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Multi-Stakeholder Opinion Statement on the Care of Individuals Born with Differences of Sex Development: Common Ground and Opportunities for Improvement

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Abstract
Background: In the last 15 years, the care provided for individuals born with differences of sex development (DSD) has evolved, with a strong emphasis on interdisciplinary approaches. However, these developments have not convinced some stakeholders to embrace the current model of care. This care model has also paid insufficient attention to socio-cultural differences and global inequalities. ***Summary:*** This article is an opinion statement, resulting from in-depth discussions and reflection among clinicians, patients, and family support organizations based in the USA and Europe, where we seek areas of common ground and try to identify opportunities to further develop resources. The product of these conversations is summarized in 10 panels. The corresponding sections provide additional discussion on some of the panel items. ***Key Messages:*** Participants identified areas of agreement, gained a deeper understanding of the reasons behind disagreements on certain matters, and identified the necessary steps to foster future consensus. We offer preliminary recommendations for guiding clinical management and resource allocation. By promoting a broader consensus, we aim to enhance the quality of care and well-being for individuals of all ages who have a DSD.

Introduction

In recent years, there have been ongoing efforts to modernize and improve medical, surgical, and psychosocial care for individuals who have differences of sex development (DSD). However, controversy has only increased, and viewpoints regarding what constitutes good care in this context currently seem to be diverging, rather than coalescing.

Healthcare, historically reliant on simplified notions of normality, now increasingly acknowledges the influence of evolving cultural dynamics and scientific progress. In parallel, there is a growing commitment to respecting individuals within the context of their family, culture, and religion. This approach seeks to provide more inclusive and patient-centered care that values diversity and recognizes the importance of cultural and social factors in health outcomes.

Through this document, we seek to engage a wide range of stakeholders, including patients and their families, clinicians, advocates, as well as human rights activists and policy-makers. We strive to prevent or minimize polarization, foster meaningful dialogue, discover areas of agreement, and identify gaps in current clinical knowledge or deficiencies in practices. Our goal is to offer preliminary recommendations for guiding clinical management and resource allocation. By promoting a broader consensus, we aim to enhance the quality of care and well-being for individuals of all ages who have a DSD.

In this article, we use "DSD" to refer to a set of congenital conditions that come to medical attention based on the presence of atypical genital appearance at birth or sometimes during puberty, requiring medical investigation, or of a discordance between one's typical-looking genitalia and that individual's karyotype [1, 2]. We do not intend for the terms "DSD" or "intersex," used here as medical terms, to carry any implications for the identity or humanity of individuals sharing these biological or physical characteristics. We adopt the principle of "person-first" language, to avoid implying that, for individuals who have a medical condition, their condition is part of their identity.

Methodology

In order to understand and address prevailing controversies surrounding the clinical care of individuals who have a DSD, and in light of developing legislation that affects such care in several countries, healthcare professionals from various disciplines, together with patients and representatives from support groups, initiated online discussions in the Fall of 2020. The objective of these discussions was to explore what might be considered elements of optimal care for individuals who have a DSD and their families. Recognizing the predominant Western representation of participants, it was acknowledged that, even within this group, there existed a wide range of differing opinions regarding this matter. Therefore, it was deemed essential to first clarify these perspectives before engaging stakeholders from diverse sociocultural or religious backgrounds. Likewise, due to the importance of involving intersex activists and human rights advocates as integral partners in the debate, it was considered crucial to crystallize viewpoints within this group first, before proceeding to next-level discussions. To ensure focused and meaningful deliberations, a limited number of professionals, patient advocates, and experts with prior work and international recognition in this field were specifically invited, enabling in-depth and thoughtful reflections on the matter at hand. The topics discussed did not focus on medical management per se. To accomplish that, a distinct methodology involving a systematic literature review and formal Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) process

[3] would be required as a step toward development of clinical practice guidelines. Instead, the group discussed the prerequisites for delivering optimal care and the setting that fosters such care. Discussions took place in a virtual mode, using the online meeting platforms MS Teams and Zoom, and were complemented with exchange of ideas through group e-mails.

The product of these conversations is summarized in 10 panels. The corresponding sections provide additional discussion on some of the panel items. Participants were able to identify areas of agreement, gained a deeper understanding of the reasons behind disagreements on certain matters, and identified the necessary steps to foster future consensus.

Terminology: Balancing Overarching Terms That Embrace Variation while Leading to Precise Medical Diagnoses (Panel 1)

The initial term "disorders of sex development" was adopted in 2006, but has since received considerable criticism [1]. First, the term "disorder" has been interpreted by some as suggesting a universal need for surgical intervention and may also be viewed as stigmatizing [4]. Second, some congenital adrenal hyperplasia (CAH) support groups have expressed strong opposition to the use of "DSD" for individuals who have 46,XX CAH because many of their members do not identify with it (or with the alternative term "intersex") [5]. Likewise, in a survey of the US-based androgen insensitivity syndrome-DSD support group [for individuals who have androgen insensitivity syndrome and related conditions, now called InterConnect], members preferred other umbrella terms, such as "variation in sex development," "difference of sex development," or "intersex" [4]. Over time, the term "differences of sex development" has been adopted by the clinical community when talking to patients, and this alternative phrasing is increasingly appearing in the medical literature. However, it is not widely used outside the clinical setting.

From a biomedical perspective, DSDs are developmental congenital conditions that result from the atypical development and/or function of one or more endocrine organs, most often the gonads and sometimes the adrenal glands. Substituting the medical term "DSD" with an identity-based term or a broader umbrella term like "differences or variations of sex characteristics" risks causing confusion or can be misleading. Moreover, it may be harmful to certain patients by diverting attention away from their specific psychosocial and medical requirements [2]. In addition, it may lead to reduced access to and/or reimbursement of healthcare. The term "variations of sex characteristics" evokes the full spectrum of physical genital appearances that exist and that contribute to the uniqueness of each individual. Variations of sex characteristics can be congenital or acquired, may or may not be associated with medical conditions, and may fluctuate over time, depending on the presence of genetic, hormonal, and environmental factors. Most individuals or patient groups prefer the specific name for their condition, if known, and clinicians are strongly encouraged to ask the patient/family what term(s) they prefer to use when referring to their/their child's medical condition [6].

Despite the limitations of an umbrella term, the 2006 nomenclature has been important and successful in many ways. First, it has allowed healthcare providers to move away from potentially stigmatizing terms such as

Panel 1: Terminology

Common ground and provisional recommendations
1 None of the currently used umbrella terms is acceptable to all stakeholders. When speaking to affected individuals and their families, we recommend using the name of the precise diagnosis, if known, and if an umbrella term is needed, to use the one preferred by them.
2 The existence of an umbrella term and common taxonomy is important as it helps delineate the conditions under consideration and to structure medical management, facilitate communication and access to healthcare, and enhance research and teaching.
3 Whichever terminology is used, the health and well-being of individuals who have a DSD should remain the primary focus of attention for all stakeholders involved in healthcare decisions.
Areas where further work, agreement, or research are needed
1 Further work is needed to identify an umbrella term that is acceptable to all stakeholders.
2 Clearer definition and demarcation of DSD (or any new umbrella term) are needed to avoid confusion with other conditions (which may occur frequently) and to avoid inflated incidence numbers.
3 Further work should investigate how prognostic parameters such as gender outcomes, fertility potential, and tumor risk can be incorporated into the current taxonomy.

"hermaphrodite" and "ambiguous genitalia." Second, the associated taxonomy provides insight into the genetic background and the pathophysiology of the various conditions, and the umbrella term "DSD" serves as a useful placeholder prior to arriving at a precise diagnosis. Third, an umbrella term remains indispensable for individuals for whom ultimately no genetic diagnosis can be identified, and it facilitates the formation of specialized teams to offer comprehensive care to address common needs that affected individuals and families may experience.

Registries: Assessment of Long-Term Outcomes and Insights in DSD Care across the Globe (Panel 2)

The new DSD terminology has promoted the development of multicenter collaborations in large international networks and registries such as the International Registries For Rare Conditions Affecting Sex Development & Maturation (the former i-DSD registry) (Europe) and the DSD-Translational Research Network (USA), and their expansion on a global scale [7]. These registries allow for detection of geographical and historical trends and analysis of outcomes of very rare diagnoses, and they can provide tools for benchmarking across centers [8]. The importance of these registries in the development of global collaboration, and the promotion of high-quality clinical research, that has resulted in substantial new insights in clinical outcomes of several DSD conditions cannot be underestimated. However, current registries have several limitations. They usually require manual input of data by trained staff. As they were established relatively recently and involve mainly pediatric centers, long-term outcome data into adulthood remain scarce. Moreover, they have mainly been designed to capture medical and surgical outcomes, and to a much lesser extent psychosocial outcomes and quality of life data, for which there are a large variation in assessment methods and a clear need to identify a core set of relevant patient-reported outcomes. Such data would become particularly meaningful if biochemical parameters, e.g., on the adequacy of hormone therapy, were included. Finally, centers from non-Western societies are greatly underrepresented in these networks, and studies from other parts of the world and other cultural and religious spheres are greatly needed to better understand the natural progression of the various DSDs, and the different socio-cultural backgrounds that guide patient care in non-Western societies. This underscores the need to expand and globalize the current registries and to ensure the availability of appropriate expertise and resources for the collection and analysis of such data.

Some (mainly Scandinavian) countries have established nationwide registries with data linkage across different registries that, in combination with accurate record-keeping, have led to an extensive network of longitudinal registries covering entire populations. Here, health data are collected through routine and automated processes which

Panel 2: Registries

Common ground and provisional recommendations
4 We recommend that centers offering specialized care for individuals who have a DSD actively participate in the development and maintenance of large, high-quality international registries, and in benchmarking initiatives.
5 These registries need to extend their reach to countries with more limited resources and diverse socio-cultural backgrounds to understand how later presentation to medical care and socio-cultural variations influence medical decision-making and clinical care practices. By doing so, these registries can facilitate more comprehensive and contextually sensitive approaches to patient care.
Areas where further work, agreement, or research are needed
4 Standardization of assessment protocols and medical records is needed to facilitate research across registries.
5 Clinicians worldwide have encountered difficulties in implementing management guidelines developed in Western societies within different cultural contexts. Despite the inclusion of patient data from various continents in large international registries like i-DSD, further research is required to facilitate the adaptation of management recommendations to diverse cultural backgrounds, enabling healthcare professionals to provide more contextually appropriate care.
6 Registries can provide tools for benchmarking center performance, but the most relevant and evidence-based parameters for this remain to be defined.
7 Stable sources of funding need to be identified for the creation, maintenance, data security, and quality control of registries.
8 Registries need to increase benefits for affected individuals who take part in them, e.g., by providing the enrollees with access to research results and to aggregated data on core outcomes. Registries can also be leveraged to facilitate secure interactions with peers worldwide.

have greatly enhanced epidemiological research and avoided manual data procuration, leading to a much better data quality [9]. The objective of future care is to enhance the quality and accessibility of patient registries, while fostering international collaboration and upholding patient privacy and data integrity [10], and to establish robust procedures for obtaining informed consent (IC) from participants.

Interdisciplinary Care: Care for Individuals Who Have a DSD Should Be Provided by Specialized Interdisciplinary Care Teams (Panel 3)

Higher specialization of care and psychosocial support for individuals who have a DSD have been associated with better physical and psychosocial outcomes [11, 12]. There is broad consensus that centralized dedicated services, integrating medical and psychosocial care, and focusing on continuity of care across all stages of life, should be the primary approach. Additionally, there is a need for the prompt development of standards and measures that define high-quality outcomes to guide these services.

Necessary qualities of care teams may include that these teams serve a sufficiently large population to have state-of-the-art scientific knowledge of the conditions under scope, and that they function in an interdisciplinary manner in which each discipline can affect the performance of the other [13]. They should function in a patient- and family-centered way [14] and foster participation of the patient and family (as appropriate) in management decisions. Transitional care from pediatric to adult services should be available [15]. Comprehensive care further implies that these centers invest in resources and staff to communicate with the patients' many environments, including primary care, schools, and workplaces, as needed [16, 17]. Measures must be in place to overcome logistical and financial hurdles, e.g., through the implementation of telehealth consultations and online interdisciplinary expert meetings to discuss the most complex cases [18]. The European Union offers a virtual platform for European Reference Networks (ERNs) to discuss difficult cases among healthcare professionals in a safe environment and with respect to patient privacy, termed clinical patient management system [18]. Further development of these and other e-consultation and e-learning initiatives may increase opportunities for patients and caregivers from different geographic regions, including those working in low- and middle-income countries, to access highly specialized care [19].

Specialized centers that offer care for individuals who have a DSD should provide assistance to local providers, and systems are needed to recognize and remunerate these activities. Moreover, specialized centers should coordinate adequate training to the broad group of healthcare workers

Panel 3: Specialized interdisciplinary care

Common ground and provisional recommendations	
6	Referral of individuals who have a DSD to a specialized center is essential. Apart from offering optimal quality care, specialized centers should provide interdisciplinary leadership, training, and support to their referring network. The quality development of standards and measures for high-quality outcomes needs to be prioritized.
7	Even in countries where such specialized centers exist, healthcare systems are currently ineffective at ensuring that all individuals who have a DSD gain access to such care. Continued efforts should be made to ensure that patients around the globe have access to such centers and/or have their care directed and monitored effectively by specialized centers.
8	In spite of available guidelines and recommendations, inadequate or outdated practices continue to exist. Essential care, particularly psychosocial care, is often unavailable, insufficiently reimbursed, or otherwise inaccessible. Standards of care need to be developed and/or implemented by all providers who care for individuals who have a DSD.
9	Given the rarity of DSD conditions, and their heterogeneity in presentation, it is crucial that specialized centers participate in multicenter research protocols.
Areas where further work, agreement, or research are needed	
9	Protocols for assessments of quality of care should be developed that involve evaluation of healthcare team composition and performance, including the quality of communication and collaboration among team specialists and the degree of involvement of patients/families in clinical decision-making.
10	The establishment of quality criteria and officially recognized training modules for DSD needs to be prioritized and to result in effective auditing and benchmarking processes, ensuring standardized and effective care practices across different healthcare settings.
11	Sites unable to provide interdisciplinary care should develop referral relationships to sites that can. Measures should be in place that ensure access to specialized care for individuals living in remote areas.

active in this field. Such training should address the specific socio-cultural context in which children are brought up and adults live. They should also participate in the creation of transparent benchmarking and certification procedures. A first attempt in this direction has been the recent publication of "good practices" in the care for children who have a DSD [20]. However, currently, few clinical practice guidelines or quality standards have been defined, no official training programs for the delivery of quality care in the context of DSD exist, and no dedicated funding is currently available for such activities. It is also unclear what group has authority to define such criteria and to develop a meaningful certification process. Moreover, in the absence of specific procedures, clinics can adopt a quality label (e.g., self-identification as "Center of Expertise") without going through an official benchmarking or assessment procedure, resulting in a broad variation in offered services and specialties. To overcome this hurdle and to provide guidance for member states on the official recognition of specialized centers, the European Union Committee of Experts on Rare Diseases (EUCERD) issued in 2011 a set of quality criteria that define Centers of Expertise in rare diseases which may also serve as a model for comparable networks and regulatory authorities outside the EU.

Genomics: Extended Genetic Testing Fosters Improvement of Clinical Care and Should Be Made More Widely Accessible (Panel 4)

Alterations in more than 100 genes are currently known to cause syndromic and non-syndromic forms of DSD, and this number continues to increase [21]. In countries with more limited resources, the karyotype, in combination with a baseline or stimulated hormonal profile, remains the cornerstone of the diagnostic pathway for a DSD [22]. In countries with sufficient access and financial resources, high-throughput sequencing has become one of the first tests performed, as it can quickly provide a definitive genetic etiology for many individuals presenting with a DSD [23]. Establishing a genetic diagnosis can lead to more precise, knowledge-based clinical management (e.g., regular screening for proteinuria in individuals who have been diagnosed with Frasier syndrome). It enables genetic counseling for heritable forms of DSD and may identify fertility preservation options (e.g., in women who are at risk of primary ovarian insufficiency associated with *NR5A1* variants).

Genomic testing may increase the psychological burden for some and is therefore not universally perceived as beneficial, and it raises important challenges. Work remains to determine the implications (e.g., for gonadal function and tumor risk) for new genetic diagnoses. Furthermore, despite scientific advances, over 50% of individuals who have a DSD other than CAH remain without a genetic diagnosis, many of whom carry so-called variants of unknown significance, for which there are insufficient data to determine whether the genetic variant is the cause of the individual's DSD. Determining the pathogenicity of such variants is challenging, and functional testing is typically not feasible in a clinical setting. Therefore, we recommend the publication of detailed phenotypic descriptions together with genomic data in public databases (e.g., https://www.ncbi.nlm.nih.gov/clinvar/) and appropriate patient registries.

Panel 4: Genomics

Common ground and provisional recommendations
10 Obtaining a diagnosis at the molecular genetic level is critical to truly understand the etiology of most DSD and, in turn, determine which diagnoses require unique guidelines to provide optimal care.
11 When available, high-throughput sequencing should be offered as a first-line diagnostic test. If a specific diagnosis is already suspected, targeted gene sequencing can occur.
Areas where further work, agreement, or research are needed
12 The role of the clinical geneticist and genetic counselor in the interdisciplinary team needs to be defined more precisely. These providers can educate individuals and their families about the implications of genetic results (e.g., on gender development and on the potential need for surgery or other interventions). They can also dispel misconceptions (e.g., that the karyotype per se determines sex assignment or gender identity). Such education can assist individuals and families in coping with the condition and facilitate genuine participation in management decisions and consideration of the full range of available options.
13 Genomic approaches should become accessible around the globe. This will require willingness and resources to establish the required networks, to train local laboratory staff, and to permit international exchange of biological samples and clinical data for centralized analysis.

Alterations causing DSD occur in multiple genes, but each gene explains the findings in a relatively small number of individuals. Conversely, for a given genetic cause, phenotypic variability can be wide. As a result, data are limited for explaining phenotypic variability and long-term outcomes. Since most DSDs are rare, we recommend that frameworks for international collaborations should be created to overcome these hurdles. Engaging with colleagues working in low-resource settings and fostering international collaborations can play a crucial role in training local staff and promoting the creation of evidence-based algorithms that aid clinical decision-making, even in the absence of advanced technical facilities. Simultaneously, global sample exchange for genetic testing can aid in deciphering rare variants and establishing their frequencies across diverse ethnic backgrounds.

Sex Assignment, Reassignment, and Stigma (Panel 5)

In this section, we use the term "sex assignment" to refer both to registration of the "Sex" or "Gender" field on a birth certificate and the decision whether to bring up a child as a girl, as a boy, or in some other way. For the latter concept, some prefer the term "sex," arguing that the term "gender" should be reserved for an individual's self-reported identity of gender. Others prefer the term "gender" because how a child is brought up is a social rather than a biological issue. In this document, we use "sex assignment," but we acknowledge that terminology continues to be discussed and to evolve.

Most human newborns are registered female or male at birth based on their genital appearance and so entered in the birth registry. In rare cases in which the external genital appearance (or other information, such as prenatal sex-chromosome results or the anatomy of internal reproductive structures) does not result in an immediate declaration, the sex of the baby is assigned using diverse criteria which have changed historically [24].

Prenatal androgens are the most important determinant of external genital differentiation, but the specific androgens involved in the sexual differentiation of other tissues, including the brain, may differ [25]. Additional factors such as variations in androgen sensitivity and genetic factors may contribute further to inter-individual differences [26, 27]. The effects of prenatal androgen exposure on later gendered behavior have been shown to be strong, but less is known about the impact on later gender identity or sexual orientation [28].

In contemporary societies with ample medical resources, sex assignment seeks to minimize the risk of later gender-related distress and follows a complex diagnostic process [22]. This process focuses on the genetic and/or

Panel 5: Sex assignment

Common ground and provisional recommendations
12 The decision to bring a child up as a boy or a girl is based on the individual's specific diagnosis, anticipated developmental trajectory, and potential for sexual function and fertility and seeks to minimize needs for hormonal or surgical therapy. This decision should be considered provisional given that the child's gender identity emerges and evolves with time.
13 For most individuals and families, sex assignment occurs within a cultural context of a binary concept of sex. We recommend that the care team supports the family within this cultural context while simultaneously encouraging openness to the complexity of gender identity formation and supporting the exploration of other options such as deferral of an assignment, if desired by families.
14 If individuals who have a DSD have questions about their gender identity or gendered behavior/attitudes in relation to physical sex characteristics or sex assignment, this should not be viewed as a failure of prior decision-making, but as an opportunity to facilitate the individual's self-exploration and understanding regarding identity development.
15 To reduce bias, we recommend that care providers acknowledge cultural diversity within their societies and critically examine their own assumptions, attitudes, and expectations about gender, genital appearance, and sexual orientation.
16 We recommend that care providers assist individuals who have a DSD and their caregivers in exploring the child's gender identity and in understanding the relationship between the medical diagnosis and personal gender experiences.
Areas where further work, agreement, or research are needed
14 Further research is needed to understand the role of genetic and hormonal factors in the sex differentiation of the brain and in modulating the development of gender expression and identity.
15 The role of parental preferences and cultural influences in the sex assignment process requires further investigation.
16 The long-term effects of the assignment of a newborn or young child who has a DSD to the sex category of "undetermined" or "nonbinary," and of deferral of sex assignment altogether, on social adjustment and gender outcome, need to be investigated.

endocrine causes of the condition and their implications for brain masculinization or feminization. Additionally, it entails a comprehensive review of long-term gender outcome data, wherever it is available for the particular condition under consideration. Active involvement of families is crucial in making informed decisions during this process.

In light of the increasing diversity of gender identity expression, particularly among individuals without DSD diagnoses, many countries have incorporated additional sex- or gender-related categories on official government documents such as passports. Likewise, categories such as "indeterminate sex" or "X" are now being offered for newborns facing challenges in sex assignment due to atypical genitalia. However, the impact of such assignments on social adjustment and long-term gender outcomes requires further investigation.

The majority of individuals who have a DSD will develop gender roles and gender identities in line with their initial sex assignment [29]. Yet, the exploration of one's gender and the questioning of sex-based cultural norms are increasingly common, particularly during the period of pubertal development. Moreover, an increasing number of people in Western societies (with or without a DSD) identify as other than male or female (e.g., gender nonbinary) [30]. This reflects the growing awareness of diverse gender identities and expressions in contemporary society. People who have a DSD may be more likely to question their gender status because of atypical appearance of the external genitalia, atypical degrees and patterns of hair growth, gender expression which may be viewed as atypical for their culture, learning of having undergone genital surgery, requiring hormone treatment for the induction of puberty, learning of having a karyotype discordant with the registered sex, realizing one is infertile, or self-discovery of patterns of non-heterosexual romantic/erotic attractions. Yet, later patient-initiated formal gender change is uncommon, although more frequent in individuals who have a DSD than in the general population [29]. It may vary with the specific DSD diagnosis, the conditions' severity, and the initial gender assignment.

The birth of children with atypical external and/or internal genitalia can cause great distress and uncertainty for caregivers. A few recent studies have documented the existence of "intersex stigma" across societies, for all developmental stages and in all spheres of life [31–33]. Specialized teams providing DSD care should possess extensive experience in effectively reducing and otherwise managing stigma. Moreover, they should be proficient in counseling families about addressing gender-related questions or gender-related distress experienced by their child [2]. They should actively support individuals who have a DSD in exploring their gender experiences and to discuss gender-related questions and/or potential feelings of gender confusion or distress with the team. An individual's culturally non-conforming gender behavior and/or gender questioning should not be interpreted as an indicator for sex reassignment unless the patient has developed and maintained for a considerable period of time marked gender-related distress and the conviction that sex reassignment is necessary.

The Psychosocial Component of Interdisciplinary Care (Panel 6)

Although consistently stated that psychosocial care is an integral feature of DSD interdisciplinary care and is essential for positive outcomes [1, 15, 34], access to expert psychosocial management remains extremely variable and challenging for patients, their caregivers, and healthcare providers [20, 35]. A model that proactively focuses on primary prevention to promote wellness and positive psychological adaptation is deemed most appropriate for DSD. Unfortunately, many centers employ a reactive model in which individualized psychosocial services are sought only upon the medical provider's identification of distress or dysfunction.

Multiple factors may interfere with the integration of behavioral health (i.e., the promotion of mental health, resilience, and well-being) in the interdisciplinary model of DSD care. Patients, caregivers, and medical providers may be ambivalent or resistant to these services for many reasons: additional financial costs, mental health stigma, limited medical specialists' experience with behavioral health, or behavioral health being conceptualized as exclusively problem-focused rather than preventive in its approach. It falls to all team members to emphasize the critical importance of psychosocial support at the earliest possible stages. Perceiving physical features of the DSD as stigmatizing may result in overweighting the value of treatments appearing to "fix" a problem and may limit thoughtful consideration of potential reasons for avoiding such treatments [2, 36].

During ongoing management, it is crucial to systematically assess the needs of patients and their families. Psychosocial interventions in DSD may encompass evidence-based approaches for assessing psychological symptoms such as depressed mood or anxiety, but a broader range of intervention strategies may be required.

Panel 6: Psychosocial aspects

Common ground and provisional recommendations
17 Identification of a DSD, whether detected in the newborn period, adolescence, or adulthood, commonly presents a psychosocial challenge for patients and their caregivers.
18 Attention to the psychosocial aspects of DSD is central to interdisciplinary care, which should focus on psychological well-being and adaptation.
19 The need for targeted psychosocial services – for the patients and their caregivers – should be assessed regularly until adulthood, with any intervention(s) guided by systematic evaluation of patient and family understanding of the condition and its implications, and the values that they attach to these consequences. Specialized centers should also provide such services to adult patients and their partners.
20 Consistent communication between providers, patients, and their caregivers is a key element of patient- and family-centered care. For this reason, all members of the healthcare team require familiarity with the psychosocial and psychosexual aspects of DSD to avoid confusion or misunderstandings regarding, e.g., terminology, factors contributing to gender development, and the process of shared decision-making (SDM).
Areas where further work, agreement, or research are needed
17 A core set of psychosocial/psychosexual measures for assessing and monitoring patient needs remains to be established. Given that families typically provide the primary source of support and care to the child, measures to identify psychosocial risk factors affecting households are also needed.
18 A high priority for research is to develop interventions to promote positive psychosocial and psychosexual adaptation. These interventions include counseling of patients and caregivers regarding the condition and its implications, prevention of negative body image, negative self-concept, internalized stigma, and modeling strategies for sharing information about the condition with others that protects privacy while avoiding secrecy.
19 Further work is needed to establish core requirements of educational training and clinical experiences of team members delivering DSD psychosocial care.
20 To create support for appropriate investments, the characteristics of the required behavioral health workforce and adequate availability of these DSD team members need to be investigated.

These should focus on decreasing shame and (perceived) stigma through education about sex development and the medical condition under scope and through facilitating discussion of the condition with extended family, close friends, and intimate others [36]. There is currently no consensus regarding core psychological measures needed to monitor the adjustment and well-being of the individual (and their caregivers) affected by a DSD. This warrants creation of a task force charged with developing such core outcome measures, ideally with input from a wide range of stakeholders including patients, parents, and providers.

Within the team, there is an important role for a dedicated team member who can help individuals who have a DSD and their families to understand and engage with the complex information that they receive, which is vital if they are to make informed decisions around treatments offered. Although this role is currently poorly defined, aspects of it are in many teams probably addressed by a patient navigator, a specialist nurse, a psychologist, an experienced social worker, a family support counselor, or any other team member. This person can help families to develop an understanding or expectation of how the DSD may impact their family and social lives, to express emotions in a safe and non-judgmental environment, and to have some understanding of what may happen at future milestones. By bridging the family with the healthcare team as well as their micro-environment, this person can reduce the chances for stigmatization and further promote acceptance of the condition. Importantly, acceptance and openness of patients and families can be influenced by their cultural and religious backgrounds and values. This team member can help all stakeholders to recognize these factors and, as such, promote long-term well-being of the individual and family within their environment, wider social network, and society as a whole.

The educational training and clinical experiences of behavioral health providers that are members of the DSD interdisciplinary team remain to be delineated. Gaps in formal education and clinical training specific to DSD represent a barrier to psychosocial services being adequately represented, and, to date, very few behavioral health providers have chosen to specialize in this field. Formal learning opportunities, such as the i-DSD training school, provide excellent opportunities for behavioral health providers to learn about the full range of topics – from embryology to genetics and genital

surgery – relating to DSD. Until formalized training opportunities become more widely available, there are emerging networks of behavioral health providers in North America and Europe that provide clinical mentorship in DSD, such as the Psychosocial Workgroup of the DSD-TRN, the DSD Special Interest Group of the Society for Pediatric Psychology, the Psychosocial Studies Intersex–International (formerly Euro-PSI), and the European-based Network of Professionals in Psychosocial Care in DSD.

Finally, the psychosocial component of healthcare in pediatric and adult services is often under-resourced [20, 35]. To define the precise needs and create support for appropriate investments, a survey assessing the required personnel, time investment, and financial resources to support an interdisciplinary team's behavioral health workforce is strongly recommended as a first step.

Informed Consent Builds upon Shared Decision-Making (SDM) (Panel 7)

Medical management decisions are made with the primary consideration of what is deemed to be in the best interest of the individual. This assessment incorporates scientific evidence, as well as the values, preferences, and beliefs of the individual, their caregivers, and the broader cultural and religious context. Additionally, the experiences of healthcare professionals and information about the potential outcomes associated with different options are taken into account to guide decision-making. For individuals with the same condition, treatment choices can differ significantly, making a formal SDM process crucial, particularly where controversies exist regarding various treatment alternatives. SDM empowers patients and their families to actively participate in the decision-making process, considering their unique situation, and the available evidence to arrive at the most suitable treatment plan [37].

SDM has been defined as "an approach where clinicians and patients share the best available evidence when faced with the task of making decisions, and where patients are supported to consider options to achieve informed preferences" [38]. The use of patient decision aids, which can take the form of web-based programs, videos, or pamphlets, can support patients and families to make choices in line with their personal values and preferences [39]. Ideally, such tools are developed jointly by multiple centers and stakeholders and endorsed by relevant professional societies, to ensure that all available options are represented and to avoid bias toward clinicians' preferences. Examples of patient decision aids and their certification can be found at Patient Decision Aids – Ottawa Hospital Research Institute.

Panel 7: Informed consent

Common ground and provisional recommendations
21 SDM is the crux of patient- and family-centered care. The member of the interdisciplinary DSD team delivering psychosocial care is well positioned to serve as a decision-making facilitator, but other members of the team can also assume this role.
22 IC documents should list in a transparent and detailed way the various perspectives discussed during the SDM process, and the person(s) signing the IC document should confirm that they have been fully informed about all individual items.
23 All information should be shared with the child in an age-appropriate way, and active involvement of the child in the decision-making process at the earliest possible stage should be encouraged. Nevertheless, caregivers and providers should be mindful that children's values, opinions, and decisions can change substantially as they mature into adulthood.
24 Throughout the SDM process, professionals should be aware of the implicit biases in data interpretation that are inherently present in each team, which may be based on multiple factors, e.g., personal experiences and socio-cultural background. Teams should put maximal efforts in minimizing such biases, through self-reflection and transparent team discussions, in order to inform families in an unbiased manner.
Areas where further work, agreement, or research are needed
21 Research is needed to understand parental attitudes and responsibilities toward SDM in the context of DSD, specifically related to high-impact and/or controversial procedures, and how they are historically and culturally influenced.
22 In various countries, agreement is needed on how to formally include the process of SDM in usual care. For example, healthcare insurance systems can incentivize providers to include written documentation of appropriate SDM for interventions in patient files. Auditing programs could be implemented at the governance level of the healthcare organization. The above requires urgent investments in the creation of training programs for SDM coaches and for obtaining appropriate IC.
23 Further work should include the development of minimal requirements of IC documents, specifically for summarizing high-impact procedures.

SDM ensures that the patient and, for minors, the patient's legal guardians are capable of making an informed and voluntary decision. It can best be guided by a team member who oversees the perspectives of the different disciplines and stakeholders. The process should be complemented with a careful consideration of the weight of all patient and caregiver values related to a given option, for that individual patient and family. For parents, it is important to realize that decisions that seem to be in the best interest of their child during childhood may not necessarily align or may even contrast with important values when their child has become an adult. For example, while children and young adolescents may favor conformity and undisturbed relations with peers, young adults may prioritize authenticity, autonomy, and freedom [40]. Age-appropriate information and involvement of the older child in therapeutic decision-making should be encouraged at the earliest possible stage. The age and maturity of each child, including the child's social and psychological development, family values and health literacy, previous health experiences, and the nature and risks of the treatment are all critical to assess a child's capacity to provide informed assent. Currently, no standardized and objective assessment tool for this capacity exists.

Despite strong evidence that SDM, and its facilitation through patient decision aids, is effective in promoting higher quality decisions, there is equally clear evidence that there are many barriers to its implementation in usual care, such as the lack of trained personnel, resources, and time [41, 42]. Implementation research to ensure robust SDM by interdisciplinary teams is urgently needed.

The SDM process ends with obtaining IC. The IC document should accurately reflect the diverse perspectives that were considered during the SDM process. This ensures that the document accurately represents the informed choices made collaboratively by the patient, their family, and the healthcare team, considering the individual's (or caregivers') values, preferences, and the available information. Prior to giving IC or assent for treatment, patients and/or their caregiver proxies need sufficient time to process all information and clarify any uncertainty. Obtaining IC is an essential component of care and is a legal obligation for all medical and surgical interventions as well as for performing medical research.

Controversies Surrounding Elective Genital Surgery in Children (Panel 8)

It is globally recognized that care pathways for children born with a genital difference should above all emphasize the provision of psychosocial support, in order to enhance acceptance and positive psychosocial adaptation. However, the extent to which this recommendation is consistently implemented, even in resource-rich countries, remains unclear. Additionally, despite apparent increased acceptance of variations in sex development, the concept of binary sex development remains deeply rooted in most societies. This makes the child and their family vulnerable to stigmatization and may pose challenges to identity development [2].

Ethical concerns rightfully exist concerning elective surgical procedures performed prior to the age of consent [40, 43]. Notwithstanding the motivation to enhance acceptance and/or reduce the risk of stigmatization of a child who has a genital difference, these procedures have the potential of violating the child's right to bodily autonomy.

Some controversies may also stem from certain hormonal treatments applied in childhood. A systematic review of surveys on patient preferences regarding the timing of genital surgery suggests, despite many methodological difficulties, that a significant majority of individuals who have 46,XX DSD and a smaller majority of those who have 46,XY DSD support elective genital surgery before the age of consent, including those who had later diagnoses and therefore underwent surgery in adolescence or adulthood [44]. Taken together, outcome studies yield a very complex picture of potential beneficial as well as harmful long-term effects and unsatisfactory outcomes of elective genital surgery in childhood. Limitations of these studies include small sample sizes with likely participation bias, and lack of comparison groups that had no surgery or deferred surgery. By definition, long-term studies often include surgical techniques that have become outdated. There are as yet no studies reporting on alternatives to surgical therapy, including psychosocial therapy [36, 45]. Studies from non-Western societies highlight the substantial impact of the cultural and spiritual context on how individuals who have a DSD shape their lives and manage sensitive aspects of their DSD, such as infertility, genital differences, and stigma [31, 32, 46]. Also, within the USA and Europe, medical professionals from our group have anecdotally experienced large differences in attitudes and coping abilities among individuals who have a DSD, their families, and the communities in which they live. This, in combination with the dearth of long-term outcome data on individuals who did not have surgery in infancy or early childhood, explains why many medical professionals are currently uncertain if growing up with a marked genital difference is, in all circumstances, in the best interest of a given child. Parent representatives in our group emphasize their

Panel 8: Genital surgery

Common ground and provisional recommendations
25 Any decision, whether or not to surgically modify the genital appearance, at any age, has the potential to irreversibly affect a person's physical integrity, sexual enjoyment, and/or psychological well-being.
26 Clinical care should prioritize psychosocial support for all individuals who have DSD, and their caregivers, to help them develop confidence in accepting a genital difference and/or a genital appearance that is atypical for the karyotype.
27 The concept of preservation of physical integrity as the sole principle guiding care in childhood insufficiently addresses the needs of patients and their caregivers, is not uniformly accepted by affected adult individuals, and requires more nuance.
28 The reduction of stigma has been a major aim of early genital surgery, but such stigma has also been said to be exacerbated by attempts to alter the body.
29 Enacting legislation that universally prohibits elective genital surgery in childhood without considering scientific evidence and the individual needs of each child and their caregivers is a matter of concern. Such a ban disrupts the fundamental principles of medical practice, which aim to provide individualized care in the best interest of each child. Additionally, there is a risk of unintended harm to patients. In cases where the appropriateness of elective surgery is uncertain, alternative measures such as bioethics consultation can be considered as alternatives to a ban.
Areas where further work, agreement, or research are needed
24 Further research is critically needed to understand the long-term outcomes of individuals with atypical genitals who do not have surgery in infancy or early childhood.
25 Strategies and psychosocial therapies need to be developed to reduce the potential negative psychosocial impact of genital variations, and studies are needed to assess their effectiveness.
26 Comprehensive mechanisms need to be developed to ensure that unnecessary, outdated, or otherwise inappropriate surgery is not performed, and that, when indicated, genital surgery is undertaken only by specially trained and highly experienced surgeons, working within the context of an interdisciplinary team.
27 Tools are needed to assess, on an individual basis, at what age a child or young person is capable of providing an informed opinion, informed assent, or IC with specific regard to medical or surgical interventions that impact the individual's autonomy.

fundamental role as a full member of the decision-making team, but also question the ability of parents to make decisions on behalf of their child when there is still so much scientific uncertainty, controversy, and inter-individual variability.

For the above reasons, all co-authors of this group are concerned that a general legislative ban on elective genital surgery in childhood in the context of DSD would not be in the best interest of all children. However, many also felt that the current situation, where not all children and families have guaranteed access to expert services, and outdated practices continue to exist in certain centers, is unacceptable. This may lead some advocates to perceive legislation that prohibits surgery as the only viable option. All co-authors agree on the need for a holistic response to this complex situation. This can have various forms, according to the specific needs, but several general principles apply.

First and foremost, the cornerstone of healthcare for all individuals who have a DSD should be to promote understanding and acceptance of the condition; to develop inclusive language that embraces genital differences and is free of normative assumptions; to address potential feelings of shame, secrecy, and taboo; and to effectively support children and their families in living with a genital difference [36]. Second, unrestricted access to specialized psychosocial services is highly desirable for all those concerned, and this requires urgent and substantial investments in research on this matter and adequate resources for training of qualified staff [45]. Third, where sufficient scientific evidence against specific surgical procedures in childhood is available, such surgery should be considered unacceptable. This includes gonadectomy before adolescence in children with complete androgen insensitivity [47], vaginoplasty as a first-line treatment for vaginal hypoplasia [48], or clitoral surgery for mild degrees of virilization [49, 50]. In the very limited situations in which childhood genital surgery may be part of a multifaceted individual management plan, all authors agree that any genital surgery requires a surgical team that can offer excellent quality, knowledge, and experience on this matter, as complication rates and the risk for tissue damage will be higher [51].

The specific criteria that define situations in which elective genital surgery in childhood may be considered require research and discussion beyond what this document can offer. However, elements may include that a child experiences harm – as diagnosed by a mental

health professional – resulting from living with atypical genitals, that all other options have been explored, that ethical board review is in place, that there is agreement among experts – including experts by experience – on the necessity of the intervention, and that extensive person- and family-centered support and therapy are provided before and will be continued after the intervention.

Peer Support (Panel 9)

The intimate nature of DSD may prevent patients and caregivers from accessing their existing community and families, and networks of peer support can therefore be particularly important. Peer support involves people drawing on their own experiences to provide information and emotional support. It can be provided through patient/parent-led support groups, clinic-based peer support workers, and informal contacts. Due to the rarity of DSD, peer support can be difficult to access, and, even when groups do exist, engagement is often limited [52]. Reasons for this are multifaceted and varied. A major barrier for accessing peer support is that clinicians rarely discuss this option with their patients, as they may fear that confidentiality may be compromised, that inaccurate information may be provided, that care provided by different teams may be compared, or simply because some clinicians do not sufficiently prioritize peer support, e.g., due to lack of knowledge, funding, or logistics. Parents may fear invading the privacy of their child, as they need to balance the right to privacy while supporting their child to grow up without secrecy and shame. Affected individuals often desire positive support and do not want to engage in controversy or conflicts between and among activist groups and healthcare providers. Some groups purport to address the needs of all individuals at all times and/or to represent the entire community of individuals who have a DSD. Such a stance may overwhelm or alienate new parents and newly diagnosed young people, who may not wish to pursue an identity label used by the group. In addition, tension may exist between support groups focusing on different aspects of DSD (e.g., those addressing medical vs. identity-related needs) or between groups targeting all conditions included under the DSD umbrella versus groups dedicated to specific diagnoses.

Peer support has the potential to deliver emotional support, facilitate exchanges and understanding of information, and increase confidence in treatment decisions [52]. Also, peers can provide information in areas that are unknown to or not prioritized by healthcare professionals. Peers sharing their experiences of discussing their child's diagnosis with the child as they age can be valuable. It allows them to offer insights into how they navigated such conversations and provides guidance to other parents facing similar situations.

For caregivers, acceptance of the condition is vital for the well-being of the child. Sharing thoughts, feelings, fears, and hopes can be an effective tool in the process of acceptance and in being open with the child when explaining their bodily differences. Opportunities to openly discuss all aspects of their child's needs with other parents can be powerfully affirming. In addition, meeting older children or adults who have a DSD can reduce fear of the future for the new parent in a way that no reassuring words from professionals can achieve. For the child and maturing adolescent, being loved and accepted for who they are by their family is key to promoting self-acceptance. Meeting others facing similar challenges or doubts can greatly reduce feelings of isolation and encourage openness. Peer support may also cover topics such as general well-being, surgery and vaginal dilation,

Panel 9: Peer support

Common ground and provisional recommendations
30 Peer support can be therapeutic and powerful and should be encouraged by healthcare providers.
31 Tension between healthcare providers and activists can complicate the process of encouraging peer support and threaten its designed benefits.
32 Healthcare providers should try to provide the required infrastructure and scientific support to facilitate peer support. Meanwhile, policy-makers need to invest in training those with lived experience becoming effective peer-to-peer resources.
Areas where further work, agreement, or research are needed
28 Clear guidance for healthcare providers is needed on how to facilitate peer support for patients and families while ensuring privacy and institutional regulations. Training standards need to be established, as well as mechanisms to compensate peer support providers for their effort in developing information brochures, attending scientific meetings, and participation in interdisciplinary care.

relationships and intimacy, (in)fertility, and day-to-day management of a condition. We encourage children to have access to peer support as young as possible.

Peer support is usually pursued on a voluntary basis, but healthcare providers can promote and encourage training in peer support, as well as making available the infrastructure and opportunities for peer support. Good peer support can be provided in a formalized support group, but also in an informal manner. To include peer support more effectively in the interdisciplinary care program, tailored training and guidance for peer support providers are needed to increase the quality of the support that is provided and also to reduce the risks of emotional over-involvement or accepting excessive responsibilities. Peer support groups, advocacy groups, and clinicians should work collaboratively on defining clear roles and expectations of confidentiality, and on establishing screening, selection, and training processes for peer support providers [53]. An example of such a peer mentor program is to be found at the University of Michigan Health System. Resources are needed to enable high-quality training for peer support providers.

Advocacy and Activism (Panel 10)

Advocacy and activism involve translation of support into actions, including changing public and medical community perceptions of the condition and attitudes toward clinical management. Both advocacy and activism play vital roles in addressing societal issues and advancing positive social change. They complement each other, with activism being more directly focused on visible actions and immediate change, and advocacy working more within existing systems to influence policies and attitudes over the long term.

At the time of the 2006 consensus statement, a working relationship, although contentious at times, existed between activists and the healthcare community [1]. However, this relationship has gradually become more adversarial. Concerns raised by activists about the healthcare community have included that the healthcare community has not adequately involved patient advocates in evolving healthcare practice, and that the pace of change has been too slow. Attempts to respond to these concerns [34] have not prevented the formulation of more polarizing viewpoints, e.g., the framing of elective surgical interventions during childhood in the context of DSD as a human rights violation. Concerns raised by the healthcare community about activism have included that some activism has been directed toward policy change, legislation to change medical practice, and potential litigation, with minimal input from healthcare professionals or from the broader community of affected individuals or their families, and in the absence of generalizable evidence supporting the proposed legislative changes [54, 55]. It is currently unclear if and how activism is taking into account recent changes in healthcare approaches, e.g., the current movement away from early genital surgery and the focus on transparency and psychosocial care. Polarization may cause affected individuals or their parents to move away from peer representation altogether, and it may induce shame in those who have experienced interventions that are disfavored by patient advocates or activists.

Meanwhile, many advocacy groups in the USA and EU have continued to work closely with healthcare professionals in their efforts to better define the contemporary role and place of some surgeries that have traditionally been performed in infancy. Other groups have been very effective in working with healthcare professionals to enhance communication and to support appropriate learning strategies rather than focus on surgical aspects. Another powerful initiative has been an international workshop grouping individuals who have a

Panel 10: Advocacy and activism

Common ground and provisional recommendations
33 Acknowledgment of past harm and full transparency in discussions on past medical practices are essential.
34 In the context of "Do no harm," any change in clinical practice warrants careful monitoring during follow-up of each individual, with data collated to assess outcomes.
Areas where further work, agreement, or research are needed
29 Stakeholders need to work collaboratively to ensure that all voices are heard and feel empowered to speak up without fear of recrimination.
30 Joint agreement is needed on actions that can reinforce the relationship between advocates, providers of peer support, and healthcare professionals, and that can enhance mutual listening.
31 Joint actions involving all stakeholders, and with a particular focus on the needs of those who have a DSD, need to be developed to inform policy-makers and society.

DSD, their family members, and representatives from advisory groups and professionals. All participants shared valuable learning points, such as the importance of peer support and of having knowledgeable and trustworthy providers [56].

Despite the differences of opinions that exist between some advocacy organizations and the healthcare community, several recommendations are supported by both. These include the need for interdisciplinary care that includes psychosocial support and for complete information and transparency. All agree that legal requirements related to sex registration of any newborn, whether born with a DSD or not, do not restrict or predict future gender identity. All agree that sex registration at birth does not, in itself, justify a need for genital or gonadal surgery.

Our concern is that antagonistic interactions between activists and the healthcare community may result in significant disenfranchisement of patients and their families from peer support. They may no longer seek peer support through particular organizations if they feel that their personal views are neither adequately represented nor respected. In addition, many of them desire to maintain a certain level of privacy to avoid perceived stigma and may not want to come forward to express their opinions, especially if they fear being challenged for their views. In the same vein, the healthcare community needs to better understand the range of opinions of their patients and to encourage patients and their families to liaise with peer support and advocacy groups where they feel safe and respected. Clinicians need to be completely open and transparent in discussion of past therapies that were experienced as harmful and be willing to accept critique of past treatments and to acknowledge the grief caused, even if the current healthcare provider did not provide those past treatments and may not even have been in practice then.

There has been increased societal awareness of gender diversity and, gradually, awareness of variations in biological sex and genital appearance. Promoting this emerging awareness and inclusiveness is a joint task that will reduce the risk of stigma for all. Further elucidation of the range of opinions of individuals who have a DSD will guide all involved in constructive next steps.

Conclusion

This work has identified several important areas where participant stakeholders from various backgrounds and who are involved in the care for individuals who have a DSD agree, while other areas need further work or research. Although challenging, all co-authors agree that productive conversations require an honest and self-reflective approach of both the clinical community and advocacy and activist groups. This may then result in a renewed level of trust that can in turn inspire a more productive working relationship. The current adversarial relationship is capable of change, to stimulate a positive and beneficial collaboration in the coming years. All parties need to acknowledge that robust evidence is needed to address current uncertainties in management and jointly need to take concrete steps in identifying gaps in our knowledge. Only by working together can they ensure that the personal, societal, and clinical needs of all individuals who have a DSD and their families are optimally addressed.

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Author Contributions

Martine Cools and Ramnath Subramaniam: conceptualization, project coordination, methodology, data curation, analysis and validation, and writing (original draft, review, and editing). Earl Y. Cheng, Joanne Hall, and David E. Sandberg: conceptualization, methodology, data curation, analysis and validation, and writing

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