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Association between autism diagnosis rates and adolescent depression: A population-based study in Sweden

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ABSTRACT

Introduction: The association between increasing diagnosis rates of autism-related disorders (ASD-R) in Swedish regions and diagnosis rates of major depressive disorders (MDD) in adolescents remains unexplored.
Methods: Following STROBE guidelines, this pre-registered (https://osf.io/duvq7) observational study, utilizing registry data from 2008 to 2022 across the 21 Swedish regions, employed a generalized linear mixed model (GLMM) to analyze the association between ASD-R (ICD-10: F84) and MDD diagnosis rates (ICD-10: F32) in 15–19 year olds, with registered primary diagnoses considered. The GLMM included psychiatric care affiliation rates (PCAR) as fixed effects and variations across years and regions as random intercepts. The model incorporated bipolar disorder (BD) rates and the male-to-female ratio of ASD-R diagnoses when justified. Separate models were created for combined sexes, males, and females.
Results: A significant inverse relationship was observed between ASD-R and MDD diagnosis rates across all sex groups. In the combined-sex model, the mean ratio was 0.40 ($P = 0.003$), while the sex-specific models showed ratios of 0.28 for males ($P < 0.001$) and 0.37 for females ($P = 0.017$). All ratios were significantly below 1, indicating a negative association between ASD-R and MDD diagnosis rates.
Conclusions: The study's observational nature limits causal inferences, but findings reveal that higher primary diagnosis rates of ASD-R correlate with lower primary diagnosis rates of MDD in adolescents of both sexes, although more pronounced in males. These results highlight the importance of further research on the relationship between ASD-R and MDD diagnosis rates, emphasizing the need for prospective, longitudinal, and individualized register data that include both primary and co-diagnoses.

1. Introduction

Depressive illness during adolescence is a critical public health concern, with Major Depressive Disorder (MDD) exhibiting a 1-year prevalence rate of approximately 4 % by the end of adolescence globally (Thapar et al., 2012a). This makes MDD a leading cause of long-term disability and a significant contributor to suicide mortality in this population (Bridge et al., 2006a). Early detection and treatment are paramount for sustained response or remission, with delayed treatment associated with poorer outcomes and longer time to remission (Curry et al., 2011a). Hence, the US Preventive Services Task Force advocates for screening MDD in adolescents aged 12–18 years, highlighting the importance of early identification and intervention to prevent disability and suicide deaths (Mangione et al., 2022a).

In recent decades, the study of Autism Spectrum Disorder (ASD) has received increased attention in research and clinical settings (Happé and

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Frith, 2020). ASD, a neurodevelopmental disorder characterized by communication deficiencies, social interaction challenges, and cognitive rigidity, has seen a substantial rise in reported prevalence rates. The latest data from the US Autism and Developmental Disabilities Monitoring Network indicates a prevalence rate of 2.76 % in the US, with profound autism observed in 26.7 % of cases (Hughes et al., 2023). However, variations in prevalence rates between regions and changes in diagnostic practices may contribute to this trend (Maenner et al., 2023). Research from Scandinavian contexts shows that the prevalence of the ASD phenotype has been relatively stable at the population level (Lundström et al., 2015b). Still, a substantial increase in diagnosis rates coincides with consistent decrease in core autism symptom severity among school-age preteens diagnosed with ASD over time. This suggests changes in diagnostic criteria and application, as well as increased focus on managing less severe cases within youth psychiatric services (Arvidsson et al., 2018a).

While ASD receives increased attention, concerns have arisen regarding the recognition and treatment of other developmental conditions and coexisting disorders (Arvidsson et al., 2018a; Avlund et al., 2021; Hansen et al., 2015). Early diagnosis and intervention have shown significant positive impacts on developmental outcomes in children with ASD aged 18–24 months (Zwaigenbaum et al., 2015; Kasari et al., 2010; Dawson et al., 2010). However, limited understanding exists regarding the effectiveness of treatments for late-diagnosed adolescents with neurodevelopmental disorders. For instance, Martini et al. (2022) conducted a study in Sweden involving females receiving ASD diagnoses at an average age of 16.1 years. By age 25 years, the majority of these individuals had received at least one additional psychiatric diagnosis (77 % females, 62 % males), with anxiety (32 % females, 15 % males), MDD (31 % females, 18 % males), and sleep disorders (38 % females, 27 % males) being the most common. It should be noted that anxiety and sleep disturbances play a crucial role in MDD, but the former is not included in the DSM criteria due to its nonspecific nature (First et al., 2022). Furthermore, a substantial proportion of these late-diagnosed individuals required psychiatric hospitalization at least once (32 % females, 19 % males) (Martini et al., 2022). These findings have been interpreted to indicate that modern psychosocial interventions for late-diagnosed ASD may be insufficient to prevent hospitalization and effectively address comorbid psychiatric disorders, pointing to the importance of excluding diagnostic overshadowing of putatively underrecognized youth psychiatric conditions that may precipitate hospitalization (Andersson et al., 2023a).

This study examines the correlation between ASD and MDD diagnoses in 15–19-year-olds. Although this age range is not typical for ASD onset, we have reported a surge in ASD cases within this range (Andersson et al., 2023a). Others have provided empirical evidence suggesting that the general increase in ASD prevalence could be partially explained by exogenous factors, a topic widely discussed by leading researchers in the field (Fombonne, 2001; Davidovitch et al., 2020; Ophir et al., 2023; Lundström et al., 2015a). Prior research indicates evolving diagnostic practices, with core ASD symptom severity decreasing (Arvidsson et al., 2018b) and concepts like camouflaging—where symptoms may not have been overtly apparent or disabling from childhood, and disabling symptoms debuting in adolescence could still be understood as autism—becoming more prominent (Happé and Frith, 2020). This suggests that ASD is increasingly considered a differential diagnosis in adolescents.

Public data from Swedish registers indicate major regional differences in ASD diagnostic practices among adolescents. Registered F84 diagnoses according to the ICD-10—which includes ASD and related disorders—show substantial variation between major Swedish regions despite universal healthcare and similar demographics. For example, the 2021 F84 prevalence rates for females aged 10–19 were 1.52 % in the Stockholm region, compared to 0.55 % in Västra Götaland and 0.59 % in Skåne. In contrast, prevalence rates in 0–4-year-old girls showed negligible regional differences (0.093–0.098 %) (Dawson et al., 2010). National rates for adolescent females increased tenfold from 2001 (0.0335 %) to 2012 (0.3546 %) and reached 0.97 % in 2021, with uninterrupted yearly consecutive increases. These data suggest that the increase in ASD diagnoses in adolescents that have been addressed in several countries may be partly explained by exogenous factors such as altered diagnostic frameworks for adolescents (Thapar et al., 2012a; Bridge et al., 2006a; Curry et al., 2011a; Mangione et al., 2022a, Happé and Frith, 2020). Previous case series from this region depict the misdiagnosis of ASD in youth with major affective disorders, particularly bipolar disorder, providing empirical evidence that ASD can sometimes be confused with major affective disorders in adolescents (Lundberg et al., 2024). Prior case reports from other demographics also depict the overshadowing of completely separate severe mental disorders by ASD in youth, indicating that the concept of ASD can negatively impact clinicians' ability to recognize other unrelated psychiatric disorders (Dhossche and Wachtel, 2010).

We hypothesize that if core diagnostic criteria for ASD are being applied less stringently (i.e. childhood onset of disabling symptoms is required less rigorously), this could potentially lead to the diagnosis of MDD in adolescents being overshadowed by ASD. MDD is one of the most prevalent psychiatric conditions in adolescents (Gutiérrez-Sacristán et al., 2022), and previous reports provide indications of substantial discrepancies across Swedish regions in its diagnosis and treatment (Desai Boström et al., 2023). Thus, multiple indications suggest that nosological frameworks for diagnosing ASD in adolescents are changing, with differential effects in major Swedish regions. Lower-quality evidence suggests that ASD diagnosis can overshadow those of major affective disorders and other severe mental disorders in youth. Given the recent and unprecedented increase in Swedish adolescents diagnosed with ASD, observed more strongly in certain regions, combined with the incidence spike in MDD in this age range (Birmaher et al., 2002) and the well-established knowledge that prompt and early identification and treatment of MDD in adolescents is paramount for sustained response or remission, with delayed treatment associated with poorer outcomes and longer time to remission (Curry et al., 2011a), it is of high clinical relevance to investigate if regional year-wise ASD diagnosis rates are associated with MDD frequencies in Swedish adolescents. Identifying potential challenges and discrepancies in diagnosing and treating both ASD and MDD in adolescents is essential for improving long-term outcomes and developing rational clinical guidelines.

The aim of this study was to investigate the potential association between year-wise regional autism spectrum disorder-related (ASD-R; ICD-10 code: F84) primary diagnosis rates and MDD (ICD-10 code: F32) primary diagnosis rates in 15–19-year-old adolescents in Sweden. Using national registry data and implementing generalized linear mixed models (GLMM) models to analyze year-wise regional MDD diagnosis rates between 2008 and 2022 in relation to ASD. Due to the close relationship between MDD and bipolar disorder—where MDD is characterized by depressed mood, low energy, low self-esteem, and anhedonia, and bipolar disorder involves alternating episodes of depressed mood and manic/hypomanic episodes marked by elevated mood, increased energy, and goal-directed activity—we considered diagnosis rates of bipolar disorder (ICD-10 code: F31) as a covariate in the statistical models where statistically motivated. The analyses were performed separately for both sexes to consider possible sex differences in prevalence rates of ASD and major affective disorders in youth (Lundström et al., 2015a; Andersson et al., 2023a; 2023c).

In this study, we included the full spectrum of ICD-10 F32 diagnoses, ranging from mild depressive episodes to major depressive disorder (MDD), severe with psychotic features. This comprehensive approach was intentional, designed to capture the complete landscape of depressive disorders in our adolescent cohort. By encompassing all F32 diagnoses, we aimed to provide a more nuanced understanding of how depressive symptoms are recognized and classified in this age group. This inclusion not only highlights the prevalence of severe MDD but also

sheds light on milder and unspecified depressive episodes, which are crucial for a holistic view of adolescent mental health. This broader scope allows for a deeper exploration of diagnostic practices and the epidemiological patterns of depressive disorders in adolescents.

2. Methods

2.1. Data sources, preregistration, initial processing, and study design

This study was conducted according to STROBE (Strengthening in Reporting of Observational Studies in Epidemiology) guidelines (Elm et al., 2007), reporting on a nationwide sex-stratified observational study of ASD-R, BD and MDD diagnosis rates in 15–19-year-olds during 2008–2022. The study was preregistered prior to analysis via the Open Science Framework (weblink: https://osf.io/duvq7). Data was retrieved on March 29th, 2023, from the Swedish National Board of Health and Welfare statistical database (Ludvigsson et al., 2011) (freely available in Swedish [dataset] (Swedish Board of National Health and Welfare, 2022)) for individuals aged 15–19 years old, covering the period from 2008 to 2022, across the 21 Swedish regions. Extracted data included registered *International Statistical Classification of Diseases and Related Health Problems, Tenth Revision (ICD-10)* category main diagnoses in both specialized outpatient and inpatient care measured per 100,000 inhabitants. The following diagnosis categories were retrieved: Pervasive developmental disorders (ICD-10: F84), bipolar disorder (ICD-10: F31) and major depressive disorder (ICD-10: F32). The data analyzed in statistical models was thus the number of primary diagnoses recorded for autism spectrum-related disorders (ASD-R) or major depressive disorder (MDD) per 100,000 individuals aged 15–19 years per year in each region with the number of primary diagnoses of bipolar disorder included as a covariate in the analysis. The primary diagnosis rates were retrieved from the Swedish National Patient Registry and reflect the primary condition for which adolescents received specialized psychiatric care during an outpatient visit or inpatient care episode.

The available data comprised main diagnoses recorded without including secondary diagnoses or other potentially relevant clinical variables at the individual level. This study, therefore, focuses on measuring care received for ASD and/or MDD based on the primary diagnosis documented during care episodes. Clinicians are required to document the primary diagnosis as the condition for which the care episode was conducted. Thus, while the study may not capture co-occurring diagnoses at the individual level if both were not recorded as the main diagnosis during different visits, it can still provide insights into regional and yearly trends in primary diagnoses of ASD and MDD.

The aggregated open-access nature of data utilized exempted the project from requirements of approval from an Institutional Review Board or retrieval of informed consent from individual participants. Sources for additional control variables, initial processing steps and statistical considerations are detailed in Supplemental Material.

2.2. Statistical considerations

Three separate GLMM-models (main, sensitivity analysis 1 and 2) were performed in consecutive order, separately for each sex-group (i.e., both sexes, males, and females) to a total of nine analyses. To ensure the robustness and validity of the results, significant models were tested for dispersion and heteroscedasticity.

Given the conceptual overlap between BD and MDD, we carefully considered whether BD's role as a moderator might obscure the variance attributed to ASD. For each of the nine models constructed, we therefore conducted a rigorous statistical comparison to assess whether the inclusion of BD was statistically justified. We compared the full model, inclusive of BD, with a null model excluding BD, using the Akaike Information Criterion (AIC), Bayesian Information Criterion (BIC), and likelihood ratio tests (LRT). The criteria for BD's inclusion were based on demonstrable model fit enhancements, indicated by lower AIC and BIC values and a significant LRT. Following these standards, BD was retained in the models for the Main Analysis (Both Sexes and Females) and Sensitivity Model 1 (Females and Males), but not in Sensitivity Model 2. Further, in light of the recognized sex differences in ASD prevalence, we integrated the male-to-female ASD-R diagnosis ratio as an independent variable in our analyses for the combined sexes. This ratio, derived from the annual regional data on ASD diagnoses, reflects the proportion of diagnosed males to females. Given the aggregated nature of the data, which presents regional prevalence rates by year, our analysis was constrained in its complexity. The inclusion of this sex ratio was intended to adjust for potential sex-related prevalence biases in assessing the association between MDD and ASD. Reporting standards have improved over time – and may influence registered regional diagnosis rates (Ludvigsson et al., 2011). Moreover, regional year-wise variations in psychiatric care affiliation rates (PCAR) could exert endogenous influence on the analysis – as high PCAR would be expected to be independently associated with higher psychiatric diagnosis rates. Thus, it is important to adjust the analysis for regional variations in reporting standards and psychiatric care affiliation rates (Ludvigsson et al., 2011). In our analysis we adjusted diagnosis rates for reporting standards across all diagnostic categories for each year and region (calculated using the following formula [(Total number of visits - Number of visits without diagnosis code) / (Total number of visits)] and PCAR (calculated using the following formula: recorded psychiatric diagnoses in outpatient care settings / proportion of visits with registered diagnoses in outpatient settings across all diagnosis categories).

For rationale for omitting multiple testing in confirmatory sensitivity analyses, please see Supplemental Material.

2.3. Model diagnostics

Significant models were tested for dispersion and heteroscedasticity. For details, please see Supplemental Materials.

2.4. Main analysis: PCAR-adjusted diagnosis variables

First, ASD-R, MDD and BD diagnosis rates were divided by PCAR for the main analysis, separately for each region, year, and sex-group, respectively – serving as an estimate of the percentage of outpatient psychiatric visits concerned with any of these diagnostic categories. It was determined that this estimate could act as a plausible proxy variable for the percentage of regional yearly psychiatric care burden concerned with ASD-R, MDD and BD (expressed as a value between 0 and 1). Based on visual inspection of the distribution of the outcome variable (regional year-wise MDD diagnosis rates divided by PCAR) it was determined that the main analyses GLMM models could be modelled on the beta distribution (Brooks et al., 2017). Collinearity on the predictor variables were investigated by analyses of the variance inflation factor (VIF), where a variable VIF value lower than 5 was not considered necessary to account for in subsequent analyses. Across all analyses, no variable exhibited collinearity (i.e., VIF < 5).

The outcome variable (MDD diagnosis rates) was investigated in relation to these exposure variables separately for both sexes, males, and females - by GLMM models specified to the beta-family distribution with a logit link function, deemed ideal for analyzing proportional outcomes. Regional ASD-R and PCAR were designated as fixed-effects variables, and random-intercept effect modifiers (region and year) were treated as random-effects. BD was included as a covariate for both combined sexes and females, a decision substantiated by improved AIC/BIC scores and a significant LRT. For the combined sexes group, we also adjusted for the regional year-wise male-to-female ratio regarding ASD diagnosis rates - note this variable was already expressed as a proportion and was thus, not, adjusted for PCAR. To ensure comparability between predictor variables, the PCAR-variable was subjected to transformation by Blom's method – maintaining the mutual relationship between observations (Ludwig, 1961). Post-hoc testing of the models indicated no

overdispersion or heteroscedasticity that could bias downstream results (Supplemental Figs. 1–3). *P*-values < 0.05 were considered significant. In the main analysis, the mean ratio of ASD-R rates to MDD rates was analyzed. Thus, a ratio larger than 1 would signify a positive association whereas a ratio below 1 would signify a negative association.

2.5. First sensitivity analysis: baseline diagnosis variables

Based on visual inspection of the distribution of the outcome variable (regional year-wise MDD diagnosis rates) it was determined that the first validation GLMM models could be modelled on the t-family of distributions (specifically, the Pearson Type VII distribution – a general class of distribution available from the 'glmmTMB' package for R that contains the Student's t distribution (Brooks et al., 2017)). Analyses were performed separately for each sex group. Across all analyses, no variable exhibited collinearity (i.e., VIF < 5).

Models were adjusted for PCAR and ASD-R diagnosis rates, while year and region constituted random-intercept effect modifiers. BD was included as a covariate for females and males, but not for the combined sexes; this decision was substantiated by improved AIC/BIC scores and a significant LRT for females and males, but not for the combined sexes. Post-hoc testing of the models indicated no overdispersion or heteroscedasticity that could bias downstream results (Supplemental Figs. 4–6). *P*-values < 0.05 were considered significant.

2.6. Second sensitivity analysis: dichotomized baseline diagnosis variables

Significant models were further explored by separate analyses. The MDD diagnosis rate variable was dichotomized based on the 25th percentile (Q1) – contrasting those observations with Q2-Q4 observations. This model thus served to validate whether lower-quartile observations regarding MDD diagnosis rates were predictive of changes to the ASD-R and/or PCAR variables. Lowest-quartile observations were thus compared to Q2-Q4 observations, separately for each sex group. Based on model selection criteria (AIC/BIC and Likelihood Ratio Tests), bipolar disorder (BD; ICD-10: F31) was excluded as a covariate for all sexes. For details, please see Supplemental Material.

3. Results

3.1. Baseline characteristics of data

The main diagnosis rates of ASD-R, BD, and MDD diagnoses per 100,000 inhabitants in 15–19-year-olds from 2008 to 2021 were calculated independently. The mean unadjusted diagnosis rate across both sexes for ASD-R was 884.6 (SD: 403.8), for BD diagnoses was 101.1 (SD: 10.8), and for MDD diagnoses was 1085.3 (SD: 279.1). These values were not adjusted for variations in reporting standards and were calculated across all regions and sexes. Female adolescents were more often diagnosed with affective disorders but less frequently with ASD-R than males, i.e., for females, mean 751.8 (SD: 412.9) [Autism-related], 150.6 (SD: 18.8) [BD] and 1570.2 [SD: 442.9] [MDD], and, for males, mean 1007.8 (SD: 403.7) [Autism-related], 55.1 (SD: 6.3) [BD] and 634.7 [SD: 138.0] [MDD]. During 2008 to 2022, non-reporting standard adjusted national diagnosis rates across all regions and sexes increased by factor 5.1 (from 276.1 to 1403.8) [Autism-related], 1.5 (from 69.8 to 104.0) [BD] and 2.2 (from 609.8 to 1317.4) [MDD] (ranges referring to 2008 vs. 2022). There were large regional variations in ASD-R, BD and MDD diagnosis frequencies across both sexes. 2022 regional diagnosis rates deviated over the national median (measured across 2008–2022), in females, by factor 0.8–3.7 [Autism-related], 0.3–6.4 [BD] and 0.5–1.6 [MDD], and, in males, by factor 0.9–4.1 [Autism-related], 0.12–2.0 [BD] and 0.6–1.6 [MDD]. Baseline data on diagnostic frequencies is displayed in Table 1.

Table 1
Regional yearly diagnostic frequencies of ASD-R, BD and MDD in 15–19-year-olds during 2008–2022.

	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022
Regional BD-diagnoses. males	42.5 (30.7)	47.9 (31.0)	49.7 (32.0)	55.1 (39.9)	62.6 (40.1)	59.8 (32.3)	57.5 (37.9)	66.8 (32.6)	57.9 (22.9)	52.8 (32.0)	60.6 (36.3)	58.4 (39.3)	54.0 (47.6)	51.9 (53.2)	49.3 (62.0)
Regional MDD-diagnoses. males	374.9 (152.5)	383.8 (153.5)	446.3 (187.7)	550.3 (157.6)	610.1 (189.5)	640.0 (167.5)	699.9 (216.3)	679.6 (194.2)	705.8 (309.4)	753.3 (223.0)	821.6 (190.6)	774.1 (172.7)	728.1 (164.0)	697.7 (209.5)	655.6 (178.9)
Regional ASD-R-diagnoses. males	336.3 (225.4)	397.9 (310.1)	468.3 (355.1)	618.5 (486.6)	758.3 (515.4)	888.9 (662.3)	998.7 (799.0)	1113.6 (662.5)	1211.6 (609.3)	1281.9 (711.4)	1345.5 (663.8)	1432.4 (589.0)	1462.5 (663.6)	1416.5 (622.4)	1386.3 (712.0)
Regional BD-diagnoses. females	98.8 (65.8)	128.8 (100.3)	151.4 (113.3)	149.9 (107.8)	154.1 (117.3)	152.9 (102.5)	139.7 (82.0)	147.1 (79.4)	157.3 (93.6)	182.0 (110.3)	167.9 (119.6)	163.8 (96.9)	154.7 (139.6)	147.7 (158.7)	162.2 (226.8)
Regional MDD-diagnoses. females	858.3 (379.8)	885.9 (405.3)	969.3 (436.3)	1 108.8 (356.6)	1 252.9 (403.0)	1 464.8 (474.6)	1 641.7 (408.5)	1 702.5 (445.8)	1 792.6 (476.9)	1 938.7 (472.2)	1 990.9 (511.5)	1 974.4 (521.6)	1 927.6 (537.1)	2 024.4 (621.3)	2 020.5 (600.2)
Regional ASD-R-diagnoses. females	212.4 (177.7)	238.6 (191.0)	260.6 (212.9)	371 (318.8)	442.6 (438.2)	534.9 (417.4)	597.2 (384.1)	708.3 (445.4)	811.3 (489.2)	945.2 (532.1)	1028.6 (444.6)	1165.5 (481.9)	1227.5 (532.9)	1311.4 (599.2)	1422.5 (668.2)

Table 1. Legend: Mean of regional diagnostic frequencies of bipolar disorder (ICD-10 code F31), major depressive disorder, (ICD-10 code F32) and autism spectrum-related disorder (ICD-10 code F84) diagnoses per 100,000 inhabitants in Swedish 15–19-year-olds during 2008–2022. These values have not been adjusted for population-size or regional heterogeneity in reporting-standards, thus, representing means of unadjusted data as was originally reported to the Swedish National Board of Health and Welfare. Values displayed are means for the 21 Swedish regions, unadjusted for population size of regions. Standard deviations in parentheses. For both sexes, non-reporting standard adjusted national diagnosis rates across all regions increased by factor 5.1 (from 276.1 to 1403.8) [Autism-related], 1.5 (from 69.8 to 104.0)[BD] and 2.2 (from 609.8 to 1317.4)[MDD] between 2008 and 2022. Affective disorder diagnosis rates were higher in females, whilst males had higher rates of ASD-R diagnoses (mean values across the entire time-period, females: 751.8 (SD: 412.9)[Autism-related], 150.6 (SD: 18.8)[BD] and 1570.2 [SD: 442.9][MDD], vs. mean values across the entire time-period, males: 1007.8 (SD: 403.7) [Autism-related], 55.1 (SD: 6.3) [BD] and 634.7 [SD: 138.0] [MDD]). Abbreviations: BD: bipolar disorder; MDD: Major depressive disorder; ASD-R: Autism spectrum-related disorder.

3.2. Main analysis of diagnosis rates divided by PCAR

In the main analyses, where regional year-wise diagnosis rates were expressed as a percentage of PCAR, ASD-R rates were associated to MDD rates across both sexes (Mean Ratio = 0.40, $P = 0.003$, 95 % CI [0.22, 0.73]), in males (Mean Ratio = 0.28, $P < 0.001$, 95 % CI [0.17, 0.46]), and in females (Mean Ratio = 0.37, $P = 0.017$, 95 % CI [0.16, 0.83]) (Fig. 1). In these analyses, MDD diagnosis rates were negatively correlated with PCAR across both sexes (Mean Ratio = 0.97, $P = 0.045$) and in males (Mean Ratio = 0.90, $P < 0.001$), with a non-significant trend in the same direction observed in females (Mean Ratio = 0.97, $P = 0.064$) (Table 2). Diagnostic assessments of the models did not demonstrate any significant problems (Supplemental Figs. 1–3).

3.3. First sensitivity analysis of baseline diagnosis rates

For the first validation analysis, which assessed baseline diagnosis rates not expressed as a percentage of PCAR, the positive association between ASD-R diagnosis frequencies and lower-than-expected MDD diagnosis rates in the combined sexes group was confirmed ($\beta = -0.15$, $P < 0.001$, 95 % CI [-0.22, -0.09]), in males ($\beta = -0.09$, $P < 0.001$, 95 % CI [-0.13, -0.05]), and in females ($\beta = -0.17$, $P = 0.005$, 95 % CI [-0.28, -0.05]) (Fig. 2). Additionally, PCAR was associated to of MDD diagnosis rates across both sexes ($\beta = 0.15$, $P < 0.001$), females ($\beta = 0.21$, $P < 0.001$), and males ($\beta = 0.09$, $P < 0.001$) (Table 3). Diagnostic assessments of the models did not demonstrate any significant problems (Supplemental Figs. 4–6).

3.4. Second sensitivity analysis of dichotomized baseline diagnosis rates

In the second validation analysis, higher autism-related diagnosis rates were associated with lower-quartile MDD diagnosis rates in Swedish 15–19-year-old across all sexes, i.e., in the combined sexes (OR = 0.14, $P = 0.0093$, 95 % CI [0.031, 0.615]), in females (OR = 0.32, $P = 0.0213$, 95 % CI [0.12, 0.85]) and males (OR = 0.50, $P = 0.0459$, 95 % CI [0.26, 0.99]). PCAR was associated to higher-quartile MDD diagnosis rates across all sex groups ($\beta = 827.08$, $P = 1.53e\text{-}07$ for both sexes; $\beta = 161.50$, $P < 0.0001$ for females; $\beta = 22.50$, $P < 0.0001$ for males) (Table 4). The diagnostic assessments of the final models did not demonstrate any significant problems (Supplemental Figs. 7–9).Diagnostic assessments of the models did not demonstrate any significant problems (Supplemental Figs. 7–9).

4. Discussion

In this pre-registered study, our aim was to investigate the possible relationship between diagnosed ASD-R related conditions and diagnosis rates of MDD in Swedish youth. We conducted a comprehensive analysis using data from all Swedish regions for the years 2008–2022, revealing substantial regional variations in ASD-R, BD, and MDD diagnoses. National main diagnosis rates for these conditions increased significantly during the study period: by a factor of 5.0 for ASD, 1.4 for BD, and 2.2 for

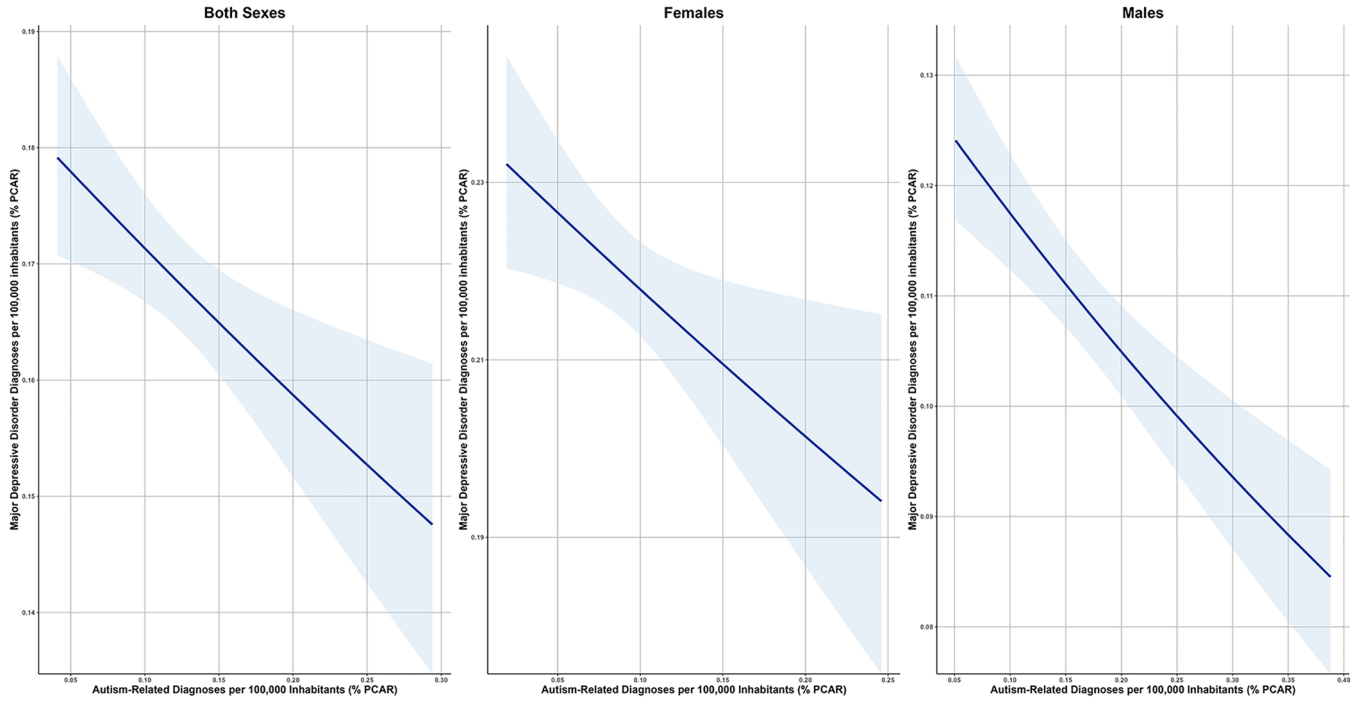

Fig. 1. Predictive analysis of PCAR-adjusted major depressive disorder diagnoses in relation to autism spectrum disorder-related diagnoses.
This figure presents the predicted diagnostic frequencies for Major Depressive Disorder (MDD; ICD-10 code: F32), on a year-wise and region-specific basis, as derived from a generalized linear mixed-effects model. The model employs a beta distribution and a logit link function. Frequencies are expressed as a percentage of the Psychiatric Care Affiliation Rates (PCAR). These predictions are based on the PCAR-adjusted Autism Spectrum Disorder-Related (ASD-R; ICD-10 code: F84) diagnosis rates, as delineated by the principal model applied to the studied population. The predictive line, represented in dark blue, is situated within a 95 % confidence interval, shaded in light blue, offering a visual representation of the predictive reliability surrounding the ASD-R diagnostic rates. Subsequent diagnostics facilitated through DHARMa underscored a homoscedastic nature in the finalized model, negating any substantial indications of heteroscedasticity or overdispersion, thereby affirming the reliability of the predictive values presented in this visualization (refer to Supplemental Figs. 1b, 2a, 3a for diagnostic details). The intricate modelling approach adopted facilitated a rigorous investigation into the diverse predictors including ASD-R and – for the combined sexes and females - bipolar diagnosis (BD; ICD-10 code: F31) rates, alongside psychiatric care affiliation rates (PCAR), incorporating region and year as random intercept-effects to yield a comprehensive insight into the dynamics governing MDD diagnosis rates. The model demonstrated a robust negative association between ASD-R and MDD diagnosis rates(i.e., in both sexes: Mean Ratio = 0.40, $P = 0.003$, 95 % CI [0.22, 0.73], in males: Mean Ratio = 0.28, $P < 0.001$, 95 % CI [0.17, 0.46], and in females: Mean Ratio = 0.37, $P = 0.017$, 95 % CI [0.16, 0.83]. **Abbreviations**: ASD-R, Autism Spectrum Disorder-Related; BD, Bipolar Disorder; MDD, Major Depressive Disorder; PCAR, psychiatric care affiliation rates.

Table 2
Analysis of associations with adjusted MDD Diagnosis Rates in Swedish Adolescents (Aged 15–19 Years).

	Mean Ratio	95 % CI Lower	95 % CI Upper	p-value
Both Sexes				
BD Rate (F31)	235.71	12.61	4405.01	<0.001
ASD-R Rate (F84)	0.40	0.22	0.73	0.003
PCAR*	0.97	0.94	0.99	0.045
Male-to-Female ratio (F84)	1.05	1.00	1.10	0.035
Females				
BD Rate (F31)	29.90	3.63	246.17	0.002
ASD-R Rate (F84)	0.37	0.16	0.83	0.017
PCAR*	0.97	0.94	1.00	0.064
Males				
ASD-R Rate (F84)	0.28	0.17	0.46	<0.001
PCAR*	0.90	0.87	0.94	<0.001

Model Details:
Dispersion parameter for beta family (Both Sexes/Females/Males): 262/124/359
AIC (Both Sexes/Females/Males): -1253.9/-1065.0/-1378.5
BIC (Both Sexes/Females/Males): -1223.9/-1038.7/-1356.0
logLik (Both Sexes/Females/Males): 635.0/539.5/695.3
Deviance (Both Sexes/Females/Males): -1269.9/-1079.0/-1390.5
Random Effects:
Region:Year (Intercept) Variance (Both Sexes/Females/Males): 2.644e-02/1.912e-02/0.045276
Year (Intercept) Std. Dev (Both Sexes/Females/Males): 1.626e-01/0.138264/0.2128
Number of observations: 315; Groups: Weights:Region:Year, 315; Region:Year, 315; Year, 15

This table details mean ratios, 95 % confidence intervals (CIs), and p-values from a beta regression model with a logit link function, ideal for analyzing proportional outcomes. We investigated the association between diagnosis rates of autism spectrum disorder (ASD; ICD-10 Code: F84) and major depressive disorder (MDD; ICD-10 Code: F32) among 15–19-year-olds. Rates were normalized against psychiatric care affiliation rates (PCAR) across multiple regions and time periods.
Blom's method was utilized to normalize PCAR, thus accommodating the proportional nature of the data. The model, adjusting for ASD-to-PCAR and PCAR, also included PCAR-normalized bipolar disorder (BD; ICD-10 code: F31) as a covariate in analyses for both combined sexes and females, a decision substantiated by improved AIC/BIC scores and a significant Likelihood Ratio Test (LRT). For the combined sexes group, we also adjusted for the regional year-wise male-to-female ratio regading ASD diagnosis rates - note this variable was already expressed as a proportion and was thus, not, adjusted for PCAR.
Employing generalized linear mixed-effects models from the beta distribution family, the fixed effects incorporated ASD-to-PCAR, PCAR, and BD-to-PCAR (for combined sexes and females), while random effects accounted for region and year. Model optimizations to mitigate potential biases are explicated in Supplemental Figs. 1b, 2a, and 3a. Abbreviations: AIC: Akaike information criterion, ASD-R: Autism Spectrum disorder related diagnosis, BD: Bipolar Disorder, BIC: Bayesian information criterion, logLik: Log Likelihood value, PCAR: Psychiatric Care Affiliation Rates, Std. Dev: Standard Deviation.

MDD. Our findings indicate that regional main diagnostic rates of ASD-R were reliably associated to regional rates of MDD diagnosis, with increased ASD-R diagnosis correlating with decreased main diagnosis rates of MDD, a relationship robust in sensitivity analyses. Moreover, higher rates of autism-related diagnoses were associated to lower-quartile MDD diagnosis rates in Swedish 15–19-year-olds of all sexes. These results remained consistent even after accounting for regional yearly adolescent psychiatric care affiliation rates, BD diagnosis rates, region, and year. While the observational nature of our study and the use of aggregated data at the regional level limit our ability to delve into causality, we nonetheless observe a clear signal at the macro level, suggesting a potential bi-directional relationship between main diagnoses of ASD-R and MDD in Swedish adolescents. Further investigation using prospective, longitudinal, and individualized data that consider co-diagnoses is warranted to explore this relationship more deeply. The clinical urgency of promptly diagnosing and treating adolescent MDD underscores the importance of such research endeavors (Thapar et al., 2012a; Mangione et al., 2022a; Curry et al., 2011a; Bridge et al., 2006a).

There are several possible explanations for the observed temporal and regional differences in the diagnostic patterns of MDD and ASD. There is prior rapport that bolsters the concept of diagnostic overshadowing of MDD in clinical contexts that could potentially contribute to the observed findings. For example and beyond the context of ASD and MDD, research observed instances where different psychopathological frameworks can result in varied diagnoses and treatments for youth with symptoms of severe mental illness (Andersson et al., 2022). Case reports also suggest that severe mental health episodes in individuals with autism can be misattributed to autism itself (Wachtel, 2019), leading to potential under-recognition from diagnostic overshadowing. Further, institutional incentives favoring recognition of certain diagnoses could be a factor influencing the observed pattern. In Sweden, policy initiatives may preferentially encourage the diagnosis of ASD-R. Legislation since 1993 affords individuals with autism spectrum conditions the right to specialized support, including dedicated care facilities and individualized assistance (SFS, 1993). Additionally, certain regions mandate timely neuropsychiatric evaluations for ASD-R, with assessments expected within 90 days, incentivized by government reimbursements upon compliance (Region Stockholm, 2023; Region Götaland, 2024). No such mandates or incentives currently exist for mood disorders or other serious mental health diagnoses. This discrepancy has been criticized in the professional press (Dagens Medicin, 2014; Dagens Medicin, 2008). However, since the analyzed data included only primary diagnoses and excluded secondary diagnoses, temporal and regional differences in how ASD and MDD are prioritized could have influenced the results. According to Swedish diagnostic guidelines (Swedish Board of National Health and Welfare, 2024), primary diagnoses are assigned based on the priorities of each care episode rather than reflecting the patient's overall health condition. Consequently, temporal and regional variations in the perceived importance of these two conditions for individuals meeting the criteria for both diagnoses may have impacted the findings. Therefore, the results should be interpreted as indicating an inverse association between the proportion of care episodes where ASD and MDD, respectively, are the primary focus of clinical attention.

Our longitudinal study revealed a notable change in the gender distribution of ASD diagnoses. The observed pattern could theoretically reflect both changes in the true population prevalence rates of the studied conditions or changes in diagnostic practices. Historically, ASD incidence has been lower in females—a trend consistent with our initial findings. However, by 2022, the gender gap in ASD diagnoses closed significantly, with female incidence rates approaching those of males. This change, more pronounced in females, suggests a shift in diagnostic recognition and practices. This observed convergence calls for detailed investigation. It may indicate a growing accuracy in diagnosing ASD in females, who can exhibit symptoms differently from males, potentially leading to historical underdiagnosis. Over the past decades, research has suggested that both clinical practices, such as diagnostic procedures and sex-specific diagnosis criteria, and patient characteristics, such as differences in presentation and the ability to engage in compensatory behaviors, contribute to the under-recognition of both Attention Deficit Hyperactivity Disorder (ADHD) and ASD in females, highlighting the need for earlier recognition of neuropsychiatric disorders in females (Martin, 2024; Mowlem et al., 2019; Lai and Szatmari, 2020). The increase in female ASD diagnoses aligns with a heightened focus on ASD

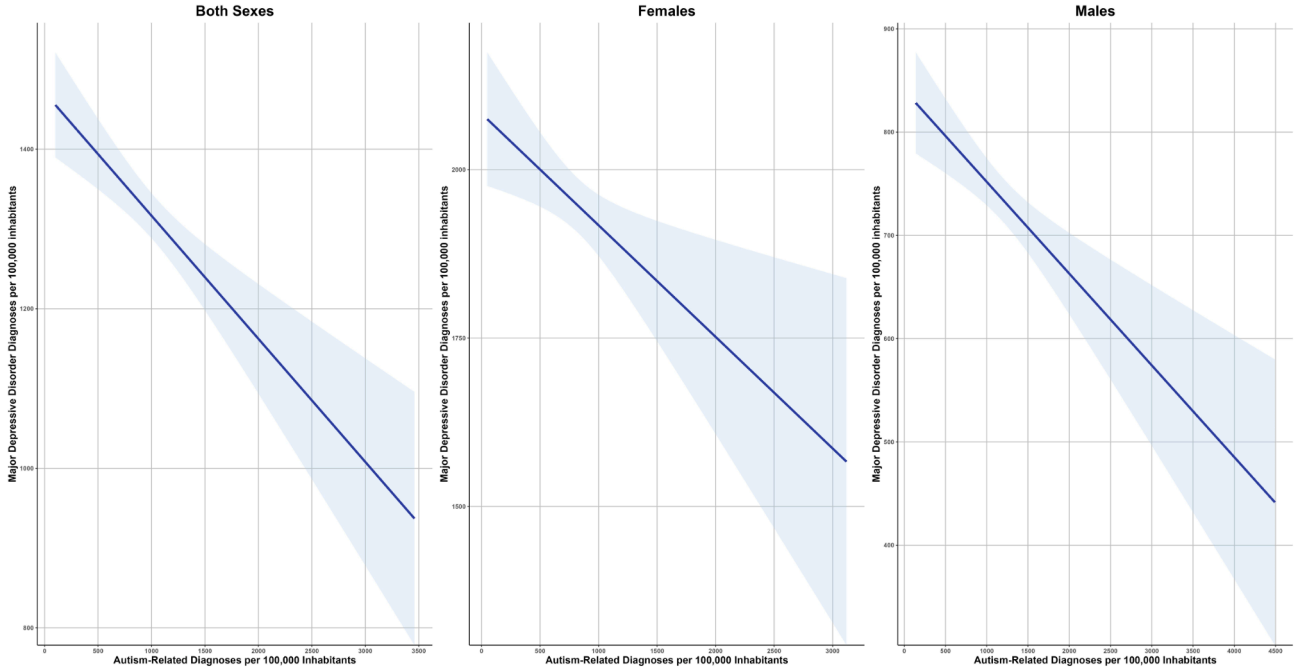

Fig. 2. Predictive analysis of major depressive disorder diagnoses in relation to autism spectrum disorder-related diagnoses – baseline diagnosis rates.
This figure delineates the predicted year-wise and region-specific diagnostic frequencies of Major Depressive Disorder (MDD) as a function of Autism Spectrum Disorder-Related (ASD-R) diagnosis rates, as discerned from the first validation model for the studied population. The predictive line, represented in dark blue, is situated within a 95 % confidence interval, shaded in steel blue, offering a visual representation of the predictive reliability surrounding the ASD-R diagnostic rates. Subsequent diagnostics facilitated through DHARMa underscored a homoscedastic nature in the finalized model, negating any substantial indications of heteroscedasticity or overdispersion, thereby affirming the reliability of the predictive values presented in this visualization (refer to Supplemental Figs. 4a, 5c, 6a for diagnostic details). The intricate modelling approach adopted facilitated a rigorous investigation into the diverse predictors including ASD-R and bipolar diagnosis rates, alongside psychiatric care affiliation rates (PCAR), incorporating region and year as random intercept-effects to yield a comprehensive insight into the dynamics governing MDD diagnosis rates. The substantial resolution achieved in addressing the heteroscedasticity concerns through a meticulous adjustment of the dispersion parameter in alignment with the ASD-R predictor, as stipulated in the pre-registered protocol, engendered a robust model demonstrative of a noteworthy negative association between ASD-R and MDD diagnosis rates combined (i.e., in both sexes: $\beta = -0.15$, $P < 0.001$, 95 % CI [-0.22, -0.09], in males: $\beta = -0.09$, $P < 0.001$, 95 % CI [-0.13, -0.05], and in females: $\beta = -0.17$, $P = 0.005$, 95 % CI [-0.28, -0.05]. **Abbreviations**: ASD-R, Autism Spectrum Disorder-Related (ICD-10 code: F84); MDD, Major Depressive Disorder (ICD-10 code: F32); PCAR, psychiatric care affiliation rates.

within this demographic. These findings highlight the need to consider gender-specific presentations in ASD diagnostic criteria and practices.

Further research with more granular data allowing for detailed analysis is warranted based on the findings presented in this paper, as they could potentially impact various aspects of psychiatric inquiry if corroborated. For instance, in epidemiological research, there may be a need for a more nuanced understanding of diagnostic criteria and regional and longitudinal changes in prevalence rates. Shifting diagnostic trends could potentially affect the perceived incidence and distribution of different disorders, thereby potentially biasing subsequent findings. In the realm of large-scale genetic studies, it would be imperative to take into account diagnostic variability and its potential impact on identifying genetic markers or predispositions.

5. Strengths and limitations

The study has several strengths, including the use of openly available data from the Swedish National Board of Health and Welfare, resulting in a transparent and fully replicable pre-registered study of real-world data. The study included all individuals aged 15–19-year-olds in Sweden from 2008 to 2022, and robust control measures were implemented to account for regional differences in reporting standards. The significant results were also validated in confirmatory analyses. However, the observational-level aggregated data utilized in the current study limits the ability to make inferences of causality. The available data comprised main diagnoses recorded, without including secondary diagnoses or other potentially relevant clinical variables at the individual level. This macro-level view precludes an investigation of the complexity of individual diagnostic trajectories often observed at the level of the individual patient. Comorbidity between autism and depressive disorders is common in both adolescents (Menezes et al., 2018) and adults, with reported incidence rates as high as 23 % in reviews of clinical samples in the latter group (Hollocks et al., 2019). Diagnostic instability is also prevalent in psychiatric services, exemplified by diagnostic changes in 43.9 % of patients transitioning from adolescent to adult services (Baldaquí et al., 2023). Additionally, detailed information regarding temporal and regional differences in institutional incentives and the structural configuration of adolescent psychiatric services, such as the existence of clinics with disease-specific specialization, was not available, limiting the ability to explore the relationship of the observed findings to such organizational-level factors. The study design and data available thus limited the possibilities to investigate the clinical characteristics of adolescents diagnosed with ASD-R or MDD, diagnostic instability, comorbidity patterns, or assessment of regional differences in institutional incentives or diagnostic procedures and organizational aspects associated to these diagnoses. It is important to note that clinicians are required to document as the primary diagnosis the condition for which the care episode was conducted. Therefore, the present study may be more accurately understood as measuring care received for ASD and/or MDD for a given year in a specific region. Moreover, the main diagnosis from the Swedish national patient register has been reliably demonstrated as a viable source for identifying individuals with certain conditions for population-based research in both somatic (Murley et al., 2019) and psychiatric conditions (Thapar et al., 2012a; Mangione et al.,

Table 3
Analysis of associations with baseline diagnostic rates of MDD in Swedish Adolescents (Aged 15–19 Years).

	Estimate	95 % CI Lower	95 % CI Upper	p-value
Both Sexes				
Intercept	276.56	104.22	448.90	0.002
ASD-R Rate (F84)	-0.15	-0.22	-0.09	<0.001
PCAR*	0.15	0.12	0.18	<0.001
Male-to-Female ratio (F84)	-67.58	-153.79	18.63	0.12
PCAR*: Male-to-Female ratio (F84)	0.01	-0.01	0.03	0.22
Females				
Intercept	135.98	23.03	248.93	0.018
BD Rate (F31)	0.59	0.16	1.03	0.008
ASD-R Rate (F84)	-0.17	-0.28	-0.05	0.005
PCAR*	0.21	0.19	0.23	<0.001
Males				
Intercept	216.78	155.19	278.37	<0.001
BD Rate (F31)	-0.14	-0.65	0.37	0.60
ASD-R Rate (F84)	-0.09	-0.13	-0.05	<0.001
PCAR*	0.09	0.08	0.10	<0.001

Model Details:
Dispersion parameter for t-family (Both Sexes/Females/Males): 262/124/359
AIC (Both Sexes/Females/Males): 4409.1/4678.3/4171.8
BIC (Both Sexes/Females/Males): 4442.9/4708.3/4201.8
logLik (Both Sexes/Females/Males): -2195.5/-2331.2/-2077.9
Deviance (Both Sexes/Females/Males): 4391.1/4662.3/4155.8
Random Effects:
Region:Year (Intercept) Variance (Both Sexes/Females/Males): 1.624e-71/8.902e-13/7.844e-23
Year (Intercept) Std. Dev (Both Sexes/Females/Males): 4.864e-01/9.444e-03/1.978e+01
Number of observations: 315; Groups: Weights:Region:Year, 315; Region:Year, 315; Year, 15

Table 3 presents coefficient estimates, 95 % confidence intervals (CIs), and p-values from a generalized linear mixed effects model, using the t-family distribution to explore the association between autism spectrum disorder (ASD; ICD-10: F84) and major depressive disorder (MDD; ICD-10: F32) diagnoses in 15–19-year-olds. For females and males, bipolar disorder (BD; ICD-10: F31) was included as a covariate based on AIC/BIC improvements and a significant Likelihood Ratio Test. For the combined sexes, the model was adjusted for the interaction between PCAR and the ASD diagnosis male-to-female ratio by region and year. Fixed effects included ASD, PCAR, and BD ratios, with random effects for region and year. Detailed model optimization strategies are presented in Supplemental Figs. 1b, 2a, and 3a.Abbreviations: AIC: Akaike information criterion, ASD-R: Autism Spectrum disorder related diagnosis, BD: Bipolar Disorder, BIC: Bayesian information criterion, logLik: Log Likelihood value, PCAR: Psychiatric Care Affiliation Rates, Std. Dev: Standard Deviation.

2022a), indicating that the registry is a good reflection of diagnostic practices in clinical settings. Therefore, while at the individual level, this study may not capture instances of co-occurring diagnoses of MDD and ASD if the patient was not coded as having both as the main diagnosis during different psychiatric care visits, it is still believed that the study can discern a clear signal regarding regional and yearly trends in ASD and MDD main diagnoses at the macro level, reflecting overall clinical attention devoted to the conditions. It is worth noting that if a patient received separate care centered on ASD and MDD during the same year, they would contribute to both the ASD and MDD metrics measured in this study. Additionally, data on the average age of onset would have been valuable for enhancing the understanding of the potential influence of temporal changes in diagnostic practices on the results observed in the current investigation .Nonetheless, further investigation using prospective, longitudinal, and individualized data that account for co-diagnoses and age of onset is warranted to delve deeper into this relationship. Studies utilizing individual-level data could incorporate potentially significant covariates into the analysis, such as socioeconomic status, family composition, and exposure to adverse childhood events. At the institutional level, approaches leveraging time-invariant analysis methods to assess the potential relationship between regulations that may incentivize clinical services towards a specific diagnosis could be valuable.

Table 4
Analysis of associations with dichotomized baseline diagnostic rates of MDD in Swedish Adolescents (Aged 15–19).

	Odds Ratio	95 % CI Lower	95 % CI Upper	p-value
Both Sexes				
Intercept	34.12	10.84	107.39	1.60e-09
ASD rate (F84)*	0.14	0.031	0.615	0.0093
PCAR*	827.08	67.34	10,158.97	1.53e-07
Male-to-Female ratio (F84)	1.86	0.942	3.66	0.0738
Females				
Intercept	21.09	9.61	46.29	<0.0001
ASD-R Rate (F84)	0.32	0.12	0.85	0.0213
PCAR*	161.50	34.39	758.34	<0.0001
Males				
Intercept	8.46	4.85	14.76	<0.0001
ASD rate (F84)*	0.50	0.26	0.99	0.0459
PCAR*	22.50	7.88	64.22	<0.0001

Model Details:
AIC (Both Sexes/Females/Males): 154.9/157.9/221.2
BIC (Both Sexes/Females/Males): 184.9/180.4/243.7
logLik (Both Sexes/Females/Males): -69.5/-72.9/-104.6
deviance (Both Sexes/Females/Males): 138.9/145.9/209.2
df.resid (Both Sexes/Females/Males): 307/309/309
Random Effects:
Region:Year (Intercept) Variance (Both Sexes/Females/Males): 6.564e-09/2.552e-08/1.316e-08
Year (Intercept) Std. Dev (Both Sexes/Females/Males): 8.102e-05/1.087e-13/1.895e-02
Weighs:Year:Region (Intercept) Variance/Std. Dev (Both Sexes): 6.564e-09/8.102e-05
Number of observations: 315; Groups: Weights:Region:Year, 315; Region:Year, 315; Year, 15

Table 4 displays the association between diagnoses of autism spectrum disorder (ASD; ICD-10: F84) and major depressive disorder (MDD; ICD-10: F32) in individuals aged 15–19, using odds ratios (ORs), 95 % confidence intervals (CIs), and p-values derived from a generalized linear mixed-effects model. The model employs a betabinomial distribution with a logit link function. MDD was dichotomized, contrasting the lower quartile (Q1) against the combined upper three quartiles (Q2-Q4), with ORs reflecting the likelihood of being in the higher MDD category. Based on model selection criteria (AIC/BIC and Likelihood Ratio Tests), bipolar disorder (BD; ICD-10: F31) was excluded as a covariate. The model for both sexes was adjusted for the presence of comorbid ASD and the male-to-female ratio of ASD diagnoses, accounting for regional and yearly variations. Additionally, the model was adjusted for the proportional population size for combined sexes. Fixed effects included ASD and PCAR with random effects specified for region and year. No significant multicollinearity was detected (Variance Inflation Factor, VIF < 5, for all variables). Detailed strategies for model optimization are presented in Supplemental Figs. 7–9. Abbreviations: AIC: Akaike information criterion, ASD-R: Autism Spectrum disorder related diagnosis, BD: Bipolar Disorder, BIC: Bayesian information criterion, logLik: Log Likelihood value, PCAR: Psychiatric Care Affiliation Rates, Std. Dev: Standard Deviation.

6. Conclusion

While the observational aspect of the investigation does not allow causal conclusions to be drawn, the results reveal a correlation: heightened primary diagnosis rates of ASD-R are linked to diminished primary diagnosis rates of MDD among adolescents and across genders, with a more pronounced effect observed in males. Given the pressing need for timely identification and management of adolescent MDD, these findings advocate for further exploration of the association between ASD-R and MDD diagnosis rates. This exploration should utilize prospective, longitudinal, and individualized register data encompassing both primary and co-diagnoses. If replicated with such detailed data, these results may suggest systemic diagnostic complexity and convergence over time, with potential implications for the configuration of youth mental health services, policy-making strategies, and the trajectory of epidemiological and genetic investigations in psychiatry.

Ethics approval and consent to participate

The work was conducted in accordance with the ethical standards of the Helsinki declaration and in accordance with the Swedish laws on research ethics. As the study pertained to openly available data, no ethical permission was required by Swedish jurisdiction. Local university regulatory standards were however followed.

Consent for publication

As the study pertained to openly available data, no consent for publication was required by Swedish jurisdiction. Local university regulatory standards were however followed.

Availability of data and materials

Data was retrieved for the 21 Swedish regions across 2008–2021 in the age-ranges 15–19 from the Swedish National Board of Health and Welfare (freely available in Swedish [dataset] (Swedish Board of National Health and Welfare, 2022)).

Role of funder statement

The funder had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

CRediT authorship contribution statement

Adrian E. Desai Boström: Writing – review & editing, Writing – original draft, Methodology, Conceptualization. **Peter Andersson:** Writing – original draft, Investigation, Conceptualization. **Lee E. Wachtel:** Writing – review & editing, Conceptualization. **Håkan Jarbin:** Writing – review & editing, Methodology. **Jussi Jokinen:** Writing – review & editing, Validation, Supervision. **Johan Lundberg:** Writing – review & editing, Supervision, Methodology.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.psychres.2024.116341.

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