

DEVELOPING A PTDA FOR FEMINIZING GENITOPLASTY FOR CAH

EXPLORING USER REQUIREMENTS FOR THE DESIGN OF AN ELECTRONIC  
PATIENT DECISION AID FOR GUARDIANS MAKING TREATMENT  
DECISIONS ABOUT CONGENITAL ADRENAL HYPERPLASIA

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## Abstract

Congenital Adrenal Hyperplasia (CAH) describes a set of autosomal recessive diseases which affect enzymes mediating steroid biochemistry in the adrenal glands. In chromosomal females, the excess androgens associated with CAH cause virilization. Females with a high degree of virilisation can undergo feminizing genitoplasty in infancy or later in life. Parents and guardians are the medical proxies for their infants and therefore make decisions on their behalf. However, decision-making about feminizing genitoplasty can be very difficult. One tool that could help in such a situation is an electronic patient decision aid (PtDA). However, a PtDA for feminizing genitoplasty does not exist and there is insufficient information in existing literature to inform its design and development.

Thus, the objectives of this study were to:

1. Identify user requirements
2. Develop specifications for the design and development of the PtDA
3. Understand the best way to implement and distribute the PtDA

We used the persona-scenario methodology to acquire user-requirements. Persona-scenario sessions were conducted with four parents of children with CAH, two adult patients with CAH, and four healthcare practitioners. Participants created fictitious personas, and scenarios wherein their personas interacted with an idealized version of the PtDA. Transcripts of these persona-scenarios and facilitator notes were analyzed to identify user-requirements, which were interpreted into specifications.

Participants provided user requirements about (1) information and decisional content in the PtDA, (2) proposed functionalities for the PtDA, (3) web usability, and (4) implementation context. Many of these requirements are supported by existing literature. The requirements identified in this project will inform the design and development of a PtDA for feminizing genitoplasty in

patients with CAH. However, further research is necessary to understand how to best implement these requirements and to ensure that the gathered information is useful for a broad range of potential end users.

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## **Dedication**

*To my parents, thank you for your support*

## Table of Contents

1. Introduction.....	1
2. Congenital Adrenal Hyperplasia .....	3
2.1. Disorder .....	3
2.2. Diagnosis .....	8
2.3. Non-surgical Treatment.....	10
2.3.1. Prenatal .....	10
2.3.2. Steroid Replacement .....	11
2.4. Surgical Treatment.....	13
2.4.1. Clitoral Surgeries .....	14
2.4.2. Vaginoplasty .....	21
2.4.3. Perineoplasty/Labioplasty.....	27
2.5. Timing of Surgical Treatment .....	28
2.6. Parents' Role and Experience in Decision Making for Feminizing Genitopasty .....	31
3. Shared Decision Making and Patient Decision Aids.....	37
4. The SDLC for the Creation of eHealth Applications .....	42
5. The Persona-Scenario Methodology .....	45
6. Methods.....	48
6.1. Sampling for Participants .....	48
6.2. Persona-Scenario Sessions.....	51
6.3. Public and Patient Engagement Evaluation Tool and Demographic Survey .....	52
6.4. Ethics .....	53



6.5. Analysis.....	53
7. Results and Analysis .....	55
7.1. Demographics.....	55
7.2. Personas and Scenarios .....	57
7.3. Coding and Analysis of Requirements .....	61
7.4. PtDA Requirements and Specifications .....	66
7.4.1. Information and Decisional Content in the PtDA.....	66
7.4.2. Proposed Functionalities for the PtDA.....	70
7.4.3. Web Usability-related Requirements .....	72
7.4.4. Implementation Context.....	74
7.5. PPEET .....	78
8. Discussion .....	81
8.1. Analysis of User Requirements .....	81
8.2. Strengths and Limitations.....	95
8.3. Future Work .....	101
9. Conclusion.....	102
10. References .....	104
11. Appendix.....	122
Appendix A: Search Strategy .....	122
Appendix B: Introduction to PtDAs and Persona-Scenario Development and Discussion Guide .....	123
Appendix C: Letters of Information and Consent for Parents, Patients and Practitioners .....	134

Appendix D: Public and Patient Engagement Evaluation Tool (PPEET) and  
Demographics Survey for Parents/Patients and Practitioners..... 146  
Appendix E: Persona-Scenario Stories ..... 154

## List of Figures

Figure 1 Biosynthetic pathway of steroids. ....	5
Figure 2 The Prader scale. ....	7
Figure 3 (A) Surgical separation of an enlarged clitoris (B) A cross section of the clitoris, showing the various components of the organ .....	17
Figure 4 Tunica Albuginea sparing surgery as described by Kaefer et al. ....	18
Figure 5 Illustration depicting the flap vaginoplasty. ....	22
Figure 6 Illustration of a pull through vaginoplasty.....	23
Figure 7 Cross sections illustrating urogenital sinus mobilization. ....	24
Figure 8 Diagrams illustrating the Anterior Sagittal Transrectal Approach (ASTRA). ....	25
Figure 9 Illustration of perineoplasty/labiaplasty. ....	28
Figure 10 Unified modelling language activity diagram showing one potential workflow for how the PtDA would be shared with and used by families and practitioners. ....	77
Figure 11 Patient and parents' responses to the Likert section of the PPEET, indicating a generally positive perception of the activity. ....	79
Figure 12 Healthcare practitioners' responses to the Likert section of the PPEET, indicating a generally perception of the activity.. ....	80

## List of Tables

Table 1 Demographic characteristics of parents of children with CAH who had feminizing genitoplasty .....	56
Table 2 Demographic characteristics of adult female patients with CAH who had feminizing genitoplasty in adolescence or as young adults .....	56
Table 3 Demographic characteristics of healthcare practitioners .....	57
Table 4 A sample of how nodes were analysed with examples from each category and some subcategories.....	63

Table 5 Some design features described by participants that aligned with IPDASi v4.0 criteria without being explicitly prompted for within the question guide or during discussion.....94

Table 6 Design features (user requirements) discussed in the persona-scenario that are beyond the scope of a PtDA for feminizing genitoplasty.....99

## **List of Abbreviations and Symbols**

ACTH: Adrenocorticotropic hormone

ASTRA: Anterior sagittal transrectal approach to vaginoplasty

CAH: Congenital adrenal hyperplasia

CRH: Corticotropin-releasing hormone

DSD: Disorder/Difference of sex development

HiREB: Hamilton integrated research ethics board

HIT: Health information technologies

IPDAS: International patient decision aids standards

PPE: Public and patient engagement

PPEET: Public and patient engagement evaluation tool

PtDA: Patient decision aid

PUM: Partial urogenital mobilization

RCT: Randomized controlled trial

SDLC: Software development lifecycle

SDM: Shared decision making

TUM: Total urogenital mobilization

UGS: Urogenital sinus

17-OHP: 17-Hydroxyprogesterone

## 1. Introduction

Treatment decisions are complex in pediatric settings, where patients, parents and guardians, and clinicians face the challenge of choosing between treatments, their benefits, side effects, and the alignment of treatments with family values. This is particularly the case for treatment of congenital adrenal hyperplasia (CAH), a disorder of sex development (DSD) which causes virilization (genital masculinization, ranging from mild clitoral enlargement to a phallic urethra) along with various endocrine, gynecologic, and reproductive repercussions. In cases of severe virilization, stakeholders in the decision process must decide and agree on whether the child has surgery in infancy or later in life. Each option carries significant advantages and disadvantages, both medically and with regards to the psycho-social and emotional development of the child and the family. However, with surgical treatment evolving over the past few decades, there is a lack of strong evidence regarding treatment outcomes for novel techniques.<sup>1</sup> This lack of evidence, along with misinformation that parents receive, means that parents are faced with confusion, worry, stress, poor-quality decision-making, and moderate decisional regret.<sup>2-7</sup> This is to the extent that some parents of children with disorders of sex development develop symptoms of post-traumatic stress.<sup>8</sup> Consequently, there is a need to understand information needs and decision-making processes in cases of CAH. This understanding will lead to the development of methods to promote high-quality decisions which are informed, in line with families' values, and result in minimal regret.

Recently, there has been an international shift towards patient-centered care. Clinicians and guardians have called for the development of patient decision aids (PtDAs) to address challenges in communicating treatment options and to promote shared decision making (SDM).<sup>9</sup> Advances in health information technologies (HIT) (a broad concept that comprises an array of technologies to store, share, and analyze health information), have expanded the scope of patient decision aids to improve decision making. Although evidence regarding its

impact on SDM is still limited, disseminating patient decision aids through the internet as electronic PtDAs allows for the integration of additional support functionalities, tailoring to individual needs, and the benefits of being highly accessible and cost-effective.

To inform the creation of an electronic PtDA to support surgical decision-making for CAH, the objectives of this research study were to:

1. Identify user requirements such as:
  - a. the information required in the PtDA,
  - b. the formats and functionalities of the PtDA,
2. Develop specifications for the design and development of the PtDA
3. Understand the best way to implement and distribute the PtDA.

The research question was:

*What is the optimal design of a patient decision aid for surgical treatment of congenital adrenal hyperplasia (i.e., both the characteristics and design of the patient decision aid, and the focus and format of the informational content)?*

To answer this question, we used the persona-scenario methodology, an innovative user-centered design approach that involves users to determine requirements for the planned output—i.e., what users require the PtDA to do to meet their needs. Data collected over several sessions (with 4 parents, 2 adult CAH patients and 4 healthcare practitioners) was transcribed and coded for user requirements, which were aggregated into higher categories of (1) information and decisional content in the PtDA, (2) proposed functionalities for the PtDA, (3) web usability-related requirements, and (4) implementation context. The research team judged each requirement for its feasibility, desirability, and viability. Then, where appropriate, requirements were translated into specifications by interpreting the requirement as requiring an action and/or a product. To gain more insight, user requirements within each of these categories were compared

between end-user groups and to the previous literature about CAH, decision making, and health information technology design.

A central aspect of user-centered design is to involve users during the design and development process. The public and patient engagement evaluation tool (PPEET) was used to evaluate the engagement of participants in the PtDA co-design and to provide an avenue for formal feedback to improve the data collection process.<sup>10</sup>

The thesis will begin with background information and identification of existing gaps in the literature. It will then describe the qualitative research and analysis methods used in the study, followed by a description of the results. Finally, the thesis will conclude with a discussion of the findings, study strengths, limitations, and next steps.

## **2. Congenital Adrenal Hyperplasia**

### **2.1. Disorder**

Congenital adrenal hyperplasia (CAH) is a disorder of sex development. It describes a set of autosomal recessive disorders which affect enzymes mediating steroid biochemistry in the adrenal glands. The most common of these, occurring in 95 per cent of individuals with CAH, is associated with mutations or deletions in the *CYP21A2* gene which encodes the adrenal cytochrome P-450 responsible for steroid hydroxylation (i.e., steroid 21-hydroxylase).<sup>1,11</sup> While inherited in an autosomal recessive fashion, CAH is one of the most common inherited metabolic disorders. The incidence of classic CAH ranges from 1:10000 to 1:20000 births.<sup>11</sup> However, in some ethnic groups, the incidence can be as high as 1:280, especially in remote geographic communities and/or communities with high rates of inbreeding (e.g., among the Yupik Eskimos of southwestern Alaska and the people of La Reunion, France).<sup>11</sup>



21-hydroxylase normally converts 17-hydroxyprogesterone to 11-deoxycortisol (the precursor to cortisol) and progesterone to deoxycorticosterone (the precursor to aldosterone). Consequently, defects in 21-hydroxylase impair cortisol and aldosterone production. Additionally, cortisol normally acts to inhibit the production of corticotropin releasing hormone (CRH) by the hypothalamus. In children with CAH, the lack of adrenal cortisol stimulates the production of CRH by the hypothalamus, causing the production and release of adrenocorticotrophic hormone (ACTH) by the anterior pituitary. High ACTH levels lead to adrenal hyperplasia and increase adrenal hormone production. Since cortisol and aldosterone cannot be produced, their precursors are diverted to the synthesis of androgen hormones. This causes the production of excessively high levels of androgen precursors, which once secreted are further metabolized to active androgens (testosterone, dihydrotestosterone, etc.), and to a lesser extent estrogens (estrone and estradiol) (see figure 1).<sup>1</sup>

Disease severity correlates well with specific *CYP21A2* alleles. The clinical phenotype is classified as classic for the severe form (of which there are salt-wasting or simple-virilizing forms, depending on the degree of aldosterone deficiency), or non-classic for the less severe form. About 50% of individuals with classic CAH have a mutation caused by large deletions or splicing mutations that remove enzyme activity.<sup>12</sup> However, more than 300 *CYP21A2* mutations are known (including point mutations, small deletions, small insertions, and complex rearrangements of the gene).<sup>13</sup> Notably, because many patients are heterozygotes for two or more different mutant *CYP21A2* alleles, CAH patients present with a wide variety of phenotypes.<sup>1</sup> The classical CAH phenotype (salt-wasting or simple virilising) is caused when a patient carries 2 severe mutations, while a non-classical phenotype is caused by a mild/mild or severe/mild genotype.

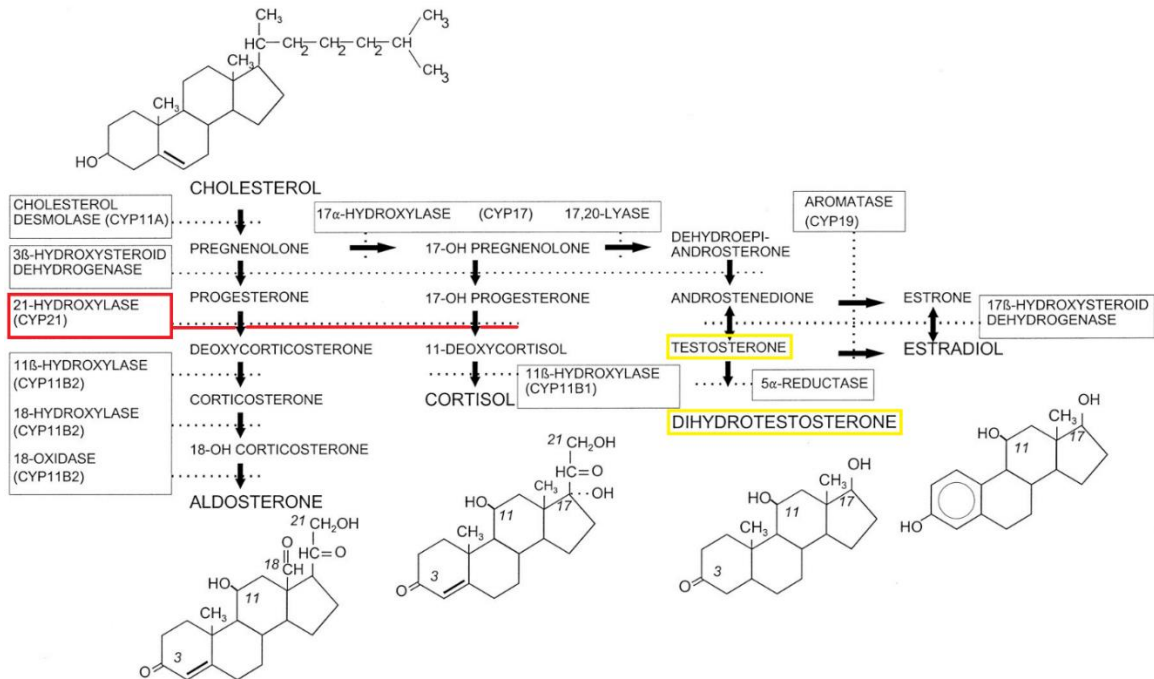


Figure 1 Biosynthetic pathway of steroids. CAH is most commonly caused by mutations in 21-hydroxylase deficiency (CYP21) (Red), which prevents normal production of aldosterone and cortisol, causing excess production of virilizing androgen hormones (Yellow).<sup>1</sup>

In cases of low to moderate enzyme deficiency, if CAH is undiagnosed or left untreated, both male and female infants undergo rapid postnatal growth and sexual precocity (the appearance of secondary sexual characteristics before the lower limit of the normal age for pubertal onset). In cases of severe enzymatic deficiency, untreated CAH can cause neonatal salt loss and death. About 75% of classic CAH cases suffer from aldosterone deficiency with salt wasting, failure to thrive, and potentially fatal hypovolemia and shock.<sup>1</sup>

In chromosomal females, in addition to the complications described above, the excess androgens associated with classic CAH cause virilization (genital masculinization), increased muscle strength, acne, hirsutism, frontal hair thinning, deepening of the voice, and menstrual disruption due to anovulation along with

<sup>1</sup> Adapted from White, P.C., Speiser, P.W., Congenital Adrenal Hyperplasia due to 21-Hydroxylase Deficiency, Endocrine Reviews, 2000, Volume 21, Issue 3, Pages 245–291, by permission of Oxford University Press.<sup>14</sup>

various other endocrine, gynecologic, and reproductive issues (if androgen production continues uncontrolled).<sup>1</sup> Genital virilization occurs because the fetal adrenal glands begin to produce excess androgens at a key stage of development when the urogenital sinus (UGS) is in the process of septation (partitions forming separate canals for the vagina and urethra). The high levels of circulating adrenal androgens not only prevent septation, they also interact with genital skin androgen receptors and induce clitoral enlargement, promote fusion of the labial folds, and cause forward migration of the urethral/vaginal perineal opening. However, internal structures are usually not virilized, presumably because that would require significantly higher local concentrations of testosterone than are present.<sup>14</sup> Genital virilization can range from mild clitoral enlargement to a phallic urethra. This spectrum was described by Andrea Prader in 1954, who developed the Prader Scale (see figure 2B) to roughly rate the degree of virilization of the genitalia and to provide a consistent vocabulary for healthcare practitioners.<sup>15,16</sup> The Prader scale identifies five distinct stages of CAH:

- **Stage 0** describes a non-virilised female.
- **Stage 1** appears normal but has a slightly enlarged clitoris and slightly reduced vaginal opening size that can go unnoticed or be considered within normal variation.
- **Stage 2** genitalia are clearly abnormal to the eye, with an enlarged clitoris and a small vaginal opening with separate urethral opening. There is posterior labial fusion (the labia are fused towards the back).
- **Stage 3** shows a further enlarged phallus, with a single urogenital sinus (the vagina and urethra share a single opening) and almost complete fusion of the labia.
- **Stage 4** illustrates a large phallus the size of a normal penis. The labia are completely joined and so appear as an empty scrotum.

The vagina and urethra share a single opening near the base of the shaft of the phallus (what would be considered a hypospadias in a male).

- **Stage 5** denotes complete male-like virilization, with a normally formed penis with the urethral opening at or near the tip. The scrotum is normally formed with rugae but without palpable gonads.<sup>17</sup>

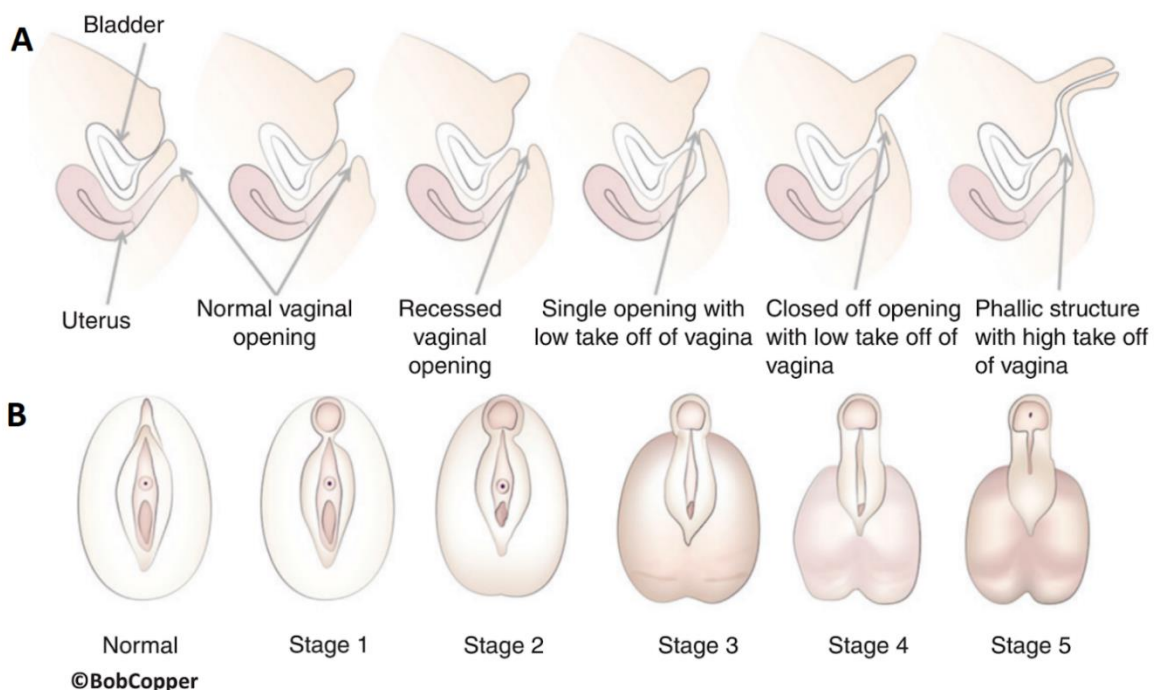


Figure 2 The Prader scale is used to coarsely rate the degree of virilization of the external genitalia (B). While ovaries and uterus remain normal, internal genitalia (A) reflect changes in the urogenital sinus.<sup>2</sup>

Importantly, while stages 1 through 5 describe the virilization of external genitalia, internally, the ovaries, fallopian tubes, and uterus develop normally (although the vagina connects internally with the urethra in stage 3, 4, and 5) (see figure 2A).<sup>18</sup> Some researchers suggest that, internally, the height of the

<sup>2</sup> Reprinted from Congenital Adrenal Hyperplasia A Comprehensive Guide, 1<sup>st</sup> Edition, Peter C. Hindmarsh and Kathy Geertsma, Chapter 2 How Males and Females Develop, Page 27, Copyright (2017).<sup>17</sup> Image Copyright Bob Cooper.

urethro-vaginal confluence (that is, how far internally the vagina and urethra connect) is not related to the degree of external masculinization.<sup>19,20</sup> However, in clinical practice, patients with Prader stage 2 or 3 are very rarely seen with high confluence and patients with Prader 4 or 5 are very rarely seen with low confluence, suggesting that there is at least some relationship between external virilisation and the height of the confluence (Private communication from Dr. Luis H. P. Braga; Department of Surgery, McMaster University, May 2018).

## **2.2. Diagnosis**

Today, most children in North America and Europe are diagnosed with CAH at birth due to wide spread incorporation of screening for 21-hydroxylase deficiency in newborn screening programs. Screening often occurs in a two-tier protocol. The first-tier assay consists of blood from a heel-prick that is used to immunoassay the concentration of 17-OH-Progesterone (17-OHP), a pre-cursor of cortisol that is increased in infants with CAH (see Figure 1).<sup>21</sup> Although the incidence of CAH is about 1:15000, the cut-off for 17-OHP considered “positive” for CAH is set such that about 1% of all tests are reported as positive as it is felt that it is more important to increase sensitivity over specificity.<sup>1</sup> Notably, there are some problems with using 17-OHP concentrations as a proxy measure for CAH. Firstly, in normal infants, 17-OHP levels are normally high at birth and decrease rapidly during the first few days after birth. In infants affected with CAH, 17-OHP levels increase with time. Consequently, heel-prick tests done in the first two days postnatally have poor diagnostic accuracy as all children will have relatively high concentrations of 17-OHP and it is only after the two-day period that significant differences arise. Secondly, premature, sick, or stressed infants typically have higher levels of 17-OHP than term or healthy infants and can generate false positives. Thirdly, 17-OHP concentrations rise with gestational-age, which must be stratified for producing appropriate cut-offs. Because of these confounders, 17-OHP immunoassays are often followed by referral to a specialized regional treatment centre, where specialists follow up with

confirmatory diagnostic tests.<sup>22</sup> While molecular genetic screens for *CYP21A2* mutations exist, no large study of efficacy of genetic screening has been reported as a second-tier screen in actual use, genotyping is fairly costly, and genetic screening focuses only on a specific gene.<sup>1</sup> Rather, evidence-based protocols recommend that the second-tier screen of choice should be the use of a biochemical screen called liquid chromatography tandem mass spectrometry to measure steroid ratios. For example, a German protocol using the ratio of the sum of 17-OHP and 21-deoxycortisol levels, divided by the cortisol level, had a positive predictive value of 100% when this ratio exceeded 0.53.<sup>1</sup> At this point, a pediatric endocrinologist is often consulted for appropriate further evaluation and treatment. If doubts remain that the child has CAH, endocrinologists may decide to order the gold standard for hormonal diagnosis of CAH, a cosyntropin (ACTH 1-24) stimulation test (the reason this is not used initially is because it takes a long time and can have serious side effects, making it difficult to perform in an urgent basis in many clinical settings).<sup>1</sup> Children will also require karyotyping to confirm chromosomal sex (i.e., XX or XY). Additionally, imaging will be necessary to fully understand where the child lies on the CAH spectrum and to cross out other possible disorders of sex development. Imaging of the internal genital tract usually involves an ultrasound to assess for the presence of a uterus and intra-abdominal gonads and a genitogram and/or cystoscopy of the urogenital sinus to determine the presence of a vagina and length of “confluence” (high or low confluence urogenital sinus).<sup>16</sup> There is some evidence indicating that cystoscopy may be better than genitography at determining the distance of the confluence.<sup>23–25</sup> If the child has visibly ambiguous genitalia, the child will often be referred to a multi-disciplinary DSD team containing pediatric endocrinologists and urologists at a local tertiary centre for proper management.

Alternatively, some children may be suspected to have CAH because their prenatal karyotype (through chorionic villus sampling etc.) is different than their genital anatomy on routine prenatal ultrasonography or does not match the

genitals they present with at birth. Regardless, even in this case, further testing (biochemical) is necessary to confirm a diagnosis of CAH.<sup>16</sup>

Female (46XX) infants with Prader 5 CAH (i.e., are not visibly ambiguous) who do not receive newborn screening are usually assumed to be ordinary boys with undescended testes.<sup>26</sup> In most cases, the diagnosis of CAH is not suspected until signs of salt-wasting develop a week (4 to 15 days) later.<sup>16,17</sup>

## **2.3. Non-surgical Treatment**

### **2.3.1. Prenatal**

Since CAH is an autosomal recessive disorder, families that have had one child with CAH have a 25% chance that a future child will also inherit the condition. Accordingly, some physicians and centres have suggested the use of prenatal therapy of pregnant mothers with dexamethasone (a corticosteroid) to suppress ACTH and adrenal production of androgens.<sup>27</sup> This would reduce prenatal female genital virilization and therefore the need for reconstructive surgery and the emotional distress and anxiety associated with having a child with ambiguous genitalia. However, prenatal therapy is not a permanent cure; children will continue to need lifelong hormonal replacement therapy and medical monitoring. While there is some evidence that this prenatal protocol is effective at decreasing virilization in children when dexamethasone was administered at or before 9 weeks of gestation (and ideally before 7 weeks),<sup>28</sup> serious questions about its safety remain. A recent article summarizing existing literature about first-trimester dexamethasone therapy in animal data and retrospective human studies suggests that treatment decreases birthweight; affects renal, pancreatic beta cell, and brain development; increases anxiety; and predisposes to adult hypertension and hyperglycemia.<sup>29</sup> Additionally, in other human studies, first-trimester dexamethasone is associated with orofacial clefts, decreased birthweight, poorer verbal working memory, and poorer self-perception of scholastic and social competence.<sup>29,30</sup> However, a review of other studies argues

that meta-analyses and recent studies indicate fewer harms for important maternal or infant outcomes.<sup>31</sup> Consequently, the long-term safety of dexamethasone must continue to be assessed. Additionally, only 1 in 8 pregnancies will actually benefit from prenatal dexamethasone treatment (the probability that the next child will inherit CAH multiplied by the probability it will be female - males do not undergo virilization and therefore would not benefit from dexamethasone suppression). While prenatal sex diagnosis is improving and becoming increasingly more accurate at earlier gestational age, since there are so many potential harms from dexamethasone and no benefit in 7 of 8 pregnancies, dexamethasone must be used cautiously.<sup>32</sup> Accordingly, the use of dexamethasone for prenatal treatment of CAH remains an off-label use primarily at scientific centres through research studies with institutional review board approval.<sup>31</sup>

### 2.3.2. Steroid Replacement

Postnatally, it is essential that infants with CAH are treated with steroids to replace reduced and missing hormones (glucocorticoids such as cortisol and mineralocorticoids such as aldosterone) and to reduce excessive androgen secretion. According to recent clinical guidelines by the Endocrinology Society, children with classic CAH (both male and female) should receive hydrocortisone (cortisol) tablets during their formative years.<sup>1</sup> Supplementation with cortisol is essential to prevent adrenal crisis (acute adrenal insufficiency), a medical emergency and potentially life-threatening situation requiring immediate treatment.<sup>1</sup> Hydrocortisone also prevents accelerated bone age and loss of growth potential. Finally, hydrocortisone acts as a negative feedback regulator of the hypothalamic-anterior pituitary-adrenal (HPA) axis, decreasing the synthesis of corticotropin releasing hormone and adrenocorticotrophic hormone. Consequently, the adrenal glands are no longer stimulated to produce excess androgen hormones, reducing their virilizing effects during pre- and peripubertal stages of development.<sup>1</sup> Treatment with glucocorticoids will be necessary for the



length of the patient's life to ensure appropriate hormonal balance. Additionally, during the neonatal and early infancy period, patients with classic CAH should be treated with fludrocortisone and sodium chloride supplements to prevent salt-wasting crisis. However, because hydrocortisone can activate mineralocorticoid receptors, mineralocorticoids are sometimes not needed when the patient is receiving pharmacological doses of hydrocortisone. Additionally, some patients can spontaneously recover from salt wasting and reduced mineralocorticoids as they grow older (because of 21-hydroxylation of precursors elsewhere in the body).<sup>1,33,34</sup> Consequently, the need to continue mineralocorticoid therapy must be reassessed periodically.<sup>1</sup>

Unfortunately, supplementation with steroids also carries inherent risks. Patients treated with steroids need monitoring throughout their life to ensure that their hormones remain carefully balanced. If too little hydrocortisone is provided, the problems associated with CAH (adrenal crisis, salt wasting, and virilization caused by excess androgens) are not resolved. However, if the patient received too much hydrocortisone or other stronger glucocorticoids (prednisone, dexamethasone, etc.), they risk growth suppression (via damage to growth plates), increased hypertension, and iatrogenic Cushing's syndrome (including reduced bone mass, obesity, and glucose intolerance).<sup>1</sup>

Recently, there has been research in improving glucocorticoid treatment of CAH by creating more effective formulations including: oral formulations that provide more sustained release (Plenadren) or mimic the body's natural circadian rhythm (Chronocort), and subcutaneous cortisol infusions via hydrocortisone pumps that approximate physiologic cortisol secretion.<sup>31,35–38</sup> Generally, these formulations improve hormonal control, improve quality of life, and are better for controlling adrenal androgen production as compared to traditional glucocorticoids. However, they remain under investigation in clinical trials and there is a lack of long term data regarding their safety and efficacy.

Beyond supplementation with glucocorticoids, there is also research investigating avenues to block the production of excess androgens by the adrenal gland (especially since glucocorticoid supplementation is insufficient to fully control androgen production). One method is to use androgen biosynthesis inhibitors, such as by targeting key enzymes in the androgen biosynthesis pathway. In a small phase I study in CAH women, the use of Abiraterone acetate (an inhibitor of CYP17A1 which is an enzyme necessary for androgen synthesis) in combination with glucocorticoids and mineralocorticoids completely normalized the level of key androgens after 6 days.<sup>39</sup> Another method is to use CRH and ACTH receptor antagonists to prevent their ability to stimulate the HPA axis as is the case in CAH. In a small phase 1 placebo-controlled study, an experimental CRH antagonist showed modest improvements in patients' ACTH and 17-OHP levels, indicating the potential for receptor antagonists to improve the hormonal control of patients with CAH.<sup>31,40</sup>

#### **2.4. Surgical Treatment**

Chromosomal females with classic CAH may be virilized due to excess androgen exposure *in utero* during key developmental stages (i.e., week 6 to 12 of gestation). Accordingly, they are often born with ambiguous genitalia ranging from clitoromegaly to fully male-appearing genitalia (see figure 2 above). The wide range of presentation means that an affected infant may require any or all of: clitoroplasty (to reduce the size of the clitoris), vaginoplasty (ranging from introitoplasty (the creation of an opening for the vagina by separating the labia) to separation of a common urogenital sinus and vaginal reconstruction), and labiaplasty (creation of labium), in infancy or later on in life (i.e., during adolescence).<sup>41</sup> The purpose of these surgeries is to create normally functioning female external genitalia that will allow for future penetrative intercourse and reproduction, appear normal, and prevent urological complications such as urinary tract infections.<sup>20,42</sup>

### 2.4.1. Clitoral Surgeries

While performing genital surgery in children with virilized genitals is intensely debated, three specific reasons for intervening are typically considered: providing anatomy suitable for penile–vaginal intercourse, achieving a manner for urination corresponding to gender identity (i.e., sitting for females, standing for males), and providing a phenotypical appearance that resembles the assigned gender. For the clitoris, it is often this last reason that is given as a rationale for surgery, and requires clitoral reduction for Prader III, IV, and V.<sup>43</sup> However, clitoral reduction surgery has evolved substantially over the past several decades as the focus of surgical outcomes changed from normalizing appearance to preserving the function and sexual sensation of the clitoris. The surgical treatments shifted from clitoridectomy (amputation), to corporal sparing techniques (clitoral recession), and then to clitoral reduction (clitoroplasty). For a thorough analysis of clitoral surgery techniques, see Kaefer and Rink's recent review.<sup>43</sup>

Since the 1930s and until the 1980s, clitoridectomy (also called clitorectomy) (partial or complete surgical removal/amputation of the clitoris) was considered the norm in management of an enlarged clitoris. This was due to early surgeons' intent to neatly fit the CAH patient into either the male or female gender. Because feminization is easier and chromosomally more congruent than masculinization of a female CAH patient, most CAH patients were assigned to the female sex. Surgeons employed the easiest way to feminize the patients, which was to remove the enlarged clitoris (which resembled a penis). Some researchers hypothesize that the complete removal of the clitoris was considered acceptable because the clitoris was considered a vestigial organ.<sup>44</sup> Additionally, clitoridectomy was rationalized by John Money et al. in the 1960s and 70s who suggested that children were psychosexually neutral until the age of 2 years and that subsequently, it was extrinsic factors such as genital appearance that reinforced gender.<sup>45</sup> However, with increasing understanding of the diversity of

gender identity and gender development, and the decreased rigidity regarding gender roles, by the late 1970s many researchers began to criticize the optimal-gender policy advocated by Money et al.<sup>46</sup> Moreover, the clitoris is a highly sensitive organ that has long been known to play an important role in sexual function.<sup>47,48</sup> Indeed, sexual pleasure is the only function of the clitoris.<sup>49</sup> As might be predicted, the removal of the clitoris generated reports of patients with sexual inhibition and ambivalence toward sexual activity, highlighting the importance of retaining sensation (via the nervous system) in the enlarged clitoris.<sup>43</sup> Accordingly, by the 1980s, clitorectomy had been phased out for clitoral recession surgery.

In clitoral recession surgery (or plication), none of the clitoral structures are removed, instead some clitoral structures are dissected out and then folded up and moved in their entirety backwards under the symphysis pubis. There they are anchored to the undersurface of the pubic bone using non-absorbable sutures.<sup>42</sup> This has the benefit of preserving the neurovascular bundle (i.e., both the vascularity and innervation of the clitoris). Additionally, in case the patient elects to reconstruct the phallus at a later date, all components of the clitoris and erectile tissue would be preserved and available. However, in cases where medical management and compliance to glucocorticoid therapy (to inhibit further productions of androgens) are not closely monitored, patients may have elevated systemic adrenal androgen, which will stimulate erectile body growth and therefore clitoral enlargement. This is problematic because the clitoral structures buried within the body will enlarge in size during growth and cause pain. Even when post-natal clitoral growth is well controlled with hormonal medication, when these patients become sexually aroused, the trapped erectile corporal bodies engorge and become painful. Cosmetic results are frequently poor and later surgical revision is often required for sexual function. Thus, clitoral recession has, for the most part, also been abandoned.<sup>50-53</sup> Recently, recognizing the potential importance of sparing the corporal bodies in case future surgery is requested to

reconstruct the phallus (since gender dysphoria has been reported in up to 5% of patients and parents are often most anxious about making the wrong irrevocable choice for surgery), Pippi Salle et al. have advocated for a technique that spares the corporal bodies by separating them and burying each in the labioscrotal folds of the patient. Their initial patients have normal phenotypic appearance and report normal sensation with lack of pain and engorgement of the corporal bodies.<sup>54</sup> However, long term outcomes are still lacking for this surgery.

Schmid was the first to describe excision of the corporal bodies while preserving the glans and neurovascular bundle in 1961 – what is now known as clitoral reduction or clitoroplasty surgeries.<sup>55</sup> In 1999, Baskin et al. used immunohistochemistry staining and three-dimensional computer modelling to map the anatomy of the clitoris, detailing the neuroanatomy in particular and again suggested that it would be prudent to attempt to preserve the nervous and vascular tissue.<sup>56</sup> Accordingly, today most clitoral reduction (or clitoroplasty) surgeries are aimed at retaining the neurovascular bundle, which is a sheath of sensory nerves and vasculature (arteries and veins) that lies along the dorsal (upper) part of the clitoris, and removing whole or parts of the corporal bodies (the components that give the enlarged clitoris its girth and become engorged during sexual arousal) (see figure 3A and B). It is essential that the neurovascular bundle remain undamaged as it is responsible for maintaining the sensory and sexual function of the clitoral tissue and glans (head of the clitoris). Several types of clitoroplasty surgeries are in use as there is no unanimous consensus as to the best technique for achieving the goal of sparing the neurovascular bundle.

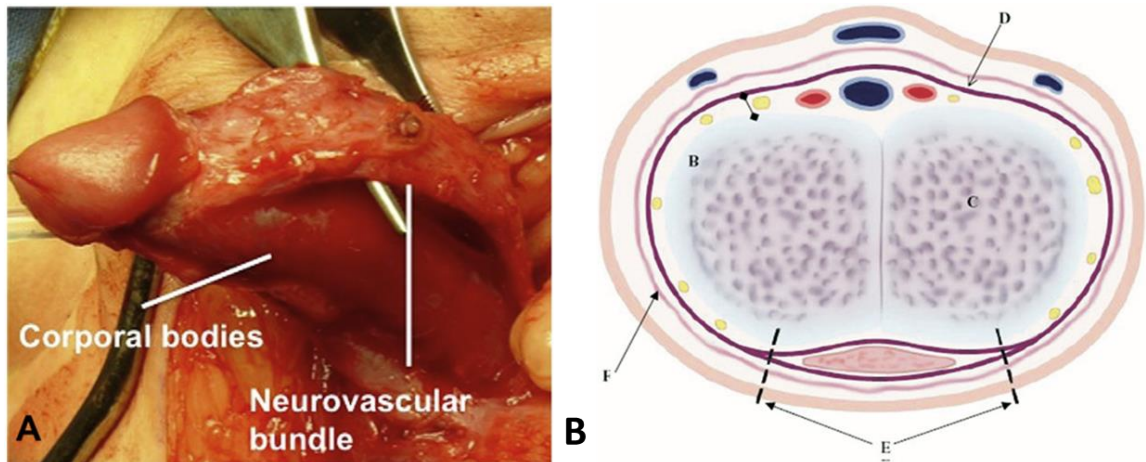


Figure 3 (A) Surgical separation of an enlarged clitoris showing the neurovascular bundle dorsally (at the top) and corporal bodies medially (towards the centre of the organ).<sup>3</sup> (B) A cross section of the clitoris, showing the various components of the organ: the neurovascular bundles is composed of nerves (yellow areas), arteries (red areas), and veins (blue areas), which are between the Buck's fascia [D] and tunica albuginea [B]. The tunica albuginea and corpora cavernosa tissue [C], comprise the corporal bodies which are excised (removed) during surgery. [E] indicates the points where incisions are made at the ventral (bottom) side of the clitoris in Poppas et al.'s nerve-sparing ventral clitoroplasty, so as not to impact the neurovascular bundle.<sup>4</sup>

Complete excision of the corporal bodies while preserving the glans and the attached ventral mucosa was described by Goodwin in 1969.<sup>57</sup> This technique was modified by others and even Goodwin himself. With improved understanding of the dorsal neurovascular bundle for clitoral innervation by Baskin et al., the modified technique approaches dissection from the ventral side of the clitoris (which has minimal innervation).<sup>58</sup> More recently, Poppas et al. showed through immunobiological staining of the excised specimens that nerve-sparing ventral clitoroplasty (see Figure 3BE which indicates that the dissection of the corporal bodies should be from the ventral side of the penis, with incisions

<sup>3</sup> Reprinted from the Journal of pediatric urology, Vol 8.6, Creighton, S., Chernausek, S., Romao, R., Pansley, P., and Salle, J.P., Timing and nature of reconstructive surgery for disorders of sex development – introduction, Pages No. 602-610, Copyright (2012), with permission from Elsevier.<sup>49</sup>

<sup>4</sup> Reprinted from The Journal of Urology, Vol 178, Issue 4, Poppas, D.P., Hochsztein, A.A., Baergen, R.N., Loyd, E., Chen, J., and Felsen, D. Nerve sparing ventral clitoroplasty preserves dorsal nerves in congenital adrenal hyperplasia, Copyright (2007), with permission from Elsevier.<sup>59</sup>

made at the 5 o'clock and 7 o'clock positions ) leads to few nerves being excised.<sup>59</sup> However, Braga and Pippi Salle have noted that, in their experience, the traditional approach from the ventral plane decreases the risk of injury to the neurovascular bundle.<sup>42</sup> Finally, there has been a recognition that separating the delicate structures of the neurovascular bundle and glans off of the Tunica Albuginea may leave them unsupported and at risk of injury. Accordingly, several techniques have been developed to preserve the Tunica Albuginea, so that the nerves and micro vessels to the glans clitoris do not have to be disturbed by dissection and can benefit from the support of the Tunica (see Figure 4). However, this technique requires precise suturing as it may otherwise lead to damage of the neurovascular bundle.

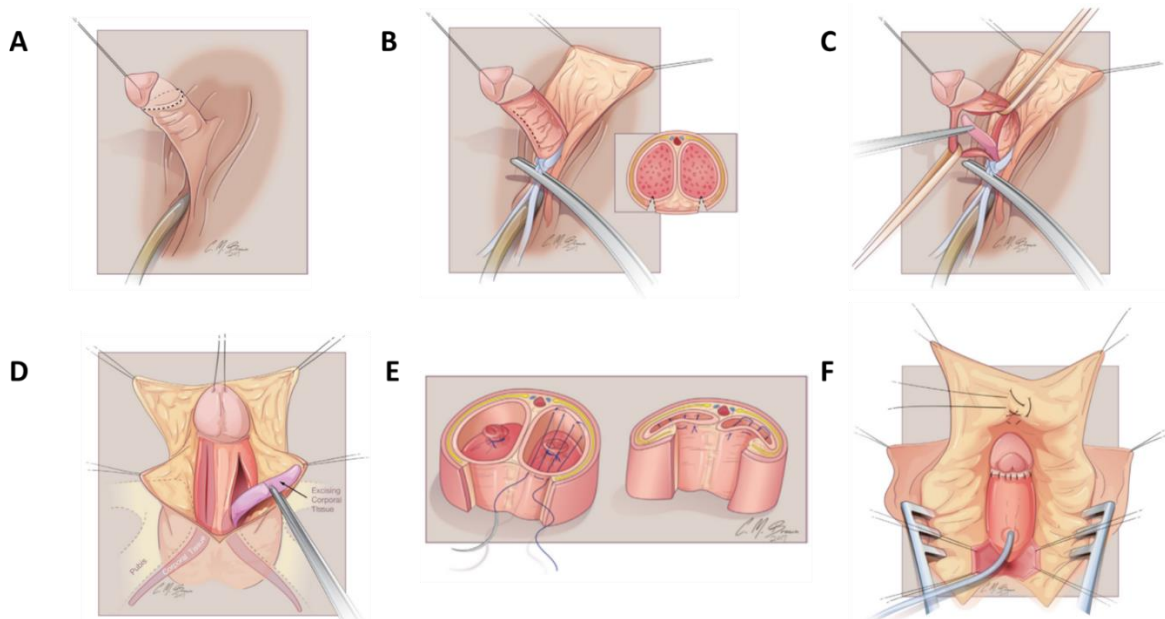


Figure 4 Tunica Albuginea sparing surgery as described by Kaefer et al. Note in (D) and (E) that only the corpora cavernosa tissue is removed while the Tunica albuginea remains intact.<sup>5</sup>

<sup>5</sup> “Creative Commons Figures 3, 4, 5, 6, 7, 8” by Kaefer and Rink, licensed under CC BY.<sup>43</sup>

### Clitoral Surgery Complications

As with any surgery, clitoral surgeries have the potential to cause serious postoperative complications:<sup>43</sup>

- Bleeding and infections due to the surgery
- **Postoperative pain** can occur in patients with CAH due to clitoral recession or incomplete reduction. This is often either because the incompletely removed corporal bodies or clitoral tissue swell during sexual arousal or, in patients with inadequate androgen suppression, grow with age. Often this pain appears during peripubertal stages of development and requires a reoperation to remove recessed and remaining corporal bodies.
- **Neurologic injury** is the most frequently discussed concern for clitoral surgery. This is especially true for older techniques, which did not consider neurologic injury at all or lacked a significant understanding of the clitoral nervous system. However, modern techniques such as clitoroplasty were created with the goal of preserving clitoral nerves. Surgeons have used intraoperative imaging of nerves as well as pre-post pudendal evoked potentials to show that electromyographic responses are not significantly compromised by clitoroplasty. While clitoroplasty aims to preserve the dorsal nerves and usually leads to normal sensation and orgasmic potential and is the currently preferred surgical technique, in one study, women who underwent a nerve-sparing clitoroplasty procedure had sensation to temperature and vibration that was poorer than control non-CAH women and CAH women who had not undergone operations (but, sensation was still better than women who had had clitoridectomy).<sup>60</sup> This was replicated in another study which also illustrated that thermal and vibratory clitoral sensation was significantly decreased in all patients compared to healthy



controls.<sup>61</sup> Another study evaluating self-reported sensation indicated that nerve-sparing clitoroplasty was the surgery that was most likely to maintain sensation.<sup>62</sup>

- **Vascular injury** leading to clitoral atrophy and necrosis is also a concern for patients who had clitoroplasty. For example, a study by Alizai et al. found that out of 14 girls who had had surgery at around 2.5 years old, four had atrophied clitoral glans (by the time they were 13 years old on average), likely due to incomplete preservation of the vasculature to the glans.<sup>63</sup>
- **Sexual Outcomes** are important considerations for clitoral surgeries as the clitoris is an important organ for sexual arousal. In one study, both non CAH and CAH women reported that they felt that the clitoris was important for their sex life and for sexual lust. However, those women who had had clitoridectomy (described as amputation) or multiple operations did not consider the clitoris important for sexual lust in their lives. Furthermore, women who had clitoridectomy had poorer outcomes (e.g., inability to experience orgasm) than women who had clitoral recession or clitoroplasty (who's reported orgasms were not statistically different to control women).<sup>62</sup> In a study by Crouch et al., reduced clitoral sensation to temperature and vibration after all types of clitoral surgery was associated with sexual dissatisfaction, with the most impaired sensation associated with the worst sexual function scores. Unlike the previous study (but like other outcome studies), Crouch et al. found that women with CAH who had clitoral surgery reported decreased intercourse frequency, and anorgasmia (difficulties with orgasm) significantly more often than CAH women who had not had clitoral surgery or non-CAH control women.<sup>60</sup>

#### 2.4.2. Vaginoplasty

In more severely virilized females (Prader levels III, IV, and V), there is a single opening for both the vagina and the urethra (a common urogenital sinus). Vaginoplasty is a type of surgery that aims to separate the vagina and the urethra, with the goal of creating a vagina that is appropriate for menstruation and sexual intercourse and connected to the pelvic floor, while also preserving urinary continence (bladder control). Like clitoral surgery, there are several surgical techniques for vaginal reconstruction. The choice of technique depends on the anatomical positioning of the vagina and the relative positions and lengths of the urethra-vaginal confluence within the urogenital sinus (that is, whether the confluence is high or low). These procedures include the relatively simple flap vaginoplasty and the more complex vaginal pull-through and partial or total urogenital sinus mobilization.<sup>49</sup>

When the vagina and the urethra separate closer to the perineum (see Figure 2A Stage 3 and 4), the urogenital sinus is termed a “low (confluence) urogenital sinus” or “low take-off vagina.” The surgery for a low or moderate confluence urogenital sinus is technically easy to address. Surgery is done using the flap technique, where a perineal skin flap is used to bridge the gap between the vagina and perineum. This flap technique was first described in 1964 by Fortunoff et al., who described a “U”-shaped incision in the perineum that is elevated as a flap and sutured to the posterior wall of the vagina (see Figure 5) (an omega shaped flap is now used as it leads to better cosmesis). It is important to note that with flap vaginoplasties, the actual anterior vaginal wall (the wall closer to the urethra) is not mobilized all the way down to the perineum to create two separate openings for the urethra and vagina at the exterior of the body. Essentially this leaves the urogenital sinus as a single opening but the perineal flap enlarges its circumference to allow for sexual intercourse (as the circumference initially would have only been as large as a urethral opening).<sup>64</sup>

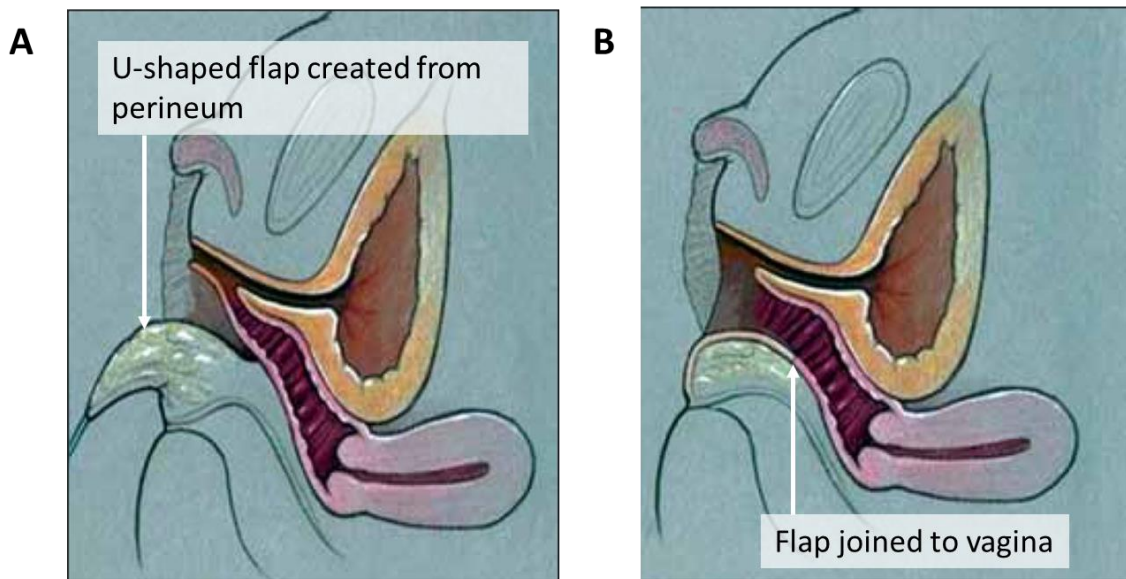


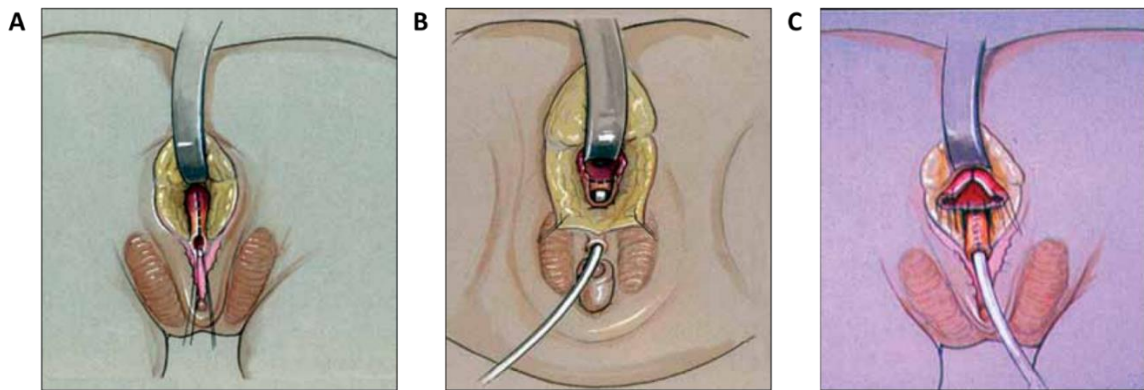
Figure 5 Illustration depicting the flap vaginoplasty. (A) A “U” shaped segment of perineal skin is cut and mobilized. (B) The mobilized flap is joined inward to the posterior vaginal wall to create a larger opening for the vagina.<sup>6</sup>

Flap vaginoplasties were initially popular even for a high urogenital sinus. However, flap techniques for high confluence UGS are prone to causing a high incidence of vaginal stenosis as patients age.<sup>49</sup> Vaginal stenosis is an abnormal condition in which the vagina becomes narrower and shorter due to the formation of fibrous tissue. This requires further surgery and long term follow up. The Passerini-Glazel technique is an extension of the traditional flap vaginoplasties that aims to avoid vaginal stenosis by using available urogenital mucosal tissue rather than the perineal tissue as in the Fortunoff flap. In this one-stage procedure (i.e., both clitoral and vaginal surgery are performed at the same time), which was first described in 1989 and has since been modified, a high confluence, short vagina is detached from the urogenital sinus and then exteriorized through a cylinder of tissue. This cylinder of tissue is made from the excised “clitoral/penile” skin and urogenital sinus tissue, is inserted into the

<sup>6</sup> “Creative Commons Figure 7a and 7b” by Leslie, Cain, and Rink, used under CC BY / 180 degrees rotation of figure 7a and addition of labels.<sup>66</sup>

perineum and is anastomosed to the native vagina. The technique is described and illustrated extensively by Lesma et al., 2007.<sup>49,65</sup>

A flap vaginoplasty alone is not suitable for higher confluence repairs because it does not bring the junction of the vagina with the urogenital sinus any closer to the perineum. Consequently, historically, most girls with a “high confluence” urogenital sinus required separation of the vagina from the urogenital sinus with a pull through vaginoplasty, which was first described by Hendren and Crawford in 1969 (see Figure 6).<sup>66,67</sup>



*Figure 6 Illustration of a pull through vaginoplasty. (A) A U-shaped flap is cut in the perineum to expose the common urogenital sinus. The urogenital sinus is opened using a midline incision indicated by the dotted line. (B) Once the point of the convergence is reached, the vagina is separated from the urethra as indicated by the black dotted line. (C) The vagina is pulled closer to the perineum and anastomosed to the U-shaped flap as in a flap vaginoplasty. The urogenital sinus tissue is formed into a tubule using absorbable sutures to create a urethra.<sup>7</sup>*

More recently, total and partial urogenital sinus mobilization (TUM and PUM) have also been introduced to aid vaginoplasties. While initially described by Peña in 1997 for the repair of cloaca, they were later adapted to the separation of the vagina from the urethra in patients with CAH.<sup>68</sup> In short, with total urogenital sinus mobilization, the complete urogenital sinus is separated from ligaments that attach it to the pelvic rim and pulled forward towards the perineum until enough length has been gained to connect the vaginal edges to

<sup>7</sup> “Creative Commons Figure 8a, 8b, and 8c” by Leslie, Cain, and Rink, licensed under CC BY.<sup>66</sup>

the perineum (see figure 7A). By doing this, a urethral and vaginal opening of near normal appearance can be created. Partial urogenital mobilization is very similar, except that it preserves the pubourethral ligaments (which are important for bladder control) (see Figure 7B). This is important because the separation of the pubourethral ligaments in total urogenital sinus mobilization has been associated with urinary incontinence. However, there is a lack of long-term outcomes comparing total and partial urogenital sinus mobilization to each other and to flap vaginoplasties (although TUM and PUM do seem to produce better short-term results than flap vaginoplasties, especially for higher confluence UGS).<sup>66,68</sup> Importantly, the extra urogenital sinus tissue in PUM and TUM can be used in other areas during the vaginoplasty and to create the introitus.

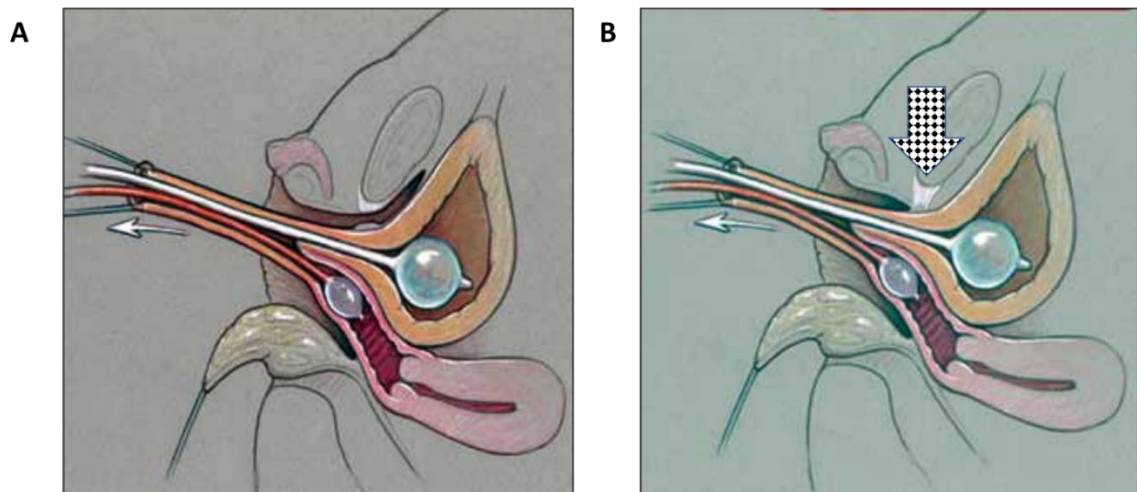


Figure 7 Cross sections illustrating urogenital sinus mobilization. (A) Total urogenital sinus mobilization, the common urogenital sinus is pulled out until the point of convergence is sufficiently close to the perineum. (B) Partial urogenital sinus mobilization. Note that the dissection stops at the pubourethral ligament anteriorly (indicated by checkered arrow).<sup>8</sup>

While urogenital mobilization is considered appropriate for cases with an intermediate to high confluence urogenital sinus, its use in patients with high confluence is still somewhat controversial since aggressive mobilization can

<sup>8</sup> “Creative Commons Figure 10b and Figure 11” by Leslie, Cain, and Rink, used under CC BY / Addition of checkered arrow.<sup>66</sup>

cause injury to adjacent structures in the body. To overcome these challenges, Dòmini et al introduced the anterior sagittal transrectal approach (ASTRA).<sup>69</sup> In this approach, an incision is made along the perineum, spanning the anterior anal border and the perineal opening of the urogenital sinus. The anterior rectal wall is incised, which allows better exposure of the high confluence. This increased exposure facilitates dissection and allows easier separation of the urethra from the vagina. The vagina is then pulled through to the perineal floor and anastomosed there and all incisions are closed using sutures (see figure 8). A recent survey by Pippi Salle et al. of international teams using ASTRA indicated that patients had good outcomes in terms of urinary and fecal continence and the absence of major complications in all but once child (who had a postoperative perineal infection that was resolved).<sup>70</sup>

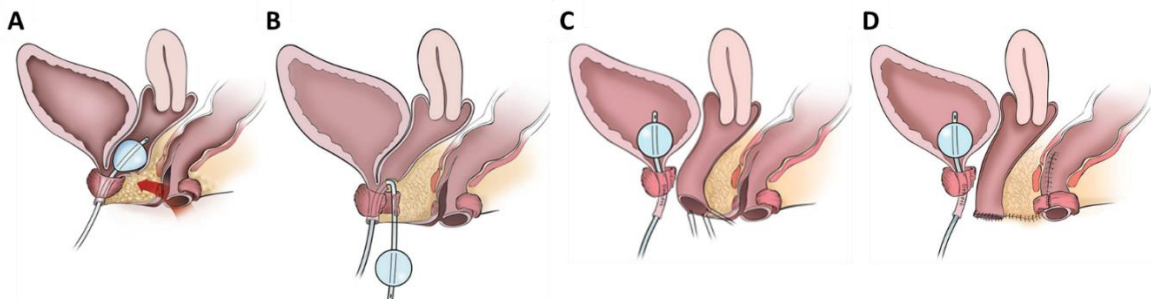


Figure 8 Diagrams illustrating the Anterior Sagittal Transrectal Approach (ASTRA). (A) An incision is made in the anterior side of the rectal wall, exposing the urogenital sinus. The red arrow indicates where the incision will be made to the vagina inserting into the urogenital sinus. (B) An incision is made into the urogenital sinus. (C) The vagina is dissected and separated from the urethra and bladder neck. The Vagina is pulled through to the perineum. (D) A final image after reconstruction is complete.<sup>9</sup>

<sup>9</sup> Reprinted from The Journal of Urology, Vol 187, Issue 3, João L. Pippi Salle, Armando J. Lorenzo, Lisieux E. Jesus, Bruno Leslie, Abdunnasser AlSaid, Francisco Nicanor Macedo, Venkata R. Jayanthi, Roberto de Castro, Surgical Treatment of High Urogenital Sinuses Using the Anterior Sagittal Transrectal Approach: A Useful Strategy to Optimize Exposure and Outcomes, Pages No. 1024-1031, Copyright (2012), with permission from Elsevier.<sup>70</sup>

### Vaginoplasty outcomes

As with clitoral surgeries, vaginal surgeries are associated with several postoperative complications including:

- **Immediate post-operative complications** such as bleeding, infections, flap necrosis and flap dehiscence (a surgical complication in which a wound ruptures along a surgical incision). To mitigate these complications, patients must be placed in restrictive dressing that constrains them from opening their legs for 4 weeks after surgery to: (a) avoid shear stress, (b) allow early neovascular ingrowth to genital tissue, and (c) prevent disruption of wound healing. However, this inability for patients (often children) to move and be active has been reported by some parents to be stressful for the children and for themselves (Private communication).<sup>50</sup>
- **Vaginal complications** including vaginal stenosis, vaginal prolapse, and urethrovaginal fistula, often requiring revision surgeries. In earlier surgeries using flap vaginoplasty for all types of confluences, complication rates were very high and revision vaginoplasties were required for up to 100% of patients.<sup>71</sup> However, as vaginoplasty techniques have evolved the rates of complications such as stenosis have declined (to 6-57% depending on the skill and experience of the surgeon, and the extent of surgery required) and accordingly the need for revision vaginoplasty has decreased to 3-36% in various centres. Generally, researchers have found that pull-through vaginoplasties require revisions vaginoplasties more frequently than flap vaginoplasties. In less severe cases of vaginal stenosis, rather than surgery, dilation can be performed using gradually increasing sizes of vaginal molds. While vaginal dilation was performed in prepubertal children in the past, it is no longer considered appropriate as dilation was often painful, traumatic, and unnecessary. Now, prepubertal vaginal stenosis is monitored until menarche, at which time the discussion of repair can be initiated.<sup>50</sup>

- **Hair growth in the vagina.** Because vaginal reconstructive surgeries often use a perineal skin flap, hair development on these flaps in peripubertal stages of development and in adulthood can be concerning for adolescent and adult women as the flap now forms the posterior wall of the vagina. This often requires treatment via professional depilation and in some cases surgical excision of the hair bearing skin and replacement with a buccal mucosal graft.<sup>50</sup>
- **Urinary dysfunction and incontinence** can be a concern for certain types of surgical techniques. While some researchers have found that greater than 95% of patients who underwent PUM and TUM are continent, others have suggested that TUM can cause significant complications with urinary incontinence, probably due to aggressive mobilization of the bladder neck and severing of the pubourethral or pubovesical ligaments.<sup>50</sup>
- **Sexual outcomes.** Vaginal stenosis can prevent patients from having satisfactory sexual intercourse. However, in one study evaluating the Passerini-Glazel feminizing genitoplasty (i.e., both clitoroplasty and vaginoplasty), there was no difference in thermal or vibratory vaginal sensation between patients and controls, greater than 90% of females described a stable satisfactory relationship, and all patients reported active sexual desire, good arousal, adequate lubrication and orgasm. The authors concluded that the Passerini-Glazel feminizing genitoplasty seems to allow normal adult sexual function.<sup>61</sup>

#### 2.4.3. Perineoplasty/Labiaplasty

The goal of the perineoplasty/labiaplasty is to create a normal external female appearance (i.e., with presence of labia minora and majora and the clitoral hood). More recent surgical techniques use the skin from the shaft of the genital tubercle (see Figure 9A) to reconstruct the two labia minora and the clitoral hood. The existing labia majora (which may appear as rugged labioscrotal folds in highly virilised patients) are mobilized, trimmed, and lowered



to reconstitute a nearly normal-looking female perineal anatomy (see Figure 9B).<sup>72,73</sup>

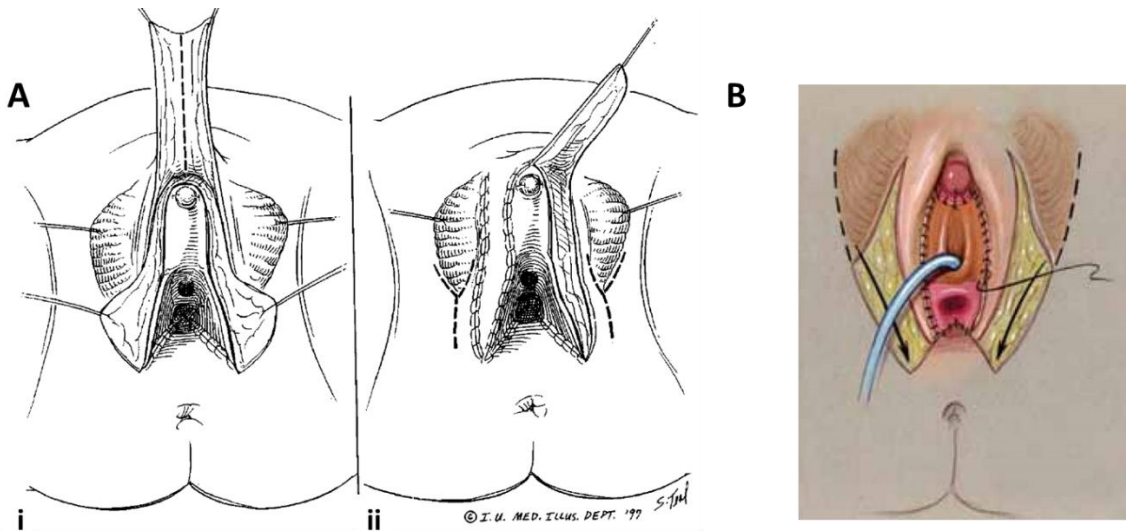


Figure 9 Illustration of perineoplasty/labiaplasty. (A) i: The phallic skin is incised along the dotted line and is split in the midline to create two “wings”. ii: The phallic skin has been brought down on the left side of the clitoris and sutured to create the left labia minora and part of the clitoral hood. A Y shaped incision is made on the posterior side of the labioscrotal skin.<sup>10</sup> (B) The labioscrotal skin is mobilized and moved posteriorly to the sides of the vaginal introitus where the labia majora are sutured in place.<sup>11</sup>

## 2.5. Timing of Surgical Treatment

Feminizing genitoplasty can be done “early” or “late”. Early surgery is considered to be within the first two years of life, ideally at age 2-6 months, while late surgery is usually performed after puberty, when patients are directly engaged in decision-making. Surgery between the ages of 12 months and adolescence is not recommended unless complications are causing medical problems.<sup>74</sup> However, there continues to be a debate about the optimal timing of feminizing genitoplasty or its component surgeries. This debate arises from the potential for suboptimal patient outcomes and the lack of strong long-term results

<sup>10</sup> Reprinted with permission from Copyright Clearance Center RightsLinks: Springer Nature, World Journal of Urology, Feminizing genitoplasty:state of the art, Richard C. Rink, Mark C. Adams [COPYRIGHT] (1998).<sup>73</sup>

<sup>11</sup> “Creative Commons Figure 6” by Leslie, Cain, and Rink, used under CC BY.<sup>66</sup>

for some of these procedures. This lack of evidence is compounded by small sample sizes, the literature being composed of short clinical series, “heterogeneity across centers”, and a lack of consistent methodology for evaluating pre vs post treatment.<sup>20</sup>

With regards to clitoral surgery, the main concern is that surgery reduces innervation of the clitoris, which can affect sexual sensation and arousal. This risk stimulates the argument that surgery should be delayed until the patient is able to make the decision (and accept the corresponding risk) for herself. On the other hand, early childhood surgery can lead to a normalized appearance of the external genitalia which can mitigate negative social interactions with peers (and the associated embarrassment and social withdrawal), avoid the psychological trauma of surgery during adolescence, and increase the bonding between parents and the child.<sup>1</sup> Additionally, the ability to do something can help parents cope with their child’s diagnosis.<sup>49</sup> To balance these concerns, the Consensus statement by the Lawson Wilkins Pediatric Endocrine Society and The European Society for Paediatric Endocrinology (2002), the Chicago Consensus Statement (2006), and the Endocrine Society Clinical Practice Guidelines (2010) recommend that clitoral surgery should not be performed during infancy for females that have only slight virilization (i.e., Prader 1 or 2).<sup>1,74,75</sup> Additionally, they suggest that even for severely virilized females (Prader  $\geq 3$ ), if surgery is performed during infancy, it should be by an experienced surgeon (having at least 3 to 4 cases per year) in a center with an experienced multidisciplinary, interdisciplinary or transdisciplinary team (including pediatric endocrinologists, mental health professionals, social workers, etc.).<sup>1,76</sup>

With regards to vaginoplasty, historically surgeons advocated for early vaginal surgery to prevent urinary reflux up the common urogenital sinus and thereby mitigating any associated urinary tract infections. However, several studies have illustrated that untreated females with CAH are no more likely to have urinary tract infections than non-CAH females, suggesting that vaginoplasty

can be delayed.<sup>50,77</sup> Additionally, because the vagina has no function in early childhood, vaginoplasty could be postponed until after puberty, especially since most early vaginoplasties need surgical revision or dilation later in life due to stenosis etc.<sup>78</sup> Delaying vaginal surgery could have the additional advantage of including the patient in the consent process. However, there are also disadvantages to performing vaginoplasty later in life. For example, if the genitoplasty is done as a two step process (clitoroplasty in infancy and vaginoplasty at a peripubertal age), the mucosal tissue from the urogenital sinus and the phallic skin could not be used to reconstruct the vulva and distal vagina (this extra mucosal tissue can be particularly useful for patients that have high confluence urogenital sinuses).<sup>50</sup> Moreover, from a medical perspective, feminizing genitoplasty before 3 months of age can have better outcomes because of increased tissue elasticity and improved vascularization due to post-natal residual maternal estrogens.<sup>42</sup>

Considering all these factors, while most intersex advocacy groups promote delaying surgery, many pediatric urology and endocrinology groups recommend early surgery. For example, the Endocrine Society released systematic consensus and evidence-based clinical practice guidelines covering the treatment of CAH, where they suggested that in patients with a low vaginal confluence, complete repair including vaginoplasty, perineal reconstruction, and clitoroplasty (if necessary) be done simultaneously at an early age. However, for individuals with higher vaginal confluence, the Endocrine Society admits that the timing is less certain, and if surgery is deferred, vaginoplasty and/or clitoroplasty may be performed in adolescence. In the end, it is important to recognize that rigorous and systematic long-term evaluations are lacking for *both* early and late surgery, especially with regards to significant postoperative complications such as urethro-vaginal fistulae, sensory loss and vaginal stenosis.

Additionally, there is minimal data comparing psychosexual health in girls and women who have undergone early and late surgery (that is, there is

inadequate evidence that either early or late surgery is better at preserving sexual function).<sup>1</sup> What little evidence exists reports on small case studies or evaluates outdated surgical methods. For example, research by Minto et al. suggested that women with clitoral surgery had higher rates of non-sensuality and inability to achieve orgasm than those who did not have surgery, however the majority of CAH patients in that study had clitoral amputations.<sup>79</sup> Research by Fagerholm et al. on a small case series suggests that while CAH patients with surgery tend to be sexually active later than non-CAH controls, there are no other statistically significant differences regarding sexual activity or function. In fact, a more recent case-control study by Binet et al. found that CAH patients with surgery reported better sexual satisfaction than age-, assigned sex-, and ethnic origin-matched non-CAH controls.<sup>80</sup>

The Endocrine society notes that, when questioned about surgical timing preferences, the majority of adult females with CAH who had surgery, stated preferences for early surgery.<sup>1</sup> This finding has been replicated a number of times in surveys and interviews of patients by various research groups.<sup>62,80–82</sup> However, in at least two studies, a not insignificant proportion of women also stated preferences for surgery in puberty.<sup>62,82</sup> The Endocrine society clinical guidelines and the Chicago Consensus statement (and its 2016 update) conclude that, because of the lack of strong evidence for either option, parents should be provided with sufficient information so that they can make the most informed decision for their child.<sup>1,75,83</sup>

## **2.6. Parents' Role and Experience in Decision Making for Feminizing Genitoplasty**

Infants clearly cannot consent to decisions related to surgery in infancy or childhood, so parents or guardians must make treatment decisions on their behalf. Surgery in infancy and childhood is generally irreversible and may impact physical and sexual functioning later in life. Moreover, there is clinical equipoise

between having surgery in infancy or delaying surgery. Accordingly, the Endocrine society clinical guidelines and the Chicago Consensus statement (and its 2016 update) advise that parents must be provided with balanced information about timing (including the option of deferring the procedure), risks and benefits of surgery, and the long-term prognosis for sexual and reproductive function.<sup>1,75,83</sup>

While parents report receiving some information and support from health professionals, the information and support was often inadequate (see below).<sup>2</sup> Additionally, previous literature has reported that parents have had poor experiences with regards to their child's diagnosis, treatment, and decision-making about their child's feminizing genitoplasty.<sup>2-5</sup> Historically, parents report that they saw surgery as obvious and necessary, without experiencing it as something that involved a decision-making process. They did not realize or were not told that delaying surgery was an option. Some have even questioned the necessity of the surgery in hindsight. Indeed, in one study, 20.5% of parents reported mild to moderate decisional regret about their child's feminizing genitoplasty (although none reported a preference for having surgery later).<sup>6</sup> Other issues that parents described include:

- Feelings of stress and isolation, especially stemming from their unfamiliarity and lack of previous awareness of the condition before their child's diagnosis.<sup>4</sup> This confusion and loneliness was compounded by parents comprehending only some of the information they were told. For example, when asked what they were told by health professionals, some parents report that they remember that they only understood parts of the information, such as the child having a chronic condition, but not the specifics of the diagnosis.<sup>2</sup>
- Feeling frustrated with the type or amount of information available to them. For example, some parents disliked that the information provided by practitioners was not clear-cut or that it was not comprehensive enough.<sup>4</sup> While the shortage of clear-cut information is not something that

can be moderated (because there is a lack of evidence to provide strong recommendations for treatment), comprehension can certainly be improved. Some parents have also mentioned the need for written information in plain nonmedical language. This was especially true for parents who were still struggling to find their feet after receiving a difficult diagnosis and going through strong emotions when information was first shared with them.<sup>2</sup> In other words, parents felt overwhelmed in facing the prospect of caring for their infant and had a limited ability to absorb the oral information provided.<sup>5</sup>

- Feeling confused about medical interventions and conflating medical constructs, often because information was shared in medical jargon that “went way above [their] heads”.<sup>5</sup> For example, some parents report having believed that karyotype findings definitively determined both their child’s sex and gender, erroneously assuming that sex chromosomes are the ultimate arbiters of gender, and making decisions about treatment or surgery based on these mistaken assumptions. Another confusion was that although there is a well-recognized distinction between biologic sex (male/female) and gender of rearing (boy/girl), parents and providers often conflated these concepts.<sup>4</sup>
- Feeling confused about which choice was right for them. This confusion may have been compounded by different clinical viewpoints regarding treatment. For example, while some groups such as the Endocrine Society advocate for early surgical treatment, others, including the United Nations, call for providers to prohibit normalizing genital surgery on infants. <sup>1,84</sup>
- Because explanations by practitioners were jargon rich or confusing, parents had to seek information from other sources and attempt to independently research information about CAH (for example through books, Internet searches and by asking questions to health care

providers). However, few parents felt comfortable asking every question they had. Many parents found material online that “frightened” them, that they found intimidating, distressing and confusing.<sup>5</sup> In at least one study, no parents had any guidance from healthcare providers about evaluating the quality of internet health information resources (parents reported using information on discussion boards and forums, which may not have been true or relevant).<sup>4,5</sup>

- The breadth and type of information that parents received varied heavily depending on their educator’s clinical role and whether they took a “medical” or “non-pathologizing and supportive” approach.
  - For example, some parents perceived healthcare practitioners (endocrinologists, urologists, nurses) as often providing a medicalized perspective to management, focusing on things such as:
    - “Disorders of sex development being static disorders that require treatment which should be function oriented,
    - That function is biologically determined,
    - That treatment regimes are predetermined [e.g., for CAH, parents have no choice regarding putting their children on steroids],
    - That the child is a passive agent, and
    - That aid should be hospital based.”<sup>3</sup>
  - Comparatively, patient advocates, activists and psychologists tend to have a more non-pathologizing perspective, noting that their approach emphasized:
    - “Disorders of sex development are dynamic and may not impair an individual,
    - That development, resilience, and coping strategies need to be fostered
    - That treatment should be geared to interests and capabilities,
    - That support must be individualized, adaptable, and dynamic,

- That the child and his or her family are active agents in defining the problem, and
- That aid should be community based.”<sup>3</sup>

The approach to educating parents is important because at least one study has found that a medical approach is much more likely to cause parents to choose to have early surgery.<sup>3</sup> Moreover, such a high degree of variation in information suggests that some parents may not receive all the information they need to make fully informed decisions, and that parents may face contrasting, uncoordinated, and contradictory information from their child’s healthcare team, leading to confusion and misinformation.<sup>2,5,85</sup> There may also be variability in care, information, and support that is provided to families by members within a clinical team.<sup>5</sup>

- Feelings of frustration or exploitation with regards to doctors using their children for teaching purposes, especially due to the high frequency with which providers interacted with their child, which parents felt was unjustified and made them feel like their child was a “show-horse”.<sup>4</sup>
- Feelings of insecurity stemming from the lack of information about coping with the situation.<sup>2</sup> Some parents even felt that healthcare providers had minimized their worries and told parents to focus on the here and now, which added to their inability to cope with the situation. This perception also negatively impacted the relationship between parents and practitioners (as they felt their concerns were not addressed). For example, parents stopped asking questions, which shut down opportunities to make shared decisions.<sup>2</sup>
- Concerns about the future that were not or could not be allayed or addressed by healthcare practitioners, such as fears about negative physical, social, or emotional changes associated with puberty and adolescence. These included concerns about future gender identity (the



personal conception of oneself as male or female), gender role (behaviors, thoughts, and characteristics consistent with expectations society and people have about a person's assigned sex), interactions with peers, interactions with romantic partners, fertility, and sexual orientation.<sup>4</sup>

- Concerns about talking with others and sharing the diagnosis and surgery for fear of stigmatization. Some felt that their child's condition was extremely difficult to explain or that sharing would generate questions that they were unable to answer.<sup>4</sup> Parents reported a dilemma of wanting to share some information to get support but not too much information to protect their child and giving them choice over disclosure.<sup>2</sup>
- Lack of information or strategies to share information about the surgery or the need for future surgery with their child, especially with children who were defensive or disengaged, which required them to invent strategies to share information or engage their child on their own.<sup>2</sup>

Because of these experiences and the lack of information and support, some parents report strong conflict and regret about their treatment decisions and a high degree of stress about their child's diagnosis and surgery.<sup>86</sup>

Additionally, at least one study indicates that 31% of mothers and 18% of fathers of children with disorders of sex development report symptoms of post traumatic stress (e.g., intrusive thoughts about the diagnosis, avoidance of reminders of the event, and/or hypersensitivity with regards to that or similar events) that meet the threshold for post traumatic stress disorder (with even more reporting subclinical but still relevant levels of symptoms). This study also found that the strongest predictor for the degree of post traumatic stress was cognitive confusion. While this study did not assess surgical decision making per se, it highlighted the importance of cognitive confusion in causing negative outcomes for parents and families of children with CAH. It also provided evidence to support the provision of patient-friendly, consistent information to parents as being a potential

mitigation strategy. The authors conclude that employing an intervention, such as tailored information about diagnosis/prognosis, could alleviate distress in parents and change the course of development for the child and family.<sup>8</sup>

### **3. Shared Decision Making and Patient Decision Aids**

A shared decision-making (SDM) approach to feminizing genitoplasty could help eliminate or mitigate many of the negative experiences parents have reported. SDM is a consultation process where patients and practitioners participate together in making a health decision. It involves the melding of the expert knowledge of a healthcare provider with the ability of a patient or their surrogate to make health care decision based on their own values, preferences, and circumstances (i.e., respecting the right to patient autonomy).<sup>87</sup> SDM is of most use when the evidence does not strongly support a single clearly superior option, as it can help patients to understand the benefits, harms and trade-offs of the various options.<sup>87</sup> There are several key aspects to good SDM: (1) both healthcare providers and the patient are involved in decision making, (2) information exchange is bidirectional (to mitigate inherent power imbalances in the patient-provider relationship), (3) thoughtful deliberation on treatment options and their consequences occurs, and (4) agreement on treatment plans is sought.<sup>87</sup> According to Siminoff and Sandberg, shared decision making is particularly important in the context of treatment of DSDs.<sup>88</sup> As a case of surrogate decision making within pediatrics, most parents with a child with DSD are highly interested in sharing treatment decisions with their child's physician.<sup>89</sup> However, this means that practitioners must be willing to engage parents and inform them thoroughly about their child's condition, including scientific controversies and uncertainties (which can be particularly difficult for care or topics related to DSD because a lack of consensus in several areas continues to persist even among clinicians). Through active participation in a shared decision-making process, parental knowledge can be increased (confusion decreased), which in turn can increase their perception of the "voluntariness" of the medical

decision (i.e., with a high level of knowledge, parents may feel empowered to contribute to medical decisions) and decrease their regret or trauma from the experience.<sup>85,90</sup>

A patient decision aid (PtDA) can support clinicians and parents to partner together in shared decision-making and to increase their engagement in decisions about a child's care. PtDAs come in various formats, such as pamphlets, leaflets, cards, videos or web-based tools that provide high quality, consistent, and organised information about a medical intervention (e.g., screening diagnostic interventions, pharmaceutical or surgical therapeutic interventions, etc.). PtDAs can help patients, families, and health care providers learn more about a condition, compare the risks and benefits of options, clarify what matters most to the patient and their family, and make a shared decision about what is the best option for the patient.

Decision aids differ from usual health education materials. While education materials help patients understand their diagnosis, treatment, and management in general terms (that is, without a focus on decision making), decision aids make the decision under consideration explicit, and provide detailed, specific, and personalized focus on options and outcomes to prepare people for decision making.<sup>91,92</sup>

Decision aids can be implemented in several ways. Decision aids can be provided before the consultation to allow the patient/family to prepare for it, have time to digest the information, and to have questions for their practitioner. Or, they can be provided during a consultation, where they help guide both the patient/family and practitioner in making healthcare choices together, helping to accomplish shared decision making. Finally, they can be provided after a clinical encounter (e.g., after an initial consultation), to provide patients/families with a supplemental evidence-based resource that can help guide them in thinking about their decision for a future consultation or intervention.<sup>91</sup>

The International Patient Decision Aids Standards (IPDAS) collaboration has set minimum standards for patient decision aids. These standards have evolved substantially since the first quality criteria checklist and quantitative patient decision assessment tool was released in 2003. Currently IPDAS has released the fourth version of their standards instrument (IPDASi v 4.0), in which they set 6 qualifying criteria, 10 certification criteria, and 28 quality criteria.<sup>93</sup> The *qualifying* criteria are those that are definitional in nature. These are criteria without which a tool would not be considered a patient decision aid (that is, they set the minimum requirement for consideration as a patient decision aid). These qualifying criteria are:

1. The patient decision aid describes the health condition or problem (treatment, procedure, or investigation) for which the decision is required.
2. The patient decision aid explicitly states the decision that needs to be considered (also called the “index decision”).
3. The patient decision aid describes the options available for the index decision.
4. The patient decision aid describes the positive features (benefits or advantages) of each option.
5. The patient decision aid describes the negative features (harms, side effects, or disadvantages) of each option.
6. The patient decision aid describes what it is like to experience the consequences of the options (e.g., physical, psychological, and social).

These qualifying criteria are assessed on a binary yes/no scale and all criteria must be met to be classified as a patient decision aid and to be considered for certification. The *certification* criteria are those that are deemed essential in order to avoid risk of harmful bias (for example, criteria related to the quality of the evidence synthesis process, open disclosure of funding source, and a balanced presentation of options). Certification criteria are scored on a 1 to 4 scale and

tools must meet scores of 3 or more on each criterion to reach certification standards. The certification score is combined with the evidence appraisal to “certify” the patient decision aid as a quality health care intervention with minimal risk of harmful bias on patients’ decisions. The final category are the *quality* criteria, which are criteria considered as desirable because they would enhance a decision aid (e.g., user experience) but are not essential for reducing risk of harmful bias. For example, a criterion like “The patient decision aid includes tools like worksheets or lists of questions to use when discussing options with a practitioner” would be considered a quality criterion, since while it would be helpful, such a functionality would not be necessary to reduce harmful bias. Quality criteria are also scored on a 1 to 4 scale.<sup>93</sup> Importantly, four of the ten certification criteria and five of the 28 quality criteria are only applicable to PtDAs about diagnostic interventions (i.e., tests) and would not be relevant to a PtDA for feminizing genitoplasty for CAH. Additionally, these IPDAS criteria were designed primarily for PtDAs that are to be used by patients alone and not for PtDAs that are to be used in a clinical encounter. Accordingly, a broader PtDA that is developed for multiple uses may not strictly meet IPDAS criteria. While lacking IPDAS certification does not preclude clinical use, adherence to these international standards can help guide the development of a decision aid. However, ultimately, it is only by assessing the impact of the PtDA on shared decision making and other important outcomes that its effectiveness and utility can be deduced.

An important body of evidence informs us on the effectiveness of PtDAs. A Cochrane systematic review of randomized controlled trials of PtDAs was first published by O’Connor et al. in 1999.<sup>94</sup> Since then, this systematic review has been updated with the addition of more studies in 2003, 2009, 2011, and 2014, with the latest update in 2017.<sup>91</sup> The 2017 systematic review and meta-analysis evaluated 105 studies involving 31 042 participants, comparing PtDAs to usual care. The review found that compared to usual care, PtDAs:

- Increased participants' knowledge (Mean Difference (MD) 13.27/100; 95% confidence interval (CI) 11.32 to 15.23; 52 studies; N = 13,316; high-quality evidence),
- Increased accuracy of risk perceptions (RR 2.10; 95% CI 1.66 to 2.66; 17 studies; N= 5096; moderate-quality evidence),
- Increased congruency between informed values and care choices (RR 2.06; 95%CI 1.46 to 2.91; 10 studies; N = 4626; low-quality evidence).
- Decreased decisional conflict\* related to feeling uninformed (MD -9.28/100; 95% CI -12.20 to -6.36; 27 studies; N = 5707; high-quality evidence),
- Decreased decisional conflict\* related to indecision about personal values (MD -8.81/100; 95%CI -11.99 to -5.63; 23 studies; N = 5068; high-quality evidence),
- Decreased the proportion of people who were passive in decision making (RR 0.68; 95% CI 0.55 to 0.83; 16 studies; N = 3180; moderate-quality evidence).

\*To clarify, decisional conflict is a multifactorial construct, measured by the decision conflict scale, that discriminates between those who make or delay decisions (high scores on the decisional conflict scale are correlated with delays in decision making).<sup>95</sup>

A number of other issues regarding the creation of electronic PtDAs exist. While a recent paper by Hoffman et al. suggests that “dissemination and implementation theories support Internet-delivery of PtDAs for providing the right information (rapidly updated), to the right person (tailored), at the right time (the appropriate point in the decision making process)”, the Cochrane systematic review noted that there is still a lack of research investigating format issues such as the web-based delivery of PtDAs.<sup>91,96</sup> The systematic review also highlighted the need to continue to methodically produce and rigorously evaluate new PtDAs. Other researchers have also noted that, to successfully implement PtDAs in clinical workflows, we need a better understanding of these workflows and any

barriers to uptake that might exist.<sup>92</sup> Of note, none of the PtDAs included (or excluded) from the Cochrane review were for surgical treatment of CAH or other disorders of sex development.

To confirm that no previous studies about PtDAs for CAH (and in particular, for feminizing genitoplasty) have been completed, a literature search with relevant terms on PUBMED/MEDLINE was performed (see Appendix A for search strategy). No research evaluating existing PtDAs for CAH treatment was discovered. However, further investigation on trial registries (clinicaltrials.gov and www.clinicaltrialsregister.eu) revealed that Sandberg et al. are in the process of developing and evaluating a web-based decision support tool for disorders of sex development (DSD), the larger umbrella group of which CAH is a part.<sup>97,98</sup> However, their decision support tool and research potentially has several limitations. Firstly, the tool is described as being for multiple DSDs. Consequently, it may not dive deeply enough to any one disorder to provide enough information for parents to make fully informed decisions about surgery. The breadth of the tool (the inclusion of information about other DSD conditions) is also problematic because parents often describe being provided “too much information” not relevant to their needs, which can cause confusion and distress.<sup>5</sup> Secondly, the tool is currently not publicly available, and is only for use in a set number of institutions that are part of the research study. Finally, it has been created for American patients for use in the American healthcare system, which is quite different as compared to the Canadian healthcare landscape. Thus, there is no relevant and easily accessible PtDA for treatment decisions about timing of feminizing genitoplasty for CAH in Canada. Moreover, the existing literature provides insufficient evidence to create an electronic PtDA for this decision.

#### **4. The SDLC for the Creation of eHealth Applications**

To create a patient decision aid that would fulfill this gap, the software development life cycle (SDLC) was adopted. The SDLC is a framework for

software development that can help “ensure a repeatable, predictable process that controls cost and improves quality of the software product or application.”<sup>99</sup> This is particularly important for sectors such as healthcare, which are considerably complex and where safety and security add additional risks. While the SDLC focuses on the development of the software/application, in practice, it is also useful for “stretching into areas such as process re-engineering so as to maximize the benefits of the software” (that is, defining and improving the contextual environment within which the software will operate).<sup>99</sup> The SDLC has several distinct phases:

- 1) **Planning and Requirements Analysis:** This phase begins with planning, which includes the formation of a project goal focusing on a particular need or outcome, establishing the scope of a project (both what is in the scope and what is outside the scope), as well as the identification of resources to accomplish the goal (e.g., funding). Then, a detailed analysis of current processes and needs of the target users is completed, including the gathering of user requirements for the new software. Requirements analysis can range from “detailed instructions on specific functions and operating parameters or more general user stories that explain in simple narrative the needs, expected workflow and outcomes for the software.” This phase of the SDLC is often the most critical and difficult phase in the healthcare sector. This difficulty arises from the need to: (a) involve all relevant stakeholders and potential end users (since healthcare is not as “top-down” as other sectors), and (b) ensure flexibility in the software because practitioner judgment is often inconsistent and adapts to ever-changing situations.<sup>99</sup>
- 2) **Design:** During this phase, analysts who have experience with the domain first turn the user requirements into suitable specifications for the software. Using these specifications, potential solutions are



explored with consideration for aspects such as system architecture, data storage, human-computer interface, costs, and potential trade-offs, as well as details such as security and performance. Then, simple mock-ups of the software are developed, and some initial testing is done with potential end-users to validate the design and identify potential problems and missing information. Depending on the approach of the development team, the complete software can be designed before it is actually developed (coded etc.), or the design and development can be an iterative process proceeding from a higher to more deeper level of the software.<sup>99</sup>

- 3) **Development:** During this phase, the software or application is actually coded or scripted.<sup>99</sup>
- 4) **Testing:** Once the software has been developed it is tested to ensure that it has the features and performs all the functions specified in the requirements (*verification*) and to show that it performs according to operational requirements specified by end-users, that it produces expected outputs, and that it can be used in a safe manner (*validation*). Often, testing is first done “in-house” by the development team and then with potential end-users to simulate a more pragmatic environment. Sometimes, testing is done after the software has been implemented or becomes “live”, in the form of a pilot with a smaller segment of the end-user population.<sup>99</sup>
- 5) **Implementation:** After testing has verified and validated the software, the software or application is “implemented” in the live environment. However, just before implementation, training is performed with any users involved with the software (e.g., healthcare practitioners). At times, implementation can be difficult in the healthcare sector because of its disruptive nature (healthcare practitioners are often highly resistant to change in their workflows, especially if they perceive their

productivity or efficiency decreasing during initial implementation when they are getting used to changes).<sup>99</sup>

- 6) **Maintenance and Evaluation:** After the software has been implemented, it must continually be maintained to correct errors and bugs as they are recognized. Additionally, applications should not be static; they must be continuously evaluated and changed as the needs of the users change.<sup>99</sup>

This thesis focuses primarily on the requirements analysis phase of the SDLC and will touch on some initial aspects of the design phase. To operationalize requirements analysis, a qualitative review of the current literature about congenital adrenal hyperplasia, parent decision making, and decision aids was conducted (see section 2 and 3 above), and we decided to utilize the narrative approach to understanding the needs of parents, patients, and practitioners, and the expected workflows and outcomes of the PtDA. To operationalize this decision, we decided to use the persona-scenario methodology.

## 5. The Persona-Scenario Methodology

Traditionally, interviews and focus groups are the most common methods of data collection employed in qualitative research.<sup>100</sup> The persona and scenario-based design approaches are alternatives to these traditional data collection methods. First described in human-computer interface design under the field of software engineering and design, personas are representations of stakeholder roles that help describe the type of person who will interact with a software or application.<sup>101</sup> Personas go beyond the superficial descriptions of roles (which are focused on actions that users perform), to introduce goals, hopes, and behaviours of each user group in detail. Scenarios are narratives of a successful path using a software or are descriptions of activities performed by individuals in specific roles in specific contexts. Essentially, the scenarios describe what users

would like to achieve through the proposed new program in plain language, making it easier for informaticians and designers to understand their expectations and needs and to discuss designs.<sup>101</sup> These scenarios can help create use cases for designers.

Traditionally, the persona and scenario-based design processes, although complimentary, are distinct from each other and have some disadvantages. For example, the two design approaches are based primarily on researchers' and designers' perceptions of end-user needs. This is because, in most applications of persona and scenario-based design, the personas and scenarios are based on user research (that is, on researchers' interpretations of interviews, focus groups, or ethnographic documentation). This has the potential to incorporate biases into the personas and scenarios. In more recent approaches, for example as described by Madsen et al., personas and scenarios have been combined into a comprehensive persona-scenario that view the user as a particular person with emotions, actions, and needs and focuses on their interaction with a system. Through this new approach, there is more emphasis on using narrative theory to create a good, coherent, and design-oriented story, and on the inclusion of customer representatives and stakeholders in the persona-scenario creation process.<sup>102</sup>

Valaitis et al. describe a fairly novel approach to the use of persona-scenarios that builds on the Madsen et al.'s description of the technique and combines it with an analysis process to create a coherent "persona-scenario methodology". In this methodology, participants who are representative of end-user groups are guided by facilitators to imagine a fictitious but authentic persona based on their lived experiences (through questions such as "What is your character's name, age, and sex?" "What is your character's experience with intervention components?" etc.). Participants are then guided to use their personas to create the potential intervention (the scenario) (for example, using questions such as "How does (character's name) learned about the

software/tool?” or “What does (character’s name) see in the tool?”, etc.). The participants then share these stories with the rest of the group, who comment on them. This adds an opportunity for member checking (a technique used by researchers to help improve the accuracy, credibility, validity, and transferability of the story). These stories and conversations are recorded, transcribed to text, and coded for content, which are the raw “user requirements”. These user requirements are then translated into specifications, which include actions (what activities or processes need to happen for the requirement to be fulfilled) and products (what product(s) and items are needed to support the requirement or action). Requirements or specifications are reviewed for feasibility, viability, and desirability, and those that meet these criteria are extracted to create a “to-do” list for development of the program/intervention. <sup>103</sup>

According to Valaitis et al. ,<sup>103</sup> this methodology has a number of benefits:

1. In a program where there are many unknowns, this method helps introduce the program components and identify potential interactions between them.
2. Because it is user-centered (it involves end-users such as caregivers and healthcare providers directly) and gives participants as much latitude as possible in determining the final program requirements, this methodology helps to reveal novel insights that the research and design team might not have otherwise considered.<sup>104</sup>
3. The methodology is useful for generating contextual information such as strategies about how to best implement and distribute a program, a factor that has been described as essential in the success of eHealth applications.<sup>96</sup>
4. Unlike focus groups where participants take turns answering the same questions one-by-one based on their experiences and context, scenarios allow for “multiple views of an interaction” and “diverse kinds and amounts of detailing.”<sup>104</sup>

5. The use of this persona-scenario methodology allows for early engagement with key stakeholders, which can help foster support and uptake of the pilot program.

Since its introduction, Valaitis et al.'s persona-scenario methodology has been used in a number of programs and interventions in healthcare, including several eHealth applications. These include the creation of online apps for heart failure and self-care for peripheral arterial disease as well as an eHealth app component of a community care intervention, and the expansion or redesign of existing products such as the My Stroke Team app and McMaster Optimal Aging Portal website.<sup>103,105–107</sup> The persona-scenario methodology was chosen for this project because of the methodology's perceived benefits and because of the similarity between the product we envision and these previous tools.

## **6. Methods**

### **6.1. Sampling for Participants**

To create a useful PtDA, it was important to first determine the user groups that would be involved in surgical decision making. From a healthcare practitioner perspective, for feminizing genitoplasty, the groups most commonly involved in the decision-making process (ordered by depth of involvement) include:

- Surgeons (pediatric urologists): perform the feminizing genitoplasty and consult with families,
- Nurses and child life specialists working in urology: educate families, prepare them for the surgery, and help post-operatively, and
- Pediatric endocrinologists and nurses working in endocrinology: refer highly virilized patients and their families to the

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urologist/surgeons for surgery and continue to see the patients for follow-ups until they become adults.

Accordingly, healthcare practitioners representing each of these groups were recruited through purposeful sampling; they were chosen to provide a diverse range of roles and to ensure perspectives of practitioners involved in surgical decision making and endocrinology. They were identified through members of the research team and were recruited by Dr. Luis Braga through his professional network who gauged interest in participation, with follow up communication done by the author through email. Three healthcare practitioners (in addition to Dr. Luis Braga) were recruited and all four of them participated in this study.

From a patient and family perspective, the group most commonly involved in decision making is the parents, who are often the surrogate decision makers for their young children. However, recognizing that young patients are beginning to play a greater role in surgical decision making, young adult patients who had surgery in adolescence were also recruited. Parents of children with CAH and adult patients were recruited through their relationship with Dr. Luis Braga, who was the patients' pediatric urologist.

With regards to sample size, generative qualitative research aims for data saturation, which “occurs when all the main variations of [an experience] have been identified” and further interviews yield little-to-no new information.<sup>108</sup> There is no clear expert consensus on the number of participant interviews needed to reach data saturation. However, one factor that impacts this number is the distribution of the experience being studied. Smaller, more homogenous experiences need fewer interviews to reach saturation.<sup>108</sup> For a relatively homogenous experience such as decision making for surgical timing for CAH, best practices in qualitative research for software design recommend at least 4 participants per “use case” and no more than 5 use cases per software, with

additional participants providing less and less new information.<sup>109</sup> A use case is a list of actions that typically define the interactions between an actor and a system to achieve a goal. Accordingly, the three use cases for our PtDA are defined by three different actor groups: parents, adolescent patients, and healthcare practitioners.

However, Valaitis et al. recently submitted an assessment of their experience using the persona-scenario in the Health Tapestry primary care intervention. They note that, “In [Health Tapestry]...most ideas (codes) were only identified once or repeated a few times, indicating that the concept of saturation may not be appropriate for the persona-scenario method” and that even if it were appropriate, determining sample size using saturation in advance of a study is difficult. Rather, they suggest that it is better to ask post-hoc “How rich (quality) and thick (quantity) is the data?” If the data is not rich or thick enough, then more participants should be recruited (Valaitis et al., 2017; manuscript submitted for publication). Moreover, Valaitis has suggested that “the purpose of the persona-scenario is not to gather enough data to reach saturation, but rather to purposefully sample the population for diverse participants to gain diverse and different perspectives about how a software/program would be used” (Private communication from Dr. Ruta Valaitis; School of Nursing, McMaster University, February 2018).

Regardless, in keeping with the minimum requirements described above, 6 parents, 2 patients and 4 health care providers were invited to participate in the persona-scenario exercise. All three families whose children had or were considering feminizing genitoplasty were approached for recruitment by Dr. Braga and informed about the study through a phone call. However, the relative rarity of adult post-surgery CAH patients at our centre limited the number that could be invited to participate. Since there were only two patients who had had surgery in adolescence, both were invited to participate. After initial interest in the study was ascertained by Dr. Braga, families were called by the author to

thoroughly explain their role and the information and consent form was emailed to them. Of the three families that were called by Dr. Braga, one refused to participate after being called again to confirm their interest.

## **6.2. Persona-Scenario Sessions**

Based on Valaitis et al.'s description of the persona-scenario methodology, a question guide was created to aid participants in thinking about a persona and a scenario in which their persona interacted with the patient decision aid (see Appendix B). The questions were adapted from Jacobsen and O'Connor's Decisional Needs Assessment in Populations: A workbook for assessing patients' and practitioners' decision-making needs.<sup>110</sup> These questions have been used frequently for the development of patient decision aids in a number of healthcare contexts. Additionally, the workbook provides separate sets of questions for patients and practitioners, recognizing important differences in these user-groups' perspectives and experiences. Consequently, the prompting questions for providers and practitioners in our question guide were slightly different. The questions cover a range of topics that are important considerations for the creation of a patient decision aid. They range from asking about the context around the surgical decision and the workflows in which the PtDA could be provided, to factors contributing to decisional conflict and decisional support, to the content users require in the PtDA.

During the persona-scenario session, participants were first asked to complete the information and consent form (see Appendix C) and were paired with other participants (i.e., as groups of mothers, fathers, and patients). The theoretical rationale for pairing participants who have similar characteristics together is to allow them to draw on similar lived experiences when creating their personas and scenarios. Previous literature has indicated that mothers and fathers have different experiences when it comes to decision making for their children and to outcomes such as posttraumatic stress.<sup>8</sup> Additionally, recognizing



that parent participants constituted of multiple couples, we decided to break up the couples so that the participants would focus less on any potential regrets they might have about their own family's experience and more on creating the personas and scenarios. They were then given a brief introduction to patient decision aids (10 mins) and an introduction to the persona-scenario method (10 mins). Following these introductions, pairs were guided by facilitators through the question guide to create a persona and a scenario in which that persona interacted with the PtDA (70 mins). Facilitators took detailed notes as they guided the participants through the questions. At the end, each table elected one representative to share the scenario (story) they had created with the room, to allow for member checking and discussion with the other participants (20 mins). Participants were then asked to complete the anonymous PPEET and demographic survey. Healthcare practitioners underwent the persona-scenario session individually and consequently did not do a "report back" to other practitioners. The sessions were held at McMaster Children's Hospital in Hamilton, Ontario and lasted about two hours (which was sufficient to complete the whole exercise and to allow participants time to interact with each other).

### **6.3. Public and Patient Engagement Evaluation Tool and Demographic Survey**

The persona-scenario method is a user-centered co-design methodology that falls under the umbrella of public and patient engagement (PPE) – "an inclusive term used to capture a wide range of efforts aimed at actively involving citizens and patients in various domains and stages of health system decision making."<sup>111</sup> As PPE becomes more commonplace, there has been a call to rigorously evaluate these activities. While a number of evaluation tools exist,<sup>112</sup> the Public and Patient Engagement Evaluation Tool (PPEET) developed by Abelson et al. was used to evaluate the person-scenario method as used in this context (see Appendix D).<sup>111,10</sup> Using the PPEET will allow for comparison with past evaluations of the persona-scenario method (unpublished). The tool consists

of fourteen statements that participants answer using a Likert scale (ranging from strongly disagree to strongly agree) as well as four open-ended questions (How do you think the results of your participation will be used?; What was the best thing about this engagement activity?; Please identify at least one improvement we could make for future engagement activities; and Additional Comments).

Additionally, to capture pertinent demographic information about the participants, they were asked to complete a demographic survey (see Appendix D).

#### **6.4. Ethics**

A detailed Research Ethics Board application was submitted to the Hamilton Integrated Research Ethics Board (HiREB) with all the supporting documents for ethics review and approval. The application received a Student Committee Research Ethics Board level of review and was approved with one stage of revision.

#### **6.5. Analysis**

Discussions at each table and the report back component of the session were audio recorded to ensure that all details were captured and that participants' perspectives were not misinterpreted during analysis. These audio recordings were transcribed and anonymized by assigning random numbers to all participants and session coordinators. All personal information was kept confidential and was only known to the two session coordinators. The facilitator notes of the discussion, supplemented by the audio recordings and the report back story, were combined for each table to create one comprehensive "source" for each of the different persona-scenarios.

NVIVO Pro 11 software (QSR International) was used to analyze each source for codes, sub-categories, and categories. We used the six phase approach to qualitative analysis described by Braun and Clarke,<sup>113</sup> but adapted it

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for the persona-scenario approach as described by Valaitis et al.<sup>103</sup> While Braun and Clarke described their methodology to code for “themes”, we chose to use their steps primarily to organize our codes into categories and to create a coherent structure that represents the relationships between the many user requirements we anticipated we would find. As described by Braun and Clarke, we performed a deductive or “theoretical” analysis, focusing less on generating a description of the overall data, and more on detailed coding and analysis to find answers to the question prompts in the question guide. We coded primarily at a semantic or explicit level, coding for requirements and categories that were identified via the explicit or surface meanings of the participants’ responses. However, at times we also coded at a latent level, where we attempted to interpret underlying ideas and requirements that participants might have. First the author and Melissa McGrath (Dr. Luis Braga’s research coordinator) read the transcripts several times to familiarize themselves with the data and to identify some distinct and reoccurring categories. Second, we coded each persona-scenario transcript together to generate the initial coding structure of user requirements mentioned by participants in their persona-scenarios. We then sorted related codes into higher level candidate sub-categories and categories. We reviewed these categories and their structure and relationships to ensure that categories were distinct from each other and that the coded extracts fit into that category. At this stage, we reviewed the persona-scenario transcripts once more to ensure that we coded any additional data within these categories that may have been missed in earlier coding stages. We verified the coding structure and our process with Dr. Ruta Valaitis.

Categories, sub-categories, and lower level nodes were formatted into a table with one column for the categories/nodes, and additional columns for the number of sources and references. The nodes were assessed for human centred design considerations, that is, whether the requirement is desirable, feasible (Yes for version one of the PTDA, yes for a later version of the PtDA, no, or needs

more investigation), and viable (yes, no, or needs more investigation).<sup>114</sup> The desirability of a requirement was contingent on it being mentioned by a potential end-user. The feasibility of specifications was based on an assessment of resources required for initial development of the feature, the relevance of the feature, and clarity of the requirement/specification. Viability was assessed by comparing the long-term ability of the research group to support and maintain the requirement or functionality. Each node was assigned specifications (i.e., products or actions), as appropriate, using researcher's interpretations of the user requirements. The specifications of nodes that meet the human-centered design considerations will form the basis of the specifications document for the design and development of the PtDA. As part of the analysis process, matrix coding queries were generated on NVIVO 11 Pro to tease out the differences in requirements between family members (patients and parents) and practitioners.

Data from the PPEET (participant scale) and demographic survey were analyzed to generate descriptive statistics (means) while data from the PPEET (open questions) were used to understand participants' perspectives about their involvement in this research study.

## **7. Results and Analysis**

### **7.1. Demographics**

We recruited four parents (out of six), 2 adult females diagnosed with CAH who had had surgery in adolescence, and 4 healthcare practitioners from a variety of fields and backgrounds (see Tables 1, 2, and 3 for an overview of important demographic characteristics).

The parents and adult patients joined the same persona-scenario session. While none of the parent and patient participants self-identified as members of minority or disadvantaged groups, participants were otherwise fairly diverse, with varied levels of education and self-rated comfort with technology (see Table 1 and 2). The two adult patients in their twenties reported being more comfortable

with technology as compared to the parent participants. While we intended to recruit a mix of families (some whose children already had surgery and others who were still considering surgery or had deferred surgery until later), all children whose families were available for contact had already undergone feminizing genitoplasty.

*Table 1 Demographic characteristics of parents of children with CAH who had feminizing genitoplasty*

Characteristic	Parents (n=4)
Proportion Female	50%
Average Age (in years)	47 (30, 33, 62,62)
Age of Child with CAH (in years)	3, 25, 27
Member of minority or disadvantaged group?	100% - NO
Marital Status	100% - Married
Highest Level of Education	50% - Completed high school 25% - Completed technical school 25% - Completed graduate degree
Level of comfort with technology (computer, internet, health websites, eHealth applications) (from 1 = no comfort to 10 = extremely comfortable)	6.5 ( $\sigma = 4.36$ )
Worked in a healthcare profession	100% - NO

*Table 2 Demographic characteristics of adult female patients with CAH who had feminizing genitoplasty in adolescence or as young adults*

Characteristic	Patients (n=2)
Proportion Female	100%
Average Age (in years)	25, 27
Member of minority or disadvantaged group?	100% - NO
Highest Level of Education	50% - Completed technical school 50% - Completed Bachelor's degree
Marital Status	100% - Single, never married
Level of comfort with technology (computer, internet, health websites, eHealth applications) (from 1 = no comfort to 10 = extremely comfortable)	8.5 ( $\sigma = 0.71$ )
Worked in a healthcare profession	100% - NO

All healthcare practitioners went through the persona-scenario sessions individually due to scheduling constraints. Healthcare practitioners provided representation from both urology and endocrinology specialities and from a number of professions (specialist physicians, nurse, and child life specialist). Practitioners reported a wide variety of years of experience providing care to children with CAH and supporting their families (from 3 to 23 years) but generally rated themselves as being very comfortable at providing families with support. Practitioners reported being quite comfortable with technology.

*Table 3 Demographic characteristics of healthcare practitioners who provide care to children with CAH who had feminizing surgery and support their families in decision making*

Characteristic	Practitioners (n=4)
Proportion Female	75%
Member of minority or disadvantaged group?	25% - Visible Minority 75% - NO
Highest Level of Education	100% - Completed graduate or professional degree or postgraduate training
Discipline	50% - Pediatric Endocrinology 25% - Pediatric Urology 25% - Pediatric Urology/Surgery
Role/occupation	25% - Urologist 25% - Endocrinology 25% - Nurse Practitioner 25% - Child life Specialist
Years of experience providing care to children with CAH and support to their families	9.75 (3, 6, 7, 23)
Level of comfort providing support to families with children diagnosed with CAH (from 1 = not at all comfortable to 10 = extremely comfortable)	9.25 ( $\sigma = 0.96$ )
Level of comfort with technology (computer, internet, apps, health websites) (from 1 = not at all comfortable to 10 = extremely comfortable)	8 ( $\sigma = 0.82$ )

## 7.2. Personas and Scenarios

In total, 7 personas and scenarios were created between the family member (parents and patients) (3) and healthcare practitioners (4). The following is a short introduction to each of those personas as summarized from the facilitator notes (see Appendix E for the final persona-scenarios shared by the participants/pairs at the end of the sessions). Parent or patient personas included:

- **Molly:** The two mothers created a persona of a 30-year-old mother of a young child with CAH who is considering whether to have her child undergo surgery now or later. Molly lives in a small rural town. She has a high school level of education and worked as a secretary before her pregnancy. Molly is very comfortable with technology, as most people are. Molly focused considerably on her emotions and feelings and the tension between involving her child with the decision and wanting her to have a normal childhood. Molly was described as being dependant on the practitioner to lead and inform the parents, but ultimately wanting to make the decision with her spouse. Within the family unit, Molly was being described as taking the stronger role in decision-making for their child. Molly learned about the PtDA through her endocrinologist or urologist, and the PtDA was used both during and after consultation.
- **Bob:** The two fathers created a persona of a 25-year-old father of a young child with CAH who is considering surgery for his child. Bob is quite educated and is studying to be a doctor, so he knows about but is not too familiar with CAH. Like others his age, Bob is great with technology and especially with [smart]phones. He lived in a large metropolitan city. He was described as wanting what was best for his child and being willing to use new health treatments. However, the two fathers stressed that Bob lets his wife make most of the decisions about surgery and how the child is raised. Bob was described as wanting healthcare providers to give him directions, but that in the end it would be a family decision to do early or late surgery.

Bob prefers that the decision aid or support tool be provided right when the child got diagnosed so that he and his spouse have the information about surgery [as early as possible].

- **Annette:** The two adult female CAH patients created the persona of Annette, a 10-year-old female with virilizing CAH who did not have surgery in infancy. She is now at an age where her family and provider have had open conversations with her about her disorder and involved her in making a shared decision about surgery. Annette is pretty experienced and comfortable with technology. Her concerns are around having a body that fits her gender and feeling embarrassed and scared about what other people will think. Annette would receive the PtDA from her specialist during a consultation about surgery. The physician would help guide her through the tool and decision, but she would also use it with her family at home.

Practitioner personas included:

- **John Smith:** The pediatric urologist created the persona of John Smith, a 45-year-old pediatric urologist who has been working for 10 years post-fellowship in a large urban tertiary care academic centre within a multidisciplinary team environment. John has considerable experience with and knowledge of CAH, having done his fellowship in a university that saw considerable CAH cases and because he is referred 5-6 patients for surgery each year. John is very comfortable with technology, having used it throughout training and in his day-to-day life; however, he is not as familiar with tools such as patient decision aids.
- **Ben:** The pediatric endocrinologist created the persona of Ben, a 45-year-old endocrinologist, who has been working for ten years in a pediatric academic centre after a fellowship at Boston Children’s Hospital. He works in an interprofessional environment with a clinic nurse and a nurse



practitioner. Ben has a moderate amount of experience with CAH, seeing about 4 females with Prader  $\geq 3$  a year and refers them on to a urologist for surgery consultations. He is moderately tech savvy but is not at all familiar with patient decision aids and how he would integrate them into his clinical practice.

- **Sarah:** The nurse practitioner (practicing in endocrinology) created the persona of Sarah, a 32-year-old pediatric endocrinology fellow who has a hunger for new and unique cases so that she can practice these cases when she is an autonomous practitioner. Sarah is overseen by a staff physician in her care for patients and works in an interprofessional environment with nurse practitioners and residents. She has some interaction with surgeons in coordinating care for patients. She sees about two children with CAH per year in her fellow patient load, so she has little-to-moderate experience with CAH. While she is very well versed in technology, she has absolutely no experience with PtDAs.
- **Shirley:** The child life specialist created the persona of Shirley, a 30-year-old child life specialist who has completed a master's in child life studies and has worked within a pediatric hospital for five years in the department of surgery. Shirley works within an interdisciplinary environment with nurses, surgeons, endocrinologists and social workers, as well as with residents and fellows. Shirley understands all aspects of CAH, including pre- and post- operative considerations, and the implications of delaying decision making. She is knowledgeable and moderately comfortable with technology and electronic tools but is new to PtDAs as they are not something that she has used in clinic.

Participants created seven scenarios (one for each of the personas). The final scenarios (see Appendix E) were of moderate depth but lacked the details participants mentioned during the facilitator-guided persona-scenario creation process. That is, the final scenarios were more superficial as compared to the

facilitator notes, which captured granular details participants were discussing while going through the question guide and building their personas and scenarios.

### **7.3. Coding and Analysis of Requirements**

After completing the coding phase of the analysis, 446 granular and highly self descriptive nodes were generated from the facilitator notes and session discussions. Each node described a unique requirement that users discussed. After several rounds of categorization, these nodes were grouped under four emerging categories (with each category having various subcategories):

- Information and Decisional Content in the PtDA (140 nodes),
- Proposed Functionalities for the PtDA (46 nodes),
- Web Usability-related requirements (40 nodes), and
- Implementation Context (220 nodes)

Each node was assessed for its feasibility, viability and desirability. All features that patients, parents, and practitioners required were considered desirable because they were mentioned as such by the potential end-users; the level of desirability can be assessed by the number of sources and references that were coded to that node. The majority of nodes were feasible and viable for implementation in the first version of the patient decision aid; however, some content and proposed functionalities were assessed as being feasible only for a later version of the patient decision aid. A few requirements were not feasible or viable. Specifications (products and actions) were interpretively generated for the nodes that passed the criteria. Depending on the category, some nodes only required a product specification (for example, most requirements related to content could be fulfilled by creating an item (the PtDA) and embedding the content within it), while others only required an action specification (for example, the description of how the PtDA would be disseminated and the workflow for its implementation). In other cases, both an action and a product would be needed

to fulfill a requirement. Examples of nodes from each of the four categories and some subcategories are included in Table 4.

Table 4 A sample of how nodes were analysed with examples from each category and some subcategories. Feasibility was assessed as Yes [V1 or L (Later version)] / No / NMI (Needs more investigation) and viability as Yes / No / NMI.

Node	Sources	References	Feasibility	Viability	Specification or Rationale
Category: Information and Decisional Content in the PtDA					
Subcategory: Information about CAH and Surgery					
What is CAH?	7	27	Yes (V1)	Yes	Product: PtDA with content about CAH including: (1) How it presents, (2) What it does to fertility, sexuality, sexual orientation, period, (3) How rare it is, (4) Kinds of CAH and levels of virilization, (5) The biomedical pathways re adrenal gland and enzymes, and (6) the genetics
Other supports and resources > Information about living with a child with CAH in general	2	4	No	Yes	Rationale: Out of scope of PtDA for surgical decision making
Subcategory: Images, Videos, and Testimonies					
Before and after surgery images	6	12	Yes (V1)	Yes	Action: Find or take images before and after surgery, including several years after surgery Product: PtDA with photos comparing before and after surgery (e.g., as a timeline of photos: -0.5 yr., +0.5 yr., +2yrs, +10 yrs. etc.)
Testimonies from families who had surgery that have only facts and no opinions	1	2	No	Yes	Rationale: All testimonies about surgical decision making will have some level of opinion imbedded in them.
Subcategory: Information that helps families consider the following values when making their decision					
Child will have pain from surgery	4	5	Yes (V1)	Yes	Product: PtDA has content about patient experiencing pain after surgery and the associated issues (e.g., need for narcotics for pain management).

Node	Sources	References	Feasibility	Viability	Specification or Rationale
Category: Proposed functionalities for the PtDA					
Subcategory: PtDA can be printed					
PtDA should have ability to highlight information you find interesting, 'save' it, and print all highlighted information	1	2	No	NMI	Rationale: This requirement would require considerable technical effort and resources to implement and is unfeasible within our budget.
Subcategory: PtDA can create a summary at the end of the tool					
Users can obtain a summary that contains their choices and what families valued as higher or lower importance	4	6	Yes (V1)	Yes	Item: PtDA contains a section or button whereby users can print or email a summary of their choices and value elicitation and rating as a PDF document
Subcategory: PtDA displays values and allows users to rate them					
Option 1: Likert scale for values is better than ranking as it allows more granularity and uniqueness	4	4	Yes (V1)	Yes	Product: PtDA has section that asks users to rate each outcome on its' perceived level of importance using a Likert-scale
Category: Web-usability related requirements					
Subcategory: Accessibility of the PtDA					
PtDA can be website or app	6	6	Yes (V1)	Yes	Product: PtDA that is available on a website
If it is an app, PtDA needs to work on both android and apple	1	1	No	NMI	Rationale: Budgetary constraints. Additionally, long-term cross-platform maintenance would likely be difficult and costly.
PtDA must be usable on all devices (i.e., computer, smartphone, tablet, etc.)	5	6	Yes (L)	Yes	Action: PtDA is developed using responsive web-design principles

Node	Sources	References	Feasibility	Viability	Specification or Rationale
Subcategory: Design-Clarity					
Users initially see basic information but are able to “dig deeper”	6	8	Yes (V1)	Yes	Product: PtDA that has concise important information and uses links and pages/sections to give users meaningful choice about learning more
Category: Implementation Context					
Subcategory: Healthcare provider workflows and context					
Healthcare providers receive training about the PtDA	2	4	Yes (V1)	Yes	Action: Generate a list of relevant healthcare practitioners that would benefit from training Action: Create training for healthcare practitioners Action: Provide practitioners with a workshop or in-service with practical run throughs (e.g., using case-studies)
Subcategory: Healthcare providers teach parents about the PtDA					
Option 1: Parents receive the tool from the healthcare provider right when the child is diagnosed	2	5	No	No	Rationale: This requirement would require considerable dissemination of the PtDA and training of practitioners. Moreover, there would not be a urologist to answer questions, which may increase parent anxiety.

## 7.4. PtDA Requirements and Specifications

Specifications from nodes that met the human centered design criteria are summarized for each category below.

### 7.4.1. Information and Decisional Content in the PtDA

Around one third of user requirements were related to information and decisional content, which were categorized into content about CAH and surgeries, content provided through images, videos, and testimonies, and content related to additional outcomes which might influence decision making.

All scenarios mentioned that the PtDA should have information about CAH and the surgery. This included content regarding:

- What is CAH?
  - (1) How it presents,
  - (2) Implications for fertility, sexuality, sexual orientation, and periods,
  - (3) Incidence of CAH,
  - (4) The kinds of CAH and levels of virilization,
  - (5) The biomedical pathways (i.e., information about the adrenal gland and enzymes), and
  - (6) The genetics
- Why is replacing hormones key?
  - (1) General information about medication emphasizing the life sustaining nature and need for regular medication and follow-up,
  - (2) Medication for crisis including information about preparing and self-injecting emergency medication, and
  - (3) Needing to control hormones before surgery
- Reasons for surgery and the surgical options, including:

- 
- (1) Why surgery may be beneficial or necessary (regardless of whether it is early or late)
  - (2) Information about the different types of surgery (i.e., one step vs two step)
  - (3) Timeline for surgery (including the potential for having revision surgery again in the future)
- The advantages and disadvantages of the different surgical options
  - The likelihood of the advantages and disadvantages
  - Impacts of each surgery option on short, intermediate, and long-term outcomes:
    - (1) Short term outcomes include risk of infection and dehiscence, pain management and need for narcotics, details regarding the preparation and hospitalization involved and physical / functional aspects of recovery from surgery (e.g., reduction of mobility and its effect on active infants or adolescents in high school etc.),
    - (2) Intermediate outcomes include cosmesis, potential for repeat surgery or dilation, and the potential for stigma, and
    - (3) Long term outcomes include ability to have normal sexual intercourse and orgasm, and to have normal sensation and fertility (including ability to deliver, have a child, and have normal periods).
  - Information regarding the physical and psychosocial effects of the various surgical options, such as:
    - (1) Letting parents know a lot is unknown for each option,
    - (2) Providing information regarding effects on peer and social pressure,
    - (3) Information regarding helping a child cope with the surgery, including information for the parents and children on how to talk to their social network and handle questions,



- 
- (4) Information regarding what parents should be looking for physically as their child heals and when seeking medical help may be necessary
- Other supports and resources, such as:
    - (1) A method of connecting with other families who have already undergone surgery,
    - (2) Definitions of medical terms,
    - (3) Reliable links to external evidence-based resources such as the Hospital for Sick Kids' "About kids" animated resources, the BC Children's Hospital booklet for CAH,<sup>115</sup> the Consortium on the Management of Disorders of Sex Development's Clinical guidelines<sup>116</sup> and Handbook for parents<sup>117</sup>,
    - (4) Support for parents on how to talk to their child about the surgery,
    - (5) A statement or section to make sure families and users know about the clinical psychological and social support available at the institution.

All scenarios also mentioned that various content should be provided through alternative formats such as:

- Images:
  - (1) To teach individuals about CAH and provide background context
  - (2) Of genitals varying in the Prader spectrum
  - (3) Before and after surgery (both for children that had surgery in infancy and later in life)
  - (4) Of the surgical procedure (drawings rather than photos)
- Videos:
  - (1) To educate the family about background information about CAH and medical treatment

- (2) Of surgery that are “live” are *not* appropriate or helpful for parents (however, a third of the persona-scenarios mentioned that there does need to be some sort of video for surgery, perhaps an animated one or one where the urologist talks about and explains the surgery)
  - (3) Testimonials or stories of older patients or families who underwent surgery early or late
- Testimonials:
    - (1) Of people who underwent surgery early or late and what their outcomes are like now

While some scenarios mentioned a concern that images and videos of “poor” outcomes could bias families against a specific surgery, most explicitly mentioned that having depictions of poor outcomes was very important to minimize bias in the PtDA, and to provide images for comparison so that parents and patients know they are healing properly.

Scenarios also discussed a need to have decision-making content, such as information about the potential values that families could consider before they make their decision. As expected, these values included a consideration of the personal importance that users attribute to the positive and negative outcomes of each surgical option, including the outcomes described above. However, participants also mentioned several additional “values/considerations” that should be reflected on, such as inclusivity and embracing differences, normalization of genitals (and the consequences, such as the ability to utilize childcare and have public outings without stigma or shame etc.), the level of willingness to involve the child in the decision, and possibility of irreversible damage (regardless of whether the surgery is performed early or late). While two scenarios mentioned that displaying these outcomes/values/considerations “out there” might bias parents who might not have otherwise thought of them, five scenarios emphasized that they needed to be mentioned in the decision aid because

parents often have difficulty verbalizing them or might not think of them in the cognitive state they might be in (i.e., due to the stress of their child's diagnosis etc.).

The specifications related to all of these content requirements will involve several actions: performing a systematic search to find evidence-based information that answers these content-requirements and then writing it into the PtDA in an accessible and lay manner. For multimedia content, it may also require creating and developing images (cartoons/drawings), videos, or testimonials to fulfil user requirements. Additionally, there needs to be more investigation about the outcomes that are important to parents during decision making and how to best represent them in the PtDA.

#### 7.4.2. Proposed Functionalities for the PtDA

The scenarios described a number of functionalities embedded into the patient decision aid. Generally, participants described a PtDA that was highly interactive and not solely textual. Interactive components included:

- Allowing users to control their movement and progression through the PtDA
- The ability to choose to see information based on a users' role (e.g., parent vs child), age, diagnosis (salt wasting vs. simple virilizing) and level of understanding (simple vs. advanced) (through filters or through sectioning of information)
- Testing users for their learning and retention of key points
- Links to evidence next to each statement, that pop into a new window with the title and abstract of the article that provides the evidence
- Branching logic that allows parents to select a surgical decision (early vs late) and prompts them with the potential outcomes of their choice (such as advantages and disadvantages)
- Prompting users with a statement asking them to reflect on their selection

- Providing users with the opportunity to provide feedback about the PtDA

Participants described a functionality related to printing or emailing the PtDA to themselves. For example, they described situations where personas would print out the PtDA at different levels of depth of information (e.g., a section of the PtDA vs. the whole PtDA). They emphasized that these paper print-out versions of the PtDA need to be created specifically for the paper medium and need to be more concise than the electronic PtDA. Participants also described a functionality to create a summary at the end of the PtDA that could be printed or emailed to themselves. These summaries would consist of the choices or selections that users made in the PtDA as well as which outcomes users rated as being of higher or lower value or importance. These summaries were also described as containing questions that users still have – questions that users would type into an open entry text box as they were going through the PtDA. Altogether, the summary was described as helping to streamline the discussion with their surgeons during their follow-up consultation.

The PtDA was described as displaying outcomes and consequences that parents should consider when making surgery and having a functionality whereby users could clarify the value they placed on these outcomes in some way, to help guide them in choosing between late or early surgery. Scenarios described three different value clarification methods: (1) Likert scales that assess each outcome in its importance to users, (2) ranking the outcomes/consequences among themselves, and (3) binning outcomes between early and late surgery. Outcomes were described as already being present in the PtDA as well as being elicited from users using a text entry field. Participants were quite clear that values clarification should not lead to a computational or algorithm-based decision about a preference for surgery that they are “stuck with”. Rather, the clarification of values should only help parents/patients and practitioners consider which way families are “leaning”.

Privacy and security was not considered a significant concern for most participants. However, it was important for the majority of participants that users ought to be told about what is happening with any data that is collected.

To implement these functionality requirements, the associated specifications would be to create/code for these features in the PtDA. For example, to print the PtDA at varying depths of information, PDFs containing the information in the PtDA would need to be created for each segment of the tool and for the PtDA as a whole and would be embedded into the PtDA graphical interface through a button. Users would click this button to access and print the PDF. To create summaries, several specifications would need to be executed, including a feature to save user selections, a text entry field feature on each page or section of the PtDA that allows users to type in questions that they have, a feature that asks users for their email, and a feature that aggregates this information and generates a report that is sent to the corresponding email. For requirements with multiple options, such as the rating/ranking/binning of values and the issues around privacy and security, one specification is that more investigation is needed to identify the option that is most suitable based on current evidence about software design and usability.

#### 7.4.3. Web Usability-related Requirements

Scenarios described several web usability related criteria, which can be further categorized into accessibility criteria and design criteria.<sup>118</sup>

Participants wanted the PtDA to be highly accessible. They felt that a website or app were both suitable but noted accessibility advantages and disadvantages for both formats. For instance, a website would allow for “use on any technology” whereas apps were suited only to smartphone or tablet devices. On the other hand, once apps are downloaded, they can be used offline in the bedside or clinic, whereas websites must be used online. Additionally, they felt

that the PtDA must be accessible on all devices, including computers, cell phones, and tablets.

Participants also contributed requirements related to the design of the PtDA. Firstly, all scenarios described a PtDA that presented information in a simple and clear manner but provided the option to “dig deeper”. One way of making information clear was by “highlighting” the important points and having summary and key points towards the end of each section and the end of the PtDA as a whole. With regards to layout, scenarios mentioned that the different surgical options (with their corresponding advantages and disadvantages) should be separated on different “sections” of the PtDA. The probabilities of each advantage and disadvantage should be next to them, and can be provided as percentages, interactive charts (that allow users to “drill down” into the probabilities), pie graphs, icon arrays (e.g., 3 icons coloured out of 100, to show a 3% risk), or statements (such as “Among 100 children like yours, xx will develop... while yy will not”). Participants suggested that probabilities need to be contextualized in some way, either by labelling the probability as low, medium, or high risk or by colour coding them as green, yellow, or red, with a legend to explain the colours.

To implement these web-usability requirements, the corresponding specifications include: developing a PtDA delivered through a website using responsive web-design principles; using accordions or tab interfaces (where appropriate) to present content clearly and allow the option to dig deeper; modularizing or segmenting content so that the different options for surgery are presented separately; investigating the probabilities of genitoplasty outcomes in the literature and the evidence regarding how to best present probabilities; and creating appropriate visual graphics to present the probability.

#### 7.4.4. Implementation Context

Nearly half of the user requirements were related to the context surrounding the implementation of the PtDA. The scenarios depicted healthcare practitioners learning about the patient decision aid in a variety of ways. They were either involved in creating the PtDA, or learned about it through specialty conferences, journals, or publications, through presentations in interdisciplinary rounds, through word-of-mouth, or through an institutions' pediatric urology website. Scenarios referenced the need to gain buy-in from staff. Additionally, several participants described the need for specialised and comprehensive training about the PtDA since none of the practitioner personas are aware of PtDAs or have used them in the past. This could involve a workshop or an in-service with "practical bed ride run throughs" using cases. Training would be for all practitioners who are or could be involved in providing surgical care for CAH patients, including the urologist, endocrinologist, anaesthetist, nurses, child life specialist, and any fellows or residents.

In all scenarios, when families begin to think about surgery, their decision is described as being between choosing surgery now or later (i.e., there is no debate over having surgery). Family members, and especially parents, are described as highly stressed and emotionally distraught, with:

- Remaining feelings of devastation from hearing that their child has a life-threatening condition that will need continuous treatment,
- Confusion and embarrassment about how to explain the condition and surgery to family and friends and about what society will think,
- Anxiety about making the wrong decision for someone else,
- Worry about regretting their decision and about the risks of surgery, and
- Eagerness for surgery because it helps normalize the external genitals (although not the underlying condition)

Some things that were described as helping to make the decision included clinical tests that helped clarify the diagnosis, having information outlined in a clear way without medical jargon, and being provided evidence about the surgeries. However, several barriers to decision making exist, including:

- Contextual or situational barriers such as:
  - Circumstances in the family life such as employment or death,
  - Family dynamics such as separated parents,
  - Poor previous interactions with the healthcare system resulting in lack of trust in healthcare practitioners,
  - A “non-compliant” or poorly tempered child, and
  - Parents or children’s feelings and emotions.
- Irreversibility of the surgery
- Lack of information or misinformation, including:
  - Lack of high-quality evidence from long-term follow up of patients,
  - Misunderstanding or conflating gender, gender identity, dysphoria, sexual orientation etc., and
  - Reading negative reviews online of bad experiences or surgeons.

The scenarios contained a number of workflows about how users learn about the PtDA and who is involved in providing them. One potential workflow that was most frequently discussed by participants is represented in the unified modeling language activity diagram in figure 10. Alternative workflows included families being provided the PtDA as soon as possible after the child is diagnosed, or by the endocrinologist rather than the urologist, or by the urology clinic in the waiting room before the consultation rather than during or after the consultation. Family members were described as using the PtDA in several settings including: the clinic, at home, in the library, a coffee shop, or a friend’s computer. Several scenarios described clinical help (e.g., a nurse) being available to help guide families or answer questions about the PtDA if families were having trouble. However other scenarios stressed the importance of having the PtDA be user-



friendly enough that no help is necessary to use it. The PtDA was described as being structured in a way that would allow it to be accessed and used both in the clinic during consultations and/or at home.

To implement these workflows, a corresponding specification would be that the urology clinic needs to have internet-enabled tablets or other devices which they can use to introduce the PtDA to families or that can be used to guide the consultation. Another specification would be that the clinic would need paper copies of the PtDA to offer to parents if they wanted it or if they did not have access to internet-enabled devices at home.

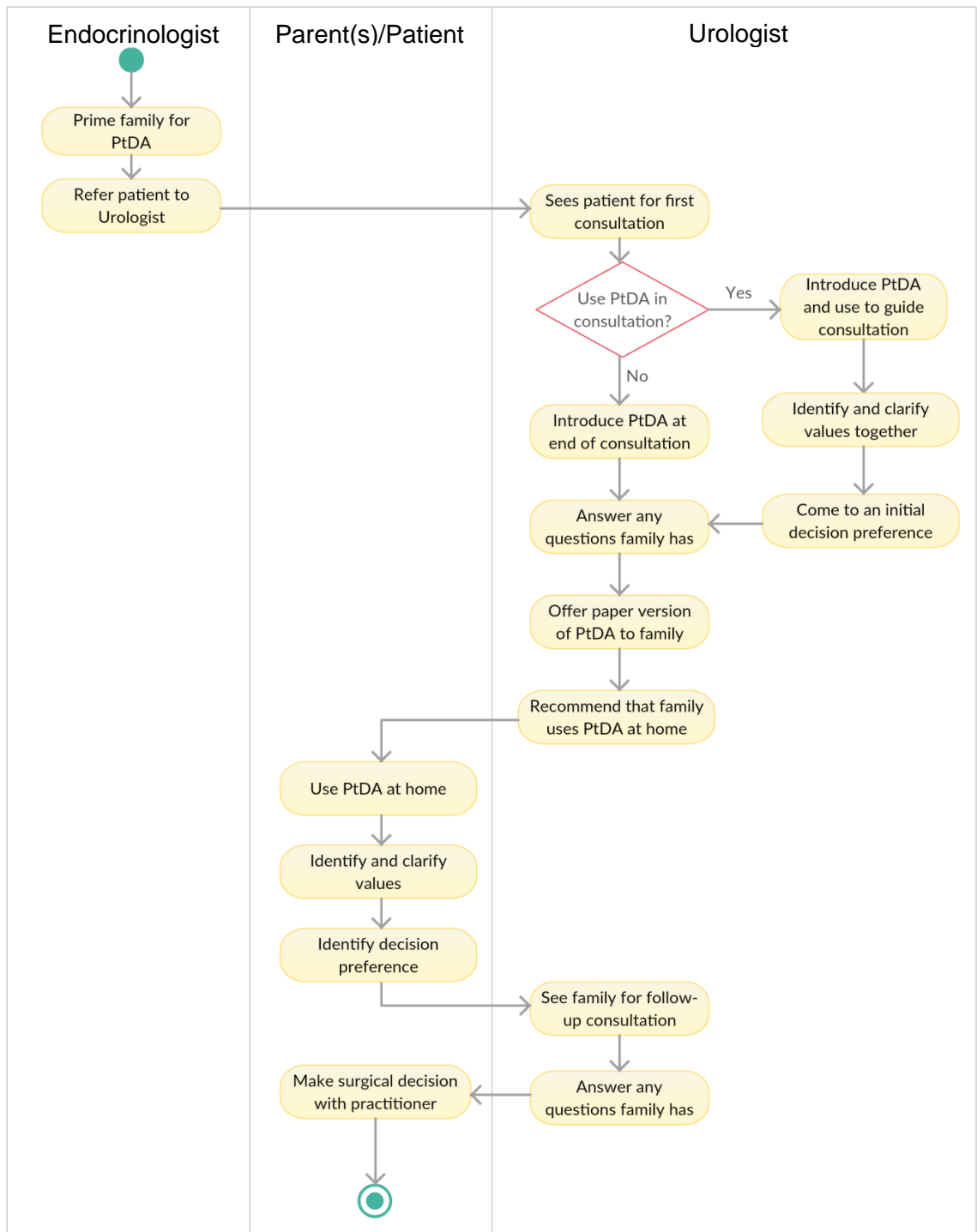


Figure 10 Unified modelling language activity diagram showing one potential workflow for how the PtDA would be shared with and used by families and practitioners. Different swim lanes show activities (cream ovals) for endocrinologists, urologists, and patients/parents. The solid green circle indicates the start and the second green circle represents the end of the workflow. Red diamond indicates a decision point with alternative options.

## 7.5. PPEET

All participants completed the PPEET. Almost all participants agreed or strongly agreed to the statements in the Likert section of the tool, suggesting an overall positive perspective towards the persona-scenario activity (see Figure 11 and 12 below). Participants revealed several interesting comments in response to the open-ended questions:

- **How do you think the results of your participation will be used?**

All participants understood that the purpose of this activity would be to inform the development of a tool to help families in information gathering and decision making.

- **What was the best thing about this engagement activity?**

Two practitioners responded that the best thing about this activity was that it was performed one-to-one, which facilitated how in-depth they could discuss their opinions about the tool. The other two thought that the best thing was being introduced to a new tool (the decision aid). On the other hand, three parents and an adult patient thought that the best thing about the session was the opportunity to meet other families who had children with CAH and to exchange information about their experiences with them.

- **At least one improvement we could make for future engagement activities:**

Three out of four practitioners felt that the most important improvement would be to disclose more information about the session before hand to prepare practitioners for the session and to reduce the time needed in-person (e.g., by sending readable material for the introduction to patient decision aids and the persona-scenario through email). Some parent and patient participants thought that the question guide should be worded better, with examples and explanations of questions.

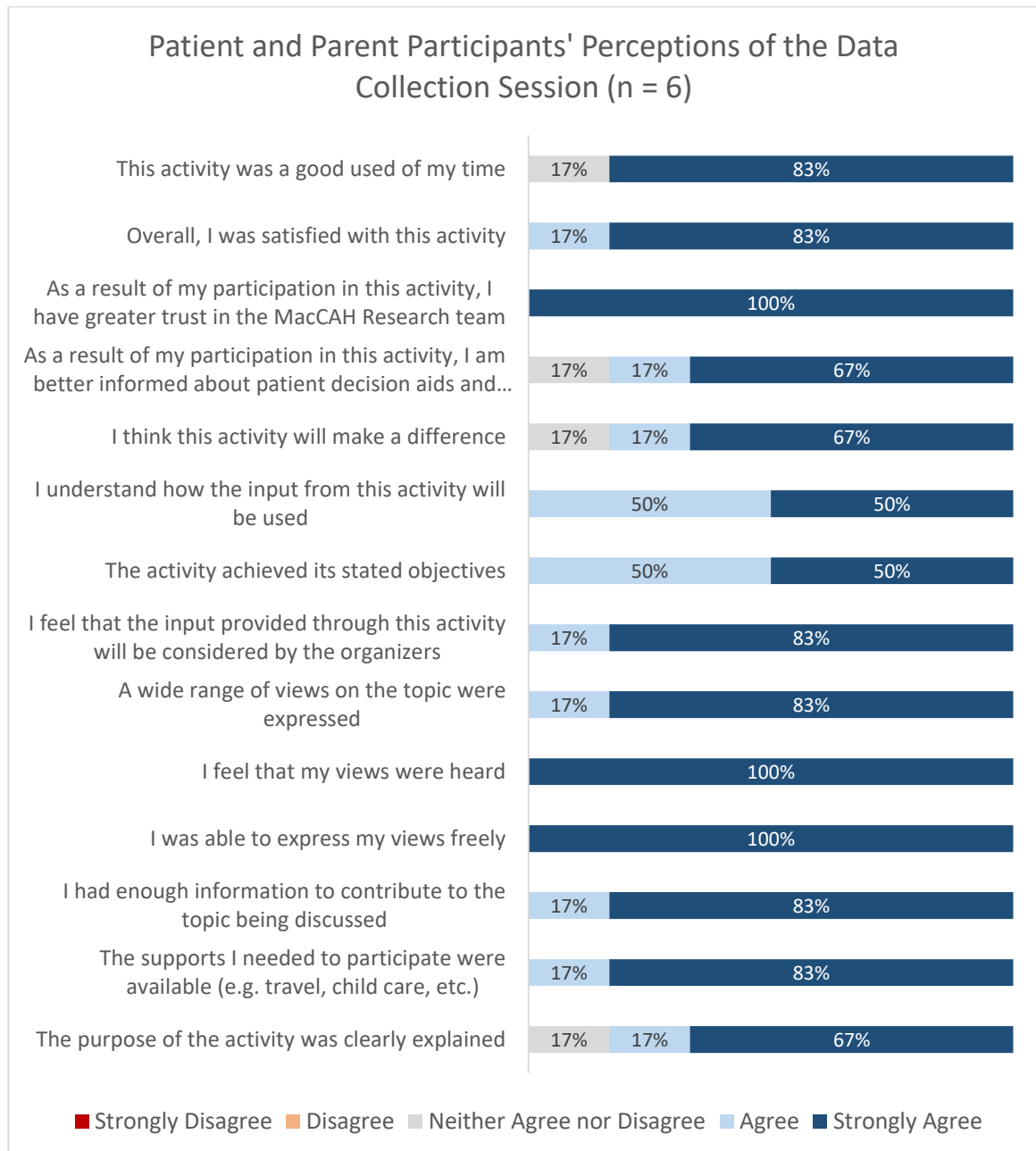
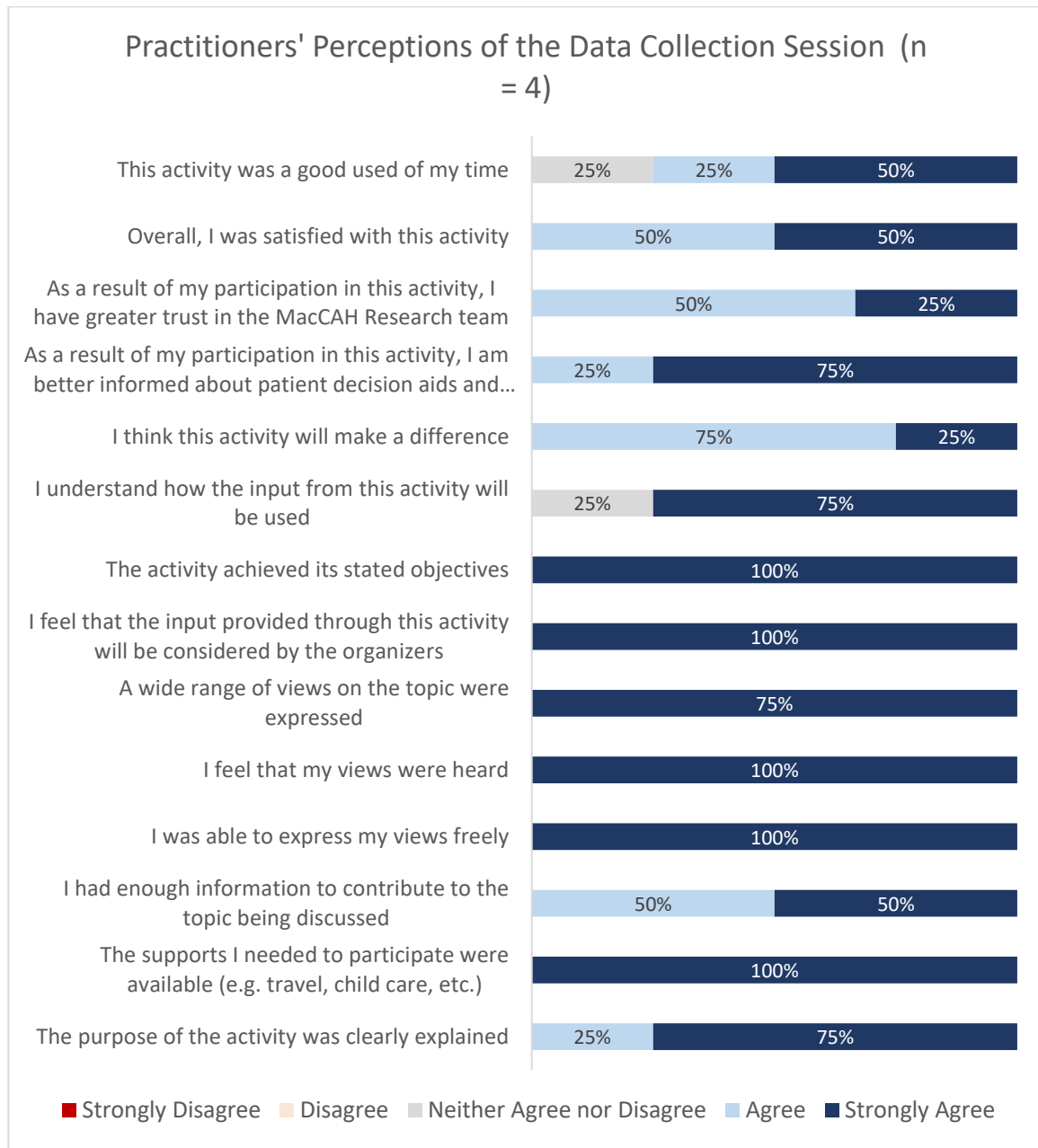


Figure 11 Patient and parents' responses to the Likert section of the PPEET, indicating a generally positive perception of the activity.



*Figure 12 Healthcare practitioners' responses to the Likert section of the PPEET, indicating a generally positive perception of the activity. Note, one participant did not provide answers to questions 3 and 9, which is why the percentages for those two statements do not add to 100%.*

## 8. Discussion

The findings fulfilled the objectives of this project, which were (1) to understand the content, format, and functionalities required in the PtDA, (2) to develop specifications for the design and development of the PtDA, and (3) to understand the best way to implement and distribute the PtDA in clinical settings.

### 8.1. Analysis of User Requirements

The content requirements identified through this project include a mix of novel content areas as well as details that had already been described in the literature. Content requirements that reaffirm what has already been described in the literature include: <sup>2,5</sup>

- Explanations of what CAH is,
- Illustrations of CAH,
- Information about future outcomes, including negative consequences of the condition [without treatment],
- Information about medication and how to give medication,
- When to seek care,
- Psychosocial and fertility issues,
- Definitions of medical terms,
- Referral for further information to trustworthy sources [that are] web-based,
- Information on how to talk to others and to the child (i.e., for the parents), and
- Information about social and psychological support.

While previous literature has explored information needs for families with children diagnosed with DSD or CAH, to our knowledge, this is the first requirements analysis for decision making for feminizing genitoplasty in particular. Accordingly, most of the novel content requirements are related to surgical decision making. This includes the findings about the short,

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intermediate, and long-term outcomes of surgical options, as well as the physical, psychological, and social impacts of the various surgical options that participants required from the PtDA. Importantly, to address these content requirements and integrate them into the PtDA, a systematic review of the literature will need to be undertaken to find evidence-based information (for example, regarding the probabilities of advantages/disadvantages/outcomes of the surgical options).

Several interesting observations can be made about the content requirements described by our participants. Firstly, it is interesting that, despite being asked to focus on a PtDA for surgical decision making, a majority of the participants highlighted the need for information about hormones, medication, and general development – indicating that information about surgery might not be their greatest priority. This is especially true of the parents and the endocrinology practitioners, who focused on the need for information dealing with adrenal crisis and stress dosing. This finding aligns well with recent work by Szymanski et al., who note that the most important concerns to parents considering feminizing genital reconstructive surgery were related to medication and development rather than surgery.<sup>7</sup>

Secondly, while information about certainty regarding probabilities of outcomes is a strong component of patient decision aids (e.g., it is an IPDASi v4.0 certification criteria) and can be understood by patients and their medical surrogates, none of the scenarios mentioned that the proposed PtDA should provide information about the levels of uncertainty around event or outcome probabilities. However, because certainty (quality of evidence) is an important aspect of informed decision making, we plan to include levels of certainty within the PtDA wherever possible, by giving a range or by using phrases such as “our best estimate is...”.<sup>93</sup>

Some interesting differences in content requirements were present between scenarios from the point of view of a practitioner as compared to a

family member (patients or parents). For example, some practitioners labelled outcomes using medical jargon, using terms such as “cosmesis” and “dehiscence”. However, no family member personas described these terms as important outcomes. Instead, they placed importance on “how to know the genitals are healing properly” (i.e., through comparison of their child’s genitals with images and descriptions in the PtDA). Another important difference was that, with regards to other supports and resources that ought to be in the decision aid, there were several supports that were only mentioned by practitioners (e.g., definitions of medical terms, information about gender, gender identity etc., and links to other resources) or by family personas (a method of connecting with other families who underwent surgery, information for the child on how to deal with and talk about surgery, and support for parents on how to talk to their child about surgery). Previous research has also illustrated that there are distinct differences between what healthcare practitioners, and parents and patients think of as helpful information. While healthcare practitioners focus on medical information such as understanding biomedical concepts and deciding on care, patients focus on strategies for coping with the experience of living with a disease or disorder (for example, managing personal tasks, home life, emotional responses, personal advocacy, etc.).<sup>2,119</sup> Ideally, the use of a PtDA to promote shared decision-making will allow practitioners and parents to go beyond this dichotomy by emphasizing information that is important to all stakeholders. Finally, the majority of the content requirements around which outcomes/consideration users should consider when making decisions about surgery (i.e., beyond the short, intermediate, and long-term outcomes), actually came from the persona-scenarios created by practitioners, suggesting caution in whether these additional values are actually important to parents.

The functionality features described by participants were highly varied. Several functionalities had not been previously considered by the research team, such as the ability to print the patient decision aid at varying depths or the ability



to email summaries of user choices, ratings, and questions to users. Considering the stigma that remains around disorders of sex development and that several participants described parents and patients as feeling embarrassed about the condition, it was surprising that most participants felt that privacy or security were not very important. In fact, several scenarios explicitly mentioned that privacy is not a factor that should limit users' access to the tool in any way and that most of the information in the PtDA should be available in the public domain.

Participants identified three methods to functionalize active values clarification within the PtDA: ranking, rating, and binning. However, rating was identified as the preferred method in the majority of persona-scenarios. Rating aligns well with the fine-grained, direct, interactive approach described by Llewellyn-Thomas and Crump.<sup>120</sup> According to Llewellyn-Thomas and Crump's taxonomy of clarification approaches, "non-interactive" approaches assume that, while viewing the PtDA's informational content, the patient will weigh the relative desirability of the options' different outcomes/ characteristics without being guided to do so and then will automatically derive a preference for one of the options. However, "interactive" approaches are "designed deliberately to engage the patient in tasks that involve explicitly comparing, ranking, and/or rating the relevant options and their characteristics." While a few persona-scenarios described non-interactive approaches using testimonies and stories, for example "reading stories about what other people valued, such as a girl who is 30 and had two surgeries, would help Annette identify what she values most", the majority of participants preferred interactive approaches to values clarification.

Interactive approaches can be *indirect* (using a predesigned set of evaluative tasks followed by a computational strategy to assess users' responses, leading to an indication of the patient's overall favored option) or *direct* (helping users to actively consider outcomes of each option and the probabilities that each outcome will be realized).<sup>120</sup> Indirect values clarification was rejected in three out of seven persona-scenarios, where participants did not

want users' decisions to be made by an algorithm. For example, one participant stated that “[t]here shouldn't be an algorithm component that makes their selection for them. It can be something that summarizes their pros/cons, but it shouldn't be misinterpreted as setting their path...because some people will make a gut decision.”

Values clarification approaches can be further categorized as *coarse-grained* (obtaining a strength-of-preference score for the users' overall favoured option), or *fine-grained* (identifying users' preferences by revealing the values that they ascribe to the various options' characteristics and outcomes). Fine-grained interactive approaches described by Llewellyn-Thomas and Crump include the Balance Technique which is very similar to the “rating” approach mentioned by participants. In the Balance Technique, which works with two options (such as early vs late surgery), “the options' positive and negative characteristics (with their probabilities) are preidentified by a clinician and summarized in two parallel columns. The user then adds other personally salient characteristics to these columns. Next, the user quantitatively rates each characteristic in terms of its personal importance [for example, by circling a number on a Likert scale].”<sup>120</sup> This is often followed by a coarse rating on a Leaning Scale (i.e., a scale with the two surgical options on either side) to identify the overall preference of the user. If there are more than two clinically relevant options, then multiple Balance Technique can be done in series. The Balance Technique is particularly useful in that, if patients still have decisional conflict, going to the ratings of individual outcomes/characteristics can help identify where the sources of the decisional conflict lie.<sup>120</sup>

Since there are *two* broad options for feminizing genitoplasty (early surgery vs. late), the Balance Technique would be appropriate for this decision. Additionally, after showing a preference for early surgery, if users wish to choose between one-stage and two-stage surgery, the first Balance Technique exercise can be followed up by a second exercise comparing these two options. Moreover,

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five of the seven scenarios preferred having a mix of preidentified characteristics and open text entry fields where users could add the characteristics and values important to them, which is a key characteristic of the Balance Technique. According to Llewellyn-Thomas and Crump, the opportunity to add such additional characteristics may be particularly important in preference-sensitive clinical situations in which there is limited or uncertain evidence to support the available options, which is especially true for the options in feminizing genitoplasty.<sup>1,120</sup> Because of how well it aligns with user-identified requirements, the Balance Technique is how the values clarification function will be operationalized in the decision aid.

Similar to what was observed about the requirements for PtDA content, there were distinct differences in which functionalities were important to practitioners as compared to family members. Practitioners focused significantly on functionalities related to making the PtDA interactive and engaging. On the other hand, functionalities identified by family member personas were mainly oriented around the ability to print the PtDA, email summaries of user choices and ratings, and how to implement values clarification.

While we categorized these features as “functionalities”, participant’s descriptions of the PtDA as being interactive and tailorable also align well with two of the usability heuristics described by Nielsen in 1994: user control and freedom, and flexibility and efficiency of use.<sup>121</sup> These usability heuristics are rules of thumb that support good user-interface design and have become pervasive in website design. One potential explanation for why so many participants cited these features is that they are drawing from their knowledge and experience with existing websites and applications.

Other web usability features involved aspects of both accessibility and design. Most participants emphasized a requirement that can be summarized as a need to “support universal access by any class of users and technology”.<sup>118</sup>

This can be best achieved by (1) producing content using simple and clear language and (2) coding the website using responsive web design principles. Responsive web design is an approach to web design that allows a single website to adapt its layout and content to viewing contexts on a variety of devices and window or screen sizes.<sup>122</sup> Consequently only one website needs to be created to meet the needs of all potential users.

Participants wanted a PtDA that was usable for a diverse set of patients. They described the PtDA as initially being simple but having the option to dig deeper using accordions/drop-downs, and links. This is in keeping with the fact that family member personas (and the participants who created them) were identified as having a wide variety of educational and work experiences, ranging from a grade 5 level of education for adolescent patients to post-graduate training for parents. The range of education suggests that the PtDA needs to be suitable for a wide range of literacy levels.<sup>92</sup> From a design perspective, participants provided substantial input regarding their preferences for the layout of advantages and disadvantages of the various options and the layout of their probabilities. What was interesting was the breadth of layout options for the probabilities. These options ranged from numerical percentages, to visual representations in the form of graphs or icon arrays, and contextual cues such as colour codes or labels.

Zipkin et al. conducted a systematic review of evidence-based risk communication to patients for shared decision making.<sup>123</sup> The authors compared various representations of risk on patients' "accuracy" (correct answers to numerical questions to assess understanding of probabilistic information), "comprehension" (a general sense of the relationship between two or more benefits or harms), and "risk perception" (participants' global sense of the magnitude of risk as measured by items, such as Likert scales). The review found very few studies comparing event rates (e.g., 4%) versus natural frequencies (e.g., 4 out of 100). The few studies they found suggest that self-reported

understanding and satisfaction were better with natural frequencies, whereas overall accuracy and comprehension were better for event rates. However, accuracy was poor overall. One study found that event rates and natural frequencies performed better when presented in tables as compared to when they were included in the text. Overall, Zipkin et al. found that the evidence was inconclusive regarding whether natural frequencies or event rates are better for representing outcome risks.

Two persona-scenarios suggested that the presentation of outcome risks should be contextualized using labels or colour codes. However, Zipkin et al.'s systematic review found that several randomized studies show that qualitative risk descriptions (e.g., "high risk") lead to lower accuracy and satisfaction and higher risk perception as compared to natural frequencies plus event rates, absolute risk reductions, or icon arrays.<sup>123</sup> A review by Burkell suggests that this decrease in accuracy was likely because the numerical probabilities that individuals assign to verbal probability labels differ across individuals, roles, and contexts (for example, a "low risk" of complications may mean 10% to one patient, 2% to another patient, and 0.1% to a practitioner).<sup>124</sup> This trade-off between accuracy and risk perception suggests that more investigation is needed to determine whether the use of qualitative risk descriptors would be appropriate for use in our PtDA.

Comparing visual displays of data, the systematic review by Zipkin et al. noted that a large randomized trial found that natural frequencies were better than visual displays for patients' accuracy but inferior for their comprehension. However, a number of studies indicated that the *addition* of visual displays to numerical formats improved accuracy and comprehension as compared to numerical formats alone.<sup>123</sup> For example, icon arrays improved accuracy and comprehension, and were perceived by patients as more helpful, effective, trustworthy, scientific, and useful, as compared to natural frequencies alone. The authors did not find any major difference between icon arrays and bar graphs,

other than one randomized trial which found that when the numerators are small, icon arrays led to better accuracy than bar graphs. Another systematic review by Garcia-Retamero and Cokely found that visual aids such as icon arrays can be particularly beneficial for vulnerable and less skilled individuals who have lower numeracy or health literacy.<sup>125</sup> For example, icon arrays can help reduce biases such as denominator neglect (a tendency to focus on the numerator) by emphasizing the part-to-whole relationship of a risk. This suggests that icon arrays will be of particular benefit for our PtDA, especially since several practitioners mentioned that the populations their personas work with have lower education. For example, one practitioner mentioned that the “population that [Ben] works with are lower SES [i.e., socioeconomic status] where education is not very high, so the information that he provides, and would suggest the tool also provides, is very simple.”

Several persona-scenarios mentioned the use of pie graphs for the representation of probabilities. Pie graphs have several advantages. They are particularly useful for exhibiting single proportions (e.g., proportion of patients who received x outcome on a binary outcome) and are familiar to the public (as compared to icon arrays etc.). They are also good at representing part-to-whole comparisons and may help diminish framing biases in low-numeracy individuals.<sup>126,127</sup> However, pie charts can be misleading when sample sizes are small and it can be difficult for viewers to compare probabilities within pie graphs or between different pie graphs.<sup>127</sup> Additionally, some research suggests that pie charts promote “gist” processing over precise quantitative processing, which is not the goal of our PtDA.<sup>126</sup> Consequently, we will not be using pie graphs in our future PtDA.

At least one persona-scenario explicitly described an interactive visual display representing the risk of outcomes with the ability to drill down into the probabilities. However, the systematic reviews by Zipkin et al., and Garcia-Retamero and Cokely found that most studies indicated that adding interactivity,

animation, and dynamic features (especially to visual aids such as icon arrays) did not improve accuracy as compared to static visual representations.<sup>123,125</sup> Accordingly, while an interactive visual display for outcome risks was a user-requirement, static icon arrays will probably be used for this PtDA.

Beyond providing requirements related to content, usability, and functionality, persona-scenarios also provided useful contextual information about how to best implement the PtDA in a clinical setting. Persona-scenarios created by healthcare practitioners emphasized that, for the PtDA to be used in any clinic, there needed to be buy-in from the staff physician, who would act as a champion to support the implementation of the PtDA in clinical practice. For example, one participant mentioned that “it would be up to Shirley’s staff physician to make [the decision to use the PtDA] and then insure their staff are knowledgeable by providing someone to come in and demonstrate how to use it.” This is supported by the literature on health technology implementation and change management, which has found that the presence of senior leadership and a “champion” is an important organizational factor in the adoption of technological innovations in healthcare.<sup>128</sup> Due to their position, senior leaders can help facilitate the re-design of workflows and ensure adequate training and support is provided to staff. Moreover, organizational culture and priorities have been identified as a major influence and potential barrier in the uptake of PtDAs. Senior leaders can facilitate a shift in organizational priorities by, for example, mandating the use of the PtDA as a requirement for obtaining informed consent (which at least one practitioner participant mentioned as a possibility).<sup>92</sup> Thus, if the research team aims to expand the use of the PtDA to additional institutions, since staff physicians often have the most power and the “final say” in their clinics, they are the optimal targets from whom to obtain buy-in and support.

With regards to the families’ context, participants identified parents as having a range of negative emotions and feelings before the decision process. Many of these emotions have been previously reported in the literature.<sup>2,5</sup> While

some of these emotions (for example, embarrassment about what society will think) cannot be tackled by a PtDA for surgical treatment, other emotions can be mitigated by a family's use of the tool. This could include their feelings of confusion and embarrassment about how to explain the surgery to others and their worries about the risks of surgery, by providing information about these content areas within the tool. Similarly, some of the barriers to decision-making identified in the persona-scenarios cannot be addressed by the PtDA. For example, situational barriers such as family circumstances are beyond the scope of the PtDA. However, one category of barriers identified by participants was a lack of information and misinformation. Patients often come into a clinical encounter with certain beliefs that arise from what they have read (e.g., online), their past personal experiences, advice from friends and family, and what they have incorporated from the media.<sup>129</sup> These beliefs can be erroneous and therefore impede informed decision-making. The proposed PtDA can fill some of these gaps and clarify the misinformation they receive by providing accurate evidence-based information about CAH and surgery. Moreover, as mentioned in section two, the lack of information or misinformation and the confusion that arose from that was found to be a significant factor in contributing to symptoms of post traumatic stress in parents of children with disorders of sex development.<sup>8</sup> By providing consistent evidence-based information and content that fulfills their needs, the PtDA can mitigate this cognitive confusion and potentially help prevent these symptoms. It was interesting that both parent scenarios emphasized that the mother in a family would be more responsible for surgical decision making, suggesting that mothers might be an important target for the PtDA within a family.

While scenarios with practitioner, patient, and parent personas all support the workflow displayed in figure 10, there are strong differences in the preferences of family members and practitioners. For example, for parents “it would have been preferable to have this decision-making tool right when the child got diagnosed” and both parents and patients mentioned being able to find it “on



a website in the public domain”. Family members were also willing to receive the PtDA from the pediatric urologist during the consultation. Conversely, practitioners did not mention early access at all and instead focused on the provision of the PtDA either immediately before, during, or immediately after the initial consultation with the urologist. Moreover, all practitioners believed that it was the role of the urology clinic, rather than the endocrinology clinic, to provide families with the PtDA and to be available for questions.

Participants generally seemed to prefer receiving/providing the decision aid during the consultation as compared to before or after the consultation. If the PtDA is provided during a consultation, that opens the possibility of using the PtDA as more than a tool to be used by family members independently outside the consultation (either in the waiting room or at home) (what could be considered as a traditional decision aid). The PtDA could also facilitate collaborative deliberation *during* the clinical encounter. Agoritsas et al. note that, while traditional decision aids promote understanding of issues (e.g., knowledge and risk perception) and can decrease the proportion of people who are passive in decision making, they do not guarantee that decisions in a healthcare context are truly “shared”.<sup>129</sup> They suggest that instead, decision aids that are used during consultations to facilitate discussion and joint deliberation may improve shared decision making. However, the “short” tools described by Agoritsas et al. are not designed to be comprehensive and do not include explicit values clarification exercises, placing the onus on clinicians to provide the time, tailored explanations and information instead.<sup>129</sup> Practitioners involved in this study perceived that the use of a PtDA in a consultation would increase the length of a consultation and accepted that as a natural consequence (in fact, the systematic review by Stacey et al. found inconsistent effects; consultation length was not significantly different in eight out of ten studies).<sup>91</sup> However, practitioners involved in this study indicated some reluctance in taking on a larger role than they currently had unless the PtDA provided significantly more utility. In addition, their

scenarios described a PtDA that took on the role of ensuring that patients and parents had a comprehensive information resource that also helped them think about their values. Moreover, all the scenarios in this study described a PtDA that would could be used independently at home. Accordingly, the requirements of this study's participants do not support the implementation of the type of short tools described by Agoritsas et al. Still, the user requirements do indicate the need to construct the PtDA in a manner that would allow for easy use within clinical encounters. One potential way to do this would be to create separate sections within the patient decision aid, one of which would be used during the clinical encounter. This clinical subsection would ideally be easy to use and could contain graphic displays of the positive and negative outcomes of different surgical options to help facilitate the conversation (putting special emphasis on the outcomes that were identified as most important to parents and patients). The reluctance of healthcare practitioners to use the PtDA suggests that the PtDA will need to be sufficiently appealing to practitioners so that they are "tempted" to use them in practice and discover that it may not prolong the consultation and increase everyone's satisfaction.

Regardless of when the PtDA is provided to families, all participants emphasized the need for practitioners (specialists or nurses) to be available to answer any questions users may have after using the PtDA. Equally, there needed to be time during the follow-up consultation for parents to ask their questions and for the practitioners to ensure that parents or patients have truly understood the information provided to them and deliberated through the decision. This was emphasized by statements like "Shirley thinks that just giving families a PtDA, without clarification or added support that they might need to understand and rationalize the decision, is not enough. There needs to be some follow through with [the PtDA], because families interpret information differently." This need for dedicated time to answer patient questions has been identified in the literature, and is an important aspect that must be integrated into clinical

workflows with the use of PtDAs.<sup>130</sup> This will broaden the scope of this project. It will require stepping beyond simply creating and implementing a patient decision aid, to reengineering existing processes and workflows so as to reorient the urology clinic towards a more patient-centered environment.

As a final comment, it was interesting that several user requirements align with the IPDASi v4.0 certification or quality criteria despite not being mentioned or explicitly asked for within the question guide. For a full list of these user requirements, see table 5. There were user requirements that also aligned with the other IPDAS criteria, but they were explicitly mentioned within the question guide to prompt participants to think about them in the context of decision making for CAH, and so are not included in the table below.

*Table 5 Some design features described by participants that aligned with IPDASi v4.0 criteria without being explicitly prompted for within the question guide or during discussion. (C = Certification criteria, Q = Quality criteria).*

Design Feature (User Requirement/Node)	Corresponding IPDASi v4.0 criteria
All statements are evidence based, links to evidence are present next to each statement and pop into a new window with title and abstract	C2: The patient decision aid (or associated documentation) provides citations to the evidence selected.
What CAH is and what it does to fertility, sexuality, sexual orientation, period	Q1: The patient decision aid describes the natural course of the health condition or problem, if no action is taken (when appropriate).
Probabilities should be represented as numbers/percentages and figures/icons/graphs	Q7: The patient decision aid provides more than 1 way of viewing the probabilities (e.g., words, numbers, and diagrams).

Summary contains questions that parents still have (questions can be typed as parents are going through the aid) and summary will help streamline discussion with surgeon	Q9: The patient decision aid includes tools like worksheets or lists of questions to use when discussing options with a practitioner.
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## 8.2. Strengths and Limitations

This study consisted of seven persona scenarios constructed by participants representing healthcare professionals, parents of children with CAH, and patients with CAH; one urologist, one endocrinologist, one nurse practitioner, one child life specialist, two fathers, two mothers, and two adult females with CAH were involved in this co-design methodology. Consequently, the breadth of participants and their diversity (with regards to education, comfort with technology, etc.), will help ensure that the requirements gathered meet multiple stakeholders' needs and that the product that is created will be suitable for a wide set of potential users. Moreover, these perspectives provided important details regarding the potential implementation of the PtDA and what roles practitioners, parents, and patients saw themselves having in the use of the PtDA. However, difficulty in recruiting practitioners and parents resulted in us having a smaller than desired number of participants, all from the same tertiary academic hospital, which may limit the relevance of the implementation-oriented specifications in other hospitals. Moreover, all family members were from families where they chose to have surgery early and the CAH child had already gone through surgery. Consequently, the perspective of parents who are still deliberating or parents who chose to defer is missing and will need to be accounted for.

Participants found the persona-scenario data collection sessions to be advantageous for several reasons. Firstly, healthcare practitioners said that the persona-scenario was a type of engagement session that was useful for learning about new tools (i.e., the PtDA). For example, one practitioner mentioned that

“after going through the [act of creating the] persona-scenario, I can now really picture how this tool [i.e., the PtDA] will look like and how we will use it.”

Secondly, parents felt that the act of bringing participants together for the group sessions was one of the most useful aspects of this data collection method (compared to individual interviews). In particular, parents and patients both loved meeting other families who had children with CAH and building a social network for the future.

The use of the persona-scenario methodology for data collection was fruitful and generated many novel requirements or reaffirmed requirements previously reported in the literature. Moreover, generally most participants provided positive feedback about the persona-scenario data collection session through the PPEET (although interestingly, one parent and one practitioner neither agreed nor disagreed that the persona-scenario session was a good use of their time). However, there were also some challenges with the way we implemented the methodology during our data collection. Firstly, we chose to include healthcare practitioners (specialist and nurse practitioner) that work in pediatric endocrinology because patients with CAH often see them throughout their adolescence. However, these healthcare practitioners had a lot of difficulty picturing how a PtDA for feminizing surgery would be implemented in an endocrinology context or how endocrinologists would be involved with the PtDA at all. Upon probing why they felt this way, these practitioners mentioned that their role was only to advise that surgery was possible and to provide a referral to a surgeon or urologist – they did not see their role as providing information about the surgeries, and so would not feel comfortable providing the PtDA.

Secondly, some parent participants had difficulty understanding or answering the questions in the question guide. The questions, which were designed to be open-ended, were suitable for parents that were more involved in the decision-making process as it allowed them the freedom to integrate their experiences into the scenarios. However, for participants that were less involved

in surgical decision making for their child, the vagueness of the open-ended questions made them difficult to answer. Some of these participants expressed that they would have preferred if the questions were better (e.g., with “explanations”) and provided examples of answers. Questions certainly could be worded better – perhaps by testing them with non-researchers/scientists before data collection. However, the provision of example answers may be difficult to implement in practice. While it is easy to understand why users might find it difficult to think about a hypothetical PtDA for CAH when this is likely their first exposure to PtDAs, providing “answers” or examples of things they might consider may bias their answers. Rather than giving them freedom to conceptualize and report their own ideas (which is why the persona-scenario methodology was chosen for this project), giving them examples could restrict their ideation to only the options presented.

Thirdly, some participants found the idea of creating a persona-scenario conceptually difficult. They often referred to their own experiences rather than creating a fictional character and story, especially as the session progressed, despite frequent prompts and reminders to generate a story from their character’s point of view. This is in keeping with previous literature regarding the persona-scenario, which has noted that, despite humans’ intuitive understanding of stories and the story form, it is nonetheless very difficult to write a scenario that follows the story form.<sup>102</sup> For example, two practitioners mentioned several times that they were struggling with creating a story about how the hypothetical PtDA might be used in clinical practice or what content it might have. However, this may also be due partly to the fact that both practitioners were from endocrinology and did not have a strong understanding of the surgical component of CAH. This finding suggests that in the future, it will be important to select the user-groups involved more carefully, to ensure that they truly represent potential end-users of the PtDA/intervention and will be able to create and provide useful scenarios. Interestingly, in scenarios where participants only superficially described content

requirements, they tended to describe layout requirements in significantly greater detail – perhaps because they were more knowledgeable about layout through their past experiences with other websites, apps, and electronic tools.

Fourthly, during patient sessions, participants were matched with each other such that pairs of mothers, fathers and patients underwent persona-scenario sessions together with a facilitator. While this pairing functioned well for the adult patient group, there were challenges with the mother and the father group. These challenges likely arose from the mismatch between the parents' experiences. For example, within the pair of mothers, one participant was a mother of a 3-year-old child with salt-wasting CAH while the other was a mother of two daughters with simple-virilizing CAH who are now in their adulthood. Consequently, there were two competing factors between the mothers' perspectives that influenced the type of persona and scenario they tried to co-create. Firstly, since salt-wasting CAH is more life-threatening than simple-virilizing CAH, the experiences that the younger mother drew on and tried to integrate into the scenario were more poignant and cogent but were focused on the hormonal rather than the surgical aspects of CAH. Secondly, since the second mother was older and had two daughters with CAH, the younger mother may have perceived her as having more "experience" and "insight" into the decision aid and consequently yielded to her comments when it came to some aspects of surgery. This occurred despite attempts from the facilitator to engage her and to tell her that her perspective was equally valid and important. Similarly, within the pair of fathers, one father described being much more involved in medical decision-making and the care for his daughter than the other. Consequently, he was much more expressive and shared significantly more details, whereas the second father often simply agreed with the first without bringing in his own perspective. While gendered-pairings did not function well in these persona-scenario data collection sessions, other alternative pairings also have potential disadvantages. For example, if pairs constituted of couples, it is

likely that they would focus on their experience with the decision rather than creating a fictitious story in which a PtDA helps with decision making. Consequently, in future persona-scenarios we will continue to match by gender, but we will also ensure that participants are close in age and have similar levels of involvement in decision making and their child's care.

Finally, this project was conducted to develop a patient decision aid specifically for feminizing genitoplasty (i.e., for surgery). However, six out of the seven scenarios asked for design features that the research team considers as being outside of the scope of a PtDA for surgery (see Table 5 for some of these features). For example, some scenarios described the importance of social support for living with a child with CAH, while others described the need for information about hormone medication and stress dosing. While many of these features align well with what is known about what parents want from information and support tools,<sup>2</sup> they go beyond our scope. However, through requirements like these, it is quite clear that when it comes to feminizing genitoplasty for CAH, families face more than the decision about surgery. Thus, what users *require* is more than a PtDA for feminizing genitoplasty, but rather a broader, more holistic support tool as well as a broader strategy to orient care towards family's needs and experiences. Accordingly, the research team has decided that these features will not be abandoned but will be left for future versions of the patient decision aid.

*Table 6 Design features (user requirements) discussed in the persona-scenario that are beyond the scope of a PtDA for feminizing genitoplasty.*

Design Feature (User Requirement/Node)	Example Quote	Number of Sources
Information about living with a child with the condition in general	"They are looking at this decision aid with the intent of finding a tool to help	2



	them navigate how to deal with this condition in general.”	
Information about the different hormone medications and their effects	“How are the medications going to affect her [daughter] as well, like even non-surgical aspects. Even with being on different types of steroids, they have different aspects, like some of them have different effects like gaining a ton of weights. Even describing the medications and their side effects.”	2
Animation that teaches parents how to prepare and inject hydrocortisone in emergencies	“[W]hen Ben prescribes injectable cortisone/hydrocortisone for emergency, it’s not premixed, they have to learn how to mix it. An animation would be helpful for that”	2
Information about CAH for other practitioners (e.g., paramedics)	“Molly feels that the patient decision aid can also be very useful for other practitioners such as ambulance professionals, to teach them about stress dosing. Because doctors and ambulance professionals don’t believe the parents when they tell them what to do.”	2
Information for child on how to talk to their social network and handle questions	“The tool has support information to help the child explain to their social network and how to handle questions.”	2
Online chat option to connect to other families	“[S]ome part of it would be a login, sort of like a mini Facebook within the app,	4

with children who have CAH	where you can communicate with other people. So, their profile would say maybe like the name and if it was the parents, the age of their child. So then maybe you could personal message the other parents just to see if they have an older child or something. You can discuss with them, ask them questions.”	
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### 8.3. Future Work

This research project has opened several new directions for further investigation. First and foremost, future studies are needed that will engage more parent and patient participants. It will be especially important to include those families that are at an earlier stage of decision making (for example those who have yet to make a firm decision about whether their child will have feminizing genitoplasty) and those families who chose to defer surgery until their child was older. Doing so will provide an understanding of their unique requirements and will also confirm whether the user requirements gained in this project are valid for a broad range of families and decision-making contexts. Secondly, before the PtDA is created, there must be systematic review of the literature to find evidence-based information that fulfills the content requirements that users have shared. The next step after this would be to use the interpreted user specifications to design and develop a prototype PtDA. This would be followed by alpha and beta testing of the prototype. Alpha-testing will consist of multiple focus group or interview feedback sessions with a subsample of persona-scenario participants, to determine the extent to which the PtDA produced met their expectations and is usable. These feedback sessions will help the research group iteratively improve the PtDA. During these feedback sessions, we will also

employ highly prolific and validated measures of system usability (System Usability Scale)<sup>131,132</sup> and user experience (User Experience Questionnaire)<sup>133</sup> to help generate quantitative assessments of the PtDA. After this initial feedback has been integrated into the prototype, phase two will then involve beta- or field-testing of the tool in a clinical setting. Interested clinicians and families who choose to use the PtDA will be observed during their encounters (through audio recording etc.) and then invited to participate in interviews and/or focus groups. The rich qualitative feedback from these sessions will be analyzed to find barriers and facilitators of use, which will help inform further refinement of the tool. Assessing early prototypes in the setting they are being designed for is an important step in ensuring that the intervention will work as intended and have the desired effect on the decision-making process.<sup>134,135</sup> Next, there will be pilot study which will assess feasibility of a protocol for a superiority, multicenter, randomized controlled trial (RCT) to determine whether use of the PtDA improves user-knowledge, decisional conflict, decision quality, and the decision-making process as compared to usual standards of care. After this pilot study is completed, the final step would ideally be a full-scale RCT. However, because of the relative rarity of the condition and low incidence rate, there would need to be buy in from multiple hospitals nationwide so that parents of all girls who present to outpatient Pediatric Urology Clinics (with CAH and considering genitoplasty) are invited to participate in the study. Alpha and beta testing as well as the randomized controlled trials will allow us to meet a number of quality criteria under IPDASi v4.0.<sup>93</sup>

## 9. Conclusion

A diverse set of healthcare practitioners (urologist, endocrinologist, nurse practitioner, and child life specialist), parents (mothers and fathers), and adult patients with CAH were recruited to co-design an electronic patient decision aid for CAH using the persona-scenario methodology. In these data collection sessions, they described scenarios in which fictitious characters used an

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idealized hypothetical PtDA to learn about CAH and guide them in their decision making for feminizing genitoplasty. More than 440 unique nodes describing user requirements were generated upon coding the transcripts of these data collection sessions. These nodes naturally grouped into four categories. “Information and decisional content in the PtDA” included information that user required to make an informed decision including information about CAH, surgical options and their likelihoods, and the types of consequences or values that they might consider. Participants also shared “proposed functionalities for the PtDA”, which included the ability to print the PtDA, generate summaries of user interactions with the PtDA (choices, selections etc.), and a system whereby users could rate or evaluate what is most important to them. “Web usability-related requirements” described the layout preferences of participants and suggestions to improve accessibility. Finally, “implementation context” described the suggestions participants had about the optimal workflow that would allow integration of the PTDA into clinical practice. The user requirements in these categories were assessed for human-centered design criteria, including feasibility, viability, and desirability. Where appropriate, specifications were created to understand how to implement the user requirements.

A significant proportion of the user requirements were novel and have not been reported in previous literature. Many user requirements were supported by previous literature, underlining their importance. In other cases, previous literature provided evidence to support a single choice between conflicting user requirements. Altogether, these requirements and their specifications will help inform the design and development of a PtDA for feminizing genitoplasty. They may also provide some insight to researchers or developers seeking to create PtDAs for other pediatric conditions.

## 10. References

1. Speiser PW, Azziz R, Baskin LS, et al. Congenital adrenal hyperplasia due to steroid 21-hydroxylase deficiency: An Endocrine Society clinical practice guideline. *J Clin Endocrinol Metab.* 2010;95(9):4133-4160. doi:10.1210/jc.2009-2631.
2. Lundberg T, Lindström A, Roen K, Hegarty P. From Knowing Nothing to Knowing What, How and Now: Parents' Experiences of Caring for their Children With Congenital Adrenal Hyperplasia. *J Pediatr Psychol.* 2016;1-10. doi:10.1093/jpepsy/jsw001.
3. Streuli JC, Vayena E, Cavicchia-Balmer Y, Huber J. Shaping parents: Impact of contrasting professional counseling on parents' decision making for children with disorders of sex development. *J Sex Med.* 2013;10(8):1953-1960. doi:10.1111/jsm.12214.
4. Crissman HP, Warner L, Gardner M, et al. Children with disorders of sex development: A qualitative study of early parental experience. *Int J Pediatr Endocrinol.* 2011;2011(1):10. doi:10.1186/1687-9856-2011-10.
5. Boyse KL, Gardner M, Marvicsin DJ, Sandberg DE. "It Was an Overwhelming Thing": Parents' needs after infant diagnosis with congenital adrenal hyperplasia. *J Pediatr Nurs.* 2014;29(5):436-441. doi:10.1016/j.pedn.2014.01.007.
6. Szymanski KM, Whittam B, Kaefer M, et al. Parental decisional regret and views about optimal timing of female genital restoration surgery in congenital adrenal hyperplasia. *J Pediatr Urol.* 2018;14(2):156.e1-e156.e7. doi:10.1016/j.jpuro.2017.11.012.
7. Szymanski KM, Whittam B, Kaefer M, Frady H, Cain MP, Rink RC. What about my daughter's future? Parental concerns when considering feminizing genital restoration surgery in girls with CAH. In: *The Societies for*

- Pediatric Urology 66th Annual Meeting*. San Francisco; 2018.  
<http://spuonline.org/abstracts/2018/24.cgi>.
8. Pasterski V, Mastroyannopoulou K, Wright D, Zucker KJ, Hughes IA. Predictors of posttraumatic stress in parents of children diagnosed with a disorder of sex development. *Arch Sex Behav*. 2014;43(11):369-375. doi:10.1007/s10508-013-0196-8.
  9. Fiks AG, Jimenez ME. The promise of shared decision-making in paediatrics. *Acta Paediatr*. 2010;99(10):1464-1466. doi:10.1111/j.1651-2227.2010.01978.x.
  10. Abelson J. *Public and Patient Engagement Evaluation Tool (Version 1.0)*.; 2015. [www.fhs.mcmaster.ca/publicandpatientengagement/](http://www.fhs.mcmaster.ca/publicandpatientengagement/)
  11. Pang SY, Wallace MA, Hofman L, et al. Worldwide experience in newborn screening for classical congenital adrenal hyperplasia due to 21-hydroxylase deficiency. *Pediatrics*. 1988;81(6):866-874. <http://www.ncbi.nlm.nih.gov/pubmed/3259306>.
  12. Krone N, Braun A, Roscher AA, Knorr D, Schwarz HP. Predicting phenotype in steroid 21-hydroxylase deficiency? Comprehensive genotyping in 155 unrelated, well defined patients from southern Germany. *J Clin Endocrinol Metab*. 2000;85(3):1059-1065. doi:10.1210/jc.85.3.1059.
  13. CYP21A2. The Human Gene Mutation Database (HGMD) at the Institute of Medical Genetics in Cardiff. <http://www.hgmd.cf.ac.uk/ac/gene.php?gene=CYP21A2>. Published 2018.
  14. White PC, Speiser PW. Congenital adrenal hyperplasia due to 21-hydroxylase deficiency. *Endocr Rev*. 2000;21(3):245-291.
  15. Prader A. Der genitalbefund beim pseudohermaphroditismus femininus des krongenitalen adrenogenitalen syndromes: morphologie, haufigkeit,

- entwicklung and vererbung der verschiedenen genitalformen. *Helv Paediat Acta*. 1954;9:231-248.
16. Allen L. Disorders of Sexual Development. *Obstet Gynecol Clin North Am*. 2009;36(1):25-45. doi:10.1016/j.ogc.2009.02.001.
  17. Hindmarsh PC, Geertsma K. *Congenital Adrenal Hyperplasia: A Comprehensive Guide*. (Broderick T, ed.). Cambridge, MA: Haley, Mica; 2017.
  18. Harris W. *Examination Paediatrics*. 3rd ed. Churchill Livingstone; 2006.
  19. Gorduza D, Tardy-Guidollet V, Robert E, et al. Late prenatal dexamethasone and phenotype variations in 46,XX CAH: Concerns about current protocols and benefits for surgical procedures. *J Pediatr Urol*. 2014;10(5):941-947. doi:10.1016/j.jpuro.2014.02.003.
  20. Mouriquand PDE, Gorduza DB, Gay CL, et al. Surgery in disorders of sex development (DSD) with a gender issue: If (why), when, and how? *J Pediatr Urol*. 2016;12(3):139-149. doi:10.1016/j.jpuro.2016.04.001.
  21. Children's Hospital of Eastern Ontario. Congenital Adrenal Hyperplasia (CAH) Screening Results. Newborn Screening Ontario. <https://www.newbornscreening.on.ca/en/disease/congenital-adrenal-hyperplasia-cah>. Published 2018. Accessed March 5, 2018.
  22. Children's Hospital of Eastern Ontario. Screen Positive Follow-Up. Newborn Screening Ontario. <https://www.newbornscreening.on.ca/en/screening-results/screen-positive-results/screen-positive-follow>. Published 2018. Accessed March 5, 2018.
  23. Rink RC, Szymanski KM. Disorders of Sexual Development: Surgical Management. In: Lima M, Manzoni G, eds. *Pediatric Urology: Contemporary Strategies from Fetal Life to Adolescence*. Vol 10. 1st ed.

- New York: Springer-Verlag Italia 2015; 2015:247-258. doi:10.1007/978-88-470-5693-0\_21.
24. Marei M, Abdelsattar AH, Fares AE, El-Kottbi M, El-Barbary M, Seif HM. Accuracy and Predictivity of Cystoscopy and Genitography to Operative Findings in Persistent Urogenital Sinus due to Virilized Female Congenital Adrenal Hyperplasia. *Kasr El Aini J Surg.* 2014;15(1).
  25. Vanderbrink BA, Rink RC, Cain MP, et al. Does preoperative genitography in congenital adrenal hyperplasia cases affect surgical approach to feminizing genitoplasty? *J Urol.* 2010;184(4 SUPPL.):1793-1797. doi:10.1016/j.juro.2010.05.082.
  26. Lee PA, Witchel SF. 46,XX patients with congenital adrenal hyperplasia: initial assignment as male, reassigned female. *J Pediatr Endocrinol Metab.* 2005;18(2):125-132. <http://www.ncbi.nlm.nih.gov/pubmed/15751601>.
  27. Forest MG, Morel Y, David M. Prenatal treatment of congenital adrenal hyperplasia. *Trends Endocrinol Metab.* 1998;9(7):284-289. doi:10.1016/j.ajog.2012.10.885.
  28. New MI, Carlson A, Obeid J, et al. Prenatal Diagnosis for Congenital Adrenal Hyperplasia in 532 Pregnancies. 2001;86(12):5651-5657.
  29. Miller WL, Witchel SF. Prenatal treatment of congenital adrenal hyperplasia: Risks outweigh benefits. *Am J Obstet Gynecol.* 2013;208(5):354-359. doi:10.1016/j.ajog.2012.10.885.
  30. Hirvikoski T, Nordenström A, Lindholm T, et al. Cognitive functions in children at risk for congenital adrenal hyperplasia treated prenatally with dexamethasone. *J Clin Endocrinol Metab.* 2007;92(2):542-548. doi:10.1210/jc.2006-1340.
  31. Bachelot A, Grouthier V, Courtillot C, Dulon J, Touraine P. Congenital



- adrenal hyperplasia due to 21-hydroxylase deficiency: update on the management of adult patients and prenatal treatment. *Eur J Endocrinol.* 2017;176(4):R167-R181. doi:10.1530/EJE-16-0888.
32. Bartha JL, Finning K, Soothill PW. Fetal sex determination from maternal blood at 6 weeks of gestation when at risk for 21-hydroxylase deficiency. *Obstet Gynecol.* 2003;101(5 SUPPL.):1135-1136. doi:10.1016/S0029-7844(03)00064-4.
  33. Gomes LG, Huang N, Agrawal V, Mendonça BB, Bachega TASS, Miller WL. Extraadrenal 21-hydroxylation by CYP2C19 and CYP3A4: Effect on 21-hydroxylase deficiency. *J Clin Endocrinol Metab.* 2009;94(1):89-95. doi:10.1210/jc.2008-1174.
  34. Speiser PW, Agdere L, Ueshiba H, White PC, New MI. Aldosterone synthesis in salt-wasting congenital adrenal hyperplasia with complete absence of adrenal 21-hydroxylase. *N Engl J Med.* 1991;324(3):145-149. doi:10.1056/NEJM199101173240302.
  35. Quinkler M, Nilsen RM, Zopf K, Vantz M, Øksnes M. Modified-release hydrocortisone decreases BMI and HbA1c in patients with primary and secondary adrenal insufficiency. *Eur J Endocrinol.* 2015;172(5):619-626. doi:10.1530/EJE-14-1114.
  36. Mallappa A, Sinaii N, Kumar P, et al. A phase 2 study of Chronocort, a modified-release formulation of hydrocortisone, in the treatment of adults with classic congenital adrenal hyperplasia. *J Clin Endocrinol Metab.* 2015;100(3):1137-1145. doi:10.1210/jc.2014-3809.
  37. Russell GM, Durant C, Ataya A, et al. Subcutaneous pulsatile glucocorticoid replacement therapy. *Clin Endocrinol (Oxf).* 2014;81(2):289-293. doi:10.1111/cen.12470.
  38. Nella AA, Mallappa A, Perritt AF, et al. A Phase 2 Study of Continuous

- Subcutaneous Hydrocortisone Infusion in Adults With Congenital Adrenal Hyperplasia. *J Clin Endocrinol Metab.* 2016;101(12):4690-4698. doi:10.1210/jc.2016-1916.
39. Auchus RJ, Buschur EO, Chang AY, et al. Abiraterone acetate to lower androgens in women with classic 21-hydroxylase deficiency. *J Clin Endocrinol Metab.* 2014;99(8):2763-2770. doi:10.1210/jc.2014-1258.
40. Turcu AF, Spencer-Segal JL, Farber RH, et al. Single-dose study of a corticotropin-releasing factor receptor-1 antagonist in women with 21-hydroxylase deficiency. *J Clin Endocrinol Metab.* 2016;101(3):1174-1180. doi:10.1210/jc.2015-3574.
41. Creighton SM, Michala L, Mushtaq I, Yaron M. Childhood surgery for ambiguous genitalia: glimpses of practice changes or more of the same? *Psychol Sex.* 2014;5(1):34-43. doi:10.1080/19419899.2013.831214.
42. Braga LH, Pippi Salle JL. Congenital adrenal hyperplasia: A critical appraisal of the evolution of feminizing genitoplasty and the controversies surrounding gender reassignment. *Eur J Pediatr Surg.* 2009;19(4):203-210. doi:10.1055/s-0029-1233490.
43. Kaefer M, Rink RC. Treatment of the Enlarged Clitoris. *Front Pediatr.* 2017;5(August). doi:10.3389/fped.2017.00125.
44. Raveenthiran V. When a woman is not a woman: Problems and perspectives of congenital adrenal hyperplasia. *J Int Med Sci Acad.* 2014;27(2):69-73.
45. Money J, Hampson JG, Hampson JL. Hermaphroditism: Recommendations concerning assignment of sex, change of sex and psychologic management. *Bull John Hopkins Hosp.* 1955;97(4):284-300.
46. Wiesemann C, Ude-Koeller S, Sinnecker GHG, Thyen U. Ethical principles

- and recommendations for the medical management of differences of sex development (DSD)/intersex in children and adolescents. *Eur J Pediatr*. 2010;169(6):671-679. doi:10.1007/s00431-009-1086-x.
47. Rodriguez SW. Rethinking the history of female circumcision and clitoridectomy: American medicine and female sexuality in the late nineteenth century. *J Hist Med Allied Sci*. 2008;63(3):323-347. doi:10.1093/jhmas/jrm044.
  48. Mazloomdoost D, Pauls RN. A Comprehensive Review of the Clitoris and Its Role in Female Sexual Function. *Sex Med Rev*. 2015;3(4):245-263. doi:10.1002/smrj.61.
  49. Creighton S, Chernausek SD, Romao R, Ransley P, Salle JP. Timing and nature of reconstructive surgery for disorders of sex development - Introduction. *J Pediatr Urol*. 2012;8(6):602-610. doi:10.1016/j.jpuro.2012.10.001.
  50. Wang LC, Poppas DP. Surgical outcomes and complications of reconstructive surgery in the female congenital adrenal hyperplasia patient: What every endocrinologist should know. *J Steroid Biochem Mol Biol*. 2017;165:137-144. doi:10.1016/j.jsbmb.2016.03.021.
  51. Allen LE, Hardy BE, Churchill BM. The surgical management of the enlarged clitoris. *J Urol*. 1982;128(2):351-354. doi:10.1016/S0022-3468(83)80143-2.
  52. Reifsnyder JE, Stites J, Bernabé KJ, Galan D, Felsen D, Poppas DP. Nerve Sparing Clitoroplasty is an Option for Adolescent and Adult Female Patients with Congenital Adrenal Hyperplasia and Clitoral Pain following Prior Clitoral Recession or Incomplete Reduction. *J Urol*. 2016;195(4):1270-1274. doi:10.1016/j.juro.2015.12.053.
  53. Lee P a, Witchel SF. Genital surgery among females with congenital

- adrenal hyperplasia: changes over the past five decades. *J Pediatr Endocrinol Metab.* 2002;15(9):1473-1477.  
doi:10.1515/JPEM.2002.15.9.1473.
54. Pippi Salle JL, Braga LP, Macedo N, Rosito N, Bagli D. Corporeal Sparing Dismembered Clitoroplasty: An Alternative Technique for Feminizing Genitoplasty. *J Urol.* 2007;178(4 SUPPLEMENT):1796-1801.  
doi:10.1016/j.juro.2007.03.167.
55. Schmid MA. Plastische Korrektur des äußeren Genitale bei einem männlichen Scheinzwitter. *Langenbecks Arch für Klin Chir.* 1961;298(1):977-982. doi:doi.org/10.1007/BF02435407.
56. Baskin LS. Fetal genital anatomy reconstructive implications. In: *Journal of Urology.* Vol 162. ; 1999:527-529. doi:10.1016/S0022-5347(05)68621-1.
57. Goodwin WE. Surgical revision of the enlarged clitoris. In: Springer-Verlag, ed. *American College of Surgeons and Deutsche Gesellschaft Fur Chirurgie. Joint Meeting.* New York; 1969.
58. Baskin LS, Erol A, Li YW, Liu WH, Kurzrock E, Cunha GR. Anatomical Studies of the Human Clitoris. *J Urol.* 1999;162(3):1015-1020.  
doi:10.1016/S0022-5347(01)68052-2.
59. Poppas DP, Hochsztein AA, Baergen RN, Loyd E, Chen J, Felsen D. Nerve Sparing Ventral Clitoroplasty Preserves Dorsal Nerves in Congenital Adrenal Hyperplasia. *J Urol.* 2007;178(4 SUPPLEMENT):1802-1806.  
doi:10.1016/j.juro.2007.03.186.
60. Crouch NS, Liao LM, Woodhouse CRJ, Conway GS, Creighton SM. Sexual function and genital sensitivity following feminizing genitoplasty for congenital adrenal hyperplasia. *J Urol.* 2008;179(2):634-638.  
doi:10.1016/j.juro.2007.09.079.

61. Lesma A, Bocciardi A, Corti S, Chiumello G, Rigatti P, Montorsi F. Sexual function in adult life following passerini-glazel feminizing genitoplasty in patients with congenital adrenal hyperplasia. *J Urol*. 2014;191(1):206-211. doi:10.1016/j.juro.2013.07.097.
62. Nordenskjöld A, Holmdahl G, Frisén L, et al. Type of Mutation and Surgical Procedure Affect Long-Term Quality of Life for Women with Congenital Adrenal Hyperplasia. *J Clin Endocrinol Metab*. 2008;93(2):380-386. doi:10.1210/jc.2007-0556.
63. Alizai NK, Thomas DFM, Lilford RJ, Batchelor AGG, Johnson N. Feminizing genitoplasty for congenital adrenal hyperplasia: What happens at puberty? *J Urol*. 1999;161(5):1588-1591. doi:10.1016/S0022-5347(05)68986-0.
64. Fortunoff S, Lattimer JK, Edson M. Vaginoplasty Technique for Female Pseudohermaphrodites. *Surg Gynecol Obs*. 1964;118:545-548. [http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list\\_uids=14133087](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=14133087).
65. Lesma A, Bocciardi A, Montorsi F, Rigatti P. Passerini-Glazel Feminizing Genitoplasty: Modifications in 17 Years of Experience with 82 Cases. *Eur Urol*. 2007;52(6):1638-1644. doi:10.1016/j.eururo.2007.02.068.
66. Leslie JA, Cain MP, Rink RC. Feminizing genital reconstruction in congenital adrenal hyperplasia. *Indian J Urol*. 2009;25(1):17. doi:10.4103/0970-1591.45532.
67. Hardy Hendren W, Crawford JD. Adrenogenital syndrome: The anatomy of the anomaly and its repair. Some new concepts. *J Pediatr Surg*. 1969;4(1):49-58. doi:10.1016/0022-3468(69)90183-3.
68. Peña A. Total urogenital mobilization - An easier way to repair cloacas. In: *Journal of Pediatric Surgery*. Vol 32. ; 1997:263-268. doi:10.1016/S0022-

- 3468(97)90191-3.
69. Dòmini R, Rossi F, Ceccarelli PL, De Castro R. Anterior sagittal transanorectal approach to the urogenital sinus in adrenogenital syndrome: Preliminary report. *J Pediatr Surg.* 1997;32(5):714-716. doi:10.1016/S0022-3468(97)90012-9.
  70. Pippi Salle JL, Lorenzo AJ, Jesus LE, et al. Surgical treatment of high urogenital sinuses using the anterior sagittal transrectal approach: A useful strategy to optimize exposure and outcomes. *J Urol.* 2012;187(3):1024-1031. doi:10.1016/j.juro.2011.10.162.
  71. Piaggio LA. Congenital Adrenal Hyperplasia: Review from a Surgeon's Perspective in the Beginning of the Twenty-First Century. *Front Pediatr.* 2014;1(January):1-7. doi:10.3389/fped.2013.00050.
  72. Vidal I, Gorduza DB, Haraux E, et al. Surgical options in disorders of sex development (dsd) with ambiguous genitalia. *Best Pract Res Clin Endocrinol Metab.* 2010;24(2):311-324. doi:10.1016/j.beem.2009.10.004.
  73. Rink RC, Adams MC. Feminizing genitoplasty: state of the art. *World J Urol.* 1998;16(3):212-218.
  74. Clayton PE, Miller WL, Oberfield SE, Ritzén EM, Sippell WG, Speiser PW. Consensus statement on 21-Hydroxylase Deficiency from The Lawson Wilkins Pediatric Endocrine Society and The European Society for Pediatric Endocrinology. *J Clin Endocrinol Metab.* 2002;87(9):4048-4053. doi:10.1210/jc.2002-020611.
  75. Hughes IA, Houk C, Ahmed SF, Lee PA. Consensus statement on management of intersex disorders. *J Pediatr Urol.* 2006;2(3):148-162. doi:10.1016/j.jpuro.2006.03.004.
  76. Lee PA, Houk CP, Ahmed SF HIICC on I organized by the LWPES and the

- ES for PE. Consensus Statement on Management of Intersex. *Ped.* 2006;118(2):488-500. doi:10.1542/peds.2006-0738.
77. Nabhan ZM, Rink RC, Eugster EA. Urinary tract infections in children with congenital adrenal hyperplasia. *J Pediatr Endocrinol Metab.* 2006;19(6):815-820.  
[http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list\\_uids=16886589](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=16886589).
78. Creighton SM. Feminizing Genital Surgery: What Should Be Done and When? *J Pediatr Adolesc Gynecol.* 2005;18:63-69.  
doi:10.1016/j.jpags.2005.01.018.
79. Minto CL, Liao LM, Woodhouse CRJ, Ransley PG, Creighton SM. The effect of clitoral surgery on sexual outcome in individuals who have intersex conditions with ambiguous genitalia: A cross-sectional study. *Lancet.* 2003;361(9365):1252-1257. doi:10.1016/S0140-6736(03)12980-7.
80. Binet A, Lardy H, Geslin D, Francois-Fiquet C, Poli-Merol ML. Should we question early feminizing genitoplasty for patients with congenital adrenal hyperplasia and XX karyotype? *J Pediatr Surg.* 2016;51(3):465-468.  
doi:10.1016/j.jpedsurg.2015.10.004.
81. Fagerholm R, Santtila P, Miettinen PJ, Mattila A, Rintala R, Taskinen S. Sexual function and attitudes toward surgery after feminizing genitoplasty. *J Urol.* 2011;185(5):1900-1904. doi:10.1016/j.juro.2010.12.099.
82. Wisniewski AB, Migeon CJ, Malouf MA, Gearhart JP. Psychosexual Outcome in Women Affected By Congenital Adrenal Hyperplasia Due To 21-Hydroxylase Deficiency. *J Urol.* 2004;171(6):2497-2501.  
doi:10.1097/01.ju.0000125269.91938.f7.
83. Lee PA, Nordenström A, Houk CP, et al. Global disorders of sex development update since 2006: Perceptions, approach and care. *Horm*

- Res Paediatr.* 2016;85(3):158-180. doi:10.1159/000442975.
84. World Health Organization. Gender and Genetics. World Health Organization.  
<http://www.who.int/genomics/gender/en/index1.html#Congenital Adrenal Hyperplasia>. Published 2018. Accessed January 1, 2018.
85. Siminoff LA, Sandberg DE. Promoting Shared Decision Making in Disorders of Sex Development (DSD): Decision Aids and Support Tools. *Horm Metab Res.* 2015;47(5):335-339. doi:10.1055/s-0035-1545302.
86. Alpern AN, Gardner M, Kogan B, Sandberg DE, Quittner AL. Development of Health-Related Quality of Life Instruments for Young Children With Disorders of Sex Development (DSD) and Their Parents. *J Pediatr Psychol.* 2016;jsw022. doi:10.1093/jpepsy/jsw022.
87. Hoffmann T, Bennett S, Del Mar C. *Evidence-Based Practice Across the Health Professions*. 3rd ed. Chatswood, NSW: Elsevier Australia; 2017.
88. Siminoff LA, Sandberg DE. Promoting Shared Decision Making in Disorders of Sex Development (DSD): Decision Aids and Support Tools. *Horm Metab Res = Horm und Stoffwechselforsch = Horm Metab.* 2015;47(5):335-339. doi:10.1055/s-0035-1545302.
89. Lipstein EA, Brinkman WB, Britto MT. What is known about parents' treatment decisions? A narrative review of pediatric decision making. *Med Decis Mak.* 2012;32(2):246-258. doi:10.1177/0272989X11421528.
90. Hong P, Gorodzinsky AY, Taylor BA, Chorney JML. Parental decision making in pediatric otoplasty: The role of shared decision making in parental decisional conflict and decisional regret. *Laryngoscope.* 2016;126:S5-S13. doi:10.1002/lary.26071.
91. Stacey D, Légaré F, Lewis K, et al. Decision aids for people facing health



- treatment or screening decisions. *Cochrane Database Syst Rev.* 2017;(4). doi:10.1002/14651858.CD001431.pub5.
92. O'Donnell S, Cranney A, Jacobsen MJ, Graham ID, O'Connor AM, Tugwell P. Understanding and overcoming the barriers of implementing patient decision aids in clinical practice. *J Eval Clin Pract.* 2006;12(2):174-181. doi:10.1111/j.1365-2753.2006.00613.x.
93. Joseph-Williams N, Newcombe R, Politi M, et al. Toward Minimum Standards for Certifying Patient Decision Aids. *Med Decis Mak.* 2014;34(6):699-710. doi:10.1177/0272989X13501721.
94. O'Connor AMA, Rostom A, Fiset V, et al. Decision aids for patients facing health treatment or screening decisions: systematic review. *BMJ.* 1999;319(7212):731-734. doi:10.1136/bmj.319.7212.731.
95. O'connor AM. Validation of a Decisional Conflict Scale. *Med Decis Mak.* 1995;15(1):25-30. doi:10.1177/0272989X9501500105.
96. Hoffman AS, Volk RJ, Saarimaki A, et al. Delivering patient decision aids on the Internet: Definitions, theories, current evidence, and emerging research areas. *BMC Med Inform Decis Mak.* 2013;13(SUPPL. 2). doi:10.1186/1472-6947-13-S2-S13.
97. Sandberg DE. Decision Support for Parents Receiving Information About Child's Rare Disease ( DSD DST ). ClinicalTrials.gov. <https://clinicaltrials.gov/ct2/show/NCT01875640>. Published 2017. Accessed January 1, 2018.
98. Sandberg D, Callens N, Sminioff L. Decision Making in DSD: Developement of a Decision Support Tool. In: *European Society for Pediatric Endocrinology.* ; 2015.
99. Shortliffe EH, Cimino JJ. *Biomedical Informatics Computer Applications in*

- Health Care and Biomedicine*. 4th ed. London: Springer-Verlag; 2014.
100. Gill P, Stewart K, Treasure E, Chadwick B. Methods of data collection in qualitative research: Interviews and focus groups. *Br Dent J*. 2008;204(6):291-295. doi:10.1038/bdj.2008.192.
  101. Reeder B, Turner AM. Scenario-based design: A method for connecting information system design with public health operations and emergency management. *J Biomed Inform*. 2011;44(6):978-988. doi:10.1016/j.jbi.2011.07.004.
  102. Madsen S, Nielsen L, Madsen S, Nielsen L, Using EP, Design C. Exploring Persona-Scenarios - Using Storytelling to Create Design Ideas. In: Springer, ed. *Second IFIP WG 13.6 Conference on HumanWork Interaction Design: Usability in Social, Cultural and Organizational Contexts (HWID)*. Pune: HAL; 2009:1-11.
  103. Valaitis R, Longaphy J, Nair K, et al. Persona-scenario exercise for codesigning primary care interventions. *Can Fam Physician*. 2014;60(3):294-296.
  104. Carroll JM. Five Reasons for Scenario-Based Design. In: *IEEE Proceedings of the 32nd Hawaii International Conference on System Sciences*. IEEE; 1999:1-11.
  105. Karimi R. Enhancing a home care eHealth application for stroke survivors with multiple chronic conditions bringing primary care into the circle of care. 2016:116.  
[https://macsphere.mcmaster.ca/bitstream/11375/19219/2/Karimi\\_Rojin\\_2016April\\_MSceHealth.pdf](https://macsphere.mcmaster.ca/bitstream/11375/19219/2/Karimi_Rojin_2016April_MSceHealth.pdf).
  106. Ariaeinejad M. User-Centred Requirements Analysis and Evidence-Informed Design Solutions for a Chronic Disease Self-Management System. 2016:90.

107. Chiu S. End user engagement in developing a self-care online app. 2015:110.  
[https://macsphere.mcmaster.ca/bitstream/11375/18774/2/Chiu\\_Stephanie\\_A\\_2015December\\_MSceHealth.pdf](https://macsphere.mcmaster.ca/bitstream/11375/18774/2/Chiu_Stephanie_A_2015December_MSceHealth.pdf).
108. Guest G, Bunce A, Johnson L. How Many Interviews Are Enough? *Field methods*. 2006;18(1):59-82. doi:10.1177/1525822X05279903.
109. Creswell JW, Poth CN. *Qualitative Inquiry and Research Design: Choosing among Five Approaches*. 4th ed. (Salmon H, Scappini J, eds.). Thousand Oaks: SAGE Publications, Inc.; 2018.
110. Jacobsen MJ, O'Connor AM, Stacey D. *Decisional Needs Assessment in Populations: A Workbook for Assessing Patients' and Practitioners' Decision Making Needs*. Ottawa; 2013. [www.ohri.ca/decisionaid](http://www.ohri.ca/decisionaid).
111. Abelson J, Li K, Wilson G, Shields K, Schneider C, Boesveld S. Supporting quality public and patient engagement in health system organizations: Development and usability testing of the Public and Patient Engagement Evaluation Tool. *Heal Expect*. 2016;19(4):817-827. doi:10.1111/hex.12378.
112. Centre of excellence on partnership with patients and the public. *Patient and Public Engagement Evaluation Toolkit*.; 2017.  
<https://nouveau.ceppp.ca/wp-content/uploads/CEPPP-publications-evaluation-toolkit-report-22062017.pdf>.
113. Braun V, Clarke V. Using thematic analysis in psychology. *Qual Res Psychol*. 2006;3(2):77-101. doi:10.1191/1478088706qp063oa.
114. Brown T. *Change by Design: How Design Thinking Transforms Organizations and Inspires Innovation*. 1st Editio. HarperBusiness; 2009.
115. Kelton S. *Congenital Adrenal Hyperplasia*. 8th ed. (Metzger D, Chanoine JP, Stewart L, Rothstein R, Connaughty S, eds.). Vancouver: C&W

- Bookstore; 2012. <http://www.bcchildrens.ca/endocrinology-diabetes-site/Documents/cahbooklet.pdf>.
116. Anthony E, Baratz AB, Boney C, et al. Clinical guidelines for the management of disorders of sex development in childhood. 2006:2. [www.dsdguidelines.org](http://www.dsdguidelines.org).
117. Intersex Society of North America. *Handbook for Parents.*; 2006. [www.isna.org](http://www.isna.org).
118. Maristella M, Rizzo F, Toffetti Carughi G. Web Usability: Principles and Evaluation Methods. *Web Eng.* 2006:143-180. doi:10.1007/3-540-28218-1\_5.
119. Hartzler A, Pratt W. Managing the personal side of health: How patient expertise differs from the expertise of clinicians. *J Med Internet Res.* 2011;13(3). doi:10.2196/jmir.1728.
120. Llewellyn-Thomas HA, Crump RT. Decision Support for Patients: Values Clarification and Preference Elicitation. *Med Care Res Rev.* 2012:1-30. doi:10.1177/1077558712461182.
121. Nielsen J. Enhancing the explanatory power of usability heuristics. *Conf companion Hum factors Comput Syst - CHI '94.* 1994:210. doi:10.1145/259963.260333.
122. Gardner BS. Responsive web design: Enriching the user experience. *Sigma J Insid Digit Ecosyst.* 2011;11(1):13-19. [http://www.noblis.org/media/2dd575c1-2de9-4d92-9bdb-f72ad9fb9a19/docs/SigmaDigEco2011\\_pdf#page=15](http://www.noblis.org/media/2dd575c1-2de9-4d92-9bdb-f72ad9fb9a19/docs/SigmaDigEco2011_pdf#page=15).
123. Zipkin DA, Umscheid CA, Keating NL, et al. Evidence-based risk communication: A systematic review. *Ann Intern Med.* 2014;161(4):270-281. doi:10.7326/M14-0295.

- 
124. Burkell J. What are the chances ? Evaluating risk / benefit information in consumer health materials. *J Med Libr Assoc.* 2004;92(2):200-208.
  125. Garcia-Retamero R, Cokely ET. Designing Visual Aids That Promote Risk Literacy: A Systematic Review of Health Research and Evidence-Based Design Heuristics. *Hum Factors Ergon Soc.* 2017;59(4):582-627. doi:10.1177/0018720817690634.
  126. Garcia-Retamero R, Galesic M. How to reduce the effect of framing on messages about health. *J Gen Intern Med.* 2010;25(12):1323-1329. doi:10.1007/s11606-010-1484-9.
  127. Spiegelhalter D, Pearson M, Short I. Visualizing uncertainty about the future. *Science (80- ).* 2011;333(6048):1393-1400. doi:10.1126/science.1191181.
  128. Cresswell K, Sheikh A. Organizational issues in the implementation and adoption of health information technology innovations : An interpretative review. *Int J Med Inform.* 2013;82(5):e73-e86. doi:10.1016/j.ijmedinf.2012.10.007.
  129. Agoritsas T, Heen AF, Brandt L, et al. Decision aids that really promote shared decision making: The pace quickens. *BMJ.* 2015;350(February). doi:10.1136/bmj.g7624.
  130. Whelan T, Sawka C, Levine M, et al. Helping Patients Make Informed Choices: A Randomized Trial of a Decision Aid for Adjuvant Chemotherapy in Lymph Node-Negative Breast Cancer. *JNCI J Natl Cancer Inst.* 2003;95(8):581-587. doi:10.1093/jnci/95.8.581.
  131. Brooke J. SUS - A quick and dirty usability scale. *Usability Eval Ind.* 1996;189(194):4-7. doi:10.1002/hbm.20701.
  132. Bangor A, Kortum PT, Miller JT. An empirical evaluation of the system

- usability scale. *Int J Hum Comput Interact*. 2008;24(6):574-594.  
doi:10.1080/10447310802205776.
133. Laugwitz B, Held T, Schrepp M. Construction and Evaluation of a User Experience Questionnaire. *HCI Usability Educ Work*. 2008;5298:63-76.  
doi:10.1007/978-3-540-89350-9\_6.
134. Coulter A, Stilwell D, Kryworuchko J, Mullen PD, Ng CJ, van der Weijden T. A systematic development process for patient decision aids. *BMC Med Inform Decis Mak*. 2013;13 Suppl 2(Suppl 2):S2. doi:10.1186/1472-6947-13-S2-S2.
135. Montori VM, Breslin M, Maleska M, Weymiller AJ. Creating a conversation: Insights from the development of a decision aid. *PLoS Med*. 2007;4(8):1303-1307. doi:10.1371/journal.pmed.0040233.

## 11. Appendix

### Appendix A: Search Strategy

PubMed on January 22<sup>nd</sup>, 2018

Order	Keyword	Articles
1	Congenital adrenal hyperplasia	7658
2	1 AND Patient decision	37
3	1 AND Decision	62
4	1 AND 2 OR 3	62
5	1 AND 2	53
6	Disorder of sexual development	1371
7	6 AND patient decision	42
8	6 AND patient decision OR decision	65

Medline on January 22<sup>nd</sup>, 2018

Order	Keyword	Articles
1	Congenital adrenal hyperplasia	7658
2	1 AND aid, decision	3
3	1 OR DSD OR 46 XX AND decision aid OR decision making	1
4	1 OR DSD OR 46 xx AND decision aid OR decision making	123

## **Appendix B: Introduction to PtDAs and Persona-Scenario Development and Discussion Guide**

### **Introduction to Patient Decision Aids**

Healthcare decisions can be confusing for patients and their families. This is particularly true when dealing with a serious condition like congenital adrenal hyperplasia. People making decisions are faced with a flood of new terms and facts about their condition and treatment(s). They are also often dealing with emotions and thoughts about the future.

One tool that can help is a patient decision aid.

#### **What are Patient Decision Aids (PtDAs)?**

Patient decision aids (PtDAs) are tools that provide high quality, combined information about a condition. PtDAs can help patients, families, and health care providers:

- Compare the risks and benefits of treatment options,
- Clarify what matters most to the patient and their family, and
- Make a shared decision about what is the best option for the individual.

Using a patient decision aid can be particularly helpful when:

- There is more than one reasonable option for treatment. This includes the option of having no treatment.
- No option has a clear advantage in terms of health outcomes, or
- Each option has benefits and harms that people may value differently.

PtDAs **do not** tell people which treatment option they should choose. They lay out pros and cons of each option. That way patients and their families can weigh the benefits and drawbacks in relation to their own values. For example, the value people put on factors such as expected side effects or inconvenience of the treatment can differ.

#### **What do PtDAs contain?**

At the very least, PtDAs contain the following parts. They:

- Describe the health condition or problem for which a treatment decision is needed
- Clearly state the treatment decision to consider
- Describe the treatment options available for the decision
- Describe the major advantages/benefits of each treatment option
- Describe the major disadvantages/harms of each treatment option
- The positive and negative aspects of treatment options can help patients imagine the physical, social and/or mental effects of the treatment.

However, PtDAs can also include many other components and functions.



**Are PtDAs actually helpful?**

Patients sometimes have medical proxies. These are people, like parents, who make medical decisions on the patient's behalf. For examples, parents are proxies for their children. Current research on PtDAs shows that when patients or their proxies use decision aids they:

- Improve their knowledge of the options
- Feel clearer about what matters most to them
- Have more accurate expectations of possible benefits and harms of their options
- Participate more in decision making.

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## **Persona-Scenario Development and Discussion Guide**

### For Parents

MacCAH (McMaster Congenital Adrenal Hyperplasia) is an **electronic** patient decision aid (PtDA). It is currently under development by Dr. Luis Braga, who works in the Pediatric Urology Clinic at McMaster Children's Hospital.

This PtDA is being created for parents who make treatment decisions for their child with congenital adrenal hyperplasia. It is aimed at parents who ask: *"Should my daughter undergo early surgery to reconstruct her genitalia or postpone it for later when she will be able to make her own decision?"*

We think it is important to have input from parents like you who have gone or are going through this decision-making process. We want your help to understand what parents want the patient decision aid to look like.

This will help us understand better ways of designing the PtDA for parents like you. It will also help us understand the informational, functional, and support needs that parents have.

Based on your knowledge and experience as a **parent of a child with congenital adrenal hyperplasia, you will create a story**. You will work with a partner.

- 1) First create an imaginary (but believable) **lead character**.
- 2) Then start to develop a story around the character. The story should address a situation in which your character obtains and uses the MacCAH PtDA. The questions below will help you create your story.
- 3) At the end, you and/or your partner will share your story with the larger group

Your scenario may involve **all or some** of the components we discussed earlier. It can also include other things that you feel would be important to have in a PtDA for parents like you.

**Step 1: Create a Character (15 minutes)**

Your character will be a parent who has a child with CAH and who is considering reconstructive genital surgery. He or she might involve another character to help him or her get health information about your child or to make decisions about treatment.

When you create your character give him or her some personality. **Consider these questions as a guide.**

What is your character's:

1. Name, age, and gender;
2. Level of education and employment background;
3. Comfort and experience with technology;
4. Health conditions related to hearing, visual, or other impairments, e.g., disability, or mobility issues;
5. Type and size of community where your character lives (i.e., metropolitan/urban/rural, large/small)
6. Social and cultural background, ethnicity, traditions, religiously-motivated values (if relevant);
7. Desires, attitudes about health;
8. Desires, attitudes about how you raise your child;
9. How much the child should be involved in decisions that affect them
10. How much health care professionals should be involved in health care decisions that affect their family;
11. Family situation, for example:
  - a. Are both parents or guardians living together?
  - b. Are both parents or guardians involved in decision-making about their child's health management?
12. Views about involving other people (providers, extended family, etc.) in this decision?

**Step 2: Create at least one Story. (45-60 minutes)**

Now create your story. Your character learns that their daughter has been diagnosed with congenital adrenal hyperplasia and that surgery is suggested. Create at least one short story for your lead character who is using the MacCAH PtDA to help him/her come to a decision about surgery.

**Consider these questions as a guide to create your story:**

1. What is the decision that your character needs to make? How does your character feel about this decision? What things make the decision difficult for him/her?
2. How did your character get involved in using the MacCAH PtDA? (Where, when, why?)
3. What is the situation that brings your character to use the MacCAH PtDA? (for example, did someone ask your character to make a decision now? Is your character worried about what he/she will have to face one day?)
4. At what point did your character learn about the PtDA?
5. Who told your character about the PtDA? In what context? In an office? Was your child present? Were both parents present?
6. What are other important characters doing in the scenario? (What, where, when, how?)
  - a. Spouse or other family
  - b. Family doctor or doctor's office staff providers
  - c. Pediatric nurses
  - d. Pediatric urologists/endocrinologists
7. What kind of information or support is your character looking for when they use the MacCAH PtDA?
8. Picture your character using the PtDA:
  - a. What kind of electronic tool is it? (e.g., a website, an app, etc.)
  - b. What kind of technology does your character use to access the PtDA (e.g., computer, cell phone, tablet) and where does he or she access it? (e.g., home, library, a relative's house, somewhere else) Is it private?
  - c. What kind of information is in the PtDA? What does the PtDA tell you about:
    - i. Congenital adrenal hyperplasia?
    - ii. Options for treatment?
    - iii. Benefits and harms of the different options?
    - iv. The likelihood of benefits and risks?
    - v. Short, intermediate, and long-term outcomes?
    - vi. The physical, psychological, and/or social effects of the various treatment options?
  - d. How much information is there and how is it presented? For example, are there key points, summaries, lists of other

- resources, or other ways information is presented? Is anything on paper or not?
- e. Describe how the information is delivered to you about CAH and its treatment options. What does your character see and hear, to get the information or support they need? Are there videos, images, links, or contact information? What kinds (e.g., surgical videos, pre/post images)?
  - f. Does your character go back to use the PtDA more than once? If so, when, where, why and how?
  - g. What are the values that your character considers when making his/her decision?
  - h. How does the PtDA help your character identify what he/she values most (i.e., the personal importance he/she places on the elements of each option)?
  - i. What other functions, supports, resources, or tools are available in the PtDA?
  - j. If your character has any physical challenges, such as vision, hearing, or mobility challenges, how does he or she overcome them to get information, support or guidance?
9. Does your character need help in using the PtDA in any way (for example, to find the information and guidance?) If yes, what kind of help does he or she get and from whom?
  10. Is privacy a concern in accessing the PtDA? How so and how does it affect how your character accesses the patient decision aid?
  11. How does the situation get resolved? What happens as a result of interacting with the MacCAH PtDA (e.g., what decisions, emotional responses, or other actions happen)? Do others talk with your character after he or she uses the PtDA?
  12. What helped your character make a decision? OR What prevented your character from making a decision?

**Step 3: Report back to larger group a summary of your character and story. (15-20 minutes per small group)**

Your discussions and presentations will be audio-taped to ensure that we do not miss anything important from your stories. The audio-tapes will be transcribed and analysed. Your names will not be used.

**Step 4: Feedback on the character-story process (5 mins)**

We want to thank you for your help today. You have provided us with important ideas about how to best develop and put a PtDA for congenital adrenal hyperplasia to use. Once we have designed and developed the PtDA, we may invite you to participate again. We will want your opinions about the way we designed the PtDA and will ask you if you think it will meet the needs of parents making treatment decisions about surgery.

Finally, we would like to take a few minutes to ask you for some feedback about this exercise. If you are willing, we have a short survey for you to complete. You can answer the survey yourself or we can go through it with you verbally. One of the note takers can fill in your answers.

**Thank you for your valuable input into the study!**

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## **Persona-Scenario Development and Discussion Guide**

### For Health Care Providers

MacCAH (McMaster Congenital Adrenal Hyperplasia) is an **electronic** patient decision aid (PtDA) currently under development by Dr. Luis Braga, who works in the Pediatric Urology Clinic at McMaster Children’s Hospital.

This PtDA is being created for parents who make treatment decisions for their child with congenital adrenal hyperplasia. It is aimed at parents who ask: *“Should my daughter undergo early surgery to reconstruct her genitalia or postpone to later in life when she would be able to make her own decision?”*

The literature highlights the importance of involving healthcare providers in the design and development of patient decision aids. Healthcare providers often have different perspectives than patients. So, we want your help to understand how healthcare providers envision the content, function, and implementation of the PtDA.

This will help us design better ways of presenting and delivering the patient decision aid. It will also help us understand the information, functionality, and support needs that parents/families have.

Based on your knowledge and experience as a **health care provider**, you will create a story. You will work with a partner.

- 4) First create an imaginary (but believable) “persona” or **lead character**.
- 5) Then start to develop the **story** or “scenario” around the character. The story should address a situation in which your character interacts with the MacCAH PtDA. The questions below will help you create your story.
- 6) At the end, you and/or your partner will share your story with the larger group

Note: your scenario may involve **all or some** of the components we discussed earlier, as well as other functionalities or components that you can think of and that you feel would be important in a PtDA for CAH.

**Step 1: Create a Character (15 minutes)**

Your persona will be health care provider working in the McMaster Pediatric Urology Clinic using the MacCAH patient decision aid in his/her clinic. When you create your character give him or her some personality. **Consider these questions as a guide.**

What is your character's:

1. Name, age, and gender;
2. Level of education and employment background;
3. Desires, attitudes about work;
4. Years of service with current employer/organization;
5. Experience with clinic health care team members (surgeons, endocrinologists, pediatric nurse practitioners, social workers, residents etc.) in providing care for patients and families receiving surgery or treatment
6. Experience with congenital adrenal hyperplasia
7. Attitudes, comfort, and experience with technology and/or eHealth Apps, and a PtDA;
8. Health conditions related to hearing, visual, or other impairments, e.g., disability, or mobility issues;
9. Hopes and fears about reconstructive genital surgery for your patients
10. Hopes and fears about managing parents / guardians of ill children

**Step 2: Create at least one Scenario. (45-60 minutes)**

Create at least one scenario for your persona who is using the MacCAH patient decision aid to provide information and decision support to clients/families in the clinic.

**Consider these questions as a guide to create your story:**

1. What is your character's usual role in helping the family make decisions about managing their child's health?
2. How does your health care provider persona become involved with the PtDA? And what is their role with respect to the use of the PtDA? How does the patient become involved? (When, where, how and why?)
3. How was your character trained about the use of the MacCAH PtDA? When and where?
4. How does your persona deliver/apply the use of the MacCAH PtDA with parents? When and where? Who is teaching parents to use it? What helps them do this?



- 
5. What are the following people doing in the scenario – what is their role? And how are they interacting with the PtDA? (What, where, when, how?)
    - a. Family or caregivers of patients –
      - i. What is the decision that parents need to make?
      - ii. How do parents/families feel when making this decision?
      - iii. How do they go about making a decision?
      - iv. What makes the decision difficult for parents/families?
      - v. What helps them make their decision?
      - vi. What gets in the way of making a decision?
      - vii. What influences them in reaching their decision?
    - b. Healthcare providers (e.g., other pediatric nurses, surgeons, endocrinologists etc.)
    - c. Anyone else involved in the decision-making process
  6. Picture the PtDA:
    - a. What kind of electronic tool is it? (e.g., a website, an app, etc.)
    - b. Is it interactive or just descriptive text? If it is interactive, how?
    - c. What kind of technology do families use to access the PtDA (e.g., computer, cell phone, tablet) and where do they access it? (e.g., in the clinic, home, library, a relative's house, somewhere else?) Does anyone help? If so, who and how?
    - d. What kind of information is in the PtDA? For example, about
      - i. Congenital adrenal hyperplasia?
      - ii. Options for surgical treatment?
      - iii. Benefits and harms of the different options?
      - iv. The likelihood of benefits and risks?
      - v. Short, intermediate, and long-term outcomes?
      - vi. The physical, psychological, and/or social effects of the various treatment options?
      - vii. Other supports and resources?
    - e. How much information is there and how is it presented? For example, are there key points, summaries, lists of other resources, or other ways information is presented?
    - f. Describe the format of the delivery of information about CAH and its treatment options. What does your character see, and hear to get the information or support they need? Are there videos, images, links, or contact information? If so, what kinds?
    - g. Is anything available in another medium such as paper?

- h. What are the values that the parents consider when making their decisions? How does the PtDA help parents/families identify what they value most?
  - i. What other functionalities, supports, or tools are available in the patient decision aid?
  - j. Is privacy a concern in accessing the patient decision aid in this situation? How so?
7. What factors make it difficult for your persona to support their patients' decision making?
8. What factors make it easier for your persona to support their patients' decision making?
9. What are the results of using the PtDA for parents/families, healthcare providers (nurses, surgeons, etc.), and patients? How does the story end?

**Step 3: Report back to larger group a summary of your character and story. (15-20 minutes per small group)**

Your discussions and presentations will be audio-taped to ensure that we do not miss anything important from your stories. The audio-tapes will be transcribed and analysed. Your names will not be used.

**Step 4: Feedback on the character-story process (5 mins)**

We want to thank you for your help today. You have provided us with important ideas about how to best develop and implement a patient decision aid for congenital adrenal hyperplasia, especially with regards to reconstructive genital surgery. Once we have designed and developed the patient decision aid, we may invite you to participate again. We will ask you if you think the way we designed the decision aid will meet the needs of parents making treatment decision about reconstructive genital surgery.

Finally, we would like to take a few minutes to ask you for some individual feedback about your experiences today. If you are willing, we have a short survey for you to complete. You can answer the survey yourself or we can go through it with you verbally (in which case one of the note takers will fill in your answers).

**Thank you for your valuable input into the study!**

## **Appendix C: Letters of Information and Consent for Parents, Patients and Practitioners**

### **LETTER OF INFORMATION AND CONSENT FOR PARENTS AND ADULT PATIENTS**

**Study Title:** Exploring User Requirements for the Design of an Electronic Patient Decision Aid for Guardians Making Treatment Decisions about Congenital Adrenal Hyperplasia

#### **Investigators:**

##### **Local Principal Investigator:**

Dr. Luis Braga  
Department of HEI  
McMaster University  
Hamilton, ON, Canada  
(905) 5215-2100 ext. 73777  
E-mail: braga@mcmaster.ca

##### **Student Investigator:**

Irtaza Tahir  
Department of HEI  
McMaster University  
Hamilton, ON, Canada  
(905) 966-4650  
E-mail: tahiri@mcmaster.ca

#### **Invitation to participate in research:**

- You are invited to participate in this study conducted by Irtaza Tahir and Dr. Luis Braga, from McMaster University.
- You are eligible to participate because you are a parent of a child diagnosed with congenital adrenal hyperplasia who has considered or is considering surgical treatment (genitoplasty, clitoroplasty, vaginoplasty etc.) for your child.
- To decide whether or not you want to be a part of this study, you should understand what is involved and the potential risks and benefits. This form gives detailed information about the study, which will be discussed with you.
- Once you understand the study, you will be asked to sign this form if you wish to participate. Please take your time to make your decision. Feel free to discuss it with your friends and family.
- Your participation is voluntary. If you agree to participate, you may withdraw from the study at any time without any penalty.
- Choosing not to participate in this study will in no way affect your access to health services or health information.

#### **What are we trying to discover?**

- Healthcare decisions can be confusing for patients and their families. This is particularly true when dealing with a serious condition like Congenital Adrenal Hyperplasia. People making decisions are faced with a flood of new terms and facts about their condition and treatment(s). They are also often dealing with emotions and thoughts about the future.
- We want to create an electronic patient decision aid (an electronic tool that will provide information and help parents make thoughtful, value-sensitive decisions) for congenital adrenal hyperplasia. This decision aid will help fill the gaps in information needs and decision support that parents and families are currently experiencing.

- To create the tool, we need the help of parents like you to understand the optimal design of a patient decision aid for surgical treatment of congenital adrenal hyperplasia (i.e., both the characteristics and design of the aid, and the focus and format of the informational content).
- We also hope to find out about the best ways to develop, and implement the patient decision aid (e.g., strategies to distribute it and share it with others).

**What will happen during the study?**

- After consenting to participate in this study, you will be asked to attend a group session. In this session, you will work with peers to create stories with support from the researchers. The purpose of the stories is to capture your ideas about how to best design, develop, and implement a patient decision aid for parents making surgical treatment decision for children diagnosed with congenital adrenal hyperplasia.
- These group sessions will take place at McMaster Children’s Hospital/Health Sciences Centre. They will last approximately 2 hours. Your travel and parking costs will be reimbursed.
- There will be 6 participants in these group sessions, along with trained facilitators who will guide the session.
- In the group session, you will first be given a small presentation that will tell you what patient decision aids are and some of the components that they contain.
- Then, you will work in a 2-person team. Facilitators will guide you through an exercise where you will develop a story together. First you will create an imaginary but realistic character who would use a patient decision aid for congenital adrenal hyperplasia. Then you will develop a situation in which your character will obtain and use the patient decision aid to decide about his or her child’s surgical treatment. Facilitators will guide your discussion using questions such as:
  - Who told your character about the PtDA?
  - Picture your character using the patient decision aid...what kind of information is in the aid?
- With your permission, facilitators will be taking notes about the story you create.
- Later in the session, each 2-person participant team will present a summary of their story to the group. These summaries will be audio-recorded with your permission. The words will be transcribed for use by the research team with your names removed. These transcriptions contain the “data” that we will use to develop tools to design and deliver the patient decision aid.
- At the end of the sessions, we will ask you to complete a short questionnaire about the session and the approach we used, as well as a short survey to gather some background information about you (such as age and education).

**Are there any risks to doing this study?**

- It is unlikely that there will be any risks or harms from participating in this study.
- However, we understand that your child’s diagnosis and treatment can be a sensitive topic that you might feel anxious or uneasy speaking about. You may worry about how others will react to what you say. You do not need to answer questions that you do not want to answer or that make you feel uncomfortable
- Remember you are free to stop participating in the study at any time.

**What will we do to minimize these risks?**

- We will have counselling resources available that you can access if you have questions or doubts about your child's care, including Dr. Braga (pediatric surgeon) as well as social workers and child life specialists in the clinic. These health care practitioners will not have access to any identifiable information that you have shared during the persona-scenario sessions. They will not know what you have said during the persona-scenarios unless you decide to share this information yourself during your discussion with them.
- Discussions will be guided by a trained facilitator who understand the sensitive nature of the topic.
- You can see below the steps we will take to protect your privacy and to keep the information you share confidential. See '*How will my personal information be kept confidential?*'.

**Are there any benefits to me and to society from participating in this study?**

- We cannot promise you any personal benefits from participating in this study. Possible benefits include:
  - feeling good that you are contributing to knowledge that will potentially help others
  - making it easier for families who have a child diagnosed with congenital adrenal hyperplasia to access health information and make decisions about treatment and surgery
  - contributing to science that may improve support for children with congenital adrenal hyperplasia and their families, in other ways.
- We hope that what is learned from this study will help us to better understand the information and support needs of parents making treatment decisions and what parents/families would require from an electronic patient decision aid to fulfill these needs. This could help us create an electronic patient decision aid in the future.

**Will I be paid to participate in this study?**

- Yes. As a token of appreciation, you will receive \$25 per hour for completing the session. In most cases, a gift card will be mailed or emailed to you after participation.

**Will there be any costs to me in this study?**

- In addition to the payment for your time as described above, you will be reimbursed for your transportation and/or parking costs at the facility where the sessions are conducted.

**How will my personal information be kept confidential?**

- The personal information collected in this study will include your contact information (to arrange your participation and provide you an honorarium and reimbursement).
- The characters and stories that you develop in your session may be based on your life experiences. Individuals can be identifiable through the stories they tell. So, we will take precautions to protect the data you provide by separating it from any information that can identify you.
- We will ask participants to use first names only during sessions.

- We will ask participants to avoid sharing information that you learn about each other outside of the session, but cannot guarantee they will respect confidentiality. Since we cannot promise complete confidentiality, you should only share what you feel comfortable sharing.
- As soon as possible, we will switch your personal identifiers (e.g., your name) in the data with identification numbers or pseudonyms to track participants in our files.
- The key to these identification numbers will be stored separately from your data in a password protected file, in a password protected server (secured against hacking using a firewall) at McMaster University.
- During the study, the data you provide (notes, recordings and transcripts of the summary of your stories, and questionnaire results) will be stored in a password protected server (secured against hacking using a firewall) at McMaster University.
- Your demographic survey answers and hardcopy data will be kept in a locked office cabinet, in a locked office at McMaster University, where only I will have access to it.
- We will omit information that could identify you from transcripts and study reports.
- Dr. Braga or other healthcare providers will not have access to any data from the persona-scenario session or surveys that has your personal identifiers.
- The data will be kept for ten years, after which hardcopy data will be securely shredded and electronic data will be digitally erased.
- Once the study is complete, an archive of the data, without identifying information, will be kept in a database that we may use for future research in developing the electronic patient decision aid or for other research purposes.

#### **Legally Required Disclosure**

- Although I will protect your privacy as outlined above, if the law requires it, I will have to reveal certain personal information (e.g., child abuse).

#### **What if I change my mind about being in the study?**

- Your participation in this study is voluntary.
- If you decide to be part of the study, you can decide to stop (withdraw), at any time, for any reason, even after signing the consent form or part-way through the study.
- If you decide to withdraw, there will be no consequence to you.
- Your decision to participate or withdraw will not affect your access to services.
- To withdraw, notify either the contact person below, or one of the researchers, as soon as possible. This can be face-to-face (such as during a session), by phone, or by email. See “*Whom should I contact?*” below.
- You will be asked for written confirmation of your intention to withdraw from the study.
- If data have already been collected during a session before you withdraw, you should indicate whether you wish to have any of your quotes included or excluded from the study.

#### **How do I find out what was learned in this study?**

- I expect to have this study completed by approximately July 2018. If you would like a brief summary of the results, please let me know how you would like it sent to you.

**Will I be contacted at a later date?**

- In the future, as we design and develop the electronic patient decision aid, we may need to contact you to clarify information that you provided or to invite you for future research (e.g., to evaluate the patient decision aid we will create to see if it meets your expectations and needs).

**If I have questions about this study, whom should I contact?**

Irtaza Tahir, M.Sc. eHealth (Candidate)

Department of Health Research Methods, Evidence, and Impact

Tel: 905-966-4650

Email: [tahiri@mcmaster.ca](mailto:tahiri@mcmaster.ca)

Mail: 1200 Main St. W., HSC 4E19

McMaster Children Hospital

McMaster University

Hamilton, ON L8S 4K1

This study has been reviewed by the Hamilton Integrated Research Ethics Board (HiREB). The HiREB is responsible for ensuring that participants are informed of the risks associated with the research, and that participants are free to decide if participation is right for them. If you have any questions about your rights as a research participant, please call the Office of the Chair, HiREB, at 905.521.2100 x 42013.

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### CONSENT

I have read the information presented in the information letter about a study being conducted by Irtaza Tahir and Dr. Luis Braga, of McMaster University.

I have had the opportunity to ask questions about my involvement in this study and to receive additional details I requested.

I understand that if I agree to participate in this study, I may withdraw from the study at any time. I have been given a signed copy of this form. I agree to participate in the study.

I permit the researchers to contact me in the future to clarify the information learned in this study or to invite me to participate in follow up research.

Yes    No

If yes, please contact me by:

Phone: \_\_\_\_\_

Email: \_\_\_\_\_

I would like to receive a summary of the study's results.

Yes    No

If yes, where would you like the results sent:

Email: \_\_\_\_\_

Mailing address: \_\_\_\_\_

\_\_\_\_\_

\_\_\_\_\_

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\_\_\_\_\_  
Name of Participant (Printed)

\_\_\_\_\_  
Signature

\_\_\_\_\_  
Date

Consent form explained in person by:

\_\_\_\_\_  
Name and Role (Printed)

\_\_\_\_\_  
Signature

\_\_\_\_\_  
Date



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## LETTER OF INFORMATION AND CONSENT FOR HEALTHCARE PRACTITIONERS

**Study Title:** Exploring User Requirements for the Design of an Electronic Patient Decision Aid for Guardians Making Treatment Decisions about Congenital Adrenal Hyperplasia

### Investigators:

#### Local Principal Investigator:

Dr. Luis Braga  
Department of HEI  
McMaster University  
Hamilton, ON, Canada  
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#### Student Investigator:

Irtaza Tahir  
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McMaster University  
Hamilton, ON, Canada  
(905) 966-4650  
E-mail: tahiri@mcmaster.ca

### Invitation to Participate in the Study

- You are invited to participate in this study conducted by Irtaza Tahir and Dr. Luis Braga, from McMaster University.
- You are eligible to participate because you are a healthcare provider involved in the care of children diagnosed with congenital adrenal hyperplasia whose families are considering/have considered surgical treatment (genitoplasty, clitoroplasty, vaginoplasty etc.) for their child.
- To decide whether you want to be a part of this study, you should understand what is involved and the potential risks and benefits. This form gives detailed information about the study, which will be discussed with you.
- Once you understand the study, you will be asked to sign this form if you wish to participate. Please take your time to make your decision.
- Your participation is voluntary. If you agree to participate, you may withdraw from the study at any time without any penalty.

### Purpose of the Study

- Healthcare decisions can be confusing for patients and their families, particularly when dealing with a condition such as Congenital Adrenal Hyperplasia (CAH). Parents and families are faced with a flood of new terms and facts about their condition and its treatment(s), and are also typically dealing with emotions and thoughts of the future.
- We want to create an electronic patient decision aid (an electronic tool that will provide information and help parents make thoughtful, value-sensitive decisions) for congenital adrenal hyperplasia, to help fill the gaps in informational and decision support that parents and families are currently experiencing.
- To create the tool, we need the help of healthcare providers to help us understand the optimal design of a patient decision aid for surgical treatment of congenital adrenal hyperplasia (i.e., both the characteristics and design of the aid, and the focus and format of the informational content).
- We also hope to find out about the best ways to develop, and implement the patient decision aid (e.g., strategies to distribute it and use it in a clinical setting).

**Procedures involved in the Research**

- After consenting to participate in this study, you will be asked to attend a group session. In this session, you will work with peers to create stories with support from the researchers. The purpose of the stories is to capture your ideas about how to best design, develop, and implement a patient decision aid for parents making surgical treatment decision for children diagnosed with congenital adrenal hyperplasia.
- These group sessions will take place at McMaster Children’s Hospital/Health Sciences Centre. They will last approximately 2 hours. Your travel and parking costs associated with participation will be reimbursed.
- There will be 4 participants in these group sessions, along with trained facilitators who will guide the session.
- In the group session, you will first be given a small presentation that will tell you what patient decision aids are and some of the components that they contain.
- Then, you will work in a 2-person team. Facilitators will guide you through an exercise where you will develop a story together. First you will create an imaginary but realistic character who would use/provide a patient decision aid for congenital adrenal hyperplasia. Then you will develop a situation in which your character will interact with the patient decision aid in their clinical setting. Facilitators will guide your discussion using questions such as:
  - How does your health care provider persona become involved with the patient decision aid? How does the patient? (When, where, why?)
  - Picture the patient decision aid...what kind of information is in the aid?
- With your permission, facilitators will be taking notes about the story you create.
- Later in the session, each 2-person participant team will present a summary of their story to the group. These summaries will be audio-recorded with your permission. The words will be transcribed for use by the research team with your names removed. These transcriptions contain the “data” that we will use to develop tools to design and deliver the patient decision aid.
- At the end of the sessions, we will ask you to complete a short questionnaire about the session and the approach we used, as well as a short survey to gather some background information about you (such as age and occupation).

**Potential Harms, Risks or Discomforts**

- It is unlikely that there will be any risks or harms from participating in this study.
- However, we understand that pediatric diagnosis and treatment can be a sensitive topic that you might feel anxious or uneasy speaking about. You may worry about how others will react to what you say. You do not need to answer questions that you do not want to answer or that make you feel uncomfortable
- Remember, you are free to stop participating in the study at any time.

**Ways Risks Will Be Minimized:**

- Discussions will be guided by a trained facilitator who understand the sensitive nature of the topic.
- You can see below the steps we will take to protect your privacy and to keep the information you share confidential. See *‘How will my personal information be kept confidential?’*.

**Potential Benefits**

- We cannot promise you any personal benefits from participating in this study. Possible benefits include:
  - feeling good that you are contributing to knowledge that will potentially help others
  - making it easier for families who have a child diagnosed with congenital adrenal hyperplasia to access health information and make decisions about treatment and surgery
  - contributing to the success of the patient decision aid by providing insights on how to best implement and distribute the aid.
  - contributing to science that may improve support for children with congenital adrenal hyperplasia and their families, in other ways.
- We hope that what is learned from this study will help us to better understand the information and support needs of parents making treatment decisions and what parents/families would require from an electronic patient decision aid to fulfill these needs. This could help us create an electronic patient decision aid in the future.

**Payment and Reimbursement**

- As a token of appreciation, you will receive \$25 per hour for completing the session. In most cases, a gift card will be mailed or emailed to you after participation.
- In addition to the payment for your time as described above, you will be reimbursed for your transportation and/or parking costs that you incurred because of participation in the study.

**Confidentiality**

- The personal information collected in this study will include your contact information (to arrange your participation and provide you an honorarium and reimbursement).
- The characters and stories that you develop in your session may be based on your life experiences. Individuals can be identifiable through the stories they tell. So, we will take precautions to protect the data you provide by separating it from any information that can identify you.
- We will ask participants to use first names only during sessions.
- We will ask participants to avoid sharing information that you learn about each other outside of the session, but cannot guarantee they will respect confidentiality. Since we cannot promise complete confidentiality, you should only share what you feel comfortable sharing.
- As soon as possible, we will switch your personal identifiers (e.g., your name) in the data with identification numbers or pseudonyms to track participants in our files.
- The key to these identification numbers will be stored separately from your data in a password protected file, in a password protected server (secured against hacking using a firewall) at McMaster University.
- During the study, the data you provide (notes, recordings and transcripts of the summary of your stories, and questionnaire results) will be stored in a password protected server (secured against hacking using a firewall) at McMaster University.
- Your demographic survey answers and hardcopy data will be kept in a locked office cabinet, in a locked office at McMaster University, where only I will have access to it.
- We will omit information that could identify you from transcripts and study reports.

- Dr. Braga or other healthcare providers will not have access to any data that has your personal identifiers.
- The data will be kept for ten years, after which hardcopy data will be securely shredded and electronic data will be digitally erased.
- Once the study is complete, an archive of the data, without identifying information, will be kept in a database that we may use for future research in developing the electronic patient decision aid or for other research purposes.

**Legally Required Disclosure**

- Although I will protect your privacy as outlined above, if the law requires it, I will have to reveal certain personal information (e.g., child abuse, malpractice).

**Participation and Withdrawal**

- Your participation in this study is voluntary.
- If you decide to be part of the study, you can decide to stop (withdraw), at any time, for any reason, even after signing the consent form or part-way through the study.
- If you decide to withdraw, there will be no consequence to you.
- To withdraw, notify either the contact person below, or one of the researchers, as soon as possible. This can be face-to-face (such as during a session), by phone, or by email. See “*Whom should I contact?*” below.
- You will be asked for written confirmation of your intention to withdraw from the study.
- If data have already been collected during a session before you withdraw, you should indicate whether you wish to have any of your quotes included or excluded from the study.

**Information About the Study Results**

- I expect to have this study completed by approximately July 2018. If you would like a brief summary of the results, please let me know how you would like it sent to you.

**Contact at a Later Date**

- In the future, as we design and develop the electronic patient decision aid, we may need to contact you to clarify information that you provided or to invite you for future research (e.g., to evaluate the patient decision aid we will create to see if it meets your expectations and needs).

**Questions About the Study**

If you have any questions or need more information about the study itself, please contact:

Irtaza Tahir, M.Sc. eHealth (Candidate)

Department of Health Research Methods, Evidence, and Impact

Tel: 905-966-4650

Email: tahiri@mcmaster.ca

Mail: 1200 Main St. W., HSC 4E19

McMaster Children Hospital

McMaster University

Hamilton, ON L8S 4K1

This study has been reviewed by the Hamilton Integrated Research Ethics Board (HiREB). The HiREB is responsible for ensuring that participants are informed of the risks associated with the research, and that participants are free to decide if participation is right for them. If you have any questions about your rights as a research participant, please call the Office of the Chair, HiREB, at 905.521.2100 x 42013.

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## Appendix D: Public and Patient Engagement Evaluation Tool (PPEET) and Demographics Survey for Parents/Patients and Practitioners

### Public and Patient Engagement Evaluation Tool

#### INSTRUCTIONS

- We are interested in your feedback about the engagement activity that you recently participated in.
- The questionnaire is composed of several statements. Please indicate your level of agreement with each statement and check only one box for each statement.
- Please provide additional feedback in the comment boxes provided throughout the questionnaire.
- All information you provide will remain confidential.
- Thank you very much for your participation!

	Strongly Agree	Agree	Neither Agree nor Disagree	Disagree	Strongly Disagree
The purpose of the activity was clearly explained.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
The supports I needed to participate were available (e.g., travel, child care, etc.).	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
I had enough information to contribute to the topic being discussed.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
I was able to express my views freely.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
I feel that my views were heard.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
A wide range of views on the topic were expressed.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

	Strongly Agree	Agree	Neither Agree nor Disagree	Disagree	Strongly Disagree
I feel that the input provided through this activity will be considered by the organizers.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
The activity achieved its stated objectives.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
I understand how the input from this activity will be used.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
I think this activity will make a difference.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
As a result of my participation in this activity, I am better informed about patient decision aids and decision support for those making treatment decisions.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
As a result of my participation in this activity, I have greater trust in the MacCAH Research team.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Overall, I was satisfied with this activity.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
This activity was a good use of my time.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>



**Open-ended questions:**

1. How do you think the results of your participation will be used?

2. What was the best thing about this engagement activity?

3. Please identify at least one improvement we could make for future engagement activities.

**Additional comments:**

## Parent/Medical Decision Maker Demographic Questions

**Finally, we would like to get a little more information about you.**

1. What is your age? \_\_\_\_\_
2. What age is your child (who is diagnosed with CAH)? \_\_\_\_\_

3. What is your gender?

<input type="checkbox"/>	Male
<input type="checkbox"/>	Female
<input type="checkbox"/>	Other: _____

4. Are you a member of any of the following groups? (Please check all that apply)

<input type="checkbox"/>	Visible minority
<input type="checkbox"/>	Persons with disabilities
<input type="checkbox"/>	Aboriginal
<input type="checkbox"/>	Recent immigrant to Canada
<input type="checkbox"/>	Other: _____

5. What is your marital status?

<input type="checkbox"/>	Single (never married)	<input type="checkbox"/>	Common-law
<input type="checkbox"/>	Married (not separated)	<input type="checkbox"/>	Divorced
<input type="checkbox"/>	Separated	<input type="checkbox"/>	Widowed

6. What is the highest level of education that you have completed?

<input type="checkbox"/>	No schooling
<input type="checkbox"/>	Completed elementary school
<input type="checkbox"/>	Completed high school
<input type="checkbox"/>	Completed community college

	Completed technical school
	Completed Bachelor's Degree (Arts, Science, etc.)
	Completed post graduate training or Professional or graduate degree

## 7. What is your current work status?

	Working for pay full time (including on strike and any form of leave)
	Working for pay part time (including retired part time, homemaker part time)
	Not in labour force, able to work
	Not in labour force, unable to work
	Retired
	Student (includes students working part time)
	Homemaker

## 8. What is your level of comfort with technology (e.g., eHealth applications, health websites, the computer, internet etc.)?

1	2	3	4	5	6	7	8	9	10
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## 9. To which of the following income category do you belong, before taxes and deductions.

	Less than \$20,000
	Between \$20,000 and \$40,000
	Between \$40,000 and \$60,000
	Between \$60,000 and \$80,000
	More than \$80,000

## 10. Have you ever worked for pay in a healthcare profession?

	Yes
	No

## Health Care Provider Demographic Questions

**Finally, we would like to get a little more information about you.**

1. What is your age? \_\_\_\_\_

2. What is your gender?

	Male
	Female
	Other: _____

3. Are you a member of any of the following groups? (Please check all that apply)

	Visible minority
	Persons with disabilities
	Aboriginal
	Recent immigrant to Canada
	Other: _____

4. What is the highest level of education that you have completed?

	Completed community college
	Completed technical school
	Completed Bachelor's Degree (Arts, Science, etc.)
	Completed post graduate training or Professional or graduate degree

5. What is your current work status?

	Working for pay full time (including on strike and any form of leave)
	Working for pay part time (including retired part time, homemaker part time)

	Not in labour force, able to work
	Not in labour force, unable to work
	Retired
	Student (includes students working part time)
	Homemaker

6. What is your discipline?

	Pediatric Urology
	Pediatric Endocrinology
	Other: _____

7. What is your role/occupation?

	Surgeon
	Endocrinologist
	Nurse Practitioner
	Social Worker
	Other: _____

8. How many years of experience do you have in providing care to children and support to families diagnosed with Congenital Adrenal hyperplasia?

\_\_\_\_\_ Years

9. What is your level of comfort providing support to families with children diagnosed with congenital adrenal hyperplasia? (Please circle: 1 – No comfort to 10 – High comfort)

1	2	3	4	5	6	7	8	9	10
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10. What is your level of comfort with technology (e.g., eHealth applications, health websites, the computer, internet etc.)?

1	2	3	4	5	6	7	8	9	10
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## **Appendix E: Persona-Scenario Stories**

### **Molly (Mother of child with virilizing CAH)**

Molly is a 30-year-old. She studied until high school and worked as a secretary. She lived in a rural community that had about 10000 people. She doesn't really have cultural or ethnic values that will affect her decision. She just wants her child to have a normal experience. She was pretty involved with her children, especially when they are little and wants them to be social like the other kids and same as the other kids. Molly struggled with involving her kid with the decision – it really depends on the age of the child. Molly and her husband are very involved but dependant on the practitioner for questions and stuff and make a shared decision. She learns about the aid from her endocrinologist or surgeon who walks her through it. The tool is open to anybody or it should be a website in the public domain. It talks about the different surgeries. She sees videos from different surgeons about the pros and cons of the surgery. Molly also sees videos from different families who had made the decision to have it earlier and who had the decision to have it later so that molly could decide for her family situation and her child what was best. The tool is in three stages, from before surgery, after surgery, and down the line what to expect. It has information about pros and cons, what is normal, what is not normal, what should I be looking for, what will I have to be involved in – all that kind of stuff. Molly likes that the app has initially more generic information, and then if you want to go more in depth with your information, that you can opt to read more and see more videos, links and pictures. Molly wants the app to be able to go into the aid at different times to see whether what is happening is normal. The app should include all the different things that could happen to a CAH child. It should have the pros and cons of each option and she should be able to rate those to how important they are for her. It should have something in it that Molly can evaluate like, “Yes I think this is important” or “I don't think that is important for me”. Molly can type in questions she is wondering throughout the tool and at the end, it would print like a summary

of questions that could be taken to the doctor. Because sometimes when you are reading all that information, you forget what you were thinking about asking or what was important. And if that was all printed in the end you could just take it to the doctor and ask all those questions. And through what she had said was her concern and not her concern, the tool kind of came up with a summary that said based on what you said, you are kind of leaning this way or that way. Not that she would have to follow that, but it would be helpful. She is also able to highlight different information that is more important to her and rate how important things are to her like through using a rating scale or something. Because depending on whether you are regular CAH or salt waster, somethings will be more important or urgent for you than others. Molly would also find it helpful if the app could be shared with other doctors who don't know what CAH is or what to do in emergency situations, like when she is up north. But really, what is helpful for molly as a mom, is that there is a way to connect with other families who have already gone through the surgery. Using the PtDA, Molly feels more informed, a sense of relief, and less stressed. She feels more supported, not as much as alone, especially if she can talk to others who have gone through the surgery.

### **Bob (Father of child with virilizing CAH)**

Bob is a healthcare practitioner. So, he knows a little about CAH but not a whole lot about it. He just had a kid and found out that the baby had CAH. The endocrinology team told him to go the website for more information about the surgery. It would be sort of a decision-making tool and to learn about the disorder: what it entails and what happens in the future, how the family can deal with it. You can use your smartphone to get access to it. There would be some parts to it that would be private. Most of it would be general information so that everyone can access. But some part of it would be a login, sort of like a mini Facebook within the app, where you can communicate with other people. So, their profile would say maybe the name and if it was the parents, the age of their child. So then maybe you could personal message the other parents just to see if



they have an older child or something. You can discuss with them, ask them questions. They might be able to give you information about things like surgery. It would be quite a visual website, it would be a lot of information, but there would be pictures and no videos of surgery because that would scare people. But videos about information would be good. And if we are including information about stories about from parent experiences, it should be just the facts, not the opinions. So, nothing like, “Oh this was terrifying, I would never do it again”. Because Bob doesn’t want their opinions to influence his decision making. He wants them to be neutral. And if there are people that are not very nice on the website, then the administrators and users should be able to block them, just like in Facebook. And in the end, it would help you to make the decision for surgery. But it is also something like a life long tool that you can keep going back to it and seeing how the disorder will take you through life. The doctor should come to talk to them about the decision aid and answer any questions they have about it. The decision is not made immediately after looking at the tool, but it is something that provides supplementary information in addition to talking with their doctor to make a decision.

### **Annette (Child with virilizing CAH)**

Annette is a ten-year-old female who is in grade five. She has two parents and she lives in a rural community of about 5000 people. She is middle class and she wants to know more about her condition that she was diagnosed with. Annette goes to her endocrinologist regularly and he is the one who tells her that she has CAH. The endocrinologist tells her that there is an app we have made for CAH patients. He logs on to a tablet and shows her and her parents how to use the app. Annette and her parents go home and they are looking through this app. When you log on, you can put in that you are a ten-year-old girl, that you are not a salt waster, and the location. From that the app will direct her to a page that will describe CAH, and support groups, and information directed to a specific age group and level of condition. As she grows, the app will direct her to more

advanced things. For example, for 30-year old's, it will say like, if you got pregnant and stuff like that, it will grow with her. In the app there is a kid's section as well as a parent's section for parents. For adults, there could be videos for the surgery, that a kid probably wouldn't want to watch before she actually has surgery. So, the parents can explain it to their child as well, if the child has more questions than the app actually answers. The app will help them too. The app should also have stories about people who have had surgery, be they younger or older and what their life looked like after. For example, with X who had two surgeries, ten-year-old Annette will see that anecdote and go oh, maybe I will need to have two surgeries as well. Then she goes back to this doctor, the endocrinologist, after using the app. And she is able to ask, with her parents, questions to him if she is confused about anything in the app or if she has made decisions about surgery or stuff like that. She has surgery and she lives a happy life. She is satisfied by the app and her parents feel good.

### **John Smith (Pediatric Urologist)**

John is an associate professor at an urban, big-city academic center, with a catchment area of 2 to 10 million people. He has been in practice for ten years after doing fellowship training that specialized in this kind of genital reconstruction. He has been working consistently with the CAH population because the cases come to him as an expert. So, he has experience. He is a member of a multidisciplinary team.

Patients will initially have access to this decision tool when they come to see John. This will be presented to them while they wait when they come into the clinic - there everything is introduced to them. They will have time to read and get familiar with the decision tool. The decision tool would be interactive. It is aesthetically pleasing, it would have colours and not be very boring. When the decision aid talks about surgeries, it would have pictures, and maybe testimonies from both sides, making sure not to bias patients (either by using various

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patients' testimonies from the clinic/hospital or from societies for and against the surgery). The patient decision aid would have the probabilities of the various outcomes. If you click the percentages and probabilities [tab or page], they are presented in terms of pie graphs or visually. And the probabilities go more in depth, if you click one it magnifies to be more detailed. At the end, the patient decision aid summarizes things and mentions the pros and cons of both options. And then John will come back in to the room and try to answer their questions, and go over some points, explaining things and showing details and sharing his experience. Mainly, John answers their questions because most families have a lot of doubts. This would be a lengthy appointment, presumably at least half an hour to an hour.

And then this family would go home and think and discuss and reflect upon what is in the aid, what they read, and what was discussed in the clinic. They would use the aid at home. And then they would come back to the follow up which would be at least half an hour again. They would come with more questions and leaning towards a decision. John can then proceed with one of the two streams [i.e., options for treatment].

If, using the tool, the family decides something that is against John's principles or intentions, he still has the opportunity to present his data and experience during the follow up appointment and tell them this would be what he would advise. But he has to respect what the family decides or if they don't change their decisions. In the end John doesn't feel frustrated that the family didn't follow a specific path because using the decision aid they were provided with a lot of information that helped inform them in choosing that alternative option or the one they think is based better on their values.

At the end, for the other doctors, nurses, social workers, fellows, and residents in John's team who are also using the same decision tool, the aid would be very helpful by providing very consistent information, so that everybody is on the same

page. This is especially important for other services that are talking about surgery at some point. Without knowing it and what it entails, talking about the surgery is difficult. With the decision aid they would have the resource to provide the same information [as the surgeon], so this improves the credibility of the organization because they don't have different information that would create confusion and uncertainty.

### **Ben the Endocrinologist**

In Ben's experience they get their act together and have a joint clinic where the endocrinologist and the urologist and the social worker and the psychologist, and the geneticist, and maybe the gynecologist, are all seeing the patient at the same time. Where its a team approach rather than isolated clinic visits and referring on to the next expert. Where perhaps this clinical decision aid can help all the team members answer the families questions the same way in the moment.

But as it stands, the story is that he sees a girl who is just born with virilization, he highly suspects CAH. Ben confirms CAH. It is salt wasting. He starts medical treatment and calls urology or sends an urgent referral to urology to see this family for surgical management down the line. He speaks to the family and explains to the family in his own way what CAH is. He gets them on board for the medical therapy. He answers to the best of his ability the surgical questions, deferring the majority of them to when they see the surgeon. [The conversation Ben has when priming the family is:] “This has probably been a long clinic visit that we’ve had together. And I’ve shared a lot of information about how we are medically going to take care of your child and to keep her safe and growing well. That is my role as a doctor. And I’m sure you are going to have a lot of questions about that. We are going to be seeing each other very very frequently because a lot of these things that we prescribe, the dose needs to change as your daughter grows. But the other part of it, which is something that you brought up, is the appearance of her genitalia, and I’ve explained to you why the genitalia look like

this. And your questions to me were whether there was something we could do about this. There is an expert and he is a urologist, that is a surgeon and he can help girls with CAH and virilization have a more typical female appearance, so I am going to refer you to that surgeon, and what I do know about that surgeon is that in his clinic, he educates families and patients about their options. But also, to help you to come to a decision that you are all comfortable with, he, with the help of other experts in the field, have developed an electronic tool that you will have the opportunity to interact with to make that decision.” The urologist answers the questions, they interact with the decision aid, they make the decision, and have the surgery. The family is happy, and the patient continues to see Ben for hormonal adjustments. He supports the family pre- and post-operatively. And he sees this girl grow up into a wonderful teenager.

### **Sarah (Endocrinology Fellow)**

For Sarah, this is actually really hard because as an endocrine fellow, she would probably not be in a position to provide the appropriate surgical options for the families. And that is why she defers to the specialist and refers to urology. Similarly, the urologist would not tell the hormone story to the family, “you need to replace x this often”. But, as an endocrine fellow, Sarah’s patient would have a diagnosis of CAH. They would come to clinic for the first time. And she would talk about the, first and foremost, the most important thing is the medical hormonal aspect of treatment. And then, what she would say is, Dr. Urologist will speak to you about the surgical options about CAH. Sarah doesn't yet know, if at that point, they would provide the PtDA for preparation for the appointment with Dr. Urologist. That is an option, absolutely. Sarah does see the value in them getting the tool ahead of time so that they can kind of going through it and have questions for the consultations. Sarah thinks she would have to weigh the family anxiety. If they are already overwhelmed with all the hormonal information, presenting something else at that visit might be more anxiety provoking. They are going to have a lot of questions when they see the PtDA. So that might be better

addressed by the urology team of specialist, surgeon and nurse practitioner. Certainly, if it was a link to the PtDA, Sarah could provide that resource. But in terms of going through that information with them, Sarah is not poised to do that. Sarah would make a referral to the urologist and other specialists. The patient goes to them and makes an informed decision because the specialist have given him/her the nitty gritty in terms of, here is the risk and benefits of each procedure, now make the decision. That is the most responsible way of going through things because those specialists are well versed with the literature and have hands on experience. But Sarah supports them through that process, she is not completely removed. However, she doesn't interject in the surgery part of the decision making.

### **Shirley (Child Life Specialist)**

Shirley is a child life specialist working in the urology clinic. There was a patient that came in for consultation for surgery. The urologist presented the surgery options for the family. They were undecided at this point because it was still new and fresh in their mind. Therefore, the family was basically told that they could speak to a child life specialist about any questions or concerns that they have about making a decision. And the child life specialist was able to come in and talk to them, or she was called later on when they were told to come back to clinic. The family was presented with the option of looking at the decision aid, having a link or app that they could go on for more information. Then they came back to clinic. The nurse practitioner or child life specialist met with the family and gathered some of the questions they may have from the information that was presented to them in the decision aid. And then the urologist was able to come in and talk to them and answer some of those specific questions. And they would come back to clinic if they had any further questions. It would probably be a couple of visits that they would have to have. For consent. If they decide to do surgery, there would be fewer visits before the surgery since the urologist could consent them quicker. But if they decided to wait, and they had more thinking to

do or they wanted someone to talk to the child about the surgery and prep them for it, the child life specialist could do that as well. There are many obstacles or things that could come into play. Ultimately through the decision aid, they will have gotten the preparation they needed to move forward in making a decision. They think and feel that it was a useful tool that helped them summarize their thoughts and feelings around making that decision around the surgery. Hopefully it will bring about questions and clarifications that they will ask or need.