Introduction

The Sexual & Gender Minority Research Office (SGMRO) works directly with NIH institutes, centers, and offices (ICOs) to coordinate research and activities related to sexual and gender minority (SGM) populations at the National Institutes of Health (NIH). SGMRO was established in September 2015 within the NIH Division of Program Coordination, Planning, and Strategic Initiatives. Since its creation, SGMRO has worked to improve the health of SGM populations by working with the ICOs to increase research and support of scientists conducting relevant research. Under Section 404N of the 21st Century Cures Act (Public Law 114-255), signed into law on December 13, 2016, the Director of NIH is encouraged to “improve research related to the health of SGM populations.”

In late 2022 and early 2023, SGMRO hosted a multiphase workshop to identify and prioritize key research needed to further gender-affirming care (GAC) for transgender and gender-diverse (TGD) populations. NIH convened researchers, advocates, and members of the community with expertise in transgender health, measurement, behavioral and social sciences, and other disciplines for a workshop that addressed not only medical considerations but also social, psychological, and behavioral considerations regarding GAC.

Phases I–III: Request for Information, Listening Sessions, and Working Group Discussions

In October 2022, SGMRO published a request for information to provide an opportunity for the public to submit comments on research opportunities related to the Scientific Workshop on Expanding the Evidence Base in Gender-Affirming Care for Transgender and Gender-Diverse Populations. The public was invited to provide comments on the following three themes: (1) pediatric and adolescent care, (2) adult and older adult care, and (3) systemic and institutional policies. In phase II, December 2022, SGMRO hosted virtual listening sessions to offer federal colleagues, community members, providers, researchers, and representatives from professional organizations an opportunity to comment on these themes, knowledge gaps, and research opportunities. During phase III, in early 2023, three working groups consisting of clinical experts, researchers, community members, and NIH staff met virtually to address the three themes. Working group members reviewed the current evidence base and the most recent scientific findings and identified crucial knowledge gaps and research opportunities for studies on GAC across the life course.

Phase IV: Public Report-Out Session

The public report-out session was held virtually on March 27, 2023. ADM Rachel Levine, Assistant Secretary for Health, U.S. Department of Health and Human Services, provided introductory remarks.
Keynote Presentation: Standards of Care

Dr. Asa Radix, Director of Research and Education, Callen-Lorde Community Health Center, and Clinical Professor of Medicine, New York University, presented on the most recent version of the World Professional Association for Transgender Health (WPATH) Standards of Care and the history of clinical practice guidelines for GAC. Quality of evidence is critical when creating clinical practice guidelines, but randomized controlled trials (RCTs) rarely are available for topics in transgender health. Outcome measures also are difficult to define when only low-quality evidence is available. The committee creating the standards must make judgments based not only on the quality of evidence but also on the weight of the benefits and harms; the acceptability, values, and preferences of the community; and the feasibility, including such considerations as resources and costs. Changes between the previous and most recent versions of the WPATH Standards of Care included an updated name, only one assessment needed for genital surgery, and an expansion of who can perform the assessment. Dr. Radix emphasized that these guidelines are designed to be used in a variety of health settings and must be flexible to meet local needs. Clinical assessment remains an important element, but the updated standards encourage shared decision-making and further recognize the diversity of gender.

The standards also provide a roadmap for future research—because none of the recommendations could be based on high-quality evidence, the standards show the need for well-designed research, multisite cohort studies, and adequate documentation, as well as the possibility for RCTs to compare two equivalent interventions. Recommendations lacking appropriate outcome measures show the need for patient-reported outcome measures (PROMs), community involvement in all phases of research, and psychometric validation. Additional topics are needed to address the lack of direct evidence to inform some screenings for TGD people, and appropriate laboratory parameters and diagnostic tools are needed. Dr. Radix noted that because of the current level of threats against TGD people, best practices should take into consideration how to support individuals participating in this research.

Overview of the U.S. Trans Survey

Dr. Sandy James, Lead Researcher, 2022 U.S. Trans Survey (USTS), presented on the 2015 and 2022 USTS deployments and results. The USTS was developed to collect data to inform policymakers, lawmakers, educators, and the public about TGD populations, as well as to provide robust data to describe TGD populations in the United States and raise issues advocates often hear anecdotally. The 2015 USTS had almost 28,000 respondents, about one-third of whom identified as nonbinary. The distribution of respondents mirrored the distribution of the U.S. population as a whole, showing that TGD people live in all constituencies and TGD issues are relevant everywhere. Many questions on the USTS were comparable to questions on federal and other national surveys. Outreach was conducted through many points of access, including social media; some sampling gaps seen in the 2015 strategy were addressed by expanding outreach for 2022. Key themes of the 2015 report included pervasive mistreatment and violence, severe economic hardship and instability, and the harmful effects of these on physical and mental health; all these experiences were compounded by other forms of discrimination against TGD people.

The 2022 USTS was conducted in late 2022 and results are not yet available. The data collection period was longer, which allowed more time for priority populations to find the survey and respond. The range of topics was expanded, and some issues with the 2015 survey were addressed. Comparability to existing and future surveys was important, and increased
participation of underrepresented populations was a priority. To respond to the changing landscape, a scientific advisory council was added, the number of questions was increased, and the age limit was lowered to 16. The team developed many “ramps” that would lead users to smaller, more specific surveys, if their responses were more suited for these areas than the main survey. Many partner organizations were engaged to help expand the reach of the survey, particularly to underrepresented populations. Although the data are not yet ready, the team expects that the number of respondents will be larger than the 2015 survey. Respondents were not deterred by the increased length of the survey. Results will provide more nuanced information about health and other experiences related to GAC, as well as evidence that can be used in legal and policy areas.

Following the presentations, representatives from each of the three working groups reported on their group’s discussions and the research opportunities identified and responded to questions submitted by other working group participants.

**Group One: Research Opportunities in Pediatric and Adolescent Care**

The Pediatric and Adolescent Care Working Group emphasized the overarching need for new research priorities for children, adolescents, and young adults to be considered in the context of prioritizing longitudinal data and outcomes across the life course, including issues related to ethics, measurement, opportunities for intervention development, and the central role of youth, caregiver, and provider voices.

The group identified the following research opportunities:

1. **Models of Care and Access to Care**
   - Defining models of GAC. Models of care may include different care team compositions, requirements prior to initiation of GAC, virtual care options, and timelines. Evaluation of best practices may include approaches to assessing readiness and facilitating fully informed shared decision-making; integration across disciplines and over time, including the transition to adult care; and models that produce higher quality outcomes.
   - Health equity in access and outcomes. Experiences of interest that may affect access to gender-affirming health care include race, ethnicity, geographic location, religion, culture, and legislation. Outcomes may be affected by key intersectional experiences and diagnoses, including mental health conditions, autism and broader neurodivergence, chronic medical conditions, and social or economic hardship.

2. **Psychosocial Well-Being, Cognitive Development, and Mental Health**
   - Mapping gender development trajectories. These trajectories include the developmental stage or age at which gender diversity or incongruence is recognized or shared with others, as well as how gender identity and expression unfold over time.
   - Psychosocial, cognitive, and adaptive outcomes associated with experiences of gender dysphoria or incongruence and gender-affirming social or medical interventions. Experiences of interest include those who do and do not pursue gender-affirming interventions. Outcomes of interest include satisfaction with embodiment goals, mental health, social and adaptive functioning, neurodevelopment, and quality of life over time.
   - The intersection of gender development trajectories with decisions and timing related to GAC, and related psychosocial, cognitive, and mental health outcomes.
3. Medical and Surgical Outcomes

- Long-term health outcomes while on or following the use of pubertal suppression (PS) or other gender-affirming medical therapies, including in populations with distinct underlying conditions, as well as for patients with and without gonads. Specific outcomes include, but are not limited to, metabolic, cardiovascular, hematologic, oncologic, bone health, height trajectory, neurocognitive, dermatologic, and autoimmune or rheumatologic outcomes.

- Pharmacokinetics and physiologic effects of hormonal therapeutics, including evaluating how these are affected by diversity in timing of initiation (e.g., chronologic age, sexual maturity rating stage), dosing schedules, delivery system (e.g., pill, topical, injectable), discontinuance of PS or gender-affirming hormone therapy (GAHT), or prolonged gaps in use.

- Surgical outcomes following gender-affirming surgeries in adolescence and young adulthood, including timing of the procedure (and how the timing is selected, including surgical decision-making, use of educational materials or written forms for decision-making, and neurocognitive or developmental stage), indications for the procedure (e.g., patient goals), use of PS or GAHT, patient satisfaction and patient-centered outcomes, and postoperative care and management.

- Sexual and reproductive health in TGD individuals (including those who may use PS, GAHT, or surgeries) including family-building goals and outcomes (including interest in specific kinds (e.g., fertility, adoption), how these evolve and how they are related to use of GAHT and or performance of surgeries, fertility outcomes), fertility preservation (including current and future potential options), sexually transmitted infections (including prevention, screening, management), and contraception.

- Decision-making regarding GAHT and surgeries with permanent effects, including how this issue is approached (e.g., use of standardized educational documents and consent forms) and how maturity or developmental stage is evaluated.

4. Impact of Social Determinants and Social Context on Gender Development and Health

- More information is needed regarding (1) individual relationships (e.g., family, peer, partner, and other social networks), (2) community context (e.g., neighborhood, school, religious institutions, other social organizations), (3) social and cultural values and norms, and (4) legislation and policies at institutional, local, state, and federal levels (e.g., sports participation, curricular inclusion, name, gender marker). The needs of key partners—such as families, communities, and schools—to optimize the healthy development of TGD youth also must be identified and addressed.

This group noted that their recommendations regarding psychological well-being include resilience and reiterated the need for research on decision aids related to maturity. Delivery systems for and patient satisfaction with GAHT should be considered under the pharmacokinetics priority.

Group Two: Research Opportunities in GAC for TGD Adults and Older Adults

The Adult and Older Adult Working Group emphasized that medical and surgical affirmation is only one type of gender-affirming support—their recommendations are inclusive of all kinds of GAC and apply to all adults who perform any sort of GAC across the life course. The group’s recommendations also include intersex and nonbinary adults across all priorities, given the lack of research on these populations.
The group identified the following research opportunities:

1. **What Are the Longitudinal Physical Health Outcomes of Gender Affirmation?**
   - NIH should expand research on longitudinal physical health and related outcomes of any gender affirmation (e.g., social, legal, medical, surgical) across the life span and across sex/gender spectra, including intersex and nonbinary adults. Examples include impacts on specific issues, organ systems, and medical conditions—both acute and chronic—such as cardiovascular physiology and disease, cancer, and dementia; effects on sexual and reproductive health; outcomes after specific interventions, such as surgical procedures or hormone therapy; definitions of TGD lay community-centered and patient-reported outcome measures; and the relationship between life stage and GAC (e.g., initiation in adolescence vs. adulthood, continuing treatment in adulthood vs. older adulthood).

2. **How Can We Optimize Mental Health Outcomes Within the Context of GAC?**
   - NIH should expand research on the effect of gender affirmation of any kind (e.g., psychosocial, legal, medical, surgical) on mental health outcomes across a range of interventions (i.e., clinical, community, structural) and outcomes (e.g., mental health care utilization, well-being, distress, diagnoses, suicidality), including patient-reported and community-centered outcomes, as well as across the life span and across sex/gender spectra, including intersex and nonbinary adults. Examples include the development and evaluation of mental and behavioral health interventions; the effect of medical GAC (e.g., hormone therapy, surgery) on the natural history, progression, development, diagnosis, and treatment of mental and behavioral health conditions; and the development and evaluation of interventions to reduce suicidal ideation and suicide risk.

3. **How Can New or Existing Binary Sex/Gender-Based Clinical Algorithms and Tools Be Inclusive of TGD Individuals?**
   - NIH should expand the evidence base on how current and future clinical algorithms and tools that use sex and/or gender as a binary variable apply to TGD people who have had any gender affirmation (e.g., social, legal, medical, surgical) across the life span and across sex/gender spectra, including intersex and nonbinary adults. Examples include decision and risk-stratification tools (e.g., cardiovascular risk estimators, breast cancer risk calculators); diagnostic tools and laboratory values (e.g., hemoglobin, substance use disorder screening, bone density); and screening guidelines (e.g., United States Preventive Services Task Force screening guidelines).

4. **What Interventions Impact Quality of Life for TGD People?**
   - NIH should expand research—including assessing the impact of peer-led, provider-level, community-level, and structural interventions—on quality of life and well-being among TGD populations, especially people with disabilities and people who are part of additional NIH health disparities populations, across the life span and across sex/gender spectra, including intersex and nonbinary adults. Examples include resilience or strengths-based research, intersectional research, TGD lay community-driven definitions and measures of quality of life, and self-initiated interventions (e.g., binding, tucking, soft-tissue fillers).
5. What Are the Most Effective Models for GAC Provision?

- NIH should expand health services research on the development and implementation of impactful GAC models, programs, and services across diverse populations (e.g., socioeconomically disadvantaged adults, adults in rural areas, aging populations) and contexts (e.g., rural areas, congregate residential settings, telehealth) across the life span and across sex/gender spectra, including intersex and nonbinary adults. Examples include infrastructure requirements, access, workforce training and qualifications, supply chain, system-level barriers, and facilitators; payment models and cost-effectiveness analyses; models for transition of care (e.g., pediatric to adult, adult to geriatric); the role of family members, caregivers, peers, and others; and collaborative or integrated models of care, especially integrating behavioral health into medical and surgical care.

The group emphasized that mental health is a component of physical health—and an exceptionally important outcome of physical interventions—but that mental health outcomes were structured as a separate research opportunity because mental health disparities are prominent and urgent, interventions are under-researched, and physical interventions alone are not sufficient to optimize mental health. Mental health interventions also are especially well positioned to include structural and community interventions. Both new and adapted existing interventions are likely to be important.

This group used an expansive understanding of sexual and reproductive health that includes function, care, experience, well-being, and satisfaction. They discussed key opportunities around conception, pregnancy, and birth experiences in particular. The conversation around pregnancy and conception was a way to bring the experience of some transgender men to the foreground, recognizing that many transgender men have different priorities. The group also explicitly discussed how to ensure each research opportunity was as inclusive as possible regarding gender identity and embodiment goals across the TGD spectrum, including for older adults, intersex people, and nonbinary individuals.

The group agreed that positive and strengths-based outcomes should be incorporated across all areas of research, which is reflected in the recommendation focused on quality of life and well-being.

Regarding the last recommendation, the group pointed out that educational outcomes research, particularly research that centers patient outcomes, creates an opportunity to define and operationalize effective and excellent care, which then can inform ethical, professional, and credentialing standards.

Group Three: Research Opportunities in Systemic, Institutional, and Ethical Issues

The Systemic, Institutional, and Ethical Issues Working Group defined its scope as including the structures and activities of organizations throughout the public health and health care systems; research and clinical standards and practices; bioethics; and public policy, law, and administration. The group emphasized that not all TGD people need medical gender affirmation and defined GAC broadly to include any type of care or support that affirms the identity and positively influences the health and well-being of TGD people. They noted that intersex people may also need GAC and are important to consider for the research opportunities highlighted.
The group identified the following research opportunities:

1. **Methodological Innovations in the Study of Intersectional Structural Influences on the Health and Well-Being of TGD Populations**
   - Develop and deploy affirming, valid, and reliable methods for identifying TGD populations in a variety of research and clinical settings (e.g., surveys, electronic health records, administrative records).
   - Develop and deploy rigorous methods for assessing intersectional structural influences—including racism, sexism, and transphobia, as well as issues related to disability, language, geography, and other factors of health disparities—on health and health care access among TGD people.
   - Develop and deploy strategies for increasing the pipeline of TGD-identified health researchers, particularly TGD people of color and others from backgrounds underrepresented in science and medicine.

2. **Ethical Considerations in Research and Clinical Practice for TGD Patients and Populations**
   - Develop and deploy ethical guidelines for research with TGD populations, particularly with regard to research around GAC.
   - Develop and deploy community-based participatory research frameworks and practice in TGD health research to ensure that these frameworks are accurately guiding the research conducted with TGD patient populations and ensure that these populations are both informing and benefiting from the research.
   - Develop and deploy ethical practice frameworks in GAC medical decision-making, TGD patient autonomy, and patient-centered care.

3. **Impacts of Policy Interventions on TGD Populations**
   - Apply legal epidemiology frameworks to assess laws and regulations affecting TGD populations.
   - Develop and deploy timely, rigorous, and intersectional methods, including quasi-experimental designs, to assess the effects of policy changes on TGD population health and on access to services, the quality of those services, and outcomes for TGD people. This includes health-specific policies, such as the effects of laws that seek to expand or restrict access to GAC, and non-health-specific policies that influence health and well-being among TGD people, such as school rules about chosen name and pronoun use for TGD youth, youth participation in sports, and legal name and gender recognition laws.

4. **System-Level Interventions to Improve Access to and Quality of Care for TGD People**
   - Assess the effects of institutional and other system-level interventions—by payors, providers, hospitals, clinics, medical educators, and other stakeholders—on care access, quality, and outcomes for TGD populations.
   - Develop and deploy training and education strategies for increasing provider clinical and cultural competency in working with TGD patients.
   - Identify optimal care coordination models for serving TGD patients, particularly with regard to GAC, integrated care (e.g., GAC and cancer screenings), and different care modalities (e.g., telehealth).
• Develop and deploy methodological advances in and application of novel health services and economic (e.g., cost-utility analysis) research methods to TGD health.

5. **Approaches to and Impacts of Science Communication on the Health of TGD People**

- Conduct research on network mapping and other quantitative and qualitative assessments of public narratives around TGD identity and access to GAC.
- Assess the effects of public narratives on access to GAC and the health and well-being of TGD people and populations, including both affirming narratives and non-affirming narratives.
- Develop and deploy strategies for addressing misinformation and driving evidence-based policymaking in relation to TGD populations.
- Develop and deploy communications strategies for reaching TGD populations with health-related information.

The dearth of information on TGD populations in federal surveys limits the extent to which existing surveys can be used to evaluate these research opportunities, although this is beginning to change and a number of long-standing longitudinal surveys now provide information on identified TGD participants. Given the speed with which restrictive policies can be created and implemented, finding ways to leverage existing data is critical. The SGMRO website includes a comprehensive overview of data sources that include TGD respondents.

Some work regarding guidelines for specific inclusion of TGD populations in research studies already has been conducted. In specific areas of inquiry and as new outcome measures are developed, issue-specific areas may need specific research guidelines, and existing guidelines will need to be updated continually to address the need to include TGD populations, who often are excluded from research when investigators feel like they cannot appropriately categorize the sex and gender of TGD or intersex participants. TGD people should be included in broad trials, as well as TGD-focused research.

Strategies for increasing cultural competency among physicians are not sufficient to increase access to care among TGD populations—systems-level factors may preclude TGD people from reaching providers. Access to care may be affected at multiple levels, including individual provider attitudes and laws and policies that may prohibit TGD people from seeking clinical help. How to ensure the safety and confidentiality of participants in community-based participatory research and protect the well-being of researchers in challenging locales is a major area for future discussion.