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Prevalence of Mental Health Conditions Among 6078 Individuals With Down Syndrome in the United States

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Abstract

Findings from a recent study of the largest documented cohort of individuals with Down syndrome (DS) in the United States described prevalence of common disease conditions and strongly suggested significant disparity in mental health conditions among these individuals as compared with age- and sex-matched individuals without DS. The retrospective, descriptive study reported herein is a follow-up to document prevalence of 58 mental health conditions across 28 years of data from 6078 individuals with DS and 30,326 age- and sex-matched controls. Patient data were abstracted from electronic medical records within a large integrated health system.

In general, individuals with DS had higher prevalence of mood disorders (including depression); anxiety disorders (including obsessive-compulsive disorder); schizophrenia; psychosis (including hallucinations); pseudobulbar affect; personality disorder; dementia (including Alzheimer's disease); mental disorder due to physiologic causes; conduct disorder; tic disorder; and impulse control disorder. Conversely, the DS cohort experienced lower prevalence of bipolar I disorder; generalized anxiety, panic, phobic, and posttraumatic stress disorders; substance use disorders (including alcohol, opioid, cannabis, cocaine, and nicotine disorders); and attention-deficit/hyperactivity disorder. Prevalence of many mental health conditions in the setting of DS vastly differs from comparable individuals without DS. These findings delineate a heretofore unclear jumping-off point for ongoing research. (*J Patient Cent Res Rev.* 2022;9:58-63.)

Keywords

Down syndrome; prevalence; mental health; depression; anxiety; dementia; substance use; ADHD

A recent study of the largest documented cohort of individuals with Down syndrome (DS) in the United States described the prevalence of a broad range of disease conditions.¹ Findings strongly suggested significant disparity in mental health conditions, in particular, among individuals with DS as compared with age- and sex-matched individuals without DS.¹ Previous research has shown that, overall, people with DS seem to be more vulnerable to mental health issues and diagnosis;²⁻⁴ however, some experts believe overdiagnosis is common due to deficits in language, communication, cognition, problem-solving, and coping.⁵ Regardless, given that the prevalence of DS itself is increasing⁶ and that the lifespan for individuals with DS has grown in recent decades,⁷⁻¹¹ a more in-

depth analysis of mental health conditions among this patient population is merited, not only for foundational knowledge but also to facilitate better diagnostics and clinical care.

To explore rates of mental health conditions among individuals with DS, this study utilizes clinical data representing the largest reported DS sample cohort in the United States, treated across a single integrated health system that includes the largest center of care for adolescents and adults with DS. The objective of this follow-up brief report to a broader study¹ was to provide critical information on mental health conditions in individuals with DS in order to better guide general practitioners, enhance specialized care, and inform future research within this unique population.

METHODS

This retrospective, descriptive cohort study utilized 28 years of available encounter data (May 1991–September 2019) abstracted from the electronic medical records of an integrated U.S. Midwest-based nonprofit health

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system. As a follow-up to a larger study conducted with this patient population, it was determined to be non-human subjects research by the applicable institutional review board. Full details on the data collection methods for this and the more generalized prevalence study can be found in the previously published primary report.¹

Participants

A total of 6078 eligible cases, ranging in age from 0 to 89 years, with at least 1 encounter registering an International Classification of Diseases (ICD) code of DS were identified. Controls included up to 5 individuals without a diagnosis of DS matched to each DS case on year of birth (± 1 year) and sex by a data analyst. There were 30,326 eligible controls. Overall, 64 cases were assigned only 4 (as opposed to 5) matched controls.

Procedures

Specific mental health conditions of interest among individuals with DS were preidentified. Conditions were chosen based on both the literature and the clinical expertise of one of the study authors (B.C.). To assess prevalence, this study used U.S. Clinical Modification (CM) codes for medical diagnoses based on the statistical classification of disease denoted in the World Health Organization's publication of the ICD,¹² specifically, 10th Revision (ICD-10-CM) and 9th Revision (ICD-9-CM) codes. See Table 1 for a complete list of mental health conditions of interest and associated ICD codes.

Statistical Methods

Demographics are reported as means with standard deviations and medians with ranges for age and total encounters per sample. Sex, race, ethnicity, and insurance are reported as counts with percentages. Clinical conditions are reported as counts with percentages and corresponding odds ratios (OR) representing the odds of having a mental health condition among cases relative to controls. Corresponding Pearson's chi-squared P-values represent statistically significant (at an alpha of <0.05) differences in prevalence of diagnoses between cases and controls. Fisher's exact P-values were interpreted when any sample count was less than 5.

RESULTS

The cohort of DS cases was predominantly White (77.35%) and of non-Hispanic or Latino ethnicity (73.51%). Cases had a median of 6 total encounters (ie, clinical visits in the health system) in the dataset. The control cohort also was predominantly White (61.97%) and of non-Hispanic or Latino ethnicity (81.72%), with a median of 7 total encounters in the dataset. Both groups were approximately 52% male and had a median age of 25 years. For complete demographics of the DS and matched control samples, the

reader is referred to the relevant table published within the parent article describing this project.¹

The following findings describe the OR and 95% CI along with associated P-value when comparing prevalence of a mental health conditions of interest among individuals with DS (ie, cases) to matched controls. See Table 2 for full results.

Statistically significant results revealed that, relative to controls, individuals with DS had *greater* odds of experiencing: any mood disorder (OR: 3.41 [2.85, 4.07]; $P<0.0001$) and, specifically, depression (OR: 1.27 [1.15, 1.39]; $P<0.0001$); any anxiety disorder (OR: 1.09 [1.01, 1.17]; $P=0.0206$) and, specifically, obsessive-compulsive disorder (OCD) (OR: 20.15 [16.43, 24.71]; $P<0.0001$); schizophrenia (OR: 1.87 [1.17, 3.00]; $P=0.0077$); any psychosis (OR: 3.87 [2.27, 6.61]; $P<0.0001$) and, specifically, hallucinations (OR: 2.35 [1.30, 4.26]; $P=0.0037$); pseudobulbar affect (OR: 49.98 [6.40, 390.47]; $P<0.0001$); any personality disorder (2.58 [1.69, 3.93]; $P<0.0001$) and, specifically, other or unspecified personality disorders (OR: 6.00 [3.02, 11.92]; $P<0.0001$); dementia (OR: 17.13 [13.39, 21.90]; $P<0.0001$) and, specifically, Alzheimer's disease (OR: 66.97 [50.39, 88.99]; $P<0.0001$); mental disorders due to physiologic causes (OR: 2.94 [1.69, 5.11]; $P<0.0001$); conduct disorders (OR: 2.01 [1.60, 2.53]; $P<0.0001$); tic disorders (OR: 1.67 [1.21, 2.31]; $P=0.0018$); and impulse control disorder (OR: 23.03 [13.40, 39.59]; $P<0.0001$).

On the other hand, statistically significant results revealed that, relative to controls, individuals with DS have *lesser* odds of experiencing: bipolar I (OR: 0.49 [0.27, 0.89]; $P=0.0174$); generalized anxiety disorder (OR: 0.25 [0.17, 0.38]; $P<0.0001$); panic disorder (OR: 0.07 [0.03, 0.18]; $P<0.0001$); phobic anxiety disorder (OR: 0.55 [0.35, 0.88]; $P=0.0109$); posttraumatic stress disorder (PTSD) (OR: 0.60 [0.39, 0.91]; $P=0.0143$); any substance use disorder (OR: 0.08 [0.06, 0.10]; $P<0.0001$) and, specifically, alcohol use (OR: 0.04 [0.02, 0.08]; $P<0.0001$), opioid use (OR: 0.12 [0.04, 0.31]; $P<0.0001$), cannabis use (OR: 0.04 [0.01, 0.15]; $P<0.0001$), cocaine use (OR: 0.18 [0.06, 0.56]; $P=0.0003$), other stimulant use (OR: 0.08 [0.04, 0.19]; $P<0.0001$), and nicotine use disorders (OR: 0.08 [0.06, 0.11]; $P<0.0001$); and, finally, attention-deficit/hyperactivity disorder (ADHD) (OR: 0.58 [0.48, 0.69]; $P<0.0001$).

DISCUSSION

Our results corroborate previous research that shows prevalences of mental health conditions in individuals with DS are vastly different relative to their non-DS matched counterparts.^{3,4,13} Importantly, these mental

Table 1. Mental Health Conditions of Interest and Associated Codes

Mental health condition	ICD-10-CM codes	ICD-9-CM codes
Mood disorders	F39	296, 2969
Manic episode(s)	F30	2961
Bipolar disorders	F31	2960, 2964, 2965, 2966, 2967, 2968
Bipolar I	F310–F3178	2960, 2964, 2965, 2966, 2967
Bipolar II	F3181	29689
Cyclothymic disorder/cyclothymia	F340	30113
Bipolar disorder, other/unspecified	F3189, F319	2968
Depression	F32–F33	2962, 2963, 311
Anxiety disorders	F40–F48	300
Generalized anxiety disorder	F411	30002
Social phobias	F401	30023
Panic disorder	F410	30001, 30021
Phobic anxiety disorder	F40	3002
Posttraumatic stress disorder	F431	30981
Obsessive compulsive disorder	F42	3003
Schizophrenia	F20	295
Schizoaffective disorder	F25	2957
Psychosis	F23	298
Hallucinations	R440–R443	7801
Delusion disorders	F22	297
Dissociative disorders	F44, F4481, F481	3001, 30012, 30014, 3006
Dissociative amnesia	F440	30012
Depersonalization disorder	F481	3006
Dissociative identity disorder	F4481	30014
Pseudobulbar affect	F482	31081
Personality disorder	F60	301
Borderline	F603	30183
Paranoid	F600	3010
Schizoid	F601	3012
Antisocial	F602	3017
Histrionic	F604	3015, 30150, 30159
Obsessive compulsive	F605	3014
Avoidant	F606	30182
Dependent	F607	3016
Narcissistic	F6081	30181
Other/Unspecified	F6089, F609	30189, 3019
Substance use/abuse	F10–F19	303–305
Alcohol	F10	303, 3050
Opioid	F11	3040, 3055
Cannabis	F12	3043, 3052
Sedative, hypnotic, anxiolytic	F13	3041
Cocaine	F14	3042, 3056
Other stimulant	F15	3044, 3054
Hallucinogen	F16	3045, 3053
Nicotine	F17	3051
Inhalant	F18	–
Other psychoactive	F19	3046, 3049
Dementia	F02–F03	2900, 29420
Alzheimer's disease	G30	3310
Mental disorders to due physiologic cause	F06	2939
Eating disorders	F50	3075
Anorexia nervosa	F500	3071
Bulimia nervosa	F502	30751
Binge eating disorder	F5081	–
Conduct disorders	F91	312
Attention-deficit/hyperactivity disorder	F90	31401
Tic disorders	F95	30720
Impulse control disorder	F639	3123

CM, Clinical Modifications; ICD, International Classification of Diseases.

Table 2. Prevalence of Mental Health Conditions of Interest Among Cases vs Controls

Mental health condition	DS sample (n=6078)	Controls (n=30,326)	OR (95% CI)	P ^a
Mood disorders	208	312	3.41 (2.85, 4.07)	<0.0001
Manic episode(s)	0	9	–	0.3721 ^b
Bipolar disorder	99	435	1.14 (0.91, 1.42)	0.2499
Bipolar I	12	121	0.49 (0.27, 0.89)	0.0174
Bipolar II	3	32	0.47 (0.14, 1.53)	0.2584 ^b
Cyclothymic disorder/Cyclothymia	0	9	–	0.3721 ^b
Bipolar disorder, other/unspecified	90	372	1.21 (0.96, 1.53)	0.1063
Depression	571	2297	1.27 (1.15, 1.39)	<0.0001
Anxiety disorders	1029	4773	1.09 (1.01, 1.17)	0.0206
Generalized anxiety disorder	24	474	0.25 (0.17, 0.38)	<0.0001
Social phobias	5	49	0.51 (0.20, 1.28)	0.1425
Panic disorder	5	332	0.07 (0.03, 0.18)	<0.0001
Phobic anxiety disorder	20	180	0.55 (0.35, 0.88)	0.0109
Posttraumatic stress disorder	25	208	0.60 (0.39, 0.91)	0.0143
Obsessive-compulsive disorder	447	119	20.15 (16.43, 24.71)	<0.0001
Schizophrenia	24	64	1.87 (1.17, 3.00)	0.0077
Schizoaffective disorder	12	49	1.22 (0.65, 2.30)	0.5328
Psychosis	24	31	3.87 (2.27, 6.61)	<0.0001
Hallucinations	16	34	2.35 (1.30, 4.26)	0.0037
Delusion disorders	6	13	2.30 (0.88, 6.06)	0.0819
Dissociative disorders	11	37	1.48 (0.76, 2.91)	0.2475
Dissociative Amnesia	0	0	–	–
Depersonalization disorder	0	0	–	–
Dissociative identity disorder	0	3	–	1.0000 ^b
Pseudobulbar affect	10	1	49.98 (6.40, 390.47)	<0.0001 ^b
Personality disorder	33	64	2.58 (1.69, 3.93)	<0.0001
Borderline	1	27	0.18 (0.03, 1.36)	0.0732 ^b
Paranoid	0	0	–	–
Schizoid	0	0	–	–
Antisocial	0	3	–	1.0000 ^b
Histrionic	0	0	–	–
Obsessive-compulsive	2	10	1.00 (0.22, 4.56)	1.0000 ^b
Avoidant	0	0	–	–
Dependent	1	3	–	–
Narcissistic	0	3	–	1.0000 ^b
Other/Unspecified	18	15	6.00 (3.02, 11.92)	<0.0001
Substance use/abuse	76	4095	0.08 (0.06, 0.10)	<0.0001
Alcohol	9	1016	0.04 (0.02, 0.08)	<0.0001
Opioid	4	172	0.12 (0.04, 0.31)	<0.0001
Cannabis	2	274	0.04 (0.01, 0.15)	<0.0001 ^b
Sedative, hypnotic, anxiolytic	2	37	0.27 (0.06, 1.12)	0.0527 ^b
Cocaine	3	85	0.18 (0.06, 0.56)	0.0003 ^b
Other stimulant	6	354	0.08 (0.04, 0.19)	<0.0001
Hallucinogen	0	9	–	0.3721 ^b
Nicotine	51	2896	0.08 (0.06, 0.11)	<0.0001
Inhalant	0	0	–	–
Other psychoactive	0	0	–	–
Dementia	276	84	17.13 (13.39, 21.90)	<0.0001
Alzheimer's disease	627	52	66.97 (50.39, 88.99)	<0.0001
Mental disorders due to physiologic cause	20	34	2.94 (1.69, 5.11)	<0.0001
Eating disorders	17	71	1.20 (0.70, 2.03)	0.5090
Anorexia nervosa	1	10	0.50 (0.06, 3.90)	0.7038 ^b
Bulimia nervosa	1	16	0.31 (0.04, 2.35)	0.3378 ^b
Binge eating disorder	0	5	1.00 (0.12, 8.54)	1.0000 ^b
Conduct disorders	104	260	2.01 (1.60, 2.53)	<0.0001
Attention-deficit/hyperactivity disorder	144	1223	0.58 (0.48, 0.69)	<0.0001
Tic disorders	49	147	1.67 (1.21, 2.31)	0.0018
Impulse control disorder	73	16	23.03 (13.40, 39.59)	<0.0001

^aStatistical significance was reached at an alpha of <0.05.

^bFisher's exact test P-value was interpreted due to low sample count.

DS, Down syndrome; OR, odds ratio.

health prevalence findings provide a baseline jumping-off point for ongoing research in DS settings. They also may compel actions for remodeled care specific to individuals with DS. A deeper investigation into the broad range of highly prevalent mental health conditions — along with the coexisting physical disorders that may contribute to their development — is merited to increase our understanding of how these conditions impact this patient population. The unique assessment and treatment barriers often faced by those with DS could be improved through more refined screening tools and treatment protocols.

While study findings represent data from only one U.S. health system, this rather large system of 26 hospitals and more than 500 outpatient locations may provide the most accurate and available review of prevalence among a U.S. sample, given the United States' fragmented storage of patient data. Furthermore, much of the data came from a specialized care center specifically serving adults with DS, which may improve diagnostic accuracy of ICD coding and subsequent prevalence findings. It should be noted that diagnostic accuracy in general can be difficult with individuals with DS for a variety of reasons.¹⁴

In general, diagnosis of mental health conditions with behavioral components can be inaccurate among individuals with DS.^{15,16} For instance, overlapping symptoms, like sensory or motor deficits, and other common comorbid medical conditions, like thyroid problems and sleep apnea, may mimic dementia or depression, affecting diagnosis.^{4,15} While our study showed increased prevalence of depression, a previous study found that half of patients with DS who were diagnosed with depression were found to not meet official diagnostic criteria, signifying a need for separate diagnostic criteria for patients with developmental disabilities.¹⁷

Research has also suggested that youth with DS are more likely to show externalizing behaviors than siblings and peers without DS.^{4,18,19} To this end, individuals with DS have shown increased prevalence of ADHD, conduct disorder, and anxiety disorder diagnoses, possibly reflecting increased diagnosis patterns versus true disease prevalence.^{3,4} While our study showed higher prevalence of conduct and anxiety disorders among individuals with DS, it also showed lesser prevalence of ADHD.

It has been noted that externalizing behaviors seen in youth with DS change into internalizing behaviors seen in adolescence and adulthood.³ Prevalence of OCD, a condition characterized by internalized symptoms of obsessions and compulsions, has been shown to range in individuals with DS, attributed to difficulty in assessment.^{3,4} However, diagnostic inaccuracies from

factors like individuals not being able to provide their own history were not studied in this paper. For example, while some research has shown PTSD to be more common in DS due to strong visual memories,²⁰ our study found it to be less common. A patient's inability or limited ability to convey the "trauma" may lead to PTSD being undiagnosed and perhaps resulting, instead, in only diagnosis of the symptomatic presentation such as mood disorder or psychoses, both of which were more common in this study's DS cohort.

Contrary to one prior study,²¹ we found higher prevalence of schizophrenia in people with DS. While the codes used to represent the conditions of interest in this study were carefully chosen and reviewed by a clinical expert in DS, it is acknowledged that the utilized codes may not be ones most commonly used to represent corresponding conditions. It is also possible that these codes over- or underrepresent diagnoses among individuals with DS relative to individuals without DS. This may be particularly true of diagnoses with primarily behavioral criteria.²²

Study Limitations

This study did not assess etiology and cause of the mental illnesses. For example, comorbid mental and physical health conditions likely impact treatment progress in both areas, so understanding the relationship between them is critical in this group. Also, reasons for differences in mental illness diagnosis, including intrinsic factors associated with or the genetics of DS, environmental factors, employment or social activities, and display of symptoms, were not explored.

While this study included both youths and adults with DS, future longitudinal analyses are necessary to look at prevalence of conditions across time, to report on youth and adult populations separately, and to track the course of conditions seen at different stages of the lifespan of individuals with DS, particularly as that lifespan continues to increase. Due to the diagnostic challenges and limited literature, we recommend cautious interpretation of mental illness data in individuals with DS. Future research should attempt to mitigate these challenges.

CONCLUSIONS

In this mental health-focused follow-up to a previously published study on the prevalence of common diseases among individuals with Down syndrome relative to matched controls,¹ it was found that, overall, individuals with DS are more likely than their non-DS counterparts to experience a variety of mental health conditions. These include mood disorders (particularly depression), anxiety disorders (particularly OCD), schizophrenia, psychosis and hallucinations, pseudobulbar affect, personality

disorders (often unspecified), dementia and Alzheimer's disease, mental disorders due to physiologic cause, conduct disorder, tic disorder, and impulse control disorder. On the other hand, individuals with DS are much less likely to experience substance use disorders relative to their non-DS counterparts and therefore may not require the same frequency or degree of screening.

Patient-Friendly Recap

- Authors collected decades of patient data from a large health system to compare the prevalence of numerous mental health diagnoses in individuals with Down syndrome (DS) to a control cohort encompassing similar patients without DS.
- Significant differences between cohorts revealed that, generally, individuals with DS were more likely to be diagnosed with mood and personality disorders, psychosis, and dementia and less likely to be diagnosed with substance use disorders than their age- and sex-matched counterparts.
- It is unclear if these differences are due to diagnostic approach or genuine prevalence; still, remodeling mental health screening and care specific to those with DS is necessary.

Author Contributions

Study design: Rivelli, Fitzpatrick, Jia, Rzhetsky, B. Chicoine. Data acquisition or analysis: Rivelli, Fitzpatrick, Wales, L. Chicoine, B. Chicoine. Manuscript drafting: Rivelli, Fitzpatrick, Wales, L. Chicoine, B. Chicoine. Critical revision: Rivelli, Fitzpatrick, Wales, L. Chicoine, B. Chicoine.

Conflicts of Interest

None.

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