A Proposal for a New Approach to Differences of Sexual Development Research

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The establishment of the term differences (disorders) of sexual development (DSD) was a significant step forward from the prior insensitive terms. However, it remains a broad, artificial definition which has little role in clinical management other than offering a placeholder label prior to arriving at a definitive diagnosis for a child born with genital ambiguity. Not only is clinical management of these complex cases based on the actual diagnosis but the patients themselves identify primarily based on their individual diagnosis. As we continue to acquire knowledge regarding these diagnoses, sweeping generalizations about a heterogeneous population like those born with DSD are not helpful due to the lack of nuance and the precision required for real-life application. Conclusions based on average outcomes in several unequally distributed, diverse groups actually do not apply to any single patient with a specific diagnosis and often represent a diluted signal from the largest group(s) enrolled in studies grouping heterogeneous diagnoses. In DSD research this typically leads to attenuated data on females with congenital adrenal hyperplasia (CAH) washing out meaningful data on individuals with other diagnoses.This realization reflects the increasingly greater understanding of issues related to genital ambiguity gained through continued work and collaboration with patients and their families. More than a decade has passed since the Chicago Consensus Statement was published, emphasizing individualized, diagnosis based, patient and family centered clinical care.1 While this approach has been incorporated into clinical management, research has lagged behind. Physicians and researchers have the responsibility to bring about this change

This is the author's manuscript of the work published in final edited form as:

Szymanski, K. M., Cain, M. P., & Rink, R. C. (2020). A Proposal for a New Approach to Differences of Sexual Development Research. *The Journal of Urology, 203*(1), 42–43. https://doi.org/10.1097/JU.0000000000000470

in research reporting.While we have made significant strides in the clinical care of patients with DSD, much DSD research remains confusing because it does not distinguish individual diagnoses. Further clinical progress and research advancement require an active paradigm shift led by researchers, experienced practitioners and funding agencies. Such an interruption, even when necessary, is rarely easy. To create a more robust body of published research that would avoid further stagnation in clinical management and understanding of individual DSD diagnoses (the culpability for which is shared by many, including the authors), we propose 3 measures for a meaningful solution.

1) Undiversified DSD research should be abandoned as it is not a helpful clinical entity. Furthermore, most patients do not identify as having DSD but rather with the individual diagnosis. This moratorium should be implemented for presentations at meetings and peer reviewed publications. Instead, we should perform and report only research on well-defined, diagnosis based populations. At least 4 groups should be reported separately: 46XX with CAH, 46XY with hypospadias, 46XY with complete androgen insensitivity and other (ideally split into individual diagnoses). Continuing to report data on DSD as a uniform group falsely assumes a nonexistent common narrative of a single voice, clinical course, expectations and outcomes. This is reflective of neither patient experience nor clinical reality.

2) Emphasis must shift from physician/surgeon centered and reported outcomes to patient and parent centered. Most current controversies concerning the treatment of a child with genital ambiguity involve patient and parental beliefs, concerns and experiences. The first question that needs to be asked is what these issues are in each group affected by a particular DSD diagnosis. We have little reliable data to provide an answer today. We must admit that it has been humbling and revealing to discover through family centered work at our institution that concerns which might keep urologists up at night are but a subset of a multitude of life-threatening and life altering issues juggled by the parents of daughters with CAH. How issues of sexuality and

fertility fit into the complex tapestry of concerns of people living with individual DSD diagnoses remains largely unknown.

3) Research should become more generalizable through interinstitutional collaborations and creative new ways of engaging the larger patient community. Similar to activists and lobbyists, who may not necessarily reflect the views of the people who did not hire them, the outcomes reported by participants in single center studies may or may not reflect those of the larger population in question. Such studies should primarily represent the initial research efforts. Given that only a small fraction of people affected by any form of DSD have until now participated in research, the outcomes in this silent majority remain unknown.

We hope that these measures will help mirror in research what we strive for in clinical care every day: taking the best possible care of our patients.

Acknowledgment

Dr. Benjamin Whittam assisted with the manuscript.

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