

Cross-Cutting Topics

The IACC has identified two topics that span across the seven Questions of the *Strategic Plan* and warrant special attention: understanding the influence of gender and sex in autism, as well as reducing disparities and promoting equity. The goal of these "cross-cutting" recommendations is to encompass the numerous research and services priorities identified by the Committee throughout the *Strategic Plan* and allow for this area to be identified as a priority for funders. In future publications tracking progress in funding for these objectives, individual projects assigned to these cross-cutting objectives will be coded to different questions of the *Strategic Plan* depending on which aspect of autism is being studied. This will ensure the funding associated with those projects will be counted toward the totals of their respective questions, but also allows the projects to be added together into a single recommendation.

Cross-Cutting Topic: Sex and Gender

The topic of sex and gender differences in autism is mentioned in several chapters of the *Strategic Plan*, indicating the Committee's strong interest in this area. In the past, many inferences about the development and trajectory of autism and its co-occurring conditions have been made based on research studies where the participants were predominantly male and/or females were disproportionately excluded¹. Thus, it will be critical in the future to understand and better serve the needs of girls, women, and/or lesbian, gay, bisexual, transgender, queer, intersex, asexual plus (LGBTQIA+) individuals on the autism spectrum.

The most recent prevalence data from the CDC suggests that autism is 4.3 times more prevalent in males vs. females²; other estimates have consistently estimated that males are 3-4 times more likely to be diagnosed with autism than females³. These estimates may not, however, reflect the true ratio of autism in females versus males, as they are based on diagnoses made using definitions that were based on how autism presents in males and using screening and diagnostic instruments that were developed using predominantly male subjects in research. A recent longitudinal study examining infants and toddlers with an autistic sibling suggests ASD-associated behaviors occur equally in males and females⁴. Many girls and women on the autism spectrum are missed early on or misdiagnosed with other mental health conditions before they receive an ASD diagnosis. It is therefore important for clinicians to be trained to recognize the differences in autism presentation among girls and women, as well as understand and recognize potential masking behaviors⁵. Additional research is also needed to understand how the presentation of autistic traits may change over time.

More research is needed to understand autism in girls and women, unique aspects of their biology, psychology, and social context, and the potential effects of various types of bias and inequities in the identification process. Girls and women may also need different or customized approaches to intervention to meet their needs. With increasing understanding, awareness, and improvement of screening and diagnostic methods, it is likely that more girls will be identified with autism earlier in life and given the opportunity to be connected with supportive services sooner. Progress in these areas and in tailoring interventions and services to meet the unique needs of girls will be critical steps in closing gender gaps.

Biological Evidence for Sex Differences in Autism

One hypothesis proposed to explain the difference in prevalence is the “female protective effect” (FPE), which suggests that females are biologically 'protected' from autism such that, on average, a greater number of genetic factors is necessary for a female to display autism traits. There has been some research that supports the FPE concept^{6,7,8}, but there are others in the field who question this hypothesis. In a recent study, researchers analyzing health records from a population-wide registry found that the unaffected sisters of autistic individuals were just as likely to have autistic children as the unaffected brothers of autistic individuals⁹. This study demonstrates that a potential FPE cannot fully account for the sex differences in prevalence¹⁰. It is therefore critical to continue exploring potential female protective effects and other genetic contributors to autism that are differentially influenced by sex.

Differences in underlying biology may account for some of the differences in autism phenotypes based on sex (discussed further in Chapter 2). For example, autistic girls have been found to activate different parts of the brain in response to social stimuli than their neurotypical girl counterparts or autistic or neurotypical boys¹¹. Girls also have been shown to activate neural reward circuits in response to social stimuli, while autistic boys decrease activation in the same part of the brain in response to similar stimuli. Another recent study used deep-learning technology to compare hundreds of brain scans of autistic and neurotypical girls and boys and found that autistic girls displayed unique brain connectivity patterns in areas of the brain involved in motor, language, and visuospatial attention^{12,13}. These biological differences may influence how autism is expressed in girls and women and how they respond to their environments. Understanding the biology of autism in girls and women may help to develop personalized interventions to better serve this population.

The Influence of Sex and Gender on the Presentation of Autism

The core features of autism often present differently in girls/women than in boys/men¹⁴. For example, restricted interests in young girls are less likely to be viewed outside of the range of normal than in boys, often because their intense interests, such as animals and fashion, are in line with social expectations for girls^{15,16}. Conversely, social communication is more likely to be affected in young girls diagnosed with ASD versus boys¹⁷. Adolescent girls and adult women on the autism spectrum are more likely to present with internalizing traits, such as anxiety and depression, while boys/men typically display externalizing traits¹⁸. Qualitative studies suggest that girls and women are also more likely to mask or camouflage their autistic features^{19,20,21}. As a result of these and other factors, autistic girls/women are diagnosed later than autistic boys/men on average^{22,23,24, 25}. Recent studies have revealed intriguing results around motor regions of the brain in autistic girls. A study using an autism screener and developmental skills assessment found that girls with autism were more likely to present with signs of motor impairment than boys²⁶. In a separate study using deep-learning to compare brain scans of girls and boys with and without autism analyses showed that girls with autism had significantly different patterns of brain connectivity in motor areas¹³. Together, these findings suggest that more investigation into motor and other brain differences in girls with autism may be warranted.

Studies have suggested that individuals on the autism spectrum are more likely to identify as LGBTQIA+ than neurotypical individuals^{27,28,29, 30}. This intersectionality between disability and gender identity or sexual orientation can result in increased social stress, stigma and discrimination, which can in turn contribute to reduced access to services and increased mental and physical health challenges. In order

to address these issues, additional research is needed to better understand the unique needs of these populations^{31,32}. It is also important to properly train medical practitioners and other service personnel on ways to properly interact with autistic individuals who identify as LGBTQIA+.

Sex- and Gender-Specific Services and Supports

Research has suggested that women on the autism spectrum have more or different physical and mental health care needs than men on the spectrum as well as neurotypical women^{33,34,35}. Autistic LGBTQIA+ individuals also have unique healthcare needs. However, many autistic women and LGBTQIA+ individuals have difficulty accessing appropriate medical care, including routine reproductive health care and prenatal care³⁵⁻³⁷. Needs for educational or employment supports may also vary. It is important for service providers to be made aware of the potential differences in need, and carefully listening and making adjustments to ensure that they are responding to the stated needs of all individuals on the autism spectrum. People of all genders and sexual orientations on the autism spectrum are more likely to report adverse sexual experiences than their neurotypical peers^{30,38}. It is critical that autistic individuals receive age-appropriate sexual education.

Summary

As researchers continue to explore the biological mechanisms that underlie autistic traits and co-occurring conditions, it will be critical to identify sex- and gender-specific influences on life outcomes. It will also be important to develop and refine screening and diagnostic tools, interventions, and services that can accommodate the unique qualities and needs of girls, women, and members of the LGBTQIA+ community.

CROSS-CUTTING RECOMMENDATION 1: Support research to understand sex and gender differences in autism.

Examples:

- Understand differences in the presentation of autistic traits in girls and women to enhance screening and diagnosis.
- Conduct research exploring the influence of sex and gender on the underlying biology of autism (differences in brain structure, function, physiology) and how this may create differences in phenotype.
- Identify genetic and environmental factors that contribute to differences in phenotype.
- Understand differences in the social context, including the societal expectations and intersectional impacts of ableism and sex/gender/sexual orientation discrimination, that may influence outcomes for females and LGBTQIA+ individuals on the autism spectrum.
- Develop strategies to better meet the intervention, service, and support needs of girls and women and of LGBTQIA+ individuals with autism.

**2021-2023 IACC Strategic Plan for Autism Research, Services, and Policy Draft
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**2021-2023 IACC Strategic Plan for Autism Research, Services, and Policy Draft
January 2023**

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**2021-2023 IACC Strategic Plan for Autism Research, Services, and Policy Draft
January 2023**

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