatal ultrasound. Of these 6, 3 were not offered additional prenatal testing or counseling.

Correction added on 20 July 2022, after first online publication: In the previous version of this article some of the authors' affiliation were wrongly cited. This has been corrected now and the updated version is re-published online.

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Most parents described tension between obtaining support through disclosure of their child's diagnosis and preserving their child's autonomy/privacy, highlighting the need for mental health support.

**Conclusion:** This is the first study to gather qualitative data from parents whose children had prenatal findings of DSD. We identified multiple targets for intervention to improve care for patients with DSD across the lifespan, including improvements in clinician education, pre- and post-test counseling, and patient education materials.

### Key points

#### What's already known about this topic? What does this study add?

- Prenatal detection of potential differences of sex development (DSD) is increasing as the availability of non-invasive prenatal screening increases.
- Algorithms have been developed for the diagnostic evaluation, but little is known about the psychosocial implications of that process.
- This study focuses on the first-hand experiences of families whose children had prenatal findings of a potential DSD, to identify existing sources of support and information, and areas for future improvement.

## 1 | INTRODUCTION

Differences of sex development (DSD), also called intersex traits, are a diverse group of diagnoses in which sex chromosomes, hormone levels, internal reproductive anatomy, and/or external genital appearance differ from typical binary male or female pathways of development.<sup>1</sup> Depending on how broadly DSD is defined, the incidence of DSD may be as high as 1 in 100–200 people, an estimate which includes certain types of congenital adrenal hyperplasia (CAH), sex chromosome aneuploidies (SCA) such as Turner syndrome (TS) and Klinefelter syndrome (KS), and other congenital genital variants such as cryptorchidism and hypospadias.<sup>2,3</sup> For this paper, “DSD” will be used in this broad and inclusive sense, acknowledging that there is debate about which conditions should be included and that nomenclature continues to evolve.<sup>4</sup>

Some types of DSD present with external genital appearance that differs from typical male or female development, referred to as non-binary, atypical or ambiguous genitalia. Historically, these types of DSD (e.g., 46,XX 21-hydroxylase deficiency CAH, mixed gonadal dysgenesis [MGD]) were detected at birth, while DSD characterized by binary male or female external genitalia, such as complete androgen insensitivity syndrome (CAIS), complete gonadal dysgenesis, or KS, commonly remained undiagnosed until adolescence/adulthood.<sup>5,6</sup> Only rarely was the possibility of a DSD known prenatally prior to the development of non-invasive prenatal screening (NIPS) such as cell-free DNA (cell-free DNA screening (cfDNA)),<sup>7–9</sup> marketed in the lay media as a “gender test” due to its ability to detect sex chromosome material.<sup>10</sup> The increased availability of cfDNA screening has led to higher rates of prenatal detection of SCA (although patients may opt out of SCA screening) as well as genotype/phenotype discordance (discordance between chromosomal sex predicted by cfDNA and genital appearance on prenatal ultrasound (ultrasound (US)) imaging)<sup>11,12</sup> though cfDNA remains an imperfect

screening tool.<sup>13,14</sup> Algorithms have been proposed to coordinate the prenatal evaluation in these situations,<sup>15–17</sup> and much research has centered around the postnatal psychosocial functioning of families with children affected by DSD.<sup>18–21</sup> However, relatively little attention has been given to the psychosocial implications of the prenatal evaluation.<sup>22,23</sup> While the primary aim of prenatal diagnosis may be to optimize medical care of the infant, an important secondary aim is anticipatory guidance to optimize the family's emotional preparation.<sup>7</sup>

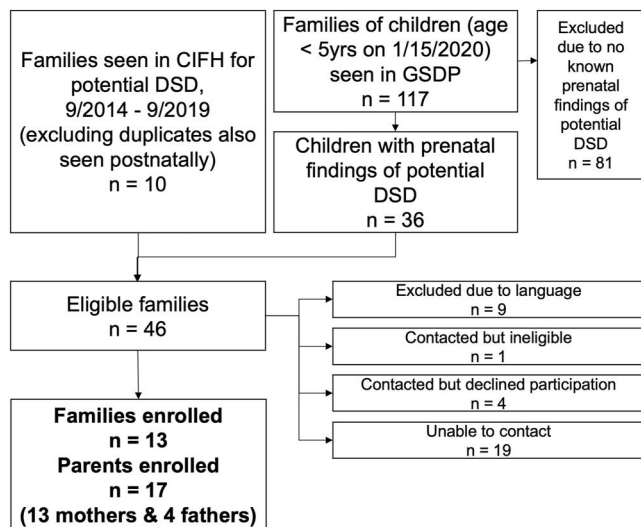
A prior study from our institution found that the parents of 70% of the infants who underwent prenatal evaluation for possible DSD were noted to experience symptoms of “distress, confusion, anxiety, and depression” two families considered pregnancy termination; and one mother reported suicidal thoughts.<sup>24</sup> The present study aimed to explore the experiences of parents whose children had prenatal findings of potential DSD, their information sources, support systems and coping mechanisms, and their levels of decisional regret regarding prenatal testing.

## 2 | METHODS

### 2.1 | Eligibility and recruitment

Parents were eligible to participate in the study if their child had prenatal detection of potential DSD because of increased chance of sex chromosome aneuploidies identified by cfDNA, genotype/phenotype discordance, or non-binary genitalia on prenatal US. Parents were eligible if any of the above characteristics were detected prenatally, even if further prenatal investigation was not offered or completed. Recruitment is outlined in Figure 1.

Potential participants were identified through chart review of pregnant patients seen for prenatal consultation at the Chicago Institute for Fetal Health between September 2014 and September



**FIGURE 1** Flowchart of parent identification and recruitment. Chicago Institute for Fetal Health (CIFH); Gender & Sex Development Program multidisciplinary clinic (GSDP); Difference of sex development (DSD).

2019 (10 patients), or pediatric patients seen in the multidisciplinary DSD clinic who were <5 years old at the time recruitment efforts commenced in January 2020 (117 patients). This age was chosen to balance the number of eligible parents with the impact of recall bias, and encompassed the time period over which prenatal diagnoses began to increase at our institution.<sup>24</sup> Of the 117 patients seen postnatally, 81 were excluded after manual chart review revealed no known prenatal findings of a potential DSD. A total of 46 patients/families were identified as eligible based on prenatal findings. Nine non-English-speaking families were subsequently excluded, as the interviewer is monolingual and interpreting services were not available for research purposes.

Potential participants were contacted by phone and/or email, with a maximum of four attempted contacts. Study staff utilized any available contact information for either parent (phone numbers, email addresses) in the medical chart. When contact was made with one parent, study staff stated that both parents (if applicable) were eligible; contact information for the other parent was then requested, if it was not already available in the medical chart. Parents received a \$30 Amazon gift card upon completion of all study procedures. Given the breadth of prenatal experiences and the relatively small eligible population, recruitment continued until no further families were able to be contacted. The study was approved by the Institutional Review Board of Ann & Robert H. Lurie Children's Hospital of Chicago (#2019-3155), and informed consent was obtained from all participants.

## 2.2 | Data collection and interview procedures

Parents completed individual interviews between July and October 2020, conducted by a single interviewer via telephone or video conferencing software (Skype for Business, Microsoft, 2020). At the time of interviews, the interviewer was a pediatric endocrinology

follow-in-training and had participated in postnatal clinical care for three of the families (ID#07-1, #09-1&2, #10-1&2), though had not participated in the prenatal care that comprised the focus of the interviews. A semi-structured interview guide covered the following topics: initial disclosure of and reaction to the potential diagnosis, questions/concerns about the prenatal evaluation and diagnosis, information sought and support utilized throughout the prenatal period, decision-making about prenatal testing, and advice for future families and clinicians faced with similar situations. The interview guide (Appendix 1) was developed and refined with input from the multidisciplinary author group. The group developed the initial topic list and then iteratively drafted and finalized the guide, after piloting with a colleague. Additional demographic data and medical history were collected by parent self-report and/or medical chart review.

Parents completed one or more Decisional Regret Scales (DRS), modified to reflect the decision point(s) of deciding to obtain or decline cfDNA testing, amniocentesis, and/or chorionic villus sampling (CVS), scored on a scale from 0 (no regret) to 100 (high regret).<sup>25</sup> These were transmitted to the study team electronically and scored manually.

## 2.3 | Data analysis

Interviews were audio-recorded, transcribed verbatim and de-identified. Thematic analysis was performed via a combined inductive (from the interviews) and deductive (from the interview guide topics) approach,<sup>26,27</sup> using MAXQDA software (VERBI Software, 2020). Three researchers (JW, JH, IR) established the initial codebook based on the first three transcripts, and two (JW and JH) collaboratively coded the remaining transcripts based on this framework, adding and modifying codes as new themes emerged. Frequencies of themes/subthemes and representative quotations were compiled. Quotes included below were minimally edited for readability only.

## 3 | RESULTS

### 3.1 | Demographics

Thirteen self-identified mothers from unique families, as well as four of their partners (all self-identified fathers), participated. Interviews averaged 43 min (range 27–93 min). Table 1 describes parent demographics.

Table 2 describes the prenatal and/or postnatal diagnostic process for each of the 13 pregnancies. Eleven of 13 pregnancies were identified as potentially affected by DSD based on cfDNA alone or in combination with findings on prenatal US indicating a genotype/phenotype discordance. The other two pregnancies were notable for non-binary appearing external genitalia on prenatal US, which in many instances triggers further diagnostic testing but in these cases did not. Seven (54%) were diagnosed with SCA, either KS or TS. Three families' experiences demonstrated missed opportunities to offer additional prenatal evaluation, had the family so desired.

TABLE 1 Demographics

Parent data (n = 17)		
Age in years at time of delivery, <sup>a</sup> median (range)		35 (23–42)
Age in years at time of interview, median (range)		37 (24–43)
		N (%)
Parental role (self-identified)	Mother	13 (76%)
	Father	4 (24%)
Race	White	15 (88%)
	Asian	1 (6%)
	Other (Egyptian)	1 (6%)
Ethnicity	Hispanic	2 (12%)
	Non-Hispanic	15 (88%)
Marital status during pregnancy	Married	14 (82%)
	Long-term relationship, unmarried	3 (18%)
Interview method	Video	11 (65%)
	Telephone	6 (35%)
Pregnancy data (n = 13)		
		N (%)
Insurance status during pregnancy	Public	2 (15%)
	Private	11 (85%)
Medical complications during pregnancy	Pre-eclampsia	3 (23%)
	Abnormality on 1 <sup>st</sup> trimester biochemical screening <sup>c</sup>	1 (8%)
	Gestational diabetes mellitus	1 (8%)
	Hyperemesis gravidarum	1 (8%)
Number pregnancy <sup>b</sup>	1 <sup>st</sup>	4 (31%)
	2 <sup>nd</sup>	4 (31%)
	3 <sup>rd</sup>	2 (15%)
	5 <sup>th</sup>	2 (15%)
	8 <sup>th</sup>	1 (8%)
Birth order of child <sup>a</sup>	1 <sup>st</sup>	6 (46%)
	2 <sup>nd</sup>	5 (38%)
	3 <sup>rd</sup>	1 (8%)
	4 <sup>th</sup>	1 (8%)

<sup>a</sup>Refers to birth/delivery of child with potential DSD.

<sup>b</sup>All spontaneous and induced abortions are included.

<sup>c</sup>Subsequent testing all normal, no further details available.

### 3.2 | Decisional regret scale—Decision to pursue or decline cfDNA testing

Fifteen parents from 12 families were offered and chose to proceed with cfDNA testing, and 12/15 scored  $\leq 15$  on the DRS-cfDNA indicating very low regret. The parent with the highest level of regret (ID#08-1, score 65/100) stated: "I don't think I would ever do testing again. ...We would rather go with the flow... It was an emotional ride." Another parent (ID#06-1) with a moderate level of regret (35/100) described initially being upset that she knew

"unnecessary" information prenatally, but upon looking back felt grateful to have known the diagnosis.

### 3.3 | Decisional regret scale—Decision to pursue or decline amniocentesis or CVS

Of the 12 parents from 9 families who were offered either amniocentesis or CVS, regret levels about their decisions were low: 11/12 scored  $\leq 15$  (6 of these 12 were offered but declined the procedure).

TABLE 2 Prenatal and postnatal diagnostic testing

Parent ID# <sup>a</sup>	cfDNA chromosomal prediction	Genitalia on prenatal US	Prenatal diagnostic testing	Postnatal genetic testing	Final diagnosis	Age at which final diagnosis confirmed	Sex of rearing
01-1	47,XXY (KS)	Not collected	Amnio obtained	N/A	47,XXY (KS)	Prenatally	Male
02-1	47,XXY (KS)	Not collected	Amnio obtained	N/A	47,XXY (KS)	Prenatally	Male
03-1	47,XXY (KS)	Not collected	Amnio obtained	N/A	47,XXY (KS)	Prenatally	Male
04-1	47,XXY (KS)	Not collected	CVS obtained	N/A	47,XXY (KS)	Prenatally	Male
05-1	47,XXY (KS)	Not collected	Amnio/CVS declined	Chromosome analysis	47,XXY (KS)	<1 month	Male
06-1, 06-2	47,XXY (KS)	Not collected	Amnio/CVS declined	Chromosome analysis	47,XXY (KS)	9 months	Male
07-1	45,X (TS)	Not collected	Amnio obtained	Chromosome analysis revealed 45,X/46,XY mosaicism	TS + Y	<1 month	Female
08-1	46,XX	Male-typical	Amnio obtained	N/A	46,XX + SRY translocation	Prenatally	Male
09-1, 09-2	46,XX	Male-typical	Amnio/CVS not offered <sup>b</sup>	DSD gene panel	Paternally-inherited heterozygous pathogenic variant in NR5A1	8 months	Male
10-1, 10-2	46,XY	Female-typical	Amnio/CVS declined	DSD gene panel	46,XY CGD	N/A, no specific genetic etiology determined	Female
11-1	46,XY	Female-typical	Amnio/CVS declined	AR sequencing declined by family	Assumed CAIS based on family history and known maternal carrier status	N/A	Female
12-1, 12-2	Not offered	Non-binary	Amnio/CVS not offered <sup>b</sup>	DSD gene panel	<i>De novo</i> heterozygous pathogenic variant in WT1	5 months	Male
13-1	46,XY	Non-binary	Amnio/CVS not offered <sup>b</sup>	DSD gene panel	Heterozygous likely pathogenic variant in NR5A1	16 months	Male

<sup>a</sup>Parent ID# ending with '-1' indicates mothers, '-2' indicates fathers (self-identified).

<sup>b</sup>Indicates missed opportunity for prenatal diagnostics.

Abbreviations: Amnio, amniocentesis; AR, androgen receptor; CAIS, complete androgen insensitivity syndrome; cfDNA, cell-free DNA; CGD, complete gonadal dysgenesis; CVS, chorionic villus sampling; KS, Klinefelter syndrome; NR5A1, Nuclear Receptor Subfamily 5 Group A Member 1, encodes Steroidogenic factor 1; TS + Y, Turner syndrome with Y-chromosome material; SRY, Sex-determining region of the Y-chromosome; US, prenatal ultrasound; WT1, Wilms' tumor 1, encodes Wilms' tumor protein.

The parent described above with the highest level of regret on the DRS-cfDNA also had a score of 90/100 on the DRS-Amnio/CVS.

### 3.4 | Qualitative results

Predominant themes included experiences of the initial diagnosis, decisions about prenatal testing, information seeking, decisions about disclosure and sources of support. Thematic saturation was reached with regards to the participants' experiences and views of prenatal testing decisions, but not with regards to their informational sources, decisions about disclosure, or sources of support.

#### 3.4.1 | Experiences of preliminary diagnosis

Initial reactions to the potential DSD diagnosis varied widely. Parents recalled having many medical concerns, which ranged from questions about life expectancy that could be shared by parents of any child with a complex medical condition, to more detailed questions of anatomy and fertility specific to DSD. Some parents worried about stigma related to the child's anatomy. The few parents who stated that they had awareness of DSD/intersex traits prior to the affected pregnancy, such as the parent for whom there was a known family history of CAIS, recalled generally less-negative reactions. Other parents were not familiar with the existence of DSD/intersex traits, or were not aware that diagnoses related to sex chromosomes were included in the prenatal screening tests. Representative quotes are shown in Table 3.

#### 3.4.2 | Information seeking

Two main sources of information accessed by parents during the prenatal period were clinicians and online sources.

Based on self-report, families most frequently received information from prenatal genetic counselors (9/13 families, 69%), high-risk obstetricians or maternal-fetal medicine specialists (7/13, 54%), and neonatologists (3/13, 23%). Comments from parents who had prenatal consults specifically addressing the possible DSD largely reflected a lack of experience with the diagnoses: one parent reported receiving conflicting information from different clinicians (ID#03-1), while several reported the information they received was no more than they had found through their own online research (ID#07-1, ID#11-1, ID#02-1), or that the clinicians did not have the volume of clinical experience with the condition needed to confidently answer their questions (ID#08-1, ID#04-1). Two families (ID#02-1, ID#04-1) had a multidisciplinary prenatal consultation with a genetic counselor and pediatric endocrinologist at a high-volume center and reported receiving helpful information and anticipatory guidance.

For three families, there was minimal opportunity to receive additional information or counseling. For one, genotype/phenotype discordance was dismissed as testing error: "it just didn't even really

cross our minds because [the clinician] just kept saying things along the lines of "this was impossible." (ID#08-1) Another family was told the discordance was "just the 0.001% chance that the genetic test was wrong," followed later by an alternative explanation that proved "devastating": "the ultrasound tech was like "oh you could have had twins, and then one died and that's where you got the [cfDNA] testing saying it was a boy" (ID#09-1). A third family had a (non-medical) 3D prenatal US showing non-binary external genitalia. When she asked her obstetrician to investigate, her recollection of the response was that "those places don't know what they're doing, you're having a boy - the blood test says you're having a boy" (ID#13-1).

Most of the parents consulted the Internet for additional information on their child's condition. Internet sources were "a lot all at once"—"what do we really take seriously?" (ID#03-1). A limiting factor for some parents was the rarity of their child's diagnosis, but even parents of children with KS expressed frustration with lack of information: "it was daunting and [online information] was inaccurate. ... It just felt like I was in the 1960s (ID#04-1)". Of the few parents who did not seek information online, one avoided the Internet intentionally due to prior experiences with misinformation. The others expressed low levels of concern and did not feel the need to seek information outside of what they learned from their medical team.

Several parents specifically cited YouTube as a helpful source for learning about real-life experiences from adults with KS. Several parents accessed the medical literature (PubMed) and expressed a high level of confidence in the information they found.

#### 3.4.3 | Disclosing to others and finding support

Inductive analysis revealed that the support systems and methods that parents used for coping were heavily influenced by the decisions they made about disclosure of the DSD diagnosis, since in many cultures genitalia is private and DSD diagnoses can be associated with significant stigma.<sup>28</sup> Seven parents from six families discussed limiting disclosure to protect their future child's privacy and allow them the autonomy to disclose their medical condition as they grew up, though this limited the support the parents were able to access. Five parents from distinct families discussed worries about disclosure based on specific family members' perceived level of social conservatism or attitudes about gender essentialism. Parents described conflicting feelings about whether attempts to maintain privacy would be perceived as creating shame and secrecy. Some parents expressed feeling burdened with the responsibility to explain the diagnosis, even though they themselves still had more questions than answers. These dichotomies are visually represented in Figure 2, along with representative quotes to illustrate the benefits and drawbacks of wider versus more limited disclosure.

Notably, all families whose child was diagnosed with the more common conditions KS or TS limited their prenatal disclosure to a few immediate family members and in one case a close friend, as did two of the four families with genotype/phenotype discordance. On the other hand, two families with discordance had a "gender reveal" where they

TABLE 3 Responses to potential DSD diagnosis or inconclusive prenatal testing

Response	Quotation	Parent ID, Child's diagnosis
Neutral/Positive emotional reaction	"I really felt fine, I mean because my husband and I have always been of the philosophy of like, we're just happy to have a baby... and this is a healthy baby. ...There are many other things that are way more difficult or scary." <sup>a</sup>	#10-1, CGD
	"This is kind of like a medical scientific mystery. So it wasn't shocking or disturbing or anything like that." <sup>a</sup>	#10-2, CGD
	"It's never been like a huge deal for me, the possibility of any of our kids having this because I've always felt that it could be a much worse thing, you know? And having [a family member] having this, I knew what we were getting in for." <sup>a</sup>	#11-1, CAIS
Surprise/Shock	"I was not prepared. [During pre-test counseling] you're like, well that's not gonna be me, I don't have to worry about any of this. And I got a phone call and I was ... not necessarily prepared for that kind of news. ...It was just kind of a lot."	#04-1, KS
	"I was taken aback because ... this wasn't discussed [as a possibility]. And so there was a bit of a surprise there because I didn't think [the child's diagnosis] was covered." <sup>a</sup>	#05-1, KS
Sad	"I went home and I think I just laid down and went to bed. And I was just super depressed."	#07-1, TS + Y
Scared/Worried	"I had a million questions. ...They wanted [husband] and me to meet with a genetic counselor [but could not be seen right away]. So for 2 weeks, we just kind of sat with this news without anyone professional to discuss it with. That was really, really hard for me."	#06-1, KS
	"It sucked. It honestly sucked. ...Of course, your mind goes to the worst-case scenario."	#06-2, KS
	"I remember my husband and I both, our stomachs kind of dropped and we were just like, what does that even mean, you know? ... You immediately are just plunged into this pool of worry. ... Because we knew absolutely nothing about it, it was pretty scary."	#01-1, KS
Questions about child's future mental health and coping	"When I look at [my child], I find that I still have these probably heteronormative fears and hopes that I put out on to him. ... I want him to feel so supported and liberated to be whoever he is. But like, internally, I am gonna battle these things, I'm like, god is his penis too small? Like are his testicles gonna be tiny, are people going to make fun of him?" <sup>a</sup>	#06-1, KS
	"We wanted [our child] to have as normal of a life growing up and we want him to be happy and healthy. So, you know, we don't want him to get teased, we just want him to be normal and feel normal. Because he is normal." <sup>a</sup>	#08-1, 46,XX + SRY
	"How are we gonna know if they're gonna wanna be like... a boy or a girl and how do I know? ... But it was more of like, how do we treat this, how do we help him cope?" <sup>a</sup>	#13-1, NR5A1 variant
Medical concerns specific to DSD	"Is he gonna need therapy and hormone therapy? Or later on in life, like if they want to have children, I mean I know, okay maybe adoption, whatever - if this happens, these are his or her options." <sup>a</sup>	#13-1, NR5A1 variant
	"The two biggest [concerns] for me were the potential for my son to have a micropenis and the potential for him not to have children." <sup>a</sup>	#05-1, KS
Other medical concerns	"That's the most terrifying thing for a parent, I think is life expectancy. ... I had no information so I was just looking for like, how difficult will this child's life be if we choose to keep the child, and how long will life expectancy [be], all the things that scare a parent."	#07-1, TS + Y
Cause of condition and reversibility	"I couldn't believe that this just happened and I must have done something to cause it. ... it must have been these medications, or maybe - I mean I	#03-1, KS

TABLE 3 (Continued)

Response	Quotation	Parent ID, Child's diagnosis
	was thinking crazy stuff - like I flew on an airplane early in pregnancy, maybe it was the radiation from the plane."	

<sup>a</sup>Indicates comments specific to DSD diagnosis.

Abbreviations: CAIS, complete androgen insensitivity syndrome; CGD, complete gonadal dysgenesis; KS, Klinefelter syndrome; NR5A1, Nuclear Receptor Subfamily 5 Group A Member 1, encodes Steroidogenic factor 1; SRY, Sex-determining region of the Y-chromosome; TS + Y, Turner syndrome with Y-chromosome material.

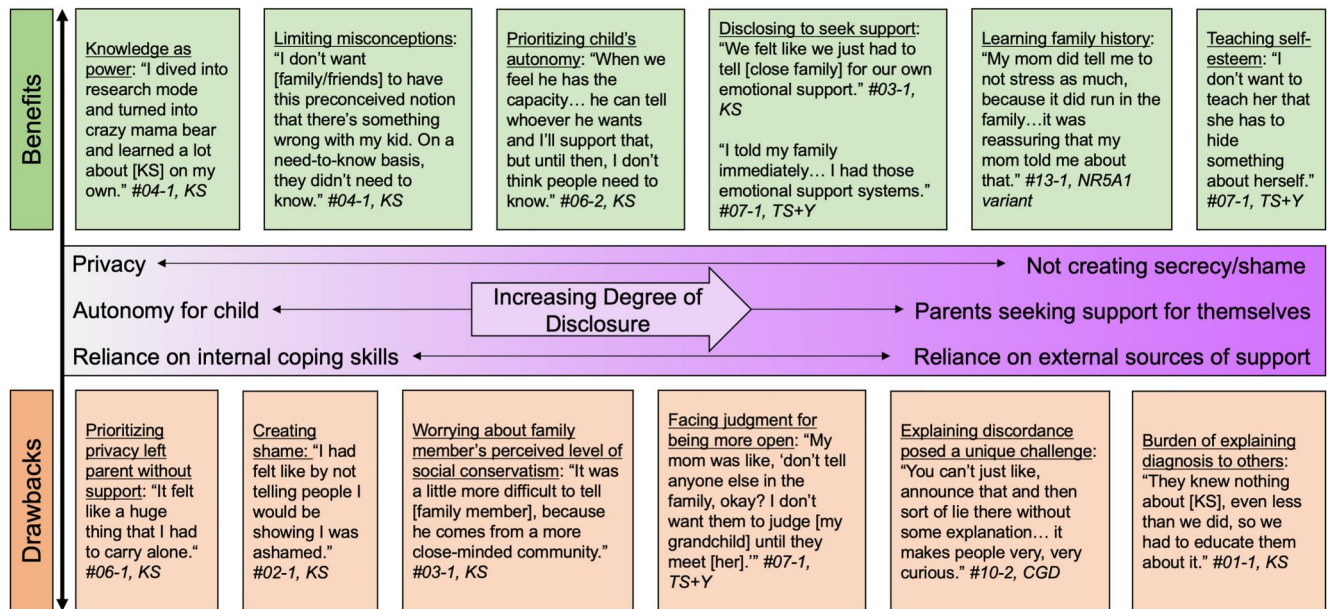


FIGURE 2 Factors affecting prenatal disclosure of diagnosis and parental support-seeking. Complete gonadal dysgenesis (CGD); Klinefelter syndrome (KS); Nuclear Receptor Subfamily 5 Group A Member 1, encodes Steroidogenic factor 1 (NR5A1); Turner syndrome with Y-chromosome material (TS+Y). Text in italics denotes parent ID and child's diagnosis [Colour figure can be viewed at [wileyonlinelibrary.com](http://wileyonlinelibrary.com)]

widely disclosed the child's initial predicted sex based on cfDNA and subsequently felt obligated to disclose the "updated" predicted sex based on US, expressing some regret about their earlier publicity. One family whose child had non-binary genitalia on US had previously announced the predicted sex based on cfDNA, but subsequently chose not to disclose the US findings. The other family whose child had non-binary genitalia on US (and did not have cfDNA testing) simply told their social networks that they were not finding out the predicted sex prenatally.

Many parents turned to the Internet for support, with mixed results. One was encouraged to advocate for herself by asking her medical team more questions after she posted in an online group (ID#09-1), and another parent found social media groups for new parents to be a valuable source of support (ID#07-1). Several families discussed being overwhelmed or disheartened by forums full of "extreme bad situations" (ID#01-1), and others found only inactive diagnosis-specific support groups and disconnected telephone numbers.

All parents mentioned their partners as sources of emotional and decision-making support, and only one parent discussed an increase

in arguments or relationship difficulties as a direct result of the DSD evaluation.

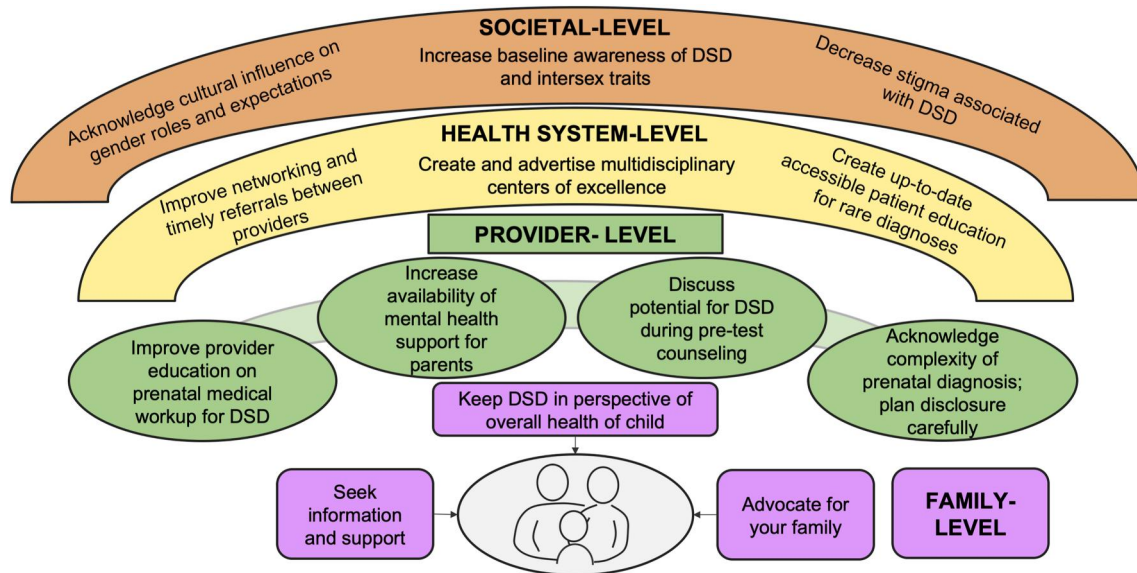
### 3.4.4 | Advising future families and clinicians

The section of the interview which addressed advice for future families and clinicians was designed to seek input on improvements to the process of prenatal testing and diagnosis and identify areas of need. The feedback shared was organized into a schematic representation of potential interventions and improvements at multiple levels—family, provider, healthcare system, and societal (Figure 3).

## 4 | DISCUSSION

The current study is the first to our knowledge to use qualitative methods to explore the experiences of parents whose children had prenatal findings of such a broad range of potential DSD diagnoses. We report insights that should guide modifications to current





**FIGURE 3** Parental perspectives on targets for improvement. Difference of sex development (DSD) [Colour figure can be viewed at [wileyonlinelibrary.com](http://wileyonlinelibrary.com)]

practice patterns in terms of counseling and managing prenatal detection of potential DSD. Parents shared their experiences with the diagnosis and testing, their sources of information and support, and their perspectives on unmet needs and ways their experiences could have been improved.

Parents without any pre-existing familiarity with DSD expressed more shock and confusion at the diagnosis. On a broad societal level, de-stigmatization of DSD and increased awareness of these conditions could substantially reduce the initial shock of the diagnosis. De-stigmatization could also be accomplished on an individual level with targeted changes in the pre-cfDNA test counseling to better prepare parents,<sup>29</sup> including dispelling the common misperception of cfDNA as a foolproof “gender test.”<sup>30</sup>

Several parents described difficulty navigating the healthcare system despite the fact that our sample was largely privately insured, older than the average age for parenthood in the United States,<sup>31</sup> and able to access care at a tertiary care center. Parents emphasized the benefits of receiving subspecialty and/or multidisciplinary consultation and recommended improved communication amongst local healthcare networks so families can receive timely referrals to teams with an appropriate level of expertise. Parents also expressed a clear desire for easily accessible and up-to-date online educational materials for families of children with rare and/or complex diagnoses, a need which has also been identified in other studies.<sup>32</sup>

Prenatal diagnosis offers time for families to process and prepare for the birth of a child with a complex medical condition.<sup>33–36</sup> It is key, though, that this gift of time be used well, with appropriate medical evaluation, thorough prenatal counseling, and consultation with subspecialists as indicated; otherwise, prenatal diagnosis risks becoming “toxic knowledge” that only increases stress levels during pregnancy.<sup>37</sup>

As noted, many parents recalled surprise, shock, and worry at the time of diagnosis, though on the quantitative DRS most parents

indicated low levels of regret about the testing decisions they made during pregnancy. These conflicting findings may indicate that there is room for improvement in the pre-test counseling or the methods of test result disclosure (these concerns were also identified in a study of mothers who expressed higher levels of regret regarding their decision to have NIPS.<sup>38</sup>) Or, perhaps over time and in retrospect, parents come to understand the benefits of earlier diagnosis, such as gaining actionable knowledge to improve their child's health.<sup>39</sup>

Three families in this study experienced missed opportunities for prenatal evaluation. The collective experiences of these families are strong evidence of the need for widespread dissemination of education on best practices<sup>40</sup> as NIPS techniques continue to advance. Medical education on controversies in the care of people with DSD has historically been limited, and as this field rapidly evolves there is a need for improved and ongoing education for clinicians.<sup>41,42</sup>

The need for formal psychological support for parents during the prenatal period is paramount,<sup>21</sup> made even more important by the limitations on peer support these families experienced due to concerns about disclosure (again, related to societal-level stigma surrounding DSD), similar to the findings of Crissman, et al.<sup>43</sup> There is emerging evidence that parental distress during pregnancy impacts the child's mental health outcomes later in life.<sup>44</sup> It is therefore essential to provide comprehensive psychosocial evaluation and intervention to help families navigate the disclosure process. Existing multidisciplinary DSD teams could expand their services to offer prenatal consultations and expand the availability of behavioral health consultation to parents as well as the children/adolescents currently seen. Peer supports and parent networks could also be expanded. The most frequent advice that our parents offered to parents in similar situations was to keep the DSD diagnosis in perspective: to seek accurate information about the diagnosis to prepare for specific challenges, but also to remember that the DSD will likely not affect every aspect of the child's life or health.

## 4.1 | Limitations

Recruitment of participants from a multidisciplinary clinic at a large academic pediatric medical center, and interviewing performed by a clinician, introduced potential biases, thus the perspectives here do not represent all parents expecting a child with a potential DSD. We were more likely to have access to up-to-date contact information for families who chose to receive ongoing post-natal care within our institution, which may bias results toward positive views of our program and services, though only two families received prenatal care within our institution. All recruited participants had chosen to continue the pregnancy, and we were not able to identify or recruit those who may have chosen to terminate the pregnancy, whether due to the potential DSD or other reasons. Those who had genotype/phenotype discordance or non-binary genital appearance on US due to non-DSD etiologies are presumably less likely to be referred to our center for subspecialty care. Given the limited pool of potential participants and the wide variety of prenatal experiences, we did appear to reach data saturation with regards to the participants' experiences and views of prenatal testing decisions, but not with regards to their informational sources, sources of support, or decisions about disclosure. As previously mentioned, children of participants were <5 years old at the time of recruitment in order to expand the pool of potential participants, with the tradeoff of potentially increased recall bias among parents of the older children.

## 5 | CONCLUSION

This study of the experiences of parents whose children were prenatally diagnosed with a wide range of DSD conditions identified many potential areas for improvement, such as increasing information availability online and from medical teams, formal psychological support services, and continued advocacy efforts to raise awareness of and de-stigmatize DSD. Given that cfDNA screening is rapidly becoming the predominant form of aneuploidy screening locally and nationally, and cfDNA technology is expected to continue to expand,<sup>45</sup> prenatal DSD diagnosis is expected to increase in frequency. Our hope is that this study will help provide the basis for future educational and clinical interventions to improve the care we provide for children with DSD and their families.

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### CONFLICT OF INTEREST

All authors declare no conflicts of interest related to this work.

### DATA AVAILABILITY STATEMENT

Members of DSD/intersex communities experience significant stigma and discrimination, and thus, since the interview transcripts and other study data contain potentially identifying information, the study team has decided not to make the data publicly available to preserve the privacy of the participants and their children.

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## SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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