Sex Differences in Mental Health Problems and Psychiatric Hospitalization in Autistic Young Adults

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**IMPORTANCE**  Psychiatric disorders are common among autistic children and adults. Little is known about sex differences in psychiatric disorders and hospitalization in early adulthood.

**OBJECTIVE**  To examine sex differences in psychiatric diagnoses and hospitalizations in autistic compared with nonautistic young adults.

**DESIGN, SETTING, AND PARTICIPANTS**  This population-based cohort study assessed all individuals born in Sweden between 1985 and 1997. A total of 1,335,753 individuals, including 20,841 autistic individuals (7,129 [34.2%] female individuals), were followed up from age 16 through 24 years between 2001 and 2013. Analysis took place between June 2021 and August 2022.

**EXPOSURES**  Autism was defined as having received at least 1 clinical diagnosis of autism based on the International Classification of Diseases.

**MAIN OUTCOMES AND MEASURES**  The cumulative incidence of 11 psychiatric diagnoses up until age 25 years was estimated, and birth year–standardized risk difference was used to compare autistic female and male individuals directly. Sex-specific birth year–adjusted hazard ratios (HRs) with 95% CIs were calculated using Cox regression. Analyses were repeated for inpatient diagnoses to assess psychiatric hospitalization.

**RESULTS**  Of 1,335,753 individuals included in this study, 650,314 (48.7%) were assigned female at birth. Autism was clinically diagnosed in 20,841 individuals (1.6%; 7,129 [34.2%] female) with a mean (SD) age of 16.1 (5.1) years (17.0 [4.8] years in female individuals and 15.7 [5.2] years in male individuals) for the first recorded autism diagnosis. For most disorders, autistic female individuals were at higher risk for psychiatric diagnoses and hospitalizations. By age 25 years, 77 of 100 autistic female individuals and 62 of 100 autistic male individuals received at least 1 psychiatric diagnosis. Statistically significant standardized risk differences were observed between autistic female and male individuals for any psychiatric disorder (−0.18; 95% CI, −0.26 to −0.10) and specifically for anxiety, depressive, and sleep disorders. Risk differences were larger among autistic than nonautistic individuals. Compared with nonautistic same-sex individuals, autistic female individuals (HR range [95% CI], 3.17 [2.50-4.04]-20.78 [18.48-23.37]) and male individuals (HR range [95% CI], 2.98 [2.75-3.23]-18.52 [17.07-20.08]) were both at increased risk for all psychiatric diagnoses. Any psychiatric hospitalization was statistically significantly more common in autistic female individuals (32 of 100) compared with autistic male individuals (19 of 100). However, both autistic female and male individuals had a higher relative risk for psychiatric hospitalization compared with nonautistic female and male individuals for all disorders (female individuals: HR range [95% CI], 5.55 [4.63-6.66]-26.30 [21.50-32.16]; male individuals: HR range [95% CI], 3.79 [3.22-4.45]-29.36 [24.04-35.87]).

**CONCLUSIONS AND RELEVANCE**  These findings highlight the need for profound mental health services among autistic young adults. Autistic female individuals, who experience more psychiatric difficulties at different levels of care, require increased clinical surveillance and support.
Mental health problems are a major concern in autistic individuals1,2 (note that we use identity-first language [autistic person] rather than person-first language [person with autism] throughout this article according to preferences reported by autistic individuals and their families). Around 70% of autistic children meet diagnostic criteria for at least 1 psychiatric disorder,4 and 54% to 79% of autistic adults receive at least 1 psychiatric diagnosis. Mental health problems are reported even among autistic individuals showing good outcomes in other areas of functioning.2

Sex differences in mental health have been observed in the general population.6 (Note: The term sex refers to biological attributes of being female or male and is assigned at birth, whereas gender refers to socially constructed attributes9 as discussed in detail elsewhere.10,11) Yet, very few studies have directly investigated sex differences in psychiatric disorders among autistic individuals. Existing evidence suggests that autistic women are particularly vulnerable to psychiatric disorders2 and access psychiatric care more often than autistic men.12 One study13 on health care claims data of children and youth younger than 21 years suggested higher odds of psychiatric difficulties such as anxiety, mood, and sleep disorders in autistic girls compared with boys. A study14 using self-reported gender (instead of sex assigned at birth) in a smaller adult sample found that autistic women experience anxiety, depression, and eating disorders at higher rates than autistic men. To our knowledge, there is only 1 large population-based investigation15 of sex differences across mental health problems in a Danish cohort of autistic and nonautistic children and adolescents. This study showed that autistic female children and adolescents were at increased risk for several psychiatric disorders, compared with autistic male counterparts.

Methods

Study Population

This register-based cohort study was approved by the Regional Ethics Review Board in Stockholm and follows the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guideline. Register studies do not require informed consent in Sweden. The study was preregistered via the Open Science Framework on June 16, 2021 (https://doi.org/10.17605/OSF.IO/QZHJS).

We linked several nationwide Swedish registers (eAppendix in the Supplement). From the Medical Birth Register20 we identified all individuals born in Sweden between 1985 and 1997 (N = 1,407,253). The follow-up period was 2001 to 2013. We excluded individuals with chromosomal abnormalities (eTable 1 in the Supplement), stillbirths, individuals who died or migrated before their 16th birthday, and whose biological mother was unidentifiable. As data on gender were unavailable, we used sex assigned at birth (male/female) in the Medical Birth Register. We additionally identified sex using the Total Population Register21 and excluded individuals whose sex was missing or reported differently in the 2 registers, since we could not determine the cause of the mismatch or missing values. After exclusions, the eligible cohort included 1,335,753 individuals who were followed up from age 16 years until a diagnosis of the respective psychiatric disorder, their 25th birthday, death, emigration, or end of follow-up on December 31, 2013, whichever came first. The cohort selection process is depicted in eFigure 1 in the Supplement.

Measures

We defined exposure as receiving at least 1 autism diagnosis from age 1 year onward based on International Classification of Diseases (ICD), Ninth Revision code 299A and ICD-10 codes F84 in the National Patient Register,22 excluding Rett syndrome, other childhood disintegrative disorders, and overactive disorder associated with intellectual disability (ID) and stereotyped movements. The validity of register-based autism diagnosis was reported to be high.23 Autism is a lifelong condition, and age at diagnosis is unlikely to accurately indicate...
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Original Investigation Research

Cohort Description

Descriptive statistics for the study population are presented in Table 1. The cohort included 1335753 individuals (650314 [48.7%] female). Detailed information on race and ethnicity was not available. Autism was clinically diagnosed in 20841 individuals (1.6%; 7129 [34.2%] female) with a mean (SD) age of 16.1 (5.1) years (17.0 [4.8] years in female individuals and 15.7 [5.2] years in male individuals) for the first recorded autism diagnosis. Percentages of individuals receiving each psychiatric diagnosis are presented in eTable 4 in the Supplement and Figure 1.

Sex Differences in Psychiatric Diagnoses

We observed sex differences in the cumulative incidence of psychiatric diagnoses between age 16 and 25 years among autistic individuals: 77 of 100 autistic female individuals, compared with 62 of 100 autistic male individuals, received at least 1 psychiatric diagnosis. Cumulative incidence was higher for autistic female individuals (0.016 [95% CI, 0.012-0.020]-0.52 [95% CI, 0.50-0.53]) than autistic male individuals (0.001 [95% CI, 0.000-0.002]-0.39 [95% CI, 0.38-0.40]) and nonautistic individuals across all individual disorders (eTable 5 in the Supplement). Comparing the standardized survival probability of autistic female and male individuals at age 25 years, we observed a statistically significant standardized risk difference for any diagnosis (−0.15; 95% CI, −0.17 to −0.13), indicating higher risk in female individuals (Figure 2). The same pattern was seen for sleep, depressive, and anxiety disorders (−0.28 [95% CI, −0.34 to −0.23] to −0.12 [95% CI, −0.14 to −0.11]; eFigure 2 in the Supplement). For most disorders risk differences between autistic female and male individuals were in the same direction yet larger than in nonautistic individuals (range of standardized risk differences at age 25 years: autistic individuals, −0.28 [95% CI, −0.34 to −0.23] to −0.007 [95% CI, −0.03 to 0.01]; nonautistic individuals, −0.10 [95% CI, −0.16 to −0.05] to 0.002 [95% CI, −0.03 to 0.03]; eTable 6 in the Supplement).

Sex-specific birth year–adjusted HRs showed an elevated relative risk for all disorders for autistic female individuals (HR range [95% CI], 3.17 [2.50-4.04]-20.78 [18.48-23.37]) and male individuals (HR range [95% CI], 2.98 [2.75-3.23]-18.52 [17.07-20.08]) compared with same-sex individuals without an autism diagnosis (Figure 3, model birth year). When adjusting for ADHD and ID, most of the HRs for female and male individuals remained statistically significant, except for alcohol use disorders (Figure 3, model birth year, ADHD, and ID; eTable 7 in the Supplement). The results of the sensitivity analyses including only individuals diagnosed before age 16 years were...
shown in Table 2 and eFigure 3 in the Supplement. Despite attenuated HRs, autistic female individuals showed higher cumulative incidences for all disorders except alcohol use disorders compared with autistic male individuals. Results from analyses including only individuals with multiple autism diagnoses resembled the main analyses (eTable 8 in the Supplement).

Sex Differences in Psychiatric Hospitalizations

Percentages of psychiatric hospitalizations are presented in eTable 9 in the Supplement and Figure 1. By age 25 years, 32 of 100 autistic female individuals compared with 19 autistic male individuals, 5 nonautistic female individuals, and 3 nonautistic male individuals were hospitalized due to any psychiatric disorder. Cumulative incidence for inpatient diagnoses was higher in autistic female individuals for all individual disorders (cumulative incidence at age 25 years [95% CI], 0.01 [0.004-0.009]-0.16 [0.14-0.17]), compared with autistic male individuals and nonautistic individuals (eTable 10 in the Supplement). The standardized risk difference comparing autistic female and male individuals was statistically significant for any psychiatric disorder (−0.18; 95% CI, −0.26 to −0.10; Figure 2) but not for individual disorders (eFigure 4 in the Supplement). However, all risk differences showed a higher absolute risk for female individuals. Standardized risk differences were larger for autistic compared with nonautistic individuals (range of standardized risk differences at age 25 years: autistic individuals, −0.18 [95% CI, −0.26 to −0.10] to −0.006 [95% CI, −0.04 to 0.03]; nonautistic individuals, −0.03 [95% CI, −0.17 to 0.11] to 0.002 [95% CI, −0.04 to 0.04]; eTable 11 in the Supplement).

Sex-specific birth year–adjusted HRs indicated a higher risk of hospitalizations for autistic female and male individuals compared with same-sex individuals without autism for all inpatient diagnoses (female individuals: HR range [95% CI], 5.55 [4.63-6.66]-26.30 [21.50-32.16]; male individuals: HR range [95% CI], 3.79 [3.22-4.45]-29.36 [24.04-35.87]; Figure 3, model birth year). After adjusting for ADHD and ID, sex-specific HRs remained statistically significant for all disorders, except alcohol use disorder (Figure 3, model birth year, ADHD, and ID; eTable 12 in the Supplement).

Discussion

To our knowledge, this is the largest study on sex differences in psychiatric disorders in autism to date, and the first study to comprehensively investigate psychiatric problems at different levels of psychiatric care in autistic young adults. Autistic young female individuals showed more mental health problems at multiple psychiatric care levels. Compared with autistic male individuals, autistic female individuals were at
higher risk for any psychiatric disorder and specifically anxiety, depressive, and sleep disorders. They were also more likely to have been hospitalized for any psychiatric disorder compared with autistic male individuals and nonautistic individuals. Overall, sex differences observed between autistic female and male individuals resembled those in nonautistic individuals (namely higher incidence in female individuals for most disorders), but the differences in cumulative incidence were larger among autistic individuals. The findings of this large, population-based sample, including, to our knowledge, the highest number of autistic female individuals (n = 7129) studied so far, demonstrate a high level of psychiatric difficulties among young autistic female individuals, and thus clearly emphasize this group’s pressing mental health needs. Nevertheless, we need to consider psychiatric disorders in both sexes as psychiatric diagnoses and hospitalizations were more likely in autistic female and male individuals compared with nonautistic individuals of the same sex.

This investigation provides an important and novel contribution by exploring sex differences in psychiatric inpatient diagnoses. Our study crucially showed that psychiatric hospitalizations are relatively common in autistic young adults. By as young as age 25 years, 22.1% of autistic female individuals and 10.9% of autistic male individuals (compared with less than 4% among nonautistic individuals) had been hospitalized for psychiatric difficulties, which have the potential to worsen over the course of their lives, if not treated appropriately. These high hospitalization rates partly reflect the severity of the disorder, indicating severe mental health problems in autistic individuals, particularly autistic female individuals. However, person-level factors often interact with system-level factors, such as availability of and barriers to services.31 Facing these barriers might make autistic individuals more likely to delay and avoid health care, thereby exacerbating their mental health problems, potentially leading to acute psychiatric crises that require hospitalization.31,32 Which factors lead to hospitalization and whether autistic individuals benefit from inpatient treatment or whether the hospital environment negatively impacts their mental health should be addressed in future studies.
Figure 2. Cumulative Incidence, Birth Year–Standardized Survival Probability, and Risk Difference for Any Disorder

A-C, Cumulative incidence, 1−birth year–standardized survival probability, and risk difference for any disorder, whereas D-F includes any inpatient diagnosis.
Hazard ratios (HRs) comparing autistic and nonautistic individuals of the same sex are reported here. Confidence intervals exceed the plot limits and are cut at 30. See eTable 12 in the Supplement for more information. ADHD indicates attention-deficit/hyperactivity disorder; HR, hazard ratio; ID, intellectual disability.

a All diagnoses indicates the inclusion of both outpatient and inpatient diagnoses. Inpatient indicates that only inpatient diagnoses were considered.

b Model birth year, male individuals–inpatient diagnoses: upper CI = 35.87 and female individuals–inpatient diagnoses: upper CI = 32.16.

c Model birth year, male individuals–all diagnoses: upper CI = 54.49 and model birth year, ADHD, and ID, male individuals–all diagnoses: upper CI = 105.04.
Possible Underlying Mechanisms for the Observed Sex Differences

Different factors may exacerbate psychiatric disorders in autistic female individuals compared with male individuals. One theoretical approach is the multiple minority theory. Being autistic and nonmale can be viewed as a form of minority identity. Individuals with a minority identity tend to experience increased distress, which adversely impacts their mental health and could explain the results observed in this study. More proximal explanations, specifically related to the experience of being an autistic female individual, include female autism presentation (a qualitatively and/or quantitatively different expression of autistic symptoms and behaviors which might not be covered by current diagnostic criteria), compensatory behaviors and camouflage, which may be more common in autistic female individuals, delays in diagnosis and access to support. These tend to be interrelated and impact mental health.

Besides contributing to psychiatric disorders through delayed diagnosis and access to support, the diagnostic bias often observed in autism (i.e., the earlier identification of autism in young male individuals), could have directly impacted our findings. Likelihood for an autism diagnosis is increased in autistic female individuals presenting with additional problems. It has therefore been suggested that diagnosed female individuals represent the extreme end of the autistic female population. Consequently, autistic female individuals without such comorbidities may be missed and not diagnosed. If additional difficulties in the form of co-occurring disorders are inherent in diagnosed autistic female individuals, this might have introduced bias toward an overestimation of psychiatric disorders in this study. However, the percentages of co-occurring ADHD and ID in our study appeared similar for both autistic female and male individuals, and our estimates are in line with community-based samples recruited from outside clinics.

Clinical Implications

Results from this study can inform clinical practice in 2 important ways. First, services for autistic adults are scarce and...
barriers to care are pervasive, subsequently causing gaps and delays in treatment. Expanding mental health services in the transitional period from childhood to adulthood, particularly for female individuals, to reduce disruption and discontinuation of essential services is a necessary first step to accommodate the needs of autistic young adults.

Second, it is essential to tailor services to autistic individuals' needs. Autistic people, particularly female individuals, often report a lack of autism knowledge and understanding of co-occurring psychiatric disorders among medical professionals, sometimes resulting in misdiagnosis. Improving communication between autistic individuals and medical staff is key, as miscommunication tends to complicate identification and management of co-occurring disorders.

Strengths and Limitations
The main strength of this study is the large nationwide sample, including a high number of autistic female individuals, which enabled us to comprehensively investigate psychiatric disorders, including rarer disorders. Using both outpatient and inpatient diagnoses based on reliable register data allowed us to investigate psychiatric problems at different psychiatric care levels and to draw more generalizable and robust conclusions. Nevertheless, the study is not without limitations.

We cannot exclude the possibility that autistic individuals in our cohort were misdiagnosed with psychiatric disorders or that autism was undiagnosed in individuals without an autism diagnosis. Misdiagnosis of psychiatric disorders, and co-occurring disorders overshadowing autistic traits, is relatively common in autistic individuals who often report disagreeing with assigned diagnoses. Psychiatric diagnoses have yet to be validated in autistic individuals. The extent to which this, together with differences in validity between outpatient and inpatient diagnoses, might have influenced our findings remains uncertain.

Although adjusting our analyses for ADHD/ID attenuated our estimates, we did not further stratify our analyses. How complex phenotypes with additional neurodevelopmental difficulties influence mental health in autism should be explored in future research. Initially, we aimed to account for the age of first recorded autism diagnosis, which was shown to influence co-occurring disorders in childhood. Underdiagnosis, misdiagnosis, or late diagnosis of autistic women alongside delays in support access may further exacerbate their psychiatric difficulties. However, outpatient care was only covered from 2001, restricting follow-up time. Earlier autism diagnoses, especially among older individuals, might have been missed, as indicated by the relatively high observed mean age of diagnosis. Studying the association of late diagnosis with mental health could help inferring mechanisms contributing to increased psychiatric difficulties in autistic female individuals.

Because no gender variable is available in the registers, we relied on sex assigned at birth to differentiate between female and male individuals. Importantly, as effects of sex and gender are entangled, this does not imply that the observed differences are solely due to biological mechanisms. This is relevant because a comparably higher proportion of autistic than nonautistic individuals do not identify with their assigned sex at birth or a binary gender. Nonbinary and nonconforming gender identity are particularly prevalent among autistic individuals assigned female at birth, potentially contributing to the observed sex differences. Findings from a study on mental health in autistic men, women, and nonbinary/transgender individuals indicated higher rates of psychiatric disorders for the latter 2, highlighting the need to identify to which degree autistic nonbinary/transgender individuals face additional barriers, stigma, and exacerbated psychiatric difficulties. Studies on intersectionality, including gender identity as well as other factors such as race, ethnicity, and socioeconomic status, their interaction and subsequent effect on autistic individuals' mental health constitute important avenues for future research.

Conclusions
In this cohort study, between ages 16 and 25 years, autistic female individuals experienced increased psychiatric difficulties at different levels of psychiatric care, from outpatient diagnoses to hospitalization, compared with autistic male individuals and nonautistic individuals. Higher rates compared with autistic male individuals were found for most psychiatric disorders with sex differences larger than among nonautistic individuals. This study expands the growing body of literature on autistic female individuals' experiences and consequently the recognition of differing needs in this understudied and underserved group.

ARTICLE INFORMATION
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Sex Differences in Mental Health Problems and Psychiatric Hospitalization in Autistic Young Adults


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