

# The Role of Mental Health and Behavioral Disorders in the Development of Temporomandibular Disorder: A SWEREG-TMD Nationwide Case-Control Study

Adrian Salinas Fredricson<sup>1,2</sup>, Carina Krüger Weiner<sup>1,2</sup>, Johanna Adami<sup>3</sup>, Annika Rosén<sup>4,5</sup>, Bodil Lund<sup>2,6</sup>, Britt Hedenberg-Magnusson<sup>2,7</sup>, Lars Fredriksson<sup>2,7</sup>, Aron Naimi-Akbar<sup>1,2,8</sup>

<sup>1</sup>Public Dental Services, Folk tandvården Stockholm, Eastmaninstitutet, Department of Oral and Maxillofacial Surgery, Stockholm, Sweden; <sup>2</sup>Division of Oral Diagnostics and Rehabilitation, Department of Dental Medicine, Karolinska Institutet, Stockholm, Sweden; <sup>3</sup>Sophiahemmet University, Stockholm, Sweden; <sup>4</sup>Department of Clinical Dentistry, Division of Oral and Maxillofacial Surgery, University of Bergen, Bergen, Norway; <sup>5</sup>Department of Oral and Maxillofacial Surgery, Haukeland University Hospital, Bergen, Norway; <sup>6</sup>Medical Unit for Reconstructive Plastic and Craniofacial Surgery, Karolinska University Hospital, Stockholm, Sweden; <sup>7</sup>Public Dental Services, Folk tandvården Stockholm, Eastmaninstitutet, Department of Orofacial Pain and Jaw Function, Stockholm, Sweden; <sup>8</sup>Health Technology Assessment-Odontology (HTA-O), Malmö University, Malmö, Sweden

Correspondence: Adrian Salinas Fredricson, Eastmaninstitutet Käkkirurgi, Dalagatan 11, Stockholm, 102 31, Sweden, Email [adrian.salinas-fredricson@regionstockholm.se](mailto:adrian.salinas-fredricson@regionstockholm.se)

**Purpose:** There is a well-known association between mental and behavioral disorders (MBD) and temporomandibular disorder (TMD), although the association has not been established in population-based samples. This study aimed to investigate this relationship using national population-based registry data.

**Patients and Methods:** This case-control study used prospectively collected data from Swedish national registries to investigate exposure to MBD and the probability of developing TMD in all Swedish citizens with hospital-diagnosed or surgically treated TMD between 1998 and 2016. Odds ratios were calculated using conditional logistic regression adjusted for educational level, living area, country of birth, musculoskeletal comorbidity, and history of orofacial/neck trauma.

**Results:** A statistically significant association between MBD and TMD was found for mood affective disorders (OR 1.4), neurotic, stress-related and somatoform disorders (OR 1.7), behavioral syndromes associated with psychological disturbances and physical factors (OR 1.4), disorders of adult personality and behavior (OR 1.4), disorders of psychological development (OR 1.3), behavioral and emotional disorders with onset usually occurring in childhood and adolescence (OR 1.4), and unspecified mental disorder (OR 1.3). The association was stronger for TMD requiring surgery, with the strongest association in patients with disorders of psychological development (OR 2.9). No significant association was found with schizophrenia, schizotypal and delusional disorders, or mental retardation.

**Conclusion:** The findings indicate an increased probability of TMD among patients with a history of certain MBD diagnoses, and a stronger association with TMD requiring surgery, specifically repeated surgery. This highlights the need for improved preoperative understanding of the impact of MBD on TMD, as TMD and chronic pain itself may have a negative impact on mental health.

**Keywords:** TMD, registry-based, case-control, epidemiology, TMJ surgery, oral and maxillofacial surgery

## Introduction

Temporomandibular disorder (TMD) is a collective term for multiple disorders affecting the muscles of mastication, the temporomandibular joint (TMJ), and the surrounding tissues and is characterized by orofacial pain and impaired function. TMD is usually reported to have a prevalence of 5% to 15% in the adult population, it is more prevalent in women, and the gender difference in persistent orofacial pain increases over time.<sup>1-3</sup>

Studies have found that psychological factors such as somatization, anxiety, depression, psychological distress, and pain-catastrophizing are predictors of both first onset of orofacial pain and chronic orofacial pain.<sup>4–10</sup> The intensity of pain has also been shown to affect recovery after treatment.<sup>11</sup> Furthermore, individuals with anxiety, depression, and substance use disorder have higher prevalence of other types of chronic pain, and the association seems to be bidirectional. However, studies on more severe mental disorders such as schizophrenia show inconclusive results with sometimes lower prevalence of chronic pain such as back pain and headaches in these patients.<sup>12</sup>

In Sweden, the vast majority of TMD patients are identified and receive conservative treatment within the dental care system and diagnostics are carried out using the Diagnostic Criteria for TMD (DC/TMD), which includes assessment of psychosocial functioning associated with the pain condition.<sup>13</sup> Some patients might seek health care for their TMD symptoms and will be diagnosed within the health care system but subsequently treated within the dental care system. Of the patients diagnosed with TMD, only 1% are referred for surgical treatment.<sup>14</sup> The surgical treatment of TMD in Sweden is conducted within the subsidized health care system and is mainly carried out on patients with articular disorders that have failed conservative treatment or patients with more complicated articular disorders such as fibrous or bony ankylosis.<sup>15</sup>

The International Classification of Diseases 10th Revision (ICD-10) (chapter 5) for mental and behavioral disorders (MBD) contains a heterogeneous group of diagnoses including a span of quite common diagnoses such as depression and anxiety as well as more rare diagnoses such as schizophrenia. Patients diagnosed or treated within the Swedish health care system are automatically registered in the National Patient Registry (NPR), which was initiated in 1964 and contains individual data from patient care with almost complete national coverage since 1987.<sup>16</sup>

This study from the Swedish National Registry Studies for Surgically Treated TMD (SWEREG-TMD) uses the unique prerequisites of prospectively collected population-based data to investigate the role of MBDs in the development of TMD. In addition, it investigates differences in odds for patients who are diagnosed but not treated for TMD within the health care system and patients who receive surgical treatment for TMD.

## Material and Methods

### Study Design and Registries

This is a registry-based case–control study with information collected from three nationwide population-based Swedish registries.

- The NPR was used to identify the cases and retrieve information on exposure variables. The registry is administered by the National Board of Health and Welfare (NBHW).<sup>16</sup>
- The Total Population Registry (TPR) was used to identify the controls. The registry is administered by Statistics Sweden (SCB) and has a coverage of 100% of all Swedish citizens.<sup>17</sup>
- The Longitudinal Integrated Database for Health Insurance and Labor Market Studies (LISA) was used to collect sociodemographic variables and is administered by SCB.<sup>18</sup>

### Study Population and Data Linking

All study subjects included were aged 18 or above. Cases were all Swedish citizens diagnosed with TMD in a hospital or surgically treated for TMD between 1998 and 2016. The TPR was used to collect the controls, who were matched 1:10 on age, sex, and living area.

The Personal Identification Number (PIN) was used to link the subjects between the various registries and to collect data on exposure, outcome, comorbidities, and sociodemographic covariates. The PIN is given to all Swedish residents and is unique for each individual.<sup>19</sup>

### Outcome

The definition of the outcome (TMD) was ICD-10 diagnostic code K07.6 (temporomandibular joint disorders) and/or any of the following treatment codes, which were used as proxy variables for TMD:

- TMJ-disc surgical procedure (EGB10)
- TMJ arthroscopy (EGA00)
- TMJ condylectomy (EGB00)
- TMJ prosthesis surgical procedure (EGC30)
- Other surgical reconstruction of TMJ (EGC99)
- TMJ synovectomy (EGB20)
- TMJ biopsy (EGA20)
- Injection of diagnostic or therapeutic substance in the TMJ (TEG10)
- TMJ condylotomy (EDC00)
- Open reposition of TMJ luxation (EGC00)
- TMJ plastic surgery (EGC10)
- TMJ plastic surgery with bone graft or other type of transplant (EGC20)

The cases were classified into three subcategories: non-surgical (NS) (ie, diagnosed but with no subsequent surgical treatment registered), surgically treated once (ST1) (ie, one surgical event), and surgically treated twice or more (ST2) (ie, multiple surgical interventions). Patients who had received bilateral surgical treatment on both TMJs but in one event were considered as surgically treated once. Injection of diagnostic or therapeutic substance in the TMJ (TEG10) was also considered a surgical intervention.

## Exposures

NPR was used to collect information on MBD diagnoses for both cases and controls. Exposure data were defined as all diagnoses from the chapter 5 of ICD-10 (F00–F99) or equivalent diagnoses from earlier versions of ICD, between 1964 and time of TMD diagnosis (cases) or inclusion in the study (controls). ICD-7 to ICD-10 codes included were:

### ICD-7 (1958–1968)

- Psychoses (300–309)
- Psychoneurotic disorders (310–318)
- Disorders of character, behavior and intelligence (320–326)

### ICD-8 (1969–1986)

- Psychoses (290–299)
- Neuroses, personality disorders and other nonpsychotic mental disorders (300–309)
- Mental retardation (310–315)

### ICD-9 (1987–1996)

- Mental disorders (290–319)

### ICD-10 (1997–2016)

- Mental and behavioral disorders (F00–F99)

The translation between ICD-7, –8, and –9 to ICD-10 was conducted using a codebook provided by the NBHW. To present coherent results, the diagnoses were divided into 11 diagnostic categories in accordance with the ICD-10 divisions:

1. Organic, including symptomatic, mental disorders (F00–F09)
2. Mental and behavioral disorders due to psychoactive substance use (F10–F19)
3. Schizophrenia, schizotypal and delusional disorders (F20–F29)
4. Mood affective disorders (F30–F39)

5. Neurotic, stress-related and somatoform disorders (F40–F48)
6. Behavioral syndromes associated with physiological disturbances and physical factors (F50–F59)
7. Disorders of adult personality and behavior (F60–F69)
8. Mental retardation (F70–F79)
9. Disorders of psychological development (F80–F89)
10. Behavioral and emotional disorders with onset usually occurring in childhood and adolescence (F90–F98)
11. Unspecified mental disorder (F99).

## Sociodemographic Covariates and Comorbidities

Sociodemographic data were collected through LISA and included information on highest acquired educational level, country of birth, and living area. Educational level was divided into three levels: 0–9 years, 9–12 years, and more than 12 years. Birth country included Sweden, other Nordic Countries, European Countries, and non-European Countries. Sweden's 290 municipalities were classified according to Eurostat's Degree of Urbanization (DEGURBA) (revised definition, 2016): cities, towns or suburbs, and rural areas.

Information on comorbidity was collected from the NPR and included musculoskeletal and connective tissue diseases (M00–M99) and history of orofacial/neck trauma (S02.4, S02.6 and S13). The translation of diagnoses from earlier versions of ICD was conducted in the same manner as the exposure data (see “Exposures”). Chronic muscular disorders have been shown to affect both the risk for TMD and the development of mental health disorders such as anxiety and depression and was therefore considered a confounding factor.<sup>20–22</sup> As history of trauma in the orofacial area and/or neck also affect both the exposure and the outcome it was included as a confounding factor.<sup>23–26</sup>

## Statistical Methods

Conditional logistic regression was used to calculate odds ratios.<sup>27</sup> Both outcome and exposures were considered binary variables, and adjustment variables were considered categorical dummy variables. Adjustment variables were educational level, country of birth, DEGURBA, musculoskeletal comorbidity, and history of orofacial/neck trauma. Musculoskeletal comorbidity and history of trauma were used as two independent binary adjustment variables to control for their presence and their influence on both mental health and the development of TMD. Missing data on educational level, country of birth, and DEGURBA were imputed using Multiple Imputation by Chained Equations (MICE).<sup>28</sup> Educational level was imputed with ordinal logistic regression, whereas country of birth and DEGURBA were imputed with multinomial logistic regression, with 20 imputations and assuming missing at random.

## Data Availability

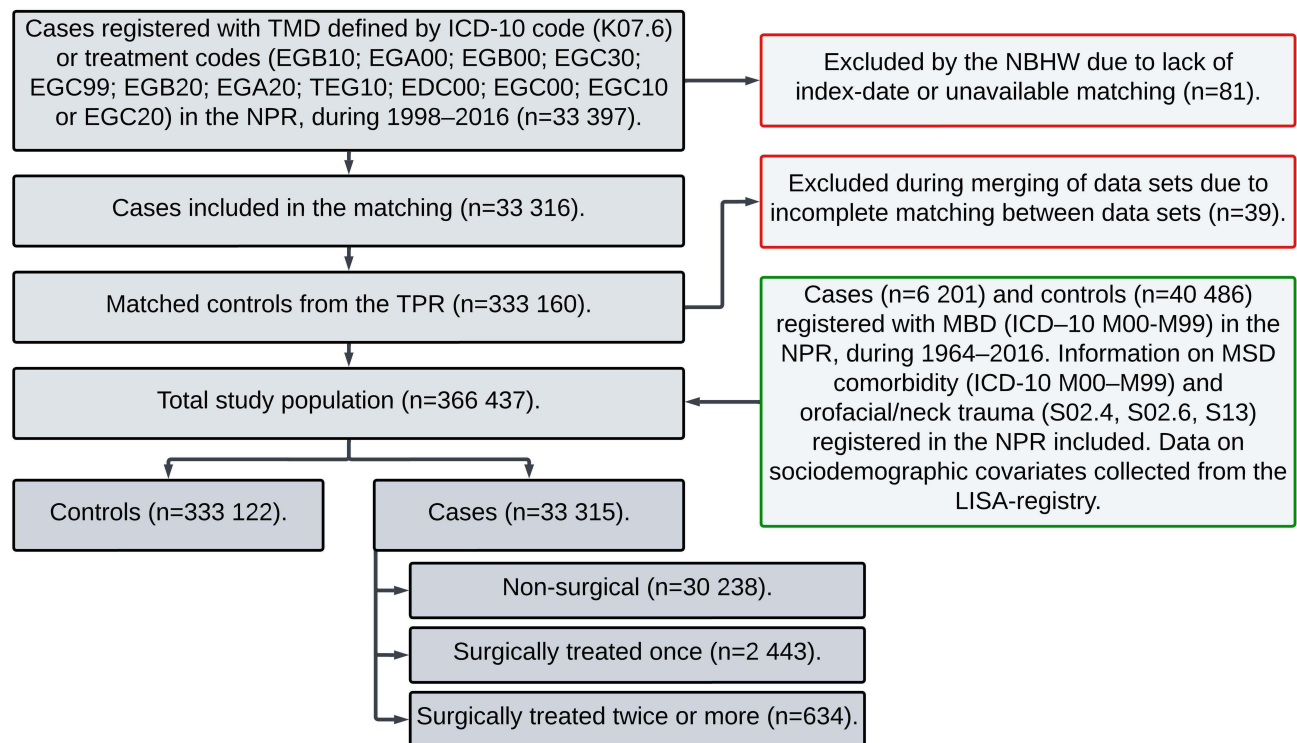
The data that support the findings of this study are available from the Swedish NBHW and Statistics Sweden. Restrictions are applied to the availability of these data, which were used under license for this study. The data are not publicly available because of privacy and/or ethical restrictions but can be retrieved through the Swedish NBHW; however, approval from the Swedish Ethical Review Authority is required.

## Ethical Declaration

This study was conducted in accordance with the Declaration of Helsinki and was comprised of a study population from Swedish national registries. The Swedish Ethical Review Authority approved the study (reference number 2018/401-31). The NBHW anonymized personal data before sending it to the researchers.

## Results

A flowchart describing the recruitment process is presented in Figure 1, which is a modified model of earlier published data.<sup>29</sup> The total study population consisted of 366 437 subjects – 33 315 cases and 333 122 controls. In total, 120 individuals were excluded due to lack of index date or because of no possible match between the delivered data sets (see Figure 1). The case subgroups consisted of NS (n = 30 238), ST1 (n = 2443), and ST2 (n = 634). A total of 6201 cases and 40 486 controls were registered with MBD exposures in the NPR before inclusion in the study.



**Figure 1** Recruitment process and registry inquiries of the study subjects as well as excluded subjects. The figure is a modified model of earlier published data.

**Abbreviations:** ICD-10, International Classification of Diseases 10th Revision; LISA, Longitudinal Integrated Database for Health Insurance and Labor Market Studies; MBD, Mental and behavioral disorders; MSD, Musculoskeletal and connective tissue diseases; NBHW, National Board of Health and Welfare; NPR, National Patient Registry; TPR, Total Population Registry.

Sociodemographic information and comorbidities of the study population are presented in [Table 1](#). No large differences were seen in the baseline data, except for slightly lower ages in the surgically treated groups. The proportion of all musculoskeletal comorbidities was higher in the surgically treated subgroups. History of trauma was more common in the surgically treated groups.

[Table 2](#) displays the crude numbers and proportions of each category of ICD-10 MBD as well as each diagnosis contained in the 11 categories. [Table 3](#) presents the results from the conditional logistic regression, which are shown with odds ratios for each diagnostic category regarding the entire case group ( $n = 33\,315$ ) and each subgroup of the cases. The model is adjusted for educational level, country of birth, DEGURBA, musculoskeletal comorbidity, and history of orofacial/neck trauma. Statistically significant association between MBD and TMD was found in individuals with mood affective disorders (OR 1.4, 95% CI 1.4–1.5), neurotic, stress-related and somatoform disorders (OR 1.7, 95% CI 1.7–1.8), behavioral syndromes associated with psychological disturbances and physical factors (OR 1.4, 95% CI 1.3–1.5), disorders of adult personality and behavior (OR 1.4, 95% CI 1.3–1.5), disorders of psychological development (OR 1.3, 95% CI 1.2–1.4), behavioral and emotional disorders with onset usually occurring in childhood and adolescence (OR 1.4, 95% CI 1.4–1.5), and unspecified mental disorder (OR 1.3, 95% CI 1.2–1.4). The association between MBD and TMD was stronger in cases who had received surgical treatment, particularly cases with multiple surgical interventions. The odds increased up to two-fold for neurotic, stress-related and somatoform disorders, behavioral syndromes associated with physiological disturbances and physical factors, disorders of adult personality and behavior, behavioral and emotional disorders with onset usually occurring in childhood and adolescence, and unspecified mental disorders. The strongest association between MBD and TMD was found in cases who had received several surgical interventions and who had earlier been diagnosed with disorders of psychological development (OR 2.9).

Slightly, albeit statistically significant, elevated probability of TMD was seen in patients with organic disorders, including symptomatic disorders (OR 1.1, 95% CI 1.0–1.2) and mental and behavioral disorders due to psychoactive

**Table I** The Sociodemographic Properties, MSD Comorbidity, and History of Orofacial/Neck Trauma of the Cases and Controls

	Controls	Cases		
	n=333 122 (%)	NS n=30,238 (%)	ST1 n=2443 (%)	ST2 n=634 (%)
<b>Sex</b>				
Female	242 868 (72.91)	21,887 (72.38)	1869 (76.50)	533 (84.07)
Male	90,254 (27.09)	8351 (27.62)	574 (23.50)	101 (15.93)
<b>Educational level</b>				
Primary/lower secondary school	64,265 (19.29)	6005 (19.86)	368 (15.06)	94 (14.83)
Upper secondary school	138 488 (41.57)	13,102 (43.33)	1149 (47.03)	301 (47.48)
Post-secondary school	125 833 (37.77)	10,837 (35.84)	914 (37.41)	238 (37.54)
Data unavailable	4536 (1.36)	294 (0.97)	12 (0.49)	1 (0.16)
<b>Country of birth</b>				
Sweden	269 829 (81.00)	23,222 (76.80)	2099 (85.92)	564 (88.96)
Other Nordic countries	11,772 (3.53)	1099 (3.63)	97 (3.97)	23 (3.63)
Other European countries	22,960 (6.89)	2192 (7.25)	87 (3.56)	18 (2.84)
Non-European countries	28,530 (8.56)	3724 (12.32)	160 (6.55)	29 (4.57)
Data unavailable	31 (0.01)	1 (<0.00)	0 (0)	0 (0)
<b>DEGURBA</b>				
Cities	150 065 (45.05)	13,092 (43.30)	1237 (50.63)	302 (47.63)
Towns and suburbs	89,917 (26.99)	9106 (30.11)	597 (24.44)	173 (27.29)
Rural areas	90,570 (27.19)	7861 (26.00)	591 (24.19)	157 (24.76)
Data unavailable	2570 (0.77)	179 (0.59)	18 (0.74)	2 (0.32)
<b>Age</b>				
Mean	49.15	49.96	41.62	39.31
Median	49	50	40	37
Standard deviation	18.43	18.39	17.00	15.96
Range	18–104	18–104	18–97	18–89
<b>Marital status</b>				
Married	142 671 (43.16)	13,544 (44.79)	890 (36.43)	240 (37.85)
Not married	119 186 (36.06)	9899 (32.74)	1140 (46.66)	311 (49.05)
Divorced	46,442 (14.05)	4720 (15.61)	320 (13.10)	68 (10.73)
Widow/widower	22,017 (6.66)	1870 (6.18)	70 (2.87)	12 (1.89)
Other*	236 (<0.00)	26 (<0.00)	1 (0.04)	1 (0.16)
Data unavailable	2570 (0.77)	179 (0.59)	18 (0.74)	2 (0.32)
<b>Comorbidities</b>				
Any MSD comorbidity (M00-M99)	93,875 (28.18)	13,781 (45.58)	1122 (45.93)	328 (51.74)
M00-M25 Arthropathies	48,165 (14.46)	7090 (23.45)	702 (28.74)	217 (34.23)
M30-M36 Systemic connective tissue disorders	4852 (1.46)	963 (3.18)	96 (3.93)	32 (5.05)
M40-M54 Dorsopathies	28,592 (8.58)	5173 (17.11)	414 (16.95)	129 (20.35)
M60-M79 Soft tissue disorders	43,775 (13.14)	7605 (25.15)	511 (20.92)	164 (25.87)
M80-M94 Osteopathies and chondropathies	9104 (2.73)	1406 (4.65)	107 (4.38)	40 (6.31)
M95-M99 Other disorders of the musculoskeletal system and connective tissue	2736 (0.82)	482 (1.59)	49 (2.01)	12 (1.89)
Any history of trauma (S02.4, S02.6, S13)	3845 (1.15)	841 (2.78)	100 (4.09)	30 (4.73)
S02.4 Fracture of malar, maxillary and zygoma bones	415 (0.12)	94 (0.31)	12 (0.49)	4 (0.63)
S02.6 Fracture of the mandible	393 (0.12)	145 (0.48)	32 (1.31)	6 (0.95)
S13 Dislocation and sprain of joints and ligaments at neck level	3051 (0.92)	618 (2.04)	57 (2.33)	22 (3.47)

**Note:** Other\*: Registered partner, divorced partner, surviving partner.

**Abbreviation:** MSD, Musculoskeletal and connective tissue diseases.



**Table 2** Crude Data on Number of Subjects with MBD-Diagnoses from Chapter 5 of ICD-10 (F00–F99) and the Division into the 11 Categories of the Chapter

	Controls	Cases		
	n=333 122 (%)	NS n=30,238 (%)	ST1 n=2443 (%)	ST2 n=634 (%)
<b>1. F00- F09 Organic, including symptomatic, mental disorders</b>	<b>6214 (1.87)</b>	<b>635 (2.10)</b>	<b>60 (2.46)</b>	<b>13 (2.05)</b>
F00 Dementia in Alzheimer disease	793 (0.24)	72 (0.24)	5 (0.20)	0 (0)
F01 Vascular dementia	384 (0.12)	20 (0.07)	2 (0.08)	1 (0.16)
F02 Dementia in other diseases classified elsewhere	703 (0.21)	33 (0.11)	2 (0.08)	3 (0.47)
F03 Unspecified dementia	2334 (0.70)	175 (0.58)	17 (0.70)	6 (0.95)
F04 Organic amnesic syndrome, not induced by alcohol and other psychoactive substances	628 (0.19)	29 (0.10)	4 (0.16)	1 (0.16)
F05 Delirium, not induced by alcohol and other psychoactive substances	1775 (0.53)	172 (0.57)	21 (0.86)	4 (0.63)
F06 Other mental disorders due to brain damage and dysfunction and to physical disease	1857 (0.56)	192 (0.63)	14 (0.57)	4 (0.63)
F07 Personality and behavioral disorders due to brain disease, damage and dysfunction	2837 (0.85)	331 (1.03)	27 (1.11)	4 (0.63)
F09 Unspecified organic or symptomatic mental disorder	135 (0.04)	14 (0.05)	1 (0.04)	1 (0.16)
<b>2. F10-F19 Mental and behavioral disorders due to psychoactive substance use</b>	<b>9919 (2.98)</b>	<b>1034 (3.42)</b>	<b>117 (4.79)</b>	<b>30 (4.73)</b>
F10 Alcohol	7320 (2.20)	726 (2.40)	80 (3.27)	19 (3.00)
F11 Opioids	2863 (0.86)	291 (0.96)	35 (1.43)	13 (2.05)
F12 Cannabinoids	2772 (0.82)	273 (0.90)	32 (1.31)	8 (1.26)
F13 Sedatives or hypnotics	3901 (1.17)	393 (1.30)	47 (1.92)	11 (1.74)
F14 Cocaine	2401 (0.72)	236 (0.78)	29 (1.19)	8 (1.26)
F15 Other stimulants, including caffeine	2646 (0.79)	254 (0.84)	33 (1.35)	8 (1.26)
F16 Hallucinogens	2399 (0.72)	232 (0.77)	29 (1.19)	8 (1.26)
F17 Tobacco	2165 (0.65)	210 (0.69)	26 (1.06)	7 (1.10)
F18 Volatile solvents	3177 (0.95)	298 (0.99)	33 (1.35)	10 (1.58)
F19 Multiple drug use and use of other psychoactive substances	4156 (1.25)	424 (1.40)	48 (1.96)	12 (1.89)
<b>3. F20-F29 Schizophrenia, schizotypal and delusional disorders</b>	<b>4044 (1.21)</b>	<b>385 (1.27)</b>	<b>41 (1.68)</b>	<b>10 (1.58)</b>
F20 Schizophrenia	1545 (0.46)	92 (0.30)	9 (0.37)	4 (0.63)
F21 Schizotypal disorder	918 (0.28)	40 (0.13)	3 (0.12)	4 (0.63)
F22 Persistent delusional disorders	2499 (0.75)	245 (0.81)	27 (1.11)	6 (0.95)
F23 Acute and transient psychotic disorders	3157 (0.95)	277 (0.92)	33 (1.35)	10 (1.58)
F24 Induced delusional disorder	370 (0.11)	36 (0.12)	2 (0.08)	0 (0)
F25 Schizoaffective disorder	1148 (0.34)	63 (0.21)	10 (0.41)	4 (0.63)
F28 Other nonorganic psychotic disorders	1427 (0.43)	103 (0.34)	10 (0.41)	4 (0.63)
F29 Unspecified nonorganic psychosis	2003 (0.60)	184 (0.61)	18 (0.74)	4 (0.63)
<b>4. F30-F39 Mood affective disorders</b>	<b>17,075 (5.13)</b>	<b>2382 (7.88)</b>	<b>192 (7.86)</b>	<b>61 (9.62)</b>
F30 Manic episode	2247 (0.67)	205 (0.68)	18 (0.74)	5 (0.79)
F31 Bipolar affective disorder	2568 (0.80)	282 (0.93)	27 (1.11)	8 (1.26)
F32 Depressive episode	13,951 (4.19)	1975 (6.53)	148 (6.06)	56 (8.83)
F33 Recurrent depressive disorder	8733 (2.62)	1100 (3.64)	93 (3.81)	31 (4.89)
F34 Persistent mood affective disorders	5818 (1.75)	752 (2.49)	60 (2.46)	21 (3.31)
F38 Other mood affective disorders	1386 (0.42)	123 (0.41)	13 (0.53)	5 (0.79)
F39 Unspecified mood affective disorder	1597 (0.48)	158 (0.52)	15 (0.65)	4 (0.63)

(Continued)

Table 2 (Continued).

	Controls	Cases		
	n=333 122 (%)	NS n=30,238 (%)	ST1 n=2443 (%)	ST2 n=634 (%)
<b>5. F40-F48 Neurotic, stress-related and somatoform disorders</b>	<b>22,271 (6.69)</b>	<b>3656 (12.09)</b>	<b>273 (11.17)</b>	<b>86 (13.56)</b>
F40 Phobic anxiety disorders	4675 (1.40)	628 (2.08)	45 (1.84)	17 (2.68)
F41 Other anxiety disorders	11,662 (3.50)	1960 (6.48)	138 (5.65)	45 (7.10)
F42 Obsessive-compulsive disorder	5314 (1.60)	736 (2.43)	59 (2.42)	20 (3.15)
F43 Reaction to severe stress, and adjustment disorders	11,877 (3.57)	1761 (5.82)	139 (5.69)	44 (6.94)
F44 Dissociative conversion disorders	7231 (2.17)	963 (3.18)	87 (3.56)	34 (5.36)
F45 Somatoform disorders	8148 (2.45)	1349 (4.46)	100 (4.09)	37 (5.84)
F48 Other neurotic disorders	5352 (1.61)	732 (2.42)	66 (2.70)	19 (3.00)
<b>6. F50-F59 Behavioral syndromes associated with physiological disturbances and physical factors</b>	<b>10,044 (3.02)</b>	<b>1352 (4.47)</b>	<b>124 (5.08)</b>	<b>47 (7.41)</b>
F50 Eating disorders	7065 (2.12)	938 (3.10)	85 (3.48)	37 (5.84)
F51 Nonorganic sleep disorders	2114 (0.63)	328 (1.08)	43 (1.76)	12 (1.89)
F52 Sexual dysfunction, not caused by organic disorder or disease	1003 (0.30)	205 (0.68)	13 (0.53)	13 (2.05)
F53 Mental and behavioral disorders associated with the puerperium, not elsewhere classified	4127 (1.24)	490 (1.62)	35 (1.43)	13 (2.05)
F54 Psychological and behavioral factors associated with disorders or diseases classified elsewhere	371 (0.11)	60 (0.20)	1 (0.04)	8 (1.26)
F55 Abuse of non-dependence-producing substance	1150 (0.35)	133 (0.44)	13 (0.53)	4 (0.63)
F59 Unspecified behavioral syndromes associated with physiological disturbances and physical factors	135 (0.04)	29 (0.10)	0 (0)	3 (0.47)
<b>7. F60-F69 Disorders of adult personality and behavior</b>	<b>7684 (2.31)</b>	<b>1076 (3.56)</b>	<b>99 (4.05)</b>	<b>34 (5.36)</b>
F60 Specific personality disorders	6634 (1.99)	928 (3.07)	81 (3.32)	26 (4.10)
F61 Mixed and other personality disorders	4047 (1.21)	521 (1.72)	40 (1.64)	12 (1.89)
F62 Enduring personality changes, not attributable to brain damage and disease	4027 (1.21)	517 (1.71)	41 (1.68)	12 (1.89)
F63 Habit and impulse disorders	4304 (1.29)	584 (1.93)	49 (2.01)	17 (2.68)
F64 Gender identity disorders	72 (0.02)	11 (0.04)	5 (0.20)	0 (0)
F65 Disorders of sexual preference	234 (0.07)	30 (0.10)	3 (0.12)	5 (0.79)
F66 Psychological and behavioral disorders associated with sexual development and orientation	234 (0.07)	33 (0.11)	3 (0.12)	5 (0.79)
F68 Other disorders of adult personality and behavior	5213 (1.56)	701 (2.32)	63 (2.58)	17 (2.68)
F69 Unspecified disorder of adult personality and behavior	4497 (1.35)	589 (1.95)	50 (2.05)	14 (2.21)
<b>8. F70-F79 Mental retardation</b>	<b>712 (0.21)</b>	<b>80 (0.26)</b>	<b>5 (0.20)</b>	<b>2 (0.32)</b>
F70 Mild mental retardation	392 (0.12)	55 (0.18)	2 (0.08)	1 (0.16)
F71 Moderate mental retardation	155 (0.05)	13 (0.04)	4 (0.16)	0 (0)
F72 Severe mental retardation	74 (0.02)	7 (0.02)	1 (0.04)	0 (0)
F73 Profound mental retardation	55 (0.02)	4 (0.01)	1 (0.04)	0 (0)
F78 Other mental retardation	5 (0.00)	0 (0)	0 (0)	0 (0)
F79 Unspecified mental retardation	247 (0.07)	23 (0.08)	2 (0.08)	1 (0.16)
<b>9. F80-F89 Disorders of psychological development</b>	<b>3603 (1.08)</b>	<b>426 (1.41)</b>	<b>48 (1.96)</b>	<b>22 (3.47)</b>
F80 Specific developmental disorders of speech and language	1989 (0.60)	276 (0.91)	34 (1.39)	14 (2.21)
F81 Specific developmental disorders of scholastic skills	757 (0.23)	98 (0.32)	17 (0.70)	3 (0.47)
F82 Specific developmental disorder of motor function	91 (0.03)	4 (0.01)	2 (0.08)	0 (0)
F83 Mixed specific developmental disorders	590 (0.18)	85 (0.28)	15 (0.61)	2 (0.32)
F84 Pervasive developmental disorders	1526 (0.46)	134 (0.44)	13 (0.53)	7 (1.10)
F88 Other disorders of psychological development	625 (0.19)	87 (0.29)	15 (0.61)	2 (0.32)
F89 Unspecified disorder of psychological development	697 (0.21)	92 (0.30)	16 (0.65)	3 (0.47)

(Continued)



**Table 2** (Continued).

	Controls	Cases		
	n=333 122 (%)	NS n=30,238 (%)	ST1 n=2443 (%)	ST2 n=634 (%)
<b>10. F90-F98 Behavioral and emotional disorders with onset usually occurring in childhood and adolescence</b>	<b>8469 (2.54)</b>	<b>1195 (3.95)</b>	<b>109 (4.46)</b>	<b>39 (6.15)</b>
F90 Hyperkinetic disorders	1803 (0.54)	283 (0.94)	23 (0.94)	8 (1.26)
F91 Conduct disorders	1216 (0.37)	145 (0.48)	19 (0.78)	5 (0.79)
F92 Mixed disorders of conduct and emotions	769 (0.23)	103 (0.34)	14 (0.57)	3 (0.47)
F93 Emotional disorders with onset specific to childhood	4772 (1.43)	630 (2.08)	52 (2.13)	19 (3.00)
F94 Disorders of social functioning with onset specific to childhood and adolescence	2043 (0.61)	293 (0.97)	35 (1.43)	9 (1.42)
F95 Tic disorders	4533 (1.36)	616 (2.04)	53 (2.17)	24 (3.79)
F98 Other behavioral and emotional disorders with onset usually occurring in childhood and adolescence	2177 (0.65)	299 (0.99)	39 (1.60)	15 (2.37)
<b>11. F99 Unspecified mental disorder</b>	<b>6884 (2.07)</b>	<b>871 (2.88)</b>	<b>80 (3.27)</b>	<b>30 (4.73)</b>
F99 Mental disorder, not otherwise specified	6884 (2.07)	871 (2.88)	80 (3.27)	30 (4.73)

**Abbreviations:** MBD, Mental and behavioral disorders; ST1, Surgically treated once; ST2, Surgically treated two or more times.

**Table 3** Odds Ratios of the Outcome in Relation to the Exposures. Calculated Through Conditional Logistic Regression and Adjusted for Educational Level, Country of Birth, DEGURBA, MSD Comorbidity, and History of Orofacial/Neck Trauma

	All Cases		NS		ST1		ST2	
	OR	[95% CI]	OR	[95% CI]	OR	[95% CI]	OR	[95% CI]
<b>1. F00-F09 Organic, including symptomatic, mental disorders</b>	<b>1.1</b>	<b>[1.0 1.2]</b>	<b>1.1*</b>	<b>[1.0 1.2]</b>	<b>1.4</b>	<b>[1.1 1.9]</b>	<b>1.3*</b>	<b>[0.7 2.5]</b>
F00 Dementia in Alzheimer disease	1.0*	[0.8 1.3]	1.0*	[0.8 1.3]	1.1*	[0.4 2.7]	†	
F01 Vascular dementia	0.6	[0.4 0.9]	0.5	[0.3 0.8]	1.2*	[0.2 5.4]	4.6*	[0.3 79.6]
F02 Dementia in other diseases classified elsewhere	0.6	[0.4 0.8]	0.6	[0.4 0.8]	0.4*	[0.1 1.6]	2.4*	[0.6 9.0]
F03 Unspecified dementia	0.9	[0.7 1.0]	0.8	[0.7 1.0]	1.2*	[0.7 2.0]	2.2*	[0.9 5.8]
F04 Organic amnesic syndrome, not induced by alcohol and other psychoactive substances	0.6	[0.4 0.8]	0.5	[0.4 0.8]	0.8*	[0.3 2.1]	1.9*	[0.2 16.1]
F05 Delirium, not induced by alcohol and other psychoactive substances	1.1*	[0.9 1.3]	1.0*	[0.9 1.2]	1.4*	[0.9 2.3]	1.5*	[0.5 4.7]
F06 Other mental disorders due to brain damage and dysfunction and to physical disease	1.0*	[0.9 1.2]	1.0*	[0.9 1.2]	1.4*	[0.8 2.6]	1.8*	[0.6 5.5]
F07 Personality and behavioral disorders due to brain disease, damage and dysfunction	1.1	[1.0 1.3]	1.2	[1.0 1.3]	1.1*	[0.7 1.6]	0.7*	[0.2 1.9]
F09 Unspecified organic or symptomatic mental disorder	1.2*	[0.7 2.0]	1.2*	[0.7 2.1]	0.6*	[0.1 4.6]	2.7*	[0.2 36.8]
<b>2. F10-F19 Mental and behavioral disorders due to psychoactive substance use</b>	<b>1.1</b>	<b>[1.0 1.1]</b>	<b>1.0*</b>	<b>[1.0 1.1]</b>	<b>1.6</b>	<b>[1.3 1.9]</b>	<b>1.4*</b>	<b>[0.9 2.2]</b>
F10 Alcohol	1.0*	[0.9 1.1]	1.0*	[0.9 1.1]	1.5	[1.2 2.0]	1.3*	[0.8 2.2]
F11 Opioids	1.0*	[0.9 1.2]	1.0*	[0.9 1.1]	1.4*	[0.9 2.0]	2.0	[1.0 3.8]
F12 Cannabinoids	1.1*	[0.9 1.2]	1.0*	[0.9 1.2]	1.4*	[1.0 2.1]	1.2*	[0.6 2.7]
F13 Sedatives or hypnotics	1.0*	[0.9 1.1]	1.0*	[0.9 1.1]	1.4	[1.0 2.0]	1.4*	[0.7 2.7]
F14 Cocaine	1.0*	[0.9 1.2]	1.0*	[0.9 1.2]	1.4*	[0.9 2.1]	1.5*	[0.7 3.3]
F15 Other stimulants, including caffeine	1.0*	[0.9 1.1]	1.0*	[0.8 1.1]	1.5*	[1.0 2.1]	1.3*	[0.6 2.9]
F16 Hallucinogens	1.0*	[0.9 1.2]	1.0*	[0.9 1.1]	1.4*	[0.9 2.1]	1.5*	[0.7 3.2]
F17 Tobacco	1.0*	[0.9 1.2]	1.0*	[0.9 1.1]	1.4*	[0.9 2.1]	1.6*	[0.7 3.8]
F18 Volatile solvents	1.0*	[0.9 1.1]	0.9*	[0.8 1.1]	1.3*	[0.9 1.9]	1.5*	[0.8 3.1]
F19 Multiple drug use and use of other psychoactive substances	1.0*	[0.9 1.1]	1.0*	[0.9 1.1]	1.4	[1.0 1.9]	1.3*	[0.7 2.6]

(Continued)

Table 3 (Continued).

	All Cases		NS		ST1		ST2	
	OR	[95% CI]	OR	[95% CI]	OR	[95% CI]	OR	[95% CI]
<b>3. F20-F29 Schizophrenia, schizotypal and delusional disorders</b>	<b>1.1*</b>	<b>[1.0 1.2]</b>	<b>1.0*</b>	<b>[0.9 1.2]</b>	<b>1.3*</b>	<b>[1.0 1.9]</b>	<b>1.5*</b>	<b>[0.7 3.1]</b>
F20 Schizophrenia	0.7	[0.6 0.9]	0.7	[0.6 0.8]	0.9*	[0.4 1.8]	1.7*	[0.6 5.0]
F21 Schizotypal disorder	0.5	[0.4 0.7]	0.5	[0.4 0.7]	0.5*	[0.2 1.7]	3.9	[1.2 13.2]
F22 Persistent delusional disorders	1.1*	[1.0 1.3]	1.1*	[0.9 1.2]	1.4*	[0.9 2.1]	1.5*	[0.6 3.6]
F23 Acute and transient psychotic disorders	1.0*	[0.9 1.1]	1.0*	[0.9 1.1]	1.4*	[0.9 2.0]	1.7*	[0.8 3.5]
F24 Induced delusional disorder	1.1*	[0.8 1.5]	1.1*	[0.8 1.6]	0.9*	[0.2 4.1]	†	
F25 Schizoaffective disorder	0.7	[0.6 0.9]	0.6	[0.5 0.8]	1.3*	[0.7 2.6]	3.0*	[0.9 10.0]
F28 Other nonorganic psychotic disorders	0.8*	[0.7 1.0]	0.8	[0.7 1.0]	0.9*	[0.5 1.8]	1.8*	[0.6 5.4]
F29 Unspecified nonorganic psychosis	1.0*	[0.9 1.2]	1.0*	[0.9 1.2]	1.2*	[0.7 2.0]	1.2*	[0.4 3.5]
<b>4. F30-F39 Mood affective disorders</b>	<b>1.4</b>	<b>[1.4 1.5]</b>	<b>1.4</b>	<b>[1.4 1.5]</b>	<b>1.5</b>	<b>[1.3 1.8]</b>	<b>1.9</b>	<b>[1.4 2.6]</b>
F30 Manic episode	1.0*	[0.9 1.2]	1.0*	[0.9 1.1]	1.2*	[0.7 1.9]	1.1*	[0.4 2.8]
F31 Bipolar affective disorder	1.1*	[1.0 1.3]	1.1*	[1.0 1.2]	1.4*	[0.9 2.1]	1.6*	[0.8 3.6]
F32 Depressive episode	1.4	[1.4 1.5]	1.4	[1.4 1.5]	1.4	[1.1 1.6]	2.0	[1.5 2.8]
F33 Recurrent depressive disorder	1.3	[1.2 1.4]	1.3	[1.2 1.4]	1.5	[1.2 1.9]	1.7	[1.1 2.7]
F34 Persistent mood affective disorders	1.3	[1.2 1.4]	1.3	[1.2 1.4]	1.3*	[1.0 1.7]	1.8	[1.1 3.0]
F38 Other mood affective disorders	1.0*	[0.8 1.2]	1.0*	[0.8 1.1]	1.4*	[0.8 2.5]	1.9*	[0.7 5.4]
F39 Unspecified mood affective disorder	1.1*	[0.9 1.3]	1.0*	[0.9 1.2]	1.5*	[0.9 2.5]	1.6*	[0.5 4.8]
<b>5. F40-F48 Neurotic, stress-related and somatoform disorders</b>	<b>1.7</b>	<b>[1.7 1.8]</b>	<b>1.7</b>	<b>[1.7 1.8]</b>	<b>1.6</b>	<b>[1.4 1.9]</b>	<b>2.2</b>	<b>[1.7 2.9]</b>
F40 Phobic anxiety disorders	1.4	[1.2 1.5]	1.4	[1.2 1.5]	1.3*	[0.9 1.8]	1.4*	[0.8 2.6]
F41 Other anxiety disorders	1.7	[1.6 1.8]	1.7	[1.6 1.8]	1.6	[1.3 2.0]	2.2	[1.5 3.1]
F42 Obsessive-compulsive disorder	1.4	[1.3 1.5]	1.4	[1.3 1.5]	1.3*	[1.0 1.7]	1.6*	[0.9 2.8]
F43 Reaction to severe stress, and adjustment disorders	1.5	[1.4 1.6]	1.5	[1.4 1.6]	1.5	[1.2 1.8]	1.9	[1.3 2.7]
F44 Dissociative (conversion) disorders	1.4	[1.3 1.5]	1.4	[1.3 1.5]	1.3	[1.0 1.7]	2.3	[1.5 3.5]
F45 Somatoform disorders	1.7	[1.6 1.8]	1.7	[1.6 1.8]	1.5	[1.2 1.8]	2.0	[1.4 3.0]
F48 Other neurotic disorders	1.4	[1.3 1.5]	1.4	[1.3 1.5]	1.4	[1.1 1.9]	1.7*	[1.0 2.9]
<b>6. F50-F59 Behavioral syndromes associated with physiological disturbances and physical factors</b>	<b>1.4</b>	<b>[1.3 1.5]</b>	<b>1.4</b>	<b>[1.3 1.5]</b>	<b>1.5</b>	<b>[1.2 1.8]</b>	<b>2.2</b>	<b>[1.6 3.2]</b>
F50 Eating disorders	1.4	[1.3 1.5]	1.4	[1.3 1.4]	1.3	[1.0 1.7]	2.5	[1.6 3.8]
F51 Nonorganic sleep disorders	1.6	[1.4 1.8]	1.5	[1.4 1.7]	2.2	[1.5 3.1]	2.9	[1.4 5.9]
F52 Sexual dysfunction, not caused by organic disorder or disease	2.0	[1.7 2.3]	2.0	[1.7 2.3]	1.6*	[0.9 3.0]	8.4	[3.4 20.5]
F53 Mental and behavioral disorders associated with the puerperium, not elsewhere classified	1.2	[1.1 1.3]	1.2	[1.1 1.3]	1.1*	[0.8 1.6]	1.4*	[0.7 2.6]
F54 Psychological and behavioral factors associated with disorders or diseases classified elsewhere	1.6	[1.2 2.1]	1.6	[1.2 2.1]	0.3*	[0.0 2.5]	5.7	[2.0 16.5]
F55 Abuse of non-dependence-producing substance	1.1*	[1.0 1.4]	1.1*	[0.9 1.3]	1.2*	[0.7 2.3]	1.5*	[0.5 4.5]
F59 Unspecified behavioral syndromes associated with physiological disturbances and physical factors	2.0	[1.4 3.0]	2.0	[1.3 3.0]	†		7.7	[1.2 49.9]
<b>7. F60-F69 Disorders of adult personality and behavior</b>	<b>1.4</b>	<b>[1.3 1.5]</b>	<b>1.4</b>	<b>[1.3 1.5]</b>	<b>1.5</b>	<b>[1.2 1.9]</b>	<b>2.3</b>	<b>[1.5 3.6]</b>
F60 Specific personality disorders	1.4	[1.3 1.5]	1.4	[1.3 1.5]	1.4	[1.1 1.8]	2.1	[1.3 3.4]
F61 Mixed and other personality disorders	1.3	[1.2 1.4]	1.3	[1.2 1.4]	1.1*	[0.8 1.6]	1.4*	[0.7 2.7]
F62 Enduring personality changes, not attributable to brain damage and disease	1.3	[1.2 1.4]	1.3	[1.2 1.4]	1.2*	[0.8 1.7]	1.4*	[0.7 2.8]
F63 Habit and impulse disorders	1.4	[1.3 1.5]	1.4	[1.3 1.5]	1.3*	[1.0 1.8]	1.9	[1.0 3.4]
F64 Gender identity disorders	2.1	[1.2 3.6]	1.6*	[0.9 3.1]	5.3	[1.5 18.6]	†	
F65 Disorders of sexual preference	1.4*	[1.0 2.0]	1.2*	[0.8 1.8]	1.5*	[0.4 5.5]	12.2	[2.2 69.5]
F66 Psychological and behavioral disorders associated with sexual development and orientation	1.5	[1.1 2.1]	1.3*	[0.9 1.9]	1.6*	[0.4 5.7]	12.2	[2.2 69.5]
F68 Other disorders of adult personality and behavior	1.4	[1.3 1.5]	1.4	[1.3 1.5]	1.4	[1.0 1.8]	1.4*	[0.8 2.6]
F69 Unspecified disorder of adult personality and behavior	1.3	[1.2 1.5]	1.3	[1.2 1.5]	1.2*	[0.9 1.7]	1.4*	[0.7 2.6]

(Continued)

Table 3 (Continued).

	All Cases		NS		ST1		ST2	
	OR	[95% CI]	OR	[95% CI]	OR	[95% CI]	OR	[95% CI]
<b>8. F70-F79 Mental retardation</b>	<b>1.2*</b>	<b>[0.9 1.5]</b>	<b>1.2*</b>	<b>[0.9 1.5]</b>	<b>0.8*</b>	<b>[0.3 2.1]</b>	<b>2.1*</b>	<b>[0.4 10.4]</b>
F70 Mild mental retardation	1.4	[1.1 1.9]	1.5	[1.1 2.0]	0.6*	[0.1 2.4]	3.4*	[0.4 29.8]
F71 Moderate mental retardation	1.1*	[0.7 1.8]	0.9*	[0.5 1.7]	3.0*	[0.8 10.4]	†	
F72 Severe mental retardation	1.0*	[0.5 2.1]	0.9*	[0.4 2.1]	3.0*	[0.3 31.1]	†	
F73 Profound mental retardation	0.9*	[0.4 2.4]	0.8*	[0.3 2.2]	4.9*	[0.4 66.8]	†	
F78 Other mental retardation	†		†		†		†	
F79 Unspecified mental retardation	1.0*	[0.6 1.5]	0.9*	[0.6 1.5]	1.1*	[0.2 4.8]	1.5*	[0.1 15.5]
<b>9. F80-F89 Disorders of psychological development</b>	<b>1.3</b>	<b>[1.2 1.4]</b>	<b>1.2</b>	<b>[1.1 1.4]</b>	<b>1.4</b>	<b>[1.0 2.0]</b>	<b>2.9</b>	<b>[1.7 5.0]</b>
F80 Specific developmental disorders of speech and language	1.5	[1.3 1.6]	1.4	[1.2 1.6]	1.7	[1.1 2.5]	3.1	[1.5 6.3]
F81 Specific developmental disorders of scholastic skills	1.4	[1.2 1.7]	1.3	[1.1 1.7]	2.0	[1.1 3.5]	1.5*	[0.4 6.2]
F82 Specific developmental disorder of motor function	0.5*	[0.2 1.3]	0.4*	[0.1 1.1]	3.1*	[0.6 17.3]	†	
F83 Mixed specific developmental disorders	1.6	[1.3 1.9]	1.5	[1.2 1.9]	2.1	[1.1 3.8]	1.4*	[0.3 7.4]
F84 Pervasive developmental disorders	1.0*	[0.9 1.2]	1.0*	[0.8 1.2]	1.1*	[0.6 2.0]	2.8	[1.2 6.9]
F88 Other disorders of psychological development	1.5	[1.2 1.9]	1.5	[1.2 1.8]	2.1	[1.1 3.8]	1.4*	[0.3 7.4]
F89 Unspecified disorder of psychological development	1.4	[1.2 1.8]	1.4	[1.1 1.7]	2.0	[1.1 3.7]	1.6*	[0.4 6.8]
<b>10. F90-F98 Behavioral and emotional disorders with onset usually occurring in childhood and adolescence</b>	<b>1.4</b>	<b>[1.4 1.5]</b>	<b>1.4</b>	<b>[1.3 1.5]</b>	<b>1.4</b>	<b>[1.2 1.8]</b>	<b>2.3</b>	<b>[1.5 3.5]</b>
F90 Hyperkinetic disorders	1.5	[1.4 1.8]	1.6	[1.4 1.8]	1.4*	[0.9 2.3]	1.7*	[0.7 4.1]
F91 Conduct disorders	1.3	[1.1 1.5]	1.2	[1.0 1.5]	1.6*	[0.9 2.6]	1.9*	[0.6 5.6]
F92 Mixed disorders of conduct and emotions	1.4	[1.2 1.7]	1.4	[1.1 1.7]	1.7*	[0.9 3.1]	1.1*	[0.3 4.2]
F93 Emotional disorders with onset specific to childhood	1.3	[1.2 1.4]	1.3	[1.2 1.4]	1.3*	[1.0 1.8]	1.8	[1.0 3.1]
F94 Disorders of social functioning with onset specific to childhood and adolescence	1.4	[1.3 1.6]	1.4	[1.2 1.6]	2.0	[1.3 2.9]	1.8*	[0.8 4.0]
F95 Tic disorders	1.4	[1.3 1.5]	1.4	[1.3 1.5]	1.3*	[0.9 1.7]	3.0	[1.8 5.2]
F98 Other behavioral and emotional disorders with onset usually occurring in childhood and adolescence	1.5	[1.3 1.6]	1.4	[1.2 1.6]	1.7	[1.2 2.4]	3.3	[1.7 6.6]
<b>11. F99 Unspecified mental disorder</b>	<b>1.3</b>	<b>[1.2 1.4]</b>	<b>1.3</b>	<b>[1.2 1.4]</b>	<b>1.4</b>	<b>[1.1 1.8]</b>	<b>2.2</b>	<b>[1.4 3.4]</b>
F99 Mental disorder, not otherwise specified	1.3	[1.2 1.4]	1.3	[1.2 1.4]	1.4	[1.1 1.8]	2.2	[1.4 3.4]

Notes: \* $p > 0.05$ . †Omitted due to too few observations.

Abbreviations: MSD, Musculoskeletal and connective tissue diseases; ST1, Surgically treated once; ST2, Surgically treated two or more times.

substance use (OR 1.1, 95% CI 1.0–1.1), these results are not expected to have any clinical relevance. No significant association between MBD and TMD was found in patients with schizophrenia, schizotypal, delusional disorders, or mental retardation.

## Discussion

This study showed that there is a strong association between certain diagnoses of MBD and TMD diagnosed and treated in a hospital setting, with stronger associations in TMD requiring surgical treatment. The relation between mental health and TMD is complex, but understanding it is imperative when dealing with patients with TMD as well as with patients with impaired mental health who might be at risk of developing chronic pain conditions. Since this study relied on prospective registry data, the risk of temporal bias, which is often associated with case–control studies, has decreased. Indeed, as with earlier findings, the results here indicate that there is a strong association present, although it is important to acknowledge that the establishment of a true casual relation requires other study designs, and that TMD itself may cause impaired psychosocial abilities thereby creating a causal nexus.<sup>30,31</sup> This is another important reason for physicians

to be familiar with the quite common conditions within the TMD umbrella and to refer patients who present with onset orofacial pain or chronic orofacial pain at an early stage.

Pain, which is the most common symptom of TMD, is associated with depression, anxiety, and stress, three psychological conditions that have a modifying role in TMD.<sup>8,32–36</sup> In addition, women have been found to experience chronic pain more often than men, a gender difference that could be related to both societal and biological factors.<sup>37</sup> Comorbidity of chronic physical and mental disorders are also risk factors for chronic pain even after adjusting for well-known confounders, such as age, education, and gender.<sup>37</sup> This is interesting considering the recognized fact that TMD patients are predominantly female as well as the obvious predisposition of comorbid diseases presented in this study. The intricate nexus of risks for chronic pain and TMD suggests that multimodal care and focused screening methods should be considered. The screening could be applied when selecting patients for TMJ surgery, with the goal of not initiating surgical intervention in patients where the rate of success is likely lower or the risk for reoperation is increased. Multimodal care and screening methods could also be applied at an earlier stage in close collaboration with oral pain clinics and in other instances of health care such as orthopedic or rheumatology clinics. These early screenings could focus on identifying early signs of TMD. National guidelines could help health care providers identify patients who should be referred for conservative treatment at an earlier stage, possibly preventing them from developing surgically demanding TMD.

Often, more severe psychiatric diagnoses are considered as absolute contraindicators of surgical treatment, but the results of this study, which might be indicative of a causal association between certain MBD and TMD, indicate that these premises perhaps need to be re-evaluated. If the cause-effect between impaired TMD and impaired mental health is bilateral, there is a possibility that the treatment of TMD, both surgical and conservative, might have the same bilateral effect. If treatment can relieve the patient from TMD symptoms, it may be possible that the psychosocial burden is reduced as well, emphasizing the need for early conservative treatment, perhaps in some form of subsidized treatment program from the health care system. The importance of optimizing treatment of MBD before TMD treatment should not be underestimated, and the impact of underlying diseases, such as MBD, and the effect on TMD treatment response should be investigated further both in relation to conservative and surgical treatment.

Preoperative psychological factors have been of interest for a long time, where methods examining the locus of control described by Rotter and later Wallston have been used to predict surgical outcome and pain management postoperatively, for example, in hand surgery.<sup>38–40</sup> More recently, Howard L Fields, describing the influence of the expectations of pain, concluded that the expectation of perceived pain is particularly important in persistent or recurrent pain such as in arthritis or chronic headache. He further described early treatment failure as a predictor itself as it may become a self-fulfilling prophecy. As most patients who are surgically treated for TMD have foregone conservative treatment that most likely would have failed to alleviate their symptoms, correctly targeted early and adequate interventions are emphasized. Similarly, pain catastrophizing has been shown to be predictive of TMD pain and should also be evaluated when considering treatment modality.<sup>7,10</sup>

The results of this study repeatedly showed stronger associations between MBD and TMD in cases who had undergone surgical treatment, with many times a two-fold increase in probability. Whether this association is the result of more severe TMD symptoms in patients with these underlying diseases and whether there is an increased risk of failing conservative treatment as the result of MBD are interesting questions; however, these questions are outside the framework of this study. Other studies that have investigated the effect of preoperative anxiety and depression on post-surgical outcome have conflicting results. Patients with preoperative depression have been found to have significantly reduced postoperative gains in quality of life after endoscopic sinus surgery, and depression has been shown to increase hospital length following coronary bypass graft surgery.<sup>41,42</sup> However, in a study on total hip or knee arthroplasty, patients with preoperative anxiety and/or depression had similar outcomes as patients without these premorbid conditions.<sup>43</sup> Similarly, a 2017 review study concluded that there were inconclusive results in the abilities to predict postoperative pain due to preoperative depression and concluded that further studies are needed.<sup>44</sup> It might also be of importance to consider the iatrogenic effects of surgical treatment, especially for aging patients with ongoing neurodegeneration, as the neuroinflammation caused by the surgical trauma itself may be the driver of further neurocognitive complications such as dementia or delirium.<sup>45</sup> Furthermore, neuroinflammation has also been suggested to alter pain perception and sensitization in individuals with attention-deficit/hyperactivity disorder (ADHD). In this study, subjects

with behavioral and emotional disorders with onset usually occurring in childhood and adolescence (F90-F98), which include neuropsychiatric disorders such as ADHD, autistic spectrum disorders and tic disorders, had a high probability of developing TMD. The odds of developing TMD that requires multiple surgical interventions were more than doubled in comparison to individuals without these comorbidities. ADHD not only increases the risk of mental health and social difficulties but is also strongly associated with extreme pain.<sup>46,47</sup> In pediatric study populations neuropsychiatric symptoms have been shown to affect how pain interferes with daily activities, and children with ADHD have even been suggested to be at increased risk of developing TMD.<sup>48,49</sup> Considering that the rates of ADHD are fairly consistent in Western countries, and that research is increasingly showing the substantial impact of ADHD on functioning, more studies on the association with TMD will advance the knowledge of how treatment of neuropsychiatric disorders might be incorporated in the management of orofacial pain.<sup>50</sup>

The strength of this study design is that it uses population-based data based on comprehensive and accurate national registries. The prospective nature of the registry data from NPR allows for assuming a temporal relationship between diagnoses of MBD and TMD, and the NPR has been validated with high reliability for many of the MBD diagnoses, but not all.<sup>51–55</sup> The largest weakness is that patients with TMD who do not require surgery but still receive a TMD diagnosis within the health care system represent a small part of the entire population, as most TMD patients in Sweden are both diagnosed and treated within the dental care system and therefore are not available in the NPR. These patients (NS) might represent a subset of the TMD population that for some reason are diagnosed within the health care system. This also means that there might be a considerable proportion of TMD patients within the control group, that have not been diagnosed within the hospital care system and thereby cause misclassification bias. However, such misclassification could most likely be considered bias towards the null.

In conclusion, the findings of this study indicate a strong association between mood affective disorders, neurotic, stress-related and somatoform disorders, behavioral syndromes associated with physiological disturbances and physical factors, disorders of adult personality and behavior, disorders of the psychological development, unspecified mental disorder, and the development of TMD. These associations suggest a causal effect, and the association seems to be stronger for TMD requiring surgery, in particular repeated surgery. The results highlight the need of multimodal care of patients with combined MBD and pain disorders, suggesting the implementation of screening methods that can identify patients with early signs of TMD as the result of MBD conditions. These types of screenings could be used to identify patients who could benefit from conservative treatment at an earlier stage. Preoperative screening for psychosocial factors could also be used to identify patients who might be at risk of persistent postoperative pain after TMJ surgery, information that can be used to design postoperative treatment plans that anticipate this pain. These results emphasize the importance of early detection and initiation of relevant treatment. In addition, these results, in terms of articular problems, suggest preferentially involving a close interdisciplinary collaboration between dental and medical specialists, such as orofacial pain specialists, TMJ surgeons, pain specialists, psychologists, and psychiatrists to obtain precision treatment.

## Abbreviations

DC/TMD, Diagnostic Criteria for Temporomandibular Disorders; DEGURBA, Eurostat's Degree of Urbanization; ICD-10, International Classification of Diseases 10th Revision; LISA, The Longitudinal Integrated Database for Labor Market and Health Insurance Studies; MBD, Mental and behavioral disorders; MSD, Musculoskeletal and connective tissue diseases; NBHW, National Board of Health and Welfare; NPR, National Patient Registry; PIN, Personal Identification Number; SCB, Statistics Sweden; ST1, Surgically treated once; ST2, Surgically treated two or more times; SWEREG-TMD, Swedish National Registry Studies for Surgically Treated TMD; TMD, Temporomandibular Disorders; TMJ, Temporomandibular Joint; TPR, Total Population Registry.

## Acknowledgments

This research was funded by the Swedish Public Dental Services, Folk tandvården Stockholm AB, and Steering Group for Collaborative Odontological Research at Karolinska Institutet and Stockholm City County.

## Disclosure

The authors report no conflicts of interest in this work. All authors approved the final version of this article.

## References

1. LeResche L. Epidemiology of temporomandibular disorders: implications for the investigation of etiologic factors. *Crit Rev Oral Biol Med.* 1997;8(3):291–305. doi:10.1177/10454411970080030401
2. Lövgren A, Häggman-Henrikson B, Visscher CM, Lobbezoo F, Marklund S, Wänman A. Temporomandibular pain and jaw dysfunction at different ages covering the lifespan—A population based study. *Eur J Pain.* 2016;20(4):532–540. doi:10.1002/ejp.755
3. Häggman-Henrikson B, Liv P, Ilgunas A, et al. Increasing gender differences in the prevalence and chronification of orofacial pain in the population. *Pain.* 2020;161(8):1768–1775. doi:10.1097/j.pain.0000000000001872
4. Macfarlane TV, Blinkhorn AS, Davies RM, Kinney J, Worthington HV. Predictors of outcome for orofacial pain in the general population: a four-year follow-up study. *J Dent Res.* 2004;83(9):712–717. doi:10.1177/154405910408300911
5. LeResche L, Mancil LA, Drangsholt MT, Huang G, Von Korff M. Predictors of onset of facial pain and temporomandibular disorders in early adolescence. *Pain.* 2007;129(3):269–278. doi:10.1016/j.pain.2006.10.012
6. Aggarwal VR, Macfarlane GJ, Farragher TM, McBeth J. Risk factors for onset of chronic oro-facial pain—results of the North Cheshire oro-facial pain prospective population study. *Pain.* 2010;149(2):354–359. doi:10.1016/j.pain.2010.02.040
7. Reiter S, Eli I, Mahameed M, et al. Pain catastrophizing and pain persistence in temporomandibular disorder patients. *J Oral Facial Pain Headache.* 2018;32(3):309–320. doi:10.11607/ofph.1968
8. Staniszewski K, Lygre H, Bifulco E, et al. Temporomandibular disorders related to stress and HPA-axis regulation. *Pain Res Manag.* 2018;2018:7020751. doi:10.1155/2018/7020751
9. Sójka A, Stelcer B, Roy M, Mojs E, Pryliński M. Is there a relationship between psychological factors and TMD? *Brain Behav.* 2019;9(9):e01360. doi:10.1002/brb3.1360
10. Willassen L, Johansson AA, Kvinnslund S, Staniszewski K, Berge T, Rosén A. Catastrophizing has a better prediction for TMD than other psychometric and experimental pain variables. *Pain Res Manag.* 2020;2020:7893023. doi:10.1155/2020/7893023
11. Staniszewski K, Willassen L, Berge T, Johansson A, Schjødt B, Rosen A. High pain intensity is a risk factor of non-resolving TMD: a three-year follow-up of a patient group in a Norwegian interdisciplinary evaluation program. *J Pain Res.* 2022;15:1283–1296. doi:10.2147/JPR.S341861
12. Velly AM, Mohit S. Epidemiology of pain and relation to psychiatric disorders. *Prog Neuropsychopharmacol Biol Psychiatry.* 2018;87(PtB):159–167. doi:10.1016/j.pnpbp.2017.05.012
13. Schiffman E, Ohrbach R, Truelove E, et al. Diagnostic Criteria For Temporomandibular Disorders (DC/TMD) for clinical and research applications: recommendations of the International RDC/TMD Consortium Network\* and orofacial pain special interest groupdagger. *J Oral Facial Pain Headache.* 2014;28(1):6–27. doi:10.11607/jop.1151
14. Widmark G. On surgical intervention in the temporomandibular joint. *Swed Dent J Suppl.* 1997;123:1–87.
15. Dimitroulis G. Management of temporomandibular joint disorders: a surgeon's perspective. *Aust Dent J.* 2018;63(Suppl 1):S79–S90. doi:10.1111/adj.12593
16. Ludvigsson JF, Andersson E, Ekblom A, et al. External review and validation of the Swedish national inpatient register. *BMC Public Health.* 2011;11(1):450. doi:10.1186/1471-2458-11-450
17. Ludvigsson JF, Almqvist C, Bonamy AK, et al. Registers of the Swedish total population and their use in medical research. *Eur J Epidemiol.* 2016;31(2):125–136. doi:10.1007/s10654-016-0117-y
18. Ludvigsson JF, Svedberg P, Olén O, Bruze G, Neovius M. The longitudinal integrated database for health insurance and labour market studies (LISA) and its use in medical research. *Eur J Epidemiol.* 2019;34(4):423–437. doi:10.1007/s10654-019-00511-8
19. Ludvigsson JF, Otterblad-Olausson P, Pettersson BU, Ekblom A. The Swedish personal identity number: possibilities and pitfalls in healthcare and medical research. *Eur J Epidemiol.* 2009;24(11):659–667. doi:10.1007/s10654-009-9350-y
20. Ayouni I, Chebbi R, Hela Z, Dhidah M. Comorbidity between fibromyalgia and temporomandibular disorders: a systematic review. *Oral Surg Oral Med Oral Pathol Oral Radiol.* 2019;128(1):33–42. doi:10.1016/j.oooo.2019.02.023
21. Pantoja LLQ, De toledo IP, Pupo YM, et al. Prevalence of degenerative joint disease of the temporomandibular joint: a systematic review. *Clin Oral Investig.* 2019;23(5):2475–2488. doi:10.1007/s00784-018-2664-y
22. Patten SB, Williams JV, Wang J. Mental disorders in a population sample with musculoskeletal disorders. *BMC Musculoskelet Disord.* 2006;7(1):37. doi:10.1186/1471-2474-7-37
23. Khan J, Zusman T, Wang Q, Eliav E. Acute and chronic pain in orofacial trauma patients. *Dent Traumatol.* 2019;35(6):348–357. doi:10.1111/edt.12493
24. Nazarevych M, Ohonovskiy R, Pohranychna K, Mokryk O, Melnychuk Y, Stasyshyn A. Frequency and nature of disorders in psycho-emotional and autonomic systems in patients with middle facial injury. *Wiad Lek.* 2022;75(1 pt 2):197–202. doi:10.36740/WLek202201209
25. Sterling M, Hendrikz J, Kenardy J. Compensation claim lodgement and health outcome developmental trajectories following whiplash injury: a prospective study. *Pain.* 2010;150(1):22–28. doi:10.1016/j.pain.2010.02.013
26. Sharma S, Ohrbach R, Fillingim RB, Greenspan JD, Slade G. Pain sensitivity modifies risk of injury-related temporomandibular disorder. *J Dent Res.* 2020;99(5):530–536. doi:10.1177/0022034520913247
27. Koletsis D, Pandis N. Conditional logistic regression. *Am J Orthod Dentofacial Orthop.* 2017;151(6):1191–1192. doi:10.1016/j.ajodo.2017.04.009
28. White IR, Royston P, Wood AM. Multiple imputation using chained equations: issues and guidance for practice. *Stat Med.* 2011;30(4):377–399. doi:10.1002/sim.4067
29. Salinas Fredricson A, Krüger Weiner C, Adami J, et al. Sick leave and disability pension in a cohort of TMD-patients - The Swedish National Registry Studies for Surgically Treated TMD (SWEREG-TMD). *BMC Public Health.* 2022;22(1):916. doi:10.1186/s12889-022-13329-z
30. Fillingim RB, Ohrbach R, Greenspan JD, et al. Psychological factors associated with development of TMD: the OPFERA prospective cohort study. *J Pain.* 2013;14(12 Suppl):T75–90. doi:10.1016/j.jpain.2013.06.009



31. Fillingim RB, Slade GD, Greenspan JD, et al. Long-term changes in biopsychosocial characteristics related to temporomandibular disorder: findings from the OPERA study. *Pain*. 2018;159(11):2403–2413. doi:10.1097/j.pain.0000000000001348
32. Bair MJ, Robinson RL, Katon W, Kroenke K. Depression and pain comorbidity: a literature review. *Arch Intern Med*. 2003;163(20):2433–2445. doi:10.1001/archinte.163.20.2433
33. Andias R, Silva AG. Impact of sex, sleep, symptoms of central sensitization and psychosocial factors in adolescents with chronic musculoskeletal pain-an exploratory study. *Pain Med*. 2022. doi:10.1093/pm/pnac053
34. Al-Khotani A, Naimi-Akbar A, Gjelsset M, et al. The associations between psychosocial aspects and TMD-pain related aspects in children and adolescents. *J Headache Pain*. 2016;17(1):30. doi:10.1186/s10194-016-0622-0
35. List T, Jensen RH. Temporomandibular disorders: old ideas and new concepts. *Cephalalgia*. 2017;37(7):692–704. doi:10.1177/0333102416686302
36. Nazeri M, Ghahreghahi HR, Pourzare A, et al. Role of anxiety and depression in association with migraine and myofascial pain temporomandibular disorder. *Indian J Dent Res*. 2018;29(5):583–587. doi:10.4103/0970-9290.244932
37. Mills SEE, Nicolson KP, Smith BH. Chronic pain: a review of its epidemiology and associated factors in population-based studies. *Br J Anaesth*. 2019;123(2):e273–e283. doi:10.1016/j.bja.2019.03.023
38. Rotter JB. Generalized expectancies for internal versus external control of reinforcement. *Psychol Monogr*. 1966;80(1):1–28. doi:10.1037/h0092976
39. Wallston KA, Wallston BS, DeVellis R. Development of the Multidimensional Health Locus of Control (MHLC) Scales. *Health Educ Monogr*. 1978;6(2):160–170. doi:10.1177/109019817800600107
40. Stewart JA, Aebischer V, Egloff N, et al. The role of health locus of control in pain intensity outcome of conservatively and operatively treated hand surgery patients. *Int J Behav Med*. 2018;25(3):374–379. doi:10.1007/s12529-018-9713-4
41. AbuRuz ME. Pre-operative depression predicted longer hospital length of stay among patients undergoing coronary artery bypass graft surgery. *Risk Manag Healthc Policy*. 2019;12:75–83. doi:10.2147/RMHP.S190511
42. Ospina J, Liu G, Crump T, Sutherland JM, Janjua A. The impact of comorbid depression in chronic rhinosinusitis on post-operative sino-nasal quality of life and pain following endoscopic sinus surgery. *J Otolaryngol Head Neck Surg*. 2019;48(1):18. doi:10.1186/s40463-019-0340-0
43. Seagrave KG, Lewin AM, Harris IA, Badge H, Naylor J. Association between pre-operative anxiety and/or depression and outcomes following total Hip or knee arthroplasty. *J Orthop Surg*. 2021;29(1):2309499021992605. doi:10.1177/2309499021992605
44. Dadgostar A, Bigder M, Punjani N, Lozo S, Chahal V, Kavanagh A. Does preoperative depression predict post-operative surgical pain: a systematic review. *Int J Surg*. 2017;41:162–173. doi:10.1016/j.ijsu.2017.03.061
45. Yang T, Velagapudi R, Terrando N. Neuroinflammation after surgery: from mechanisms to therapeutic targets. *Nat Immunol*. 2020;21(11):1319–1326. doi:10.1038/s41590-020-00812-1
46. Thapar A, Cooper M. Attention deficit hyperactivity disorder. *Lancet*. 2016;387(10024):1240–1250. doi:10.1016/S0140-6736(15)00238-X
47. Stickley A, Koyanagi A, Takahashi H, Kamio Y. ADHD symptoms and pain among adults in England. *Psychiatry Res*. 2016;246:326–331. doi:10.1016/j.psychres.2016.10.004
48. Suligowska K, Mikietyńska M, Pakalska-Korcala A, Wolańczyk T, Prośba-Mackiewicz M, Zdrojewski T. Parafunctions, signs and symptoms of Temporomandibular Disorders (TMD), in children with Attention-Deficit Hyperactivity Disorder (ADHD): the results of the SOPKARD-Junior study. *Psychiatr Pol*. 2021;55(4):887–900. doi:10.12740/PP/OnlineFirst/113438
49. Balter LJT, Wiwe Lipsch C, Wicksell RK, Lekander M. Neuropsychiatric symptoms in pediatric chronic pain and outcome of acceptance and commitment therapy. *Front Psychol*. 2021;12:576943. doi:10.3389/fpsyg.2021.576943
50. Cortese S, Coghill D. Twenty years of research on attention-deficit/hyperactivity disorder (ADHD): looking back, looking forward. *Evid Based Ment Health*. 2018;21(4):173–176. doi:10.1136/ebmental-2018-300050
51. Dalman C, Broms J, Cullberg J, Allebeck P. Young cases of schizophrenia identified in a national inpatient register—are the diagnoses valid? *Soc Psychiatry Psychiatr Epidemiol*. 2002;37(11):527–531. doi:10.1007/s00127-002-0582-3
52. Ekholm B, Ekholm A, Adolfsson R, et al. Evaluation of diagnostic procedures in Swedish patients with schizophrenia and related psychoses. *Nord J Psychiatry*. 2005;59(6):457–464. doi:10.1080/08039480500360906
53. Sellgren C, Landén M, Lichtenstein P, Hultman CM, Långström N. Validity of bipolar disorder hospital discharge diagnoses: file review and multiple register linkage in Sweden. *Acta Psychiatr Scand*. 2011;124(6):447–453. doi:10.1111/j.1600-0447.2011.01747.x
54. Rück C, Larsson KJ, Lind K, et al. Validity and reliability of chronic tic disorder and obsessive-compulsive disorder diagnoses in the Swedish National Patient Register. *BMJ Open*. 2015;5(6):e007520. doi:10.1136/bmjopen-2014-007520
55. Kouppis E, Ekselius L. Validity of the personality disorder diagnosis in the Swedish National Patient Register. *Acta Psychiatr Scand*. 2020;141(5):432–438. doi:10.1111/acps.13166