ADHD & Addiction

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CHAPTER 5

VARIABILITY IN THE PREVALENCE OF ADULT ADHD IN TREATMENT SEEKING SUBSTANCE USE DISORDER PATIENTS: RESULTS FROM AN INTERNATIONAL MULTI-CENTER STUDY EXPLORING DSM-IV AND DSM-5 CRITERIA

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ABSTRACT

Background: Available studies vary in their estimated prevalence of attention deficit/ hyperactivity disorder (ADHD) in substance use disorder (SUD) patients, ranging from 2% to 83%. A better understanding of the possible reasons for this variability and the effect of the change from DSM-IV to DSM-5 is needed.

Methods: A two stage international multi-center, cross-sectional study in 10 countries, among patients from inpatient and outpatient addiction treatment centers for alcohol and/or drug use disorder patients. A total of 3558 treatment seeking SUD patients were screened for adult ADHD. A subsample of 1276 subjects, both screen positive and screen negative patients, participated in a structured diagnostic interview.

Results: Prevalence of DSM-IV and DSM-5 adult ADHD varied for DSM-IV from 5.4% (CI 95%: 2.4-8.3) for Hungary to 31.3% (CI 95%: 25.2-37.5) for Norway and for DSM-5 from 7.6% (CI 95%: 4.1-11.1) for Hungary to 32.6% (CI 95%: 26.4-38.8) for Norway. Using the same assessment procedures in all countries and centers resulted in substantial reduction of the variability in the prevalence of adult ADHD reported in previous studies among SUD patients (2-83% à 5.4-31.3%). The remaining variability was partly explained by primary substance of abuse and by country (Nordic versus non-Nordic countries). Prevalence estimates for DSM-5 were slightly higher than for DSM-IV.

Conclusions: Given the generally high prevalence of adult ADHD, all treatment seeking SUD patients should be screened and, after a confirmed diagnosis, treated for ADHD since the literature indicates poor prognoses of SUD in treatment seeking SUD patients with ADHD.

INTRODUCTION

Attention Deficit/Hyperactivity Disorder (ADHD) is one of the most common mental health disorders affecting children and adolescents.[1] The prevalence of childhood ADHD in general population surveys varies from 6-9% ,[2] whereas for adult ADHD a pooled estimated prevalence of 2.5% was reported.[3] A meta-analysis of longitudinal data suggests that in two-thirds of the cases childhood ADHD persists into adulthood.[4]

Studies in adults with substance use disorders (SUD) show a higher prevalence of adult ADHD compared to the general population.[5-11] This is important since research suggests that co-occurring ADHD and SUD are associated with a more severe course of substance use and poorer treatment outcome.[12, 13] Moreover, patients with these co-occurring disorders have higher rates of other psychiatric disorders.[2, 14]

Prevalence rates of ADHD in SUD patients show an enormous variation ranging from 2% in substance abusing Icelandic adolescents[15] to 83% in Japanese methamphetamine and inhalant abusers.[16] In a recent meta-analysis by Van Emmerik-van Oortmerssen et al.[17] reporting on 12 studies in adult treatment seeking SUD patients, the pooled ADHD prevalence rate was 23.3%, ranging from 10.0% to 54.1% in individual studies. Possible explanations for this huge variability include differences in diagnostic criteria, primary drug of abuse, country specific factors (treatment offer, service structure), treatment setting (e.g. inpatient vs. outpatient treatment), clinical biases and demographic factors. However, the relative effect of these factors has not been studied, because the studies so far vary considerably in the definition of adult ADHD and the diagnostic procedures and assessment instruments. Hence, although there is increasing recognition of the importance of adult ADHD in treatment seeking SUD subjects, there is considerable uncertainty about the magnitude of the problem in this population, and the factors that affect variability of the prevalence.

In addition, changes in criteria for adult ADHD in the newest edition of the Diagnostic and Statistical Manual of Mental Disorders, DSM-5 [18] may affect the prevalence of adult ADHD in SUD patients. First, the increase in the age threshold for the *onset* of ADHD symptoms from 'prior to the age of 7 years' to 'prior to the age of 12 years', may increase the prevalence of ADHD. Second, the reduction in the minimum *number of symptoms* needed for a diagnosis of adult ADHD from 6 to 5 out of 9 symptoms for either inattention and/or hyperactivity/impulsivity may increase the prevalence of adult ADHD. These changes have been criticized because they may inflate the prevalence of ADHD with serious consequences for practice, policy and research.[19, 20] Nonetheless there has been no empirical examination of this issue in clinical samples of SUD patients so far.

The IASP study represents the first cross-national study of ADHD among treatment seeking SUD patients. Data was collected from participating addiction treatment centers all using the same diagnostic criteria and conducting the same sampling design and assessment procedures and instruments. In 10 countries across the globe, this study examines the effect of changes in the diagnostic system (DSM-IV vs. DSM-5) and the effects of country,

age, gender, setting (inpatient vs. outpatient) and primary substance of abuse (alcohol vs. drugs) on the variation in the prevalence of childhood and adult ADHD in treatment seeking SUD patients.

METHOD

Design and procedure

Data was collected in the context of the *International ADHD in Substance Use Disorders Prevalence* study (IASP), completed within the framework of the *International Collaboration on ADHD and Substance Abuse* (ICASA). The IASP is an international, multi-centre, cross-sectional study consisting of a screening stage and a full assessment stage. Australia, Belgium, France, Hungary, the Netherlands, Norway, Spain, Sweden, Switzerland and the United States participated in the screening stage. France, Hungary, the Netherlands, Norway, Spain, Sweden, and Switzerland also participated in the full assessment stage. For a detailed description of the methodology (including choice of instruments, translation and training procedures), study population and screening results the reader is referred to Van de Glind et al.[21] The IASP study is a large study with many different aspects, and data on other research topics have been and will be published. For example, results on the psychometric quality of the Adult ADHD Self-Report Scale (ASRS V 1.1)[2] were published in Van de Glind et al.[22] and a paper on the psychiatric comorbidity of SUD patients with and without ADHD is currently under revision.[23]

Participants

A random sample of 3558 patients, 18-65 years, seeking treatment for SUD for a new treatment episode, were asked to participate in the study in each participating center/ward. Patients with insufficient language skills or unwilling to sign informed consent were excluded from the study. Patients who were intoxicated or currently suffering from severe physical or mental problems were asked to join the study when their clinical condition improved. All participants gave signed informed consent after receiving verbal and written information about the study. They did not receive financial compensation, except for Australia, where patients received AUD $20 reimbursement for associated costs. The study was approved by the local Ethical Review Board in each participating country.

Assessments

In the first stage, all participants filled out a questionnaire on demographics and substance use. In addition, the ASRS V 1.1 [24] was administered assessing ADHD symptoms in adulthood.[25] ADHD symptoms in the ASRS are rated from "never" to "very often" and scored from 0 to 4. Items 1-3 are positively endorsed with scores ≥ 2, items 4-6 with scores ≥ 3. The first six items have been found most predictive of ADHD diagnosis, and were used as a screener with a cut off of four positively endorsed items for a positive screening result.

Three countries (Belgium, Australia, United States of America) with 963 subjects participated

in the screening stage only. All patients from the other 7 countries, regardless of their ASRS result, were referred to the second stage, resulting in 1276 subjects from seven countries. In this stage, a psychiatric interview was administered to assess the presence of SUD, ADHD and other commonly occurring psychiatric disorders in SUD patients.

For the diagnosis of ADHD, we applied the Conners' Adult ADHD Diagnostic Interview for DSM-IV (CAADID),[26] a valid semi-structured interview. CAADID-Part I was filled out by the patient before the interview, collecting information on demographics, developmental course, ADHD risk factors, and psychopathology. CAADID-Part II was administered by trained clinicians and is designed to evaluate the presence of DSM-IV ADHD criteria in childhood and in adulthood, as follows: A) presence of symptoms (six out of nine symptoms of inattention and/or hyperactivity/impulsivity), B) age of onset before the age of seven, C) pervasiveness of the symptoms, D) impairment caused by the symptoms, and E) the symptoms are not better explained by another disorder.

To evaluate Criterion E, further information was collected using two additional semi-structured interviews: the Mini International Neuropsychiatric Interview (M.I.N.I.) Plus version 5.0.0 [27] to assess prior and current episodes of mood disorders, bipolar disorder and antisocial personality disorder (APD); and the borderline module of the Structured Clinical Interview for DSM-IV personality disorders (SCID II)[28] to assess borderline personality disorder (BPD).

The DSM-IV also includes a code ADHD–Not Otherwise Specified (ADHD-NOS) for individuals not meeting the age criteria (symptoms present before the age of 12 instead of before the age of 7) and/or symptom criteria for ADHD but showing ADHD symptoms (≥4 instead of ≥6 out of 9) and who do fulfill criteria of pervasiveness and impairment. In addition, the American Psychiatric Association (APA) presented the main changes in criteria for ADHD in childhood and adulthood for DSM-5.[18]

To assess ADHD diagnosis according to the ADHD-NOS criteria and DSM-5 criteria, we adapted the diagnostic algorithm of the CAADID using a different cut off for the *age of onset criterion* of <12 and different cut offs for the *number of symptom* criterion of 4 (DSM-IV ADHD-NOS) and 5 (DSM-5) respectively.

There is debate on whether or not a retrospectively obtained diagnosis of childhood ADHD should be mandatory for the diagnosis of adult ADHD.[29] For this paper we used the CAADID algorithm for the diagnosis of adult ADHD, including a retrospectively obtained diagnosis of childhood ADHD meeting all of the 5 criteria. This procedure results in conservative prevalence rates of adult ADHD as it is stricter than the DSM criteria that does not expressly demand meeting full childhood ADHD criteria.

SUD was assessed via self-report measures related to the current primary substance of abuse, and it included only current use of either alcohol or illicit drugs, assuming that all of those coming for treatment to an addiction treatment centre have a SUD.

For more detailed information on validation of the ASRS and CAADID, the reader is referred to van de Glind et al.[21, 22]

Statistical analyses

Although all of the participants were referred to the second stage, the proportion of ASRS positives (40.0%) participating in the second stage slightly differed from the proportion of ASRS positives (36.3%) in those who dropped out after stage one (in those countries participating in stage 2).[21, 22] Because this effect was different for the different countries, we constructed weights based on the percentage of ASRS positives, CAADID cases, and country. To prevent biased standard errors, these weights were constructed in such a way that the overall number of participants did not change. All tests, estimates and confidence intervals are based on weighted data. SPSS 20 was used for analyzing the data.

RESULTS

Preliminary analyses

Of the 2595 patients screened in the seven countries participating in stage two, 1276 patients completed the CAADID. There were no significant differences between the patients who completed the CAADID and the drop-outs, with two exceptions: the mean age in Norway and Spain was significantly higher for participants than for drop outs, and the above mentioned difference in ASRS score. The latter was taken into account as described in the methods section. Of 1276 included subjects with completed CAADID interviews, 511 had a positive score and the remaining 765 had a negative score on the ASRS.

Demographics

Table 1 describes the demographic and substance use characteristics of the 1276 participants. Mean age varied between 37 years in France to 43 years in Hungary, approximately one in four were women, fewer than one third were employed, almost one in ten were homeless and only one in four were currently married or had a partner. The primary substance of abuse varied considerably between the countries. Alcohol was the most frequent primary substance of abuse in the total sample (54.6%), followed by stimulants (15.1%), cannabis (10.8%), opiates (10.8%) and other drugs (8.6%). With the exception of housing status, there was a significant country effect for all demographic and clinical characteristics ($p<.001$; adjusted for multiple testing). The number of ASRS positives varied between countries ranging from 20.8% in Hungary to 65.9% in Norway.

Ranges of ADHD prevalence rates

Table 2 presents the ranges of weighted prevalence rates of childhood and adult ADHD according to DSM-IV and DSM-5 and for adult ADHD-NOS according to DSM-IV. The prevalence of adult ADHD-DSM-IV differed markedly across countries with Hungary having the lowest and Norway having the highest rate: 5.4% (CI 95%: 2.4- 8.3) and 31.3% (CI 95%: 25.2-37.5), respectively. Based on DSM-5 criteria the prevalence for adult ADHD were slightly higher, ranging from 7.6% (CI 95%: 4.1- 11.1) in Hungary to 32.6% (CI 95%: 26.4-38.8) in Norway. However the DSM-5 rates were within the range of rates observed for adult ADHD-

Table 1: Main characteristics of the study population (N=1,276).

	France (n=157)	Hungary (n=226)	Netherlands (n=129)	Norway (n=220)	Spain (n=222)	Sweden (n=168)	Switzerland (n=154)	Total (N=1276)		p
Age M(SD)	36·8(10·6)	43·1(12·1)	40·4(10·3)	38·1(10·7)	37·0 (9·8)	42·6 (11·6)	42·5 (10·8)	40·0 (11·2)	F(6,1265)= 11.55	<.001
ASRS screen positive (%)	40.1	20.8	53.5	65.9	35.6	37.5	28.6	40.0	Wald(6) =89.01	<.001
Female (%)	44 (28·0)	55 (24·3)	23 (17·8)	69 (31·3)	46 (20·7)	52 (31·0)	51 (33·6)	340 (26·7)	Wald(6) = 16.64	.010
Employed (%)	51 (32·5)	53 (24·0)	68 (53·1)	55 (26·4)	81 (36·7)	56 (35·9)	20 (13·4)	384 (31·0)	Wald(6) = 54.80	<.001
Homeless/shelter (%)	9 (5·7)	27 (13·2)	10 (7·8)	14 (6·9)	19 (8·6)	18 (5·9)	9 (11·0)	106 (8·6)	Wald(6) = 11.56	.073
Married/partner (%)	35 (22·3)	71 (31·7)	30 (23·3)	39 (18·4)	58 (26·4)	47(28·7)	47 (30·9)	327 (25·9)	Wald(6) = 14.57	.024
Main substance (missing):	0	0	0	6	1	3	2	12		
- Alcohol (%)	79 (50·3)	169 (74·8)	79 (61·2)	68 (31·8)	57 (25·8)	92 (55·8)	146 (96·1)	690 (54·6)	Wald(6)=189.31	<.001
- Stimulants (%)	10 (6·4)	13 (5·8)	12 (9·3)	57 (26·6)	81 (36·7)	16 (9·7)	2 (1·3)	191 (15·1)	Wald(6)=117.16	<.001
- Opiates (%)	15 (9·6)	8 (3·5)	1 (0·8)	37 (17·3)	39 (17·6)	35 (21·2)	2 (1·3)	137 (10·8)	Wald(6) =51.79	<.001
- Cannabis (%)	32 (20·4)	4 (1·8)	31 (24·0)	30 (14·0)	30 (13·6)	10 (6·1)	0 (0·0)	137 (10·8)	Wald(6) =39.25	<.001
- Other drugs (%)	21 (13·4)	32 (14·2)	6 (4·7)	22 (10.3)	14 (6·3)	12(7·3)	2 (1·3)	109 (8·6)	Wald(6) =24.77	<.001

NOS (DSM-IV): 8.2% (CI 95%: 3.9-12.5) in Switzerland to 34.5% (CI 95%: 28.2-40.7) in Norway.

The percentage of patients with DSM-IV childhood ADHD also meeting criteria for DSM-IV adult ADHD (ADHD persistence into adulthood) varied considerably between countries, ranging from 38% in Hungary to 90% in Spain.

Stratified analyses: setting and primary substance of abuse

We were unable to statistically control for country, because country was confounded with setting (inpatient vs. outpatient) and/or by primary substance of abuse (alcohol vs. drugs) with only one country (Norway) including both inpatients and outpatients and one country (Switzerland) including almost only patients with alcohol use disorders (see table S1 in supplementary material). Therefore, we performed analyses stratified by setting and primary substance of abuse (see Table 3). In these results the exact binomial confidence intervals were calculated using a method proposed by Morisette and Khorram.[30]

Using DSM-IV criteria for adult ADHD based on the CAADID algorithm (including the mandatory presence of full childhood ADHD diagnosis), the prevalence is lower among treatment seeking SUD patients whose primary substance of abuse was alcohol, compared to those whose primary substance of abuse was illicit drugs. Similarly, the prevalence of adult ADHD was lower among outpatients than among the inpatients.

However, even within these strata, there was a large country effect, with prevalence rates ranging from 5% to 22% in inpatients with alcohol use disorders (AUD) and 4% to14% in AUD outpatients. Among inpatients with dug use disorders (DUD), prevalence rates ranged from 5% to 52% and, among DUD outpatient, from 10% to 33%. These large country differences were mainly due to the relatively high prevalence rates for all subgroups in the Nordic countries (Norway and Sweden). After adjustment for age, gender, occupational status, housing and marital status there was still a large and statistically significant effect of Nordic versus non-Nordic countries on the prevalence estimates. After post-hoc stratification on Nordic versus non-Nordic countries the difference in prevalence of ADHD within Nordic and within non-Nordic countries was no longer significant (see Tables 3 and 4).

DISCUSSION

The present study is, to our knowledge, the first multinational study on the prevalence of ADHD in adult treatment seeking SUD patients. Based on DSM-IV criteria, the reported rates of adult ADHD were much higher in our sample of treatment seeking SUD patients than in the general population (6-9% childhood ADHD; 2.5% adult ADHD).[31, 3] The prevalence of DSM-IV adult ADHD varied between countries from 5.4% (CI 95%: 2.4- 8.3) in Hungary to 31.3% (CI 95%: 25.2-37.5) in Norway. Although this is a broad range of prevalence rates, the range is much smaller than the ranges reported on ADHD in SUD patients in the literature so far (2-85%)[15, 16] and the range reported in a recent meta-analysis in treatment seeking SUD patients (10-54%)[17]; a finding that is probably related to the fact that in the current study the same classification and the same diagnostic procedures and instruments were

Table 2: Prevalence of childhood (retrospective) and adult (current) ADHD and ADHD-NOS according to DSM-IV criteria and to DSM-5 criteria.

	France (n=157)	Hungary (n=226)	Netherlands (n=129)	Norway (n=220)	Spain (n=222)	Sweden (n=168)	Switzerland (n=154)	Range (N=1276)
Childhood ADHD DSM-IV % (CI 95 %)	21·3 (14·9-27·7)	12· 9 (8·6-17·3)	15·0 (8·9-21·2)	41·0 (34·5-47·5)	10·6 (6·5-14·6)	27·7 (20·9-34·5)	15·1 (9·4-20·8)	10·6-41·0
Childhood ADHD DSM-5 age of onset <12 % (CI 95 %)	23·2 (16·6-29·8)	12·9 (8·6-17·3)	15·0 (8·9-21·2)	42·3 (35·7-48·8)	13·0 (8·5-17·4)	29·1 (22·2-36·0)	15·6 (9·8-21·3)	12·9-42·3
Adult ADHD DSM-IV % (CI 95 %)[a]	11·2 (6·3-16·2)	5·4 (2·4- 8·3)	10·1 (4·9-15·3)	31·3 (25·2-37·5)	9·2 (5·4-13·0)	19·7 (13·7- 25·7)	6·1 (2·3-9·9)	5.4 – 31.3
Adult ADHD DSM-5[b] age of onset <12 and # symptoms 5/9 % (CI 95 %)	16·2 (10·5-22·0)	7·6 (4·1- 11·1)	11·8 (6·2-17·3)	32·6 (26·4-38·8)	10·6 (6·6-14·7)	22·4 (16·1-28·7)	7·7 (3·5-12·0)	7.6 – 32.6
Adult ADHD DSM-IV ADHD-NOS)[b] Combined: age of onset <12 and # symptoms 4/9 % (CI 95 %)	16·9 (11·0-22·7)	8·9 (5·2-12·7)	12·3 (6·7-18·0)	34·5 (28·2-40·7)	10·6 (6·6-14·7)	22·4 (16·1-28·7)	8·2 (3·9-12·5)	8.2 – 34.5

[a] Prerequisite: Diagnosed Childhood ADHD based on CAADID retrospective diagnosis; DSM-IV criteria for Childhood ADHD;
[b] Prerequisite: Diagnosed Childhood ADHD based on CAADID retrospective diagnosis; DSM-5: adjusted age of onset <12 criterion for childhood

Table 3: Prevalence of ADHD (DSM-IV).

	Inpatients Alcohol (n=339) 1, weighted data					Inpatients Drugs (n=1091), weighted data				
	Childhood DSM-IV		Adult ADHD DSM-IV			Childhood DSM-IV		Adult ADHD DSM-IV		
	prevalence	95% ci[2]	prevalence	95% ci[2]		prevalence	95% ci[2]	prevalence	95% ci[2]	
Hungary (169[1])	12 %	7-18	5 %	02-10	Hungary (57[1])	16 %	8-28	5 %	1-15	
Norway (24[1])	43 %	23-64	22 %	08-44	Norway (52[1])	57 %	42-71	52 %	37-66	
Switzerland (146[1])	15 %	09-21	5 %	02-10						
- All countries[6]	15 %	12-20	6 %	4-10	- All countries[6]	35 %	26-44	27 %	19-36	
- Without Nordic[5]	13 %	10-17	5 %	3-8						
- Only Nordic	43 %	23-64	22 %	8-44						
Observed range					Observed range					
- All countries	12-43 %		5-22 %		- All countries	16-57 %		5-52 %		
- Without Nordic	12-15 %		5·1-5·4 %							
- Only Nordic	n.a.[4]		n.a.[4]							
Effect country[3]					Effect country[3]					
- all countries Wald(2); (p)	16·67 (<.001)		8·00 (.018)		- All countries Wald(1); (p)	10.58 (.001)		14.13 (<.001)		
- Without Nordic Wald(1); (p)	.024 (.878)		.585 (.444)							
- Only Nordic	n.a.[4]		n.a.[4]							

Inpatients alcohol (n=339) and inpatients drugs (n=109), weighted data.
1) Presented is the non-weighted n.
2) Exact binomial confidence interval using the approach by Morisette and Khorram.[30]
3) Effect of country on prevalence adjusted for age, sex, occupational status, housing and marital status.
4) Not applicable.
5) Nordic countries: Norway and Sweden.
6) All countries: meaning all countries with subjects in this setting.

Table 4: Prevalence of ADHD (DSM-IV).

	Outpatients Alcohol (n=351[1]), weighted data					Outpatients Drugs (n=454[1]), weighted data				
	Childhood DSM-IV		Adult ADHD DSM-IV			Childhood DSM-IV		Adult ADHD DSM-IV		
	prevalence	95% ci[2]	prevalence	95% ci[2]		prevalence	95% ci[2]	prevalence	95% ci[2]	
France (79[1])	12 %	6-22	6 %	2-14	France (78[1])	30 %	20-42	16 %	9-27	
Netherlands (79[1])	14 %	7-23	10 %	5-19	Netherlands (50[1])	17 %	7-32	10 %	3-22	
Norway (44[1])	25 %	14-40	14 %	6-27	Norway (89[1])	41 %	30-52	33 %	23-43	
Spain (57[1])	4 %	0·5-13	4 %	1-13	Spain (164[1])	12 %	8-19	11 %	7-17	
Sweden (92[1])	17 %	10-27	13 %	6-21	Sweden (73[1])	37 %	26-49	26 %	16-37	
- all countries[6]	14 %	11-18	9 %	7-13	- all countries[6]	26 %	21-30	18 %	15-22	
- without Nordic[5]	11 %	7-16	7 %	4-12	- Without Nordic[5]	14 %	14-23	12 %	9-17	
- only Nordic	20 %	14-28	13 %	8-20	- only Nordic	39 %	32-47	29 %	22-37	
Observed range					Observed range					
- all countries[5]	4-25 %		4-14 %		- all countries[6]	12-41%		10-33%		
- Without Nordic[4]	4-12 %		4-10 %		- Without Nordic[5]	12-30%		10-16%		
- only Nordic	17.25 %		13-14 %		- only Nordic	37-41%		26-33%		
Effect country[3]					Effect country[3]					
- all countries Wald(4); (p)	10·23 (.037)		7·06 (.133)		- all countries Wald(4); (p)	30.54 (<.001)		18.47 (.001)		
- without Nordic Wald(2); (p)	4·62 (.099)		2·79 (.248)		- without Nordic Wald(2); (p)	9.33 (.009)		1.60 (.449)		
- only Nordic Wald(1); (p)	.003 (.957)		.60 (.440)		- only Nordic Wald(1); (p)	.15 (.699)		.016 (.889)		

Outpatients alcohol (n=351) and outpatients drugs (n=454), weighted data.
[1]) Presented is the non-weighted n.
[2]) Exact binomial confidence interval using the approach by Morisette and Khorram.[30]
[3]) Effect of country on prevalence adjusted for age, sex, occupational status, housing and marital status.
[4]) Not applicable.
[5]) Nordic countries: Norway and Sweden.
[6]) All countries: meaning all countries with subjects in this setting.

used. Furthermore, post-hoc analyses showed that the remaining variation in prevalence of adult ADHD between the various countries was mainly caused by the high prevalence in the Nordic countries (Norway and Sweden). Moreover, these differences between the Nordic and non-Nordic countries were independent of gender, age, occupational status, housing and marital status. One explanation may be latitude which may affect circadian rhythm[32] and circadian rhythm may be related to the incidence and prevalence of ADHD.[33] An important indication for such an influence of region related to solar intensity on the prevalence of ADHD has recently been reported,[34] indicating high solar intensity as a protective factor, possibly via improving circadian clock disturbances. However, the prevalence rates of childhood ADHD in Scandinavian countries lye well within the range as found in other countries as reported by Faraone et al.[35] In Sweden two independent studies found childhood ADHD prevalence of 4.0% [36] and 3.7% [37] using DSM-III-R resp. DSM-IV. A Norwegian study recently reported childhood ADHD prevalence of 5.2%.[38] Thus, other explanations are likely to of more importance. These other explanations may be found in country specific reasons, leading to more or less subjects with ADHD within addiction treatment centers, e.g. differences in the public awareness of ADHD frequently coexisting with SUD resulting in differences in recognition and referral, and differences in treatment availability and treatment approach for patients with co-occurring ADHD and SUD. Unfortunately, no data is currently available to support these explanations. Moreover, selection of treatment centers within the various countries was not random and thus the observed differences in prevalence may also be a result of selection bias at the center level. However, all participating centers indicated that their center was representative for the national situation. Moreover, national non-representativeness does not directly explain the Nordic vs. non-Nordic gradient and it is thus rejected as a plausible explanation.

The observed range of adult ADHD prevalence rates among inpatients (AUD: 5-22%; DUD: 5-52%) is difficult to interpret as these reflect participating sites from 3 countries with inpatient AUD sites and 2 countries with inpatient DUD sites only (see Table 3). The AUD outpatient adult ADHD prevalence rates ranged from 4-14% and the DUD outpatient adult ADHD prevalence rates ranged from 10-33%. These results show that ADHD is more prevalent in patients with illicit drug use than in patients with alcohol use as their primary addiction. This is consistent with the finding that ADHD and DUDs are familially/genetically related, whereas ADHD and AUDs are not.[39] However, this finding is inconsistent with the meta-regression analysis of Van Emmerik-van Oortmerssen et al.[17] reporting a lower prevalence of adult ADHD in treatment seeking cocaine dependent patients compared to treatment seeking alcohol and opioid dependent patients.

Although it is possible to calculate overall prevalence rates for ADHD for the total sample, we resisted this temptation. In presenting overall rates we would overrule the important finding of the large variability in prevalence rates due to Nordic-non-Nordic country effects, primary substance of abuse and probably other unknown factors influencing referral and access of subjects with adult ADHD and SUD to addiction treatment centers.

The use of DSM-5 criteria resulted in a modest increase in prevalence rates: 7.6% (CI

95%: 4.1- 11.1) in Hungary to 32.6% (CI 95%: 26.4-38.8) in Norway. The observed DSM-5 prevalence rates were all within the rates based on ADHD-NOS criteria in DSM-IV, indicating that DSM-5 may reduce the use of the NOS category without increasing the prevalence of clinical relevant ADHD syndromes in treatment seeking SUD patients. Therefore the fear that DSM-5 would inflate the prevalence of ADHD[19] seems not justified and the change from DSM-IV to DSM-5 will have, if any, minimal implications for clinical practice in addiction treatment centers.

LIMITATIONS

Although our study included a large sample based on a similar recruitment strategy and assessed with identical instruments for the diagnosis of adult ADHD, there are several limitations to consider.

Because of the lack of information about the initial number of referred patients and the dropout rates in some countries, it remains unclear to what extent the current sample is representative of all service attendees, let alone all people affected by a SUD in the various countries. Although the participants dropping out from the full assessment stage of the study were very similar to those who participated,[21, 22] the possibility that there were ADHD related differences that could have biased the estimates of ADHD cannot be fully discounted. In addition, requiring sustained abstinence as a criterion for inclusion might have resulted in more reliable information, but would have potentially excluded some of the more severely dependent participants, thereby leading to a possible underestimation of the prevalence of ADHD.[40]

The diagnostic accuracy of adult ADHD can be enhanced by obtaining additional information from parents or other individuals who knew the patient well during childhood. In this study, patients were approximately 40 years old and often came from dissolved families; hence it would be difficult if not impossible to track down parents or other key informants. When requiring attainment of collateral information to include SUD patients for this study, many would have been excluded. This decision however may have lowered the prevalence rates based on the CAADID.[41]

Furthermore, we obtained information on the primary substance of abuse via self-report measures during the screening procedure (stage one), and it included only current use of either alcohol or illicit drugs. This is a simplification of reality, as many patients use multiple substances and no clear distinction between primary and non-primary substance of abuse can be made. It is unclear how this may have had a specific impact on the prevalence rates.

In addition, we have no measures of severity of SUD in our sample. Since severity of substance use may be related to treatment type with inpatients using more substances, this in turn may have an effect on the prevalence rates.

Finally, we had limited data on the reliability of the interviews in the various study locations.[1] This may have influenced the prevalence rates in some of the countries. However, all sites were trained in the use of the MINI and the CAADID by the same clinical researcher (GvdG)

and all interviewers at all sites were extensively trained using the same training manual for all assessment instruments.

CONCLUSIONS

Using the same definitions and diagnostic instruments in all countries and centers resulted in substantial reduction of the variability in the prevalence of adult ADHD reported in previous studies among SUD patients (2-83%) and treatment seeking SUD patients (10.0-54.1%) to 5.4-31.3%. The remaining variability was partly explained by primary substance of abuse and country. Prevalence estimates for DSM-5 were slightly higher than for DSM-IV and all within the rates based on ADHD-NOS criteria in DSM-IV. Therefore, the change from DSM-IV to DSM-5 will hardly have any effect on the clinical practice in addiction treatment centers. However, given the generally high prevalence of adult ADHD in treatment seeking SUD patients and given the fact that efficacious pharmacologic42 and cognitive behavioral43 interventions exist for the treatment of adult ADHD and its potential impact upon the outcomes of SUD treatment, all treatment seeking SUD patients should be screened and, after confirmed diagnosis, treated for ADHD since the current literature indicates poor prognoses of SUD in treatment seeking SUD patients with ADHD.[40]

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SUPPLEMENTARY MATERIAL

Supplement 1 (S1): Confounding variables: country with setting.

	alcohol		Drugs		
	inpatient	outpatient	inpatient	outpatient	Total
France	--	79	--	78	157
Hungary	169	--	57	--	226
The Netherlands	--	79	--	50	129
Norway	24	44	52	89	209
Spain	--	57	--	164	221
Sweden	--	92	--	73	165
Switzerland	146	--	6	--	152
Total	339	351	115	454	1259[1]

[1]) although we have 1,276 patients with valid CAADID and ASRS data, 17 patients had missing values on primary substance of abuse and/or setting (Norway, 11; Spain, 1; Sweden, 3; Switzerland, 2)

Looking at the table it is obvious that, with the exception of Norway, the variables country and setting overlap (as the grey shaded cells show, for example: France has only outpatient settings, Hungary has only inpatient settings etc.)