Treatments and Treatment Predictors in Patients With Substance Use Disorders and Comorbid Attention-Deficit/Hyperactivity Disorder:

First Results From the International Naturalistic Cohort Study of ADHD and SUD (INCAS)

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Abstract

Background: Treatment of attention-deficit/hyperactivity disorder (ADHD) in patients with a substance use disorder (SUD) and comorbid ADHD (SUD + ADHD) may have positive effects on the outcome of both conditions, but controversy exists regarding the preferred ADHD treatment in these patients. Little is known about the treatments that are provided for these patients in routine addiction care practice and the factors that are associated with treatment provision.

Objective: To describe the treatments provided in everyday clinical practice and to explore factors associated with ADHD treatment provision in patients with SUD + ADHD.

Methods: An international multicenter observational prospective cohort design was employed. Patients with moderate to severe SUD and comorbid ADHD according to *DSM-5* were invited to participate at the start of a new SUD treatment episode between June 2017 and May 2021. Clinical and sociodemographic data were collected at 12 study sites in 9 countries through patient interviews, interviews with treatment providers, and patient files. Treatment variation across studies was described, and mixed-effect logistic regression was used to identify factors associated with ADHD treatment provision.

Results: A total of 578 treatment-seeking patients with SUD + ADHD (274 inpatients, 303 outpatients, and 1 unknown) were recruited. About two-thirds received some kind of ADHD treatment (62.8%), with 54.0% receiving pharmacologic, 34.0% receiving psychological treatment, and 25.1% receiving combined pharmacologic and psychological treatment. The treatment site explained more of the variation in ADHD treatment provision than individual patient factors. In addition, higher ADHD symptom severity and sobriety at intake were associated with receiving ADHD treatment.

Conclusion: These findings suggest that treatment of SUD + ADHD patients is suboptimal even in specialized centers with substantial practice variation. Further research is needed to better understand the barriers to implement treatment guidelines for ADHD + SUD and, thus, to improve quality of care.

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Clinical Points

- Very little is known about treatments that are provided to patients with substance use disorder and comorbid attention-deficit/hyperactivity disorder in everyday clinical settings.
- The current observational study shows that there is considerable treatment provision variation across clinics and/or countries.
- Future research is needed to investigate the reasons for this variation to develop strategies for the implementation of currently existing treatment guidelines.

It is well established that attention-deficit/hyperactivity disorder (ADHD) is an important risk factor for developing substance use disorder (SUD),[1,2] and studies have also shown that comorbid SUD + ADHD, compared to having only one of these conditions, is associated with a more severe clinical course, including an increased mortality rate.[3–6] ADHD and SUD share neurocognitive deficits[7–9] and symptoms,[10] and a growing body of evidence suggests that these are further aggravated in individuals with SUD + ADHD.[10–13] This highlights the importance of effective and targeted treatment strategies in this comorbid population.

A meta-analysis of randomized controlled studies (RCTs) investigating the effect of pharmacotherapy on SUD + ADHD, demonstrated a small to moderate effect on ADHD symptoms, but no effect on substance use.[14] However, the limited number of included studies was heterogeneous regarding study medication, study population, and presence of adjunct treatments.[15] Two later RCTs on stimulant treatment in stimulant use disorder patients showed significant positive effects of treatments with higher-than-standard doses of extended-release stimulants on both ADHD and substance use.[16,17] Furthermore, 2 large registry studies found a dose-dependent effect of methylphenidate on adherence to treatment[18] and a decrease in substance use.[19] Finally, research suggests that pharmacotherapy in SUD + ADHD is effective in reducing ADHD symptoms without negative effects on SUD outcomes.[20–22] These findings constitute the scientific bases for recent treatment guidelines that recommend a combination of pharmacotherapy and psychological treatment.[23–25]

However, controversy remains about ADHD treatment in patients with SUD.[21] For instance, there is a concern that prescribing stimulants might lead to an increased risk for misuse and/or diversion, which may result in a reluctance towards prescribing stimulants to patients with SUD + ADHD.[22] This likely contributes to practice variation, but data on treatments that are provided to patients with SUD + ADHD in clinical settings are lacking.

Few studies have investigated predictors for treatment allocation in psychiatric populations. One study showed that patient factors, such as sociodemographic status, were associated with psychiatric treatment allocation in primary care.[26] To the best of our knowledge, no previous study has investigated sociodemographic and clinical predictors, such as self-rated symptom severity and presence of other psychiatric comorbidities, for treatment allocation in treatment-seeking patients with SUD + ADHD.

This study aimed to describe the treatment modalities provided to treatment-seeking patients with SUD + ADHD and explore factors that are associated with ADHD treatment provision.

METHOD

Study Design

An international multicenter observational prospective cohort design was employed at 12 study sites in 9 countries (Belgium, France, Germany, Hungary, the Netherlands, Spain, Sweden, Switzerland, and the US). All study sites were existing SUD treatment centers connected to academic research groups with a specific interest and expertise in SUD + ADHD.

The study was preregistered (https://doi.org/10.1186/ISRCTN15998989), and the protocol and some baseline data were published in 2022.[27]

Data were collected at baseline, 4 weeks, 3 months, and 9 months using self-rating scales, interviews with patients and clinicians, and patient files. Information on treatment provision was not limited to the specific treatment center, and patients and clinicians were instructed to provide data on all treatments they received (including self-help groups and/or parallel caregivers).

Participants

Treatment-seeking adults (≥18 years) with moderate to severe SUD and comorbid ADHD, according to *DSM-5*, were invited to participate at the start of a new SUD treatment episode between June 2017 and May 2021. The diagnostic assessments were performed according to local clinical routines and regulations.

A new treatment episode was defined as either (a) the first visit in 3 months or (b) the first visit after receiving the diagnosis of ADHD. There were no formal exclusion criteria.

Participants received written and oral information before providing written informed consent. The study was approved by the Swedish Ethical Review Authority (2017/240–31) and the local ethics committees and was conducted in accordance with the Declaration of Helsinki—Ethical Principles for Medical Research Involving Human Subjects.

Table 1.

Baseline Descriptives of Complete Sample[a]

	Total sample N = 578	Belgium-Antwerpen N = 37	Spain N = 35	Belgium-Brussels N = 28	Germany N = 56	Hungary N = 15	Netherlands N = 72	France N = 8	Sweden N = 152	Switzerland N = 135	United States N = 41	*P* value
Female	137 (24%)	4 (11%)	6 (18%)	8 (29%)	18 (32%)	3 (20%)	13 (18%)	1 (13%)	45 (30%)	24 (18%)	15 (37%)	.04*
Treatment initiator												<.01*
Other (eg, law enforcement and social service)	193 (33%)	20 (54%)	10 (29%)	16 (57%)	14 (25%)	1 (7%)	16 (22%)	1 (13%)	53 (35%)	41 (30%)	21 (51%)	
Patient	381 (66%)	17 (46%)	24 (71%)	12 (43%)	42 (75%)	14 (93%)	55 (76%)	7 (88%)	99 (65%)	93 (69%)	18 (44%)	
Unknown	4 (0.7%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (1.4%)	0 (0%)	0 (0%)	1 (0.7%)	2 (5%)	
Treatment setting at baseline												<.01*
Outpatient	303 (52%)	0 (0%)	31 (91%)	7 (25%)	21 (38%)	15 (100%)	19 (26%)	8 (100%)	152 (100%)	11 (8%)	39 (95%)	
Unknown	1 (0.2%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (2%)	
Substance use												
Tobacco user	500 (87%)	34 (92%)	32 (94%)	27 (96%)	51 (93%)	12 (80%)	64 (91%)	4 (57%)	119 (81%)	128 (95%)	29 (81%)	<.01*
Polysubstance use	353 (62%)	32 (87%)	23 (70%)	22 (79%)	35 (63%)	7 (47%)	53 (76%)	5 (63%)	67 (44%)	84 (63%)	25 (66%)	<.01*
Injected during last 12 mo	37 (7%)	1 (3%)	5 (15%)	0 (0%)	1 (2%)	0 (0%)	4 (6%)	0 (0%)	16 (11%)	6 (5%)	4 (13%)	.04*
Alcohol use disorder	376 (66%)	28 (76%)	18 (55%)	17 (61%)	42 (75%)	3 (20%)	41 (59%)	7 (88%)	103 (68%)	99 (74%)	18 (47%)	<.01*
Opioid use disorder	100 (18%)	0 (0%)	10 (30%)	1 (4%)	2 (4%)	1 (7%)	15 (21%)	0 (0%)	18 (12%)	30 (23%)	23 (61%)	<.01*
Cannabis use disorder	261 (46%)	23 (62%)	21 (64%)	23 (82%)	24 (43%)	7 (47%)	36 (51%)	4 (50%)	45 (30%)	60 (45%)	18 (47%)	<.01*
Hallucinogen use disorder	36 (6%)	0 (0%)	3 (9%)	4 (14%)	1 (2%)	0 (0%)	10 (14%)	0 (0%)	2 (1%)	13 (10%)	3 (8%)	<.01*
Inhalant use disorder	25 (4%)	0 (0%)	2 (6%)	0 (0%)	0 (0%)	0 (0%)	8 (11%)	0 (0%)	1 (1%)	11 (8%)	3 (8%)	<.01*
Stimulant use disorder	297 (52%)	30 (81%)	25 (76%)	18 (64%)	34 (61%)	10 (67%)	46 (66%)	2 (25%)	60 (40%)	58 (44%)	14 (37%)	<.01*
Sedatives use disorder	94 (17%)	10 (27%)	6 (18%)	6 (21%)	4 (7%)	1 (7%)	12 (17%)	0 (0%)	29 (19%)	19 (14%)	7 (18%)	.27
Self-reported abstinence during 30 d before enrollment (TLFB)	113 (21%)	5 (14%)	8 (24%)	2 (7%)	18 (38%)	2 (13%)	15 (21%)	0 (0%)	35 (25%)	22 (16%)	6 (27%)	.03
Self-reported ADHD symptoms and quality of health												
ASRS	47.3 (10.0)											.08
EQ-5D—VAS	62.9 (19.5)											<.01*

[a]Descriptive data on sex, treatment initiation, treatment setting, clinical data of substance use and self-reported ADHD symptoms and quality of health. Presented as total number and proportion except for ASRS and EQ-5D, which are presented as mean (SD). *P* values refer to statistical test of differences between sites/countries.

*Statistically significant *P* value.

Abbreviations: ADHD = attention-deficit/hyperactivity disorder, ASRS = ADHD Self-Report Scale, EQ-5D = EuroQol 5 Dimension, TLFB = Timeline Follow-Back, VAS = visual analog scale.

Table 2.

Treatments Provided for SUD

	Total N = 578	Belgium-Antwerpen N = 37	Spain N = 35	Belgium-Brussels N = 28	Germany N = 56	Hungary N = 15	Netherlands N = 72	France N = 8	Sweden N = 152	Switzerland N = 135	United States N = 41	*P* value
Treatment during 30 d before enrollment												
Any SUD treatment	371 (66.9%)	22 (59.5%)	21 (61.8%)	21 (75%)	51 (91.1%)	8 (53.3%)	54 (77.1%)	6 (85.7%)	61 (42.4%)	115 (85.2%)	12 (41.4%)	<.01*
Inpatient treatment	212 (38.6%)	17 (45.9%)	4 (11.8%)	7 (25%)	34 (60.7%)	0 (0%)	34 (50.7%)	0 (0%)	10 (7%)	104 (77.6%)	2 (6.9%)	<.01*
Pharmacotherapy SUD during first month												
Total	224 (39.2%)	10 (27%)	31 (91.2%)	17 (60.7%)	12 (21.4%)	9 (60%)	38 (52.8%)	3 (37.5%)	42 (27.6%)	34 (25.2%)	28 (80%)	<.01*
Opioid use disorder[a]	41 (43.2%)	-	9 (90%)	1 (100%)	1 (50%)	1 (100%)	6 (40%)	-	3 (16.7%)	10 (33.3%)	10 (55.6%)	<.01*
Alcohol use disorder[a]	105 (28.1%)	5 (17.9%)	10 (55.6%)	10 (58.8%)	8 (19%)	1 (33.3%)	12 (29.3%)	1 (14.3%)	38 (36.9%)	8 (8.1%)	12 (75%)	<.01*
Stimulant use disorder[a]	51 (17.3%)	2 (6.7%)	16 (64%)	3 (16.7%)	4 (11.8%)	6 (60%)	7 (15.2%)	1 (50%)	0 (0%)	6 (10.3%)	6 (50%)	<.01*
Tobacco use disorder[a]	33 (6.7%)	2 (5.9%)	1 (3.1%)	3 (11.1%)	0 (0%)	1 (8.3%)	12 (18.8%)	0 (0%)	0 (0%)	7 (5.5%)	7 (29.2%)	<.01*
Pharmacotherapy for SUD at 3 mo visit												
All SUDs[b]	106 (32.3%)	2 (11.8%)	25 (83.3%)	6 (60%)	3 (10%)	5 (56%)	8 (19%)	2 (33.3%)	35 (31.8%)	15 (22.4%)	5 (71.4%)	<.01*
Pharmacotherapy SUD at 9 mo visit												
All SUDs[b]	67 (29.5%)	2 (22.2%)	20 (83.3%)	3 (60%)	2 (11.8%)	3 (33.3%)	5 (19.2%)	1 (33.3%)	21 (24.7%)	8 (17.8%)	2 (50%)	<.01*

[a]Percentage of pharmacotherapy targeting a specific SUD represents the proportions who received treatment out of those that had the specified substance use disorder.
[b]For the follow-up visits, percentages refer to the proportion out of those in treatment at the specific follow-up visit. *P* values refer to statistical differences between sites/countries as tested by χ^2 test.
*Statistically significant *P* value.
Abbreviation: SUD = substance use disorder.

Instruments and Measurements

Outcomes. Data on pharmacologic SUD treatment (yes/no) were collected for specific groups of SUDs (in accordance with *DSM-5*). For instance, for "stimulant use disorder" the exact proportions that primarily used cocaine, (meth)amphetamine or other stimulants were not specified. Data on ADHD treatments were collected in detail, including dosing. Presence of other comorbid psychiatric disorders was collected along with data on pharmacologic treatments for these disorders.

Predictors of treatment provision. Sociodemographic and clinical data were collected using study-specific questionnaires. The following predictors of treatment provision were assessed: study site, educational level, occupational status, marital status, housing, age, sex, presence of poly-SUD and/or additional psychiatric comorbidity, self-rated ADHD symptom severity, and substance use at baseline. ADHD symptoms were assessed with the 18-item Adult ADHD Self-Report Scale (ASRS).[28] Self-rated perception of health was assessed with item 6 of the EuroQol-5D (EQ-5D),[29] ie, a visual analog scale (VAS) ranging from 0 to 100, where 100 is "the best health you can imagine." Substance use during the 30 days preceding treatment initiation was assessed through a structured interview (Timeline Follow-Back interview[30]). For details, we refer the reader to the aforementioned publication on methods and measurement issues of the study.[27]

Statistical Analysis

Analyses were conducted in R version 4.2.0.[31] Proportions or mean values with standard deviation (SD) were calculated for the total sample and per site. Differences between sites regarding categorical variables of sociodemographic and clinical data were tested utilizing χ^2 tests or Fisher exact test if the assumptions of χ^2 tests were not met.

Mixed-effect logistic regression models ("lme4" package in R[32]) were built, based on variable selection with "Least Absolute Shrinkage and Selection Operator" (LASSO) ("glmmLasso" package[33]), to investigate predictors for treatment status (operationalized as a binary variable) during the first 4 weeks of treatment. Patient factors (eg, sociodemographic data) were included as fixed effects and site as a random effect.

Missing data were deleted listwise. Test statistics and adjusted odds ratios (aOR) with 95% confidence intervals (CIs) were calculated. The area under the receiver operating characteristic curve (AUC) was calculated, and the marginal and conditional R2 was calculated ("performance" package[34]). Marginal R2 is a measure of the explanatory power of the fixed effects alone (in this case, specific patient factors), and the conditional R2 reflects the entire model. The explanatory power of the random effect (ie, the effect of site) is calculated by subtracting marginal R2 from conditional R2.

RESULTS

Sample Characteristics

In total, 578 patients with SUD + ADHD were recruited, 274 inpatients (47.4%) and 303 (52.4%) outpatients and 1 unknown (0.2%), 137 females (23.7%) and 441 males (76.3%), and a mean (SD) age of 36.7 (11.0) years. Sample size differed significantly between sites (minimum 8 and maximum 152), with the largest samples from Bern (Switzerland n = 135) and Stockholm (Sweden n = 152) and the smallest from Budapest (n = 15) and Paris (n = 8). Further socio- and clinical characteristics are presented in Table 1 or have been previously published.[30]

In general, inpatient treatment lasted between 2 and 12 weeks and followed by outpatient treatment at the same or another clinic, as per local routines. Most sites reported no specific local routines regarding local pharmacologic ADHD treatment and that they adhere to (inter)national guidelines, whereas some sites (eg, Syracuse, US) reported that stimulant treatment was generally not offered due to concerns of misuse and/or diversion.

Treatment Provision

SUD treatments received. Two-thirds (66.9%) received SUD treatment (defined as being in contact with a health care provider due to SUD) in the 30 days preceding enrollment with 38.6% receiving inpatient treatment prior to inclusion. Within 4 weeks after enrollment, 39.2% received pharmacologic SUD treatment, and at 3 and 9 months, the proportions receiving pharmacologic SUD treatment were even lower (28.3% and 23.7%, respectively). Details are presented in Table 2.

ADHD treatments received. In the first month, 62.8% of the participants received ADHD treatment (psychological and/or pharmacologic). About half (54%) received pharmacologic ADHD treatment (40.9% received stimulants). The most common pharmacotherapies at baseline were long-acting methylphenidate (45.8% of patients receiving ADHD pharmacotherapy), nonstimulant medication (27.3%), and short-acting methylphenidate (21.2%), with lisdexamfetamine prescribed to only 9.7%. Generally, stimulants were within standard dose range or in the lower ranges. For instance, at 3 months, 74.3% of those with lisdexamfetamine received 60 mg/d or less and 73.8% of those with methylphenidate received 70 mg/d or less. One-third (34%) received psychological ADHD treatment, and of those, most common treatments were cognitive-behavioral therapy (32%), coaching (23%), and skills training (22.1%). Details are presented in Table 3.

Pharmacologic treatment for other psychiatric comorbidities. Half (47.6%) received pharmacologic treatments for other psychiatric disorders (than

Table 3.

ADHD and Other Psychiatric Comorbidity Treatments Provided

	Total N = 578	Belgium-Antwerpen N = 37	Spain N = 35	Belgium-Brussels N = 28	Germany N = 56	Hungary N = 15	Netherlands N = 72	France N = 8	Sweden N = 152	Switzerland N = 135	US N = 41	*P* value[a]
ADHD treatment during the first month												
Pharmacotherapy	311 (54.0%)	22 (59.5%)	23 (67.6%)	21 (75%)	41 (73.2%)	7 (46.7%)	40 (55.6%)	6 (75%)	48 (31.6%)	68 (50.4%)	35 (89.7%)	<.01*
Stimulant treatment	235 (40.9%)	19 (51.4%)	17 (50%)	9 (32.1%)	32 (57.1%)	4 (26.7%)	37 (51.4%)	6 (75%)	40 (26.3%)	63 (46.7%)	8 (21.1%)	<.01*
Psychotherapy	195 (34.0%)	7 (18.9%)	25 (73.5%)	7 (25%)	2 (3.6%)	13 (86.7%)	31 (43.1%)	6 (75%)	16 (10.5%)	55 (40.7%)	33 (91.7%)	<.01*
Combined pharmacotherapy and psychotherapy	144 (25.1%)	6 (16.2%)	17 (50%)	6 (21.4%)	2 (3.6%)	6 (40%)	25 (34.7%)	4 (50%)	5 (3.3%)	41 (30.4%)	32 (88.9%)	<.01*
ADHD treatment at 3 mo visit												
Pharmacotherapy[b]	205 (56.9%)	11 (61%)	18 (58.1%)	8 (72.7%)	22 (71%)	5 (45.5%)	31 (63.3%)	4 (66.7%)	49 (41.5%)	40 (59.7%)	17 (94.4%)	<.01*
Stimulant treatment[b]	151 (42.2%)	10 (55.6%)	14 (45.2%)	2 (18.2%)	14 (45.2%)	3 (27.3%)	24 (50%)	4 (66.7%)	41 (34.7%)	38 (56.7%)	1 (5.9%)	<.01*
Psychotherapy[b]	112 (31.6%)	4 (22.2%)	18 (58.1%)	3 (27.3%)	2 (5.6%)	10 (90.9%)	14 (29.8%)	3 (50%)	23 (19.8%)	24 (35.8%)	11 (68.8%)	<.01*
Combined pharmacotherapy and psychotherapy[b]	74 (20.9%)	2 (11.1%)	12 (38.7%)	3 (27.3%)	2 (6.5%)	5 (45.5%)	10 (21.3%)	1 (16.7%)	10 (8.6%)	18 (26.9%)	11 (68.8%)	<.01*
ADHD treatment at 9 mo visit												
Pharmacotherapy[b]	153 (61.4%)	5 (55.6%)	15 (60%)	6 (75%)	13 (72.2%)	4 (44.4%)	16 (55.2%)	2 (66.7%)	54 (59.3%)	29 (63%)	9 (81.2%)	.8
Stimulant treatment[b]	117 (47.8%)	5 (55.5%)	12 (48%)	1 (12.5%)	9 (50%)	3 (33.3%)	11 (37.9%)	2 (66.7%)	46 (51.1%)	27 (60%)	1 (11.1%)	.11
Psychotherapy[b]	69 (28.3%)	1 (11.1%)	16 (64%)	1 (12.5%)	0 (0%)	8 (88.9%)	9 (32.1%)	3 (100%)	11 (12.4%)	14 (30.4%)	6 (66.7%)	<.01*
Combined pharmacotherapy and psychotherapy[b]	51 (21%)	0 (0%)	11 (44%)	1 (12.5%)	0 (0%)	4 (44.4%)	6 (21.4%)	2 (66.7%)	9 (10.2%)	12 (26.1%)	6 (66.7%)	<.01*
Pharmacotherapy for other psychiatric disorders												
Baseline	273 (47.6%)	10 (27%)	18 (52.9%)	18 (64.3%)	30 (54.5%)	9 (60%)	23 (32.4%)	6 (75%)	60 (39.5%)	76 (56.3%)	23 (59%)	<.01*
Month 3	176 (50.1%)	8 (44.4%)	12 (40%)	8 (72.7%)	18 (62.1%)	6 (54.5%)	13 (27.7%)	4 (66.7%)	62 (53.9%)	35 (52.2%)	10 (58.8%)	.05
Month 9	125 (51.2%)	1 (11.1%)	13 (54.2%)	7 (87.5%)	10 (62.5%)	7 (77.8%)	7 (24.1%)	2 (66.7%)	47 (52.8%)	24 (52.2%)	7 (63.6%)	<.08

[a]*P* values refer to statistical differences between sites/countries as tested by χ^2 test.
[b]Percentages at the follow-up visits represent the proportions out of those in treatment at the specific follow-up visit.
*Statistically significant *P* value.
Abbreviation: ADHD = attention-deficit/hyperactivity disorder.

SUD + ADHD) at baseline. Of those still in treatment at follow-up, 36.8% and 26.8% received pharmacotherapy at 3 and 9 months, respectively.

Predictors of Receiving ADHD Treatment

Only significant associations between variables and specific treatments are presented. The variables that were considered in analysis are presented in the method section.

Any ADHD treatment. The final mixed-effect logistic regression model for overall ADHD treatment receipt had a mean AUC of 0.76 (95% CI, 0.697–0.827), indicating good ability to discriminate between receiving treatment or not. Higher ASRS scores were associated with an increased likelihood of ADHD treatment receipt (aOR = 1.04, 95% CI, 1.02–1.06, $P < .001$), whereas a higher score on the EQ-5D-VAS (indicating better overall perceived health) was associated with a decreased likelihood (aOR = 0.98, 95% CI, 0.97–0.99, $P < .001$). The conditional R2 was 0.31 and the marginal R2 was 0.1, and, thus, site was a much better predictor for the likelihood of ADHD treatment than patient factors were (0.31–0.10 = 0.21).

Pharmacologic ADHD treatment. The final model for receiving pharmacologic ADHD treatment had a mean AUC of 0.74 (95% CI, 0.71–0.77) and, thus, had a good ability to discriminate between receiving pharmacologic ADHD treatment. Higher ASRS scores ($P < .01$, aOR = 1.03, 95% CI, 1.01–1.05) and complete abstinence from substance use 30 days prior to enrollment ($P = .03$, aOR 1.76, 95% CI, 1.05–2.95) were associated with a higher likelihood of receiving pharmacologic ADHD treatment, whereas a higher EQ-5D-VAS score was associated with a decreased likelihood ($P = .01$, aOR = 0.986, 95% CI, 0.974–0.997). Conditional R2 was calculated to 0.22 and marginal R2 to 0.07, indicating that differences in pharmacologic ADHD treatment between sites had more explanatory power for treatment receipt than individual patient factors.

Stimulant ADHD treatment. The final model had a mean AUC of 0.67 (95% CI, 0.62–0.72), indicating that the model only had fair discriminative ability. Higher ASRS scores ($P < .01$, aOR 1.03, 95% CI, 1.01–1.05) and abstinence from substance use in the 30 days before the start of the study ($P = .03$, aOR 1.65, 95% CI, 1.06–2.59) were significantly associated with an increased likelihood of stimulant treatment receipt. Conditional R2 was calculated to 0.09 and marginal R2 to 0.04, indicating that patient- and site-specific factors had similarly low explanatory power for the likelihood of receiving stimulant treatment.

Psychological ADHD treatment. The final model for receiving psychological ADHD treatment had a mean AUC of 0.84 (95% CI, 0.80–0.88), indicating that the model had a very good discriminative ability for receiving psychological ADHD treatment. The calculated conditional R2 of 0.5, compared to the marginal R2 of 0.03, indicates that site differences almost completely explained the variability in the likelihood of receiving psychological ADHD treatment (compared to patient factors).

Combined psychological and pharmacologic ADHD treatment within 4 weeks. The final model had a mean AUC of 0.80 (95% CI, 0.76–0.84), indicating that the model has very good discriminative ability. Poly-SUD was negatively and significantly associated with combined ADHD treatment receipt ($P = .04$, aOR = 0.58, 95% CI, 0.35–0.97). Marginal R2 was calculated to 0.41 and conditional R2 to 0.04, suggesting that the effect of site almost completely explained the variability in the likelihood of receiving combined psychological and pharmacologic ADHD treatment (compared to patient factors).

DISCUSSION

Summary

This observational multicenter study aimed to describe treatments received in standard clinical practice and to explore predictors for receiving ADHD treatments in patients with SUD + ADHD. The results show substantial variability across sites, with site as the main predictor of ADHD treatment provision. About 60% of the patients with SUD + ADHD did not receive pharmacologic treatment for their SUD and almost 40% did not receive any ADHD treatment. Notably, only 40% received stimulant treatment, which is first-line treatment for ADHD,[23] and only 25% received a combined pharmacotherapy with psychotherapy. Study site, baseline ADHD symptom severity, and level of quality of health were significantly associated with ADHD treatment provision.

Discussion

The finding that almost 40% of SUD + ADHD patients were not treated for ADHD, and the substantial variability in treatments across sites, is in line with the controversy related to ADHD treatment in this population.[21] These results indicate a gap between treatment guidelines and clinical practice.[23,24] Moreover, it suggests that treatment provision may be highly influenced by local routines and clinicians' attitudes towards ADHD treatment.

It is important to understand why patients with SUD + ADHD do not receive (certain) ADHD treatments. Possible explanations may include contraindications, patient's attitude towards certain treatments, and the availability/costs of psychotherapy and pharmacotherapy. However, the latter would likely not explain the choice between nonstimulants vs stimulants. Some study sites seem to systematically provide nonstimulant treatment more often than stimulants which affirms previous research that some clinicians are reluctant to prescribe stimulants to patients with SUD (or require a period of abstinence).[21] While this practice variation reflects the need for more research on the effectiveness of ADHD

treatment in this population, it should be noted that current guidelines recommend targeted ADHD treatment and that stimulants should not be avoided in SUD + ADHD.[23,24]

While practice variation was mainly explained by site, also a higher ASRS score and a lower EQ-5D-VAS score slightly increased the likelihood of ADHD treatment provision, indicating that those with less symptoms were less likely to receive treatment. This practice may be influenced by the clinicians' judgment and/or the patient and may in some cases be justified. However, by definition, patients with ADHD have significant impairments, and while some factors may predict treatment response,[35,36] there is today no evidence-based way to reliably predict treatment nonresponse. Therefore, treatment guidelines do not suggest therapists to refrain from ADHD treatment in SUD-ADHD patients.[23,24] Interestingly, abstinence for 30 days prior to treatment enrollment increased the likelihood of receiving pharmacologic ADHD treatment, specifically with stimulants. This is in line with previous research,[21] suggesting that for some clinicians, abstinence is a prerequisite to consider pharmacologic ADHD treatment, especially stimulant treatment. Indeed, some international guidelines do recommend abstinence before treatment initiation, but not all of them consider complete abstinence as a necessity.[21] However, there is little research on a positive effect of stabilization of substance use prior to ADHD treatment on treatment outcomes. In fact, pharmacotherapy, particularly with robust doses of stimulants, may facilitate treatment retention[37] and reductions in both ADHD symptoms and substance use.[16,17,37] Notably, 1 study found that stimulant treatment-related reduction in ADHD symptoms precipitated a reduction in substance use, indicating the importance of treating ADHD symptoms to achieve stabilization in SUD symptoms for some patients.[38]

In the current sample, pharmacotherapy targeting SUD was utilized in less than half, eg, for alcohol use disorder less than a third received pharmacologic treatment whereas for opioid use disorder, with opioid agonist being the main treatment, less than half received pharmacologic treatment. Importantly, while almost 9 of 10 in this sample reported regular tobacco use, only approximately 7% received pharmacotherapy targeting tobacco use. In contrast, two-thirds of those with a comorbid psychiatric disorder other than ADHD (eg, depression) received pharmacologic treatment for that comorbidity. This is in line with previous epidemiologic research on common psychiatric disorders in primary care settings, showing that most conditions are treated pharmacologically, but not SUD (with or without ADHD).[26,39] Taken together, this suggests that pharmacotherapy for SUD and ADHD might be underutilized compared to other psychiatric disorders.

Overall, these findings suggest that many patients with SUD + ADHD do not receive ADHD treatment and that there is a substantial variability in ADHD treatment provision across clinics. This may reflect that psychiatrists are uncertain about best practice and implies a need to examine the psychiatrists' decision-making process in treatment allocation for patients with SUD + ADHD. Moreover, it highlights the urgency of research on ADHD treatment in SUD populations to guide clinicians and, importantly, dissemination of available evidence and implementation of guidelines.

Finally, although psychotherapy as an add-on intervention to pharmacologic treatment is associated with better outcomes[23] and is recommended,[24] only a quarter of the patients in the current study received a combined treatment, possibly due to higher costs and lower availability of these combined treatments. This is unfortunate since adequate (pharmacologic) treatment of ADHD may also have a positive effect on the effectiveness of psychological treatments of SUD and on general well-being and social functioning.

Study Strengths and Limitations

This observational study has several strengths and limitations. The most important strengths are the large sample size, the use of the same structured assessments at all study sites, and the prospective design. There are, however, also limitations. First, the selected treatment facilities are all connected to academic research groups with a specific interest and expertise in SUD + ADHD. Therefore, the present results cannot be generalized to other treatment centers. Particularly, in treatment centers, not specifically trained to identify and treat ADHD in patients with SUD, treatment levels for ADHD are likely to be much lower.[40] Furthermore, the results of the current study cannot be generalized to persons with SUD + ADHD who do not seek treatment or have no access to health care. For instance, while the sample was heterogeneous in terms of clinical and sociodemographic variables,[27] only a very small proportion reported homelessness and/or had not completed elementary school. Thus, the current study likely was not able to assess the impact of certain factors on treatment allocation (such as homelessness). Second, there were site differences in diagnostic procedures.[27] For many participants, no structured instruments were utilized to diagnose SUD and/or ADHD. However, since data were collected at addiction treatment centers, we are confident that SUD diagnoses are in line with *DSM-5* criteria. Additionally, the baseline mean ASRS score (47.3) was high, with 99% of the study participants scoring above the cutoff of 24. This adds to the likelihood that the study sample had a genuine ADHD diagnosis. Third, neither the clinicians'

nor the participants' attitudes towards pharmacotherapy were investigated. It is unknown to what extent participants were offered treatment but declined. Since approximately 50% of those who did not receive pharmacotherapy for ADHD received pharmacotherapy for either SUD or another psychiatric comorbidity, these participants may not, however, have a general aversion to pharmacotherapy. Furthermore, information on other site-specific factors, such as available resources (eg, the number of psychologists/psychiatrists in relation to the number of patients treated), was not collected. However, the observed treatment variation between sites is important, and the uncertainty in estimates caused by differences in local routines has partly been accounted for by statistical modeling. Overall, this calls for studies with a specific focus on the clinic-specific reasons for the observed treatment variation.

Conclusions

Many treatment-seeking SUD patients with comorbid adult ADHD do not receive ADHD treatment. Moreover, there are significant differences in treatment strategies between clinics. While some factors, such as ADHD symptom severity and current substance use, were associated with ADHD treatment provision, treatment site is the main predictor of ADHD treatment receipt. These findings suggest unwarranted practice variation and underutilization of evidence-based effective and safe treatments for adult ADHD in SUD patients. Future research should examine clinic-specific reasons, specifically, for not providing ADHD treatment in SUD populations. This can, for instance, be investigated using qualitative research with in-depth interviews and/or focus groups with caregivers and patients. Overall, further research is needed regarding facilitators and barriers to the implementation and dissemination of existing treatment guidelines for SUD + ADHD.[23,24]

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