

Project Information?

5R01HD093450-03

Title: DISORDERS/DIFFERENCES OF SEX DEVELOPMENT (DSD) - TRANSLATIONAL RESEARCH NETWORK

Awardee Organization: UNIVERSITY OF MICHIGAN AT ANN ARBOR

Abstract Text:

PROJECT SUMMARY Disorders/Differences of Sex Development (DSD) is an umbrella term covering congenital conditions in which chromosomal, gonadal, or anatomic sex development is atypical. DSD are phenotypically heterogeneous, ranging from genital malformations (hypospadias, cryptorchidism, clitoral hypertrophy) to genital ambiguity. DSD have a collective incidence of about 1% and can result in serious consequences for fertility, cancer risk and quality of life across the lifespan. Debate over clinical management, in particular gender assignment and genital or gonadal surgery, has intensified; yet scientific data informing best practices remain limited. Clinical care in DSD is hampered by a fragmented research agenda and lack of standardization, leaving fundamental gaps in knowledge of DSD pathology and links between treatment options and desired outcomes. Major obstacles include gaps in understanding of pathophysiology (impeding precise diagnostic categorization), the absence of prospective longitudinal studies of psychosocial outcomes, and the potential moderating influence of biomedical, psychosocial and legal factors on medical decision making. This project is the first of its kind, globally, to prospectively study the variable pathways from DSD diagnosis and clinical management to psychosocial adaptation. This goal will be accomplished by exploiting the infrastructure and robust collaboration of the DSD–Translational Research Network (DSD-TRN). The Network comprises a consortium of 12 interdisciplinary healthcare teams across the nation in conjunction with patient stakeholder and bioethics representation. Our guiding principle is that evidence-based standardization of diagnostic and treatment protocols will be associated with higher rates of definitively diagnosed DSD, reduced variation in clinical practice, enhanced patient/family healthcare-related experiences, and improved psychosocial outcomes for patients and their families. The proposed project will deliver evidence needed to raise the quality of healthcare in DSD to levels observed for other rare diseases. Specific aims include: 1. Genetics. Improving and expanding the molecular diagnosis of DSD; 2. Psychosocial. Identifying diagnostic, clinical care, and family risk and resilience factors associated with variability in psychological outcomes of patients with DSD and their families; 3. Determinants of clinical management. Identifying biomedical, legal, and psychosocial determinants of clinical management decisions.

Public Health Relevance Statement:

PROJECT NARRATIVE A defining moment of our lives begins when we embark on a male or female path in the womb; disruption of typical male or female development results in Disorders/Differences of Sex Development (DSD), which collectively occur

frequently – in about 1% of the human population. The quality of life of people affected by DSD and their families is often threatened by uncertainty about what caused the condition, doubt over choices in care, and the chronic stress associated with anticipated or experienced stigma, and lifelong clinical care. To inform emerging clinical practice guidelines for the assessment and management of DSD, we propose a study that uncovers the genetic causes of DSD and examines connections between the genetics, patient and family psychological adaptation, and both medical and surgical decisions.
