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The International ADHD in Substance Use Disorders Prevalence (IASP) study: background, methods and study population

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Abstract

Attention deficit/hyperactivity disorder (ADHD) is an increasingly recognized comorbid condition in subjects with substance use disorders (SUDs).

This paper describes the methods and study population of the International ADHD in Substance Use Disorders Prevalence (IASP) study. Objectives of the IASP are to determine the prevalence of ADHD in adult treatment seeking patients with SUD in different countries and SUD populations, determine the reliability and validity of the Adult ADHD Self-report Scale V 1.1 (ASRS) as ADHD screening instrument in SUD populations, investigate the comorbidity profile of SUD patients with and without ADHD, compare risk factors and protective factors in SUD patients with and without a comorbid diagnosis of ADHD, and increase our knowledge about the relationship between ADHD and the onset and course of SUD.

In this cross-sectional, multi-centre two stage study, subjects were screened for ADHD with the ASRS, diagnosed with the Conner's Adult ADHD Diagnostic Interview for DSM-IV (CAADID), and evaluated for SUD, major depression, bipolar disorder, anti social personality disorder and borderline personality disorder.

Three thousand five hundred and fifty-eight subjects from 10 countries were included. Of these 40.9% screened positive for ADHD.

This is the largest international study on this population evaluating ADHD and comorbid disorders.

Introduction

Attention deficit/hyperactivity disorder (ADHD) is a complex, multifactorially determined neurodevelopmental disorder, based on a genetic predisposition, which in interaction with negative environmental factors leads to neurobiological disregulations (Kiesling & Rohde, 2012) and serious behavioural problems. In children and adolescents the disorder is documented worldwide (Faraone *et al.*, 2003) with an estimated prevalence of 5.3% (Polancyk *et al.*, 2007). Increasing evidence documents ADHD persistence into adulthood: Fayyad *et al.* (2007) reported a worldwide prevalence of adult ADHD in the general population of 3.4% with lower prevalence rates in lower-income countries (1.9%) compared with higher-income countries (4.2%). In a recent meta-analysis, Simon *et al.* (2009) calculated a slightly lower worldwide prevalence of adult ADHD of 2.5%. A lower prevalence of ADHD in adults compared with children is consistent with the age dependent decline of the disorder, which has been confirmed in a meta-analysis (Faraone *et al.*, 2006).

ADHD frequently co-occurs in patients with substance use disorders (SUDs) (Lee *et al.*, 2010; Charach *et al.*, 2011; Wilens *et al.*, 2011). In a recent meta-analysis, the prevalence of ADHD in substance abusing adults ($N = 2635$) was 21.0% [95% confidence interval (CI) 15.9–27.2] (Van Emmerik-van Oortmerssen *et al.*, 2011). The majority of studies in adults in this meta-analysis were from the United States (eight studies, $N = 1574$) (Clure *et al.*, 1999; King *et al.*, 1999; Levin *et al.*, 1998; Rounsaville *et al.*, 1991; Schubiner *et al.*, 2000; Tang *et al.*, 2007; Wood *et al.*, 1983; Ziedonis *et al.*, 1994).

The differences in prevalence rates between the studies could only partly be explained by differences in ADHD assessment instruments [with ADHD assessment with the Diagnostic Interview for Children and Adolescents (DICA) and the Schedule for Affective Disorders and Schizophrenia – lifetime version (SADS-L) resulting in higher rates of comorbid ADHD than other ADHD interviews] and differences in the primary substance of abuse (with lower rates of ADHD in patients with cocaine as their primary substance of abuse). These results raise several unresolved questions: are there differences in the prevalence of ADHD in SUD populations between different countries; are there differences in the prevalence of ADHD in SUD populations with different substances and severity of abuse; are there still differences in the prevalence of ADHD in SUD populations when the same methods and the same outcome measures are used; finally can the lower prevalence rate of ADHD in cocaine dependent patients be corroborated?

Another important issue is the fact that the American Psychiatric Association (APA) is currently in the process of evaluating and possibly revising the criteria for ADHD in both childhood and adulthood (DSM-5 website). The proposed revisions were still under review at the time of the submission of this paper. The first major change, and most likely to be implemented in DSM-5, is the *Age of onset* of the ADHD symptoms, which is likely to be changed from "prior to the age of seven years" to "prior to the age of 12 years", for both ADHD in children and adults. The second proposed change, which at the time of conducting this paper was (according to the DSM-5 website) "still under consideration", is that the diagnostic threshold will be lowered as the number of symptoms needed for a diagnosis of adult ADHD will drop from six symptoms to four symptoms (out of nine symptoms for either inattention and/or hyperactivity/impulsivity). Note that for diagnosing adult ADHD both in DSM-IV and DSM-5 it is required that the adult must also meet criteria for onset of ADHD in childhood (http://www.dsm5.org). Questions have been raised about the consequences of the proposed criteria for mental disorders in general. It is hypothesized that the new criteria would inflate the prevalence of the disorder, with serious consequences for practice, policy and research (Batstra & Frances, 2012; Frances & Widiger, 2012). This raises the question to what extent the proposed DSM-5 criteria for ADHD, if implemented, will inflate the prevalence rate of ADHD in subjects with SUD.

Furthermore, for many professionals working in addiction treatment centres, screening, diagnosing and treating ADHD in subjects with SUD is not part of their routine practice (McAweeney *et al.*, 2010; Fatseas *et al.*, 2012). These professionals often lack the knowledge, skills and instruments required to detect ADHD in their patients. The Adult ADHD Self-report Scale V 1.1 (ASRS) includes questions for each of the 18 DSM-IV symptoms. The six-item short version had a sensitivity of 69% and specificity of 99% in a population survey (Kessler *et al.*, 2005). In a second study in a population of US managed care subscribers, sensitivity and specificity was less good (sensitivity 39% and specificity 65%), but these results could be drastically improved (sensitivity 88% and specificity 94%) by using an alternative scoring approach on the six-item version (Kessler *et al.*, 2007). The few studies available on the validity of the ASRS in SUD populations show mixed results with good sensitivity/specificity (Daigre Blanco *et al.*, 2009; Pérez Pedrero & García, 2007; Adler *et al.*, 2009) and low sensitivity/specificity (Chiasson *et al.*, 2011). It is therefore prudent to evaluate the sensitivity and specificity of the ASRS in a large sample of SUD patients, in several countries, using the same diagnostic procedure for the external criterion. Moreover it is uncertain whether the alternative scoring method (Kessler *et al.*, 2007) would increase sensitivity and/or specificity of this instrument in a population of SUD subjects.

Finally, it should be noticed that when SUD occurs with ADHD, it is associated with a greater severity of SUD compared to other SUD patients (Wilens, 2004). This has also been shown in its earlier age at onset (Arias *et al.*, 2008; Johann *et al.*, 2003; Riggs *et al.*, 1999), and more severe clinical features in several domains: suicidal ideation (Arias *et al.*, 2008; Johann *et al.*, 2003), antisocial behavior (Biederman *et al.*, 1995; Johann *et al.*, 2003), risk for depression (Ilomaki *et al.*, 2008), chronicity of substance use (Biederman *et al.*, 1995), need for hospitalization (Arias *et al.*, 2008) and likelihood of a complicated course (Biederman *et al.*, 1998). The effects of ADHD on SUD outcomes have been documented to be independent of other psychiatric comorbidities (Biederman *et al.*, 1995). These findings are, however, based on a small number of studies mainly from the United States and it remains to be seen whether this is true in other countries with different (addiction) treatment services.

Objectives of the IASP study

The frequent co-occurrence of adult ADHD and SUD is important because early detection and treatment of ADHD in patients with both ADHD and SUD may result in a better outcome of both ADHD and SUD symptoms; and because knowledge about the risk factors and protective factors for the development of SUD in ADHD patients may result in the development of better strategies for the prevention of SUD in children and adolescents with ADHD. With these general objectives in mind, the International Collaboration on ADHD and Substance Abuse (ICASA) started its work in 2005 and became a formal foundation by Dutch law in September 2010 (ICASA, 2011). The ICASA Foundation is an international research group with participants from Europe, Australia, the United States (USA), Africa and South America. The first research priorities of ICASA were to determine the prevalence of ADHD in adult treatment seeking patients with SUD in different countries, to determine the reliability and validity of an ADHD screening instrument in SUD populations, to compare risk factors and protective factors in SUD patients with and without a comorbid diagnosis of ADHD, and to increase our knowledge about the relationship between ADHD and the onset and course of SUD by

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retrospectively comparing SUD patients with and without ADHD. In order to address these issues, the International ADHD in Substance Use Disorders Prevalence (IASP) study was developed.

This paper describes the design of the IASP study, documents the methods that were used for data collection, informs the reader about the measures that were taken to guarantee the quality of the data, and describes recruitment, sample characteristics and the percentage of ADHD screen positive subjects. This paper therefore is the basis for subsequent papers in which the results related to the IASP objectives will be published.

Methods

Study design

A cross-sectional study was designed in such a way that it was relatively easy for countries and addiction treatment organizations to participate, while still adding valuable data to the study. Data collection consisted of two stages: a screening stage and a diagnostic stage (see Figure 1). During stage 1, the screening stage, all subjects with a SUD referred to an addiction treatment service were screened for the possible presence of adult ADHD. In stage 2, the full assessment or diagnostic stage, subjects were assessed with structured interviews to establish the presence of DSM-IV SUDs, DSM-IV and DSM-5 ADHD and other psychiatric disorders.

The screening instrument, the ASRS, was re-administered at stage 2. Comparing the results of these ASRS administrations provides an answer to the question whether the ASRS can be used as a screening instrument for ADHD at the front door of addiction treatment centres or whether the use of the ASRS should be postponed until subjects are in a more stable situation, i.e. not intoxicated, no withdrawal symptoms and/or sustained abstinence. A scheme of the design and instruments used in the study is presented in Figure 1.

Study population: inclusion and exclusion criteria

All adult subjects (age 18–65 years) consecutively referred to the selected addiction treatment centres during the course of the study (July 2008–November 2011; each site sampled subjects for one year) were invited to participate in the study. Norway, Sweden, the Netherlands, Belgium, France, Spain, Switzerland, Hungary, Australia and the USA participated, resulting in a total sample of 3578 cases, from 10 countries and 47 sites. However not all participants completed all instruments. Figure 2 shows the number of patients per group of instruments. These groups of instruments reflect the information that is needed for answering specific research questions. Table 1 summarizes the main characteristics of the participating sites. A wide range of different treatment settings was included: outpatient and inpatient settings dedicated to the treatment of

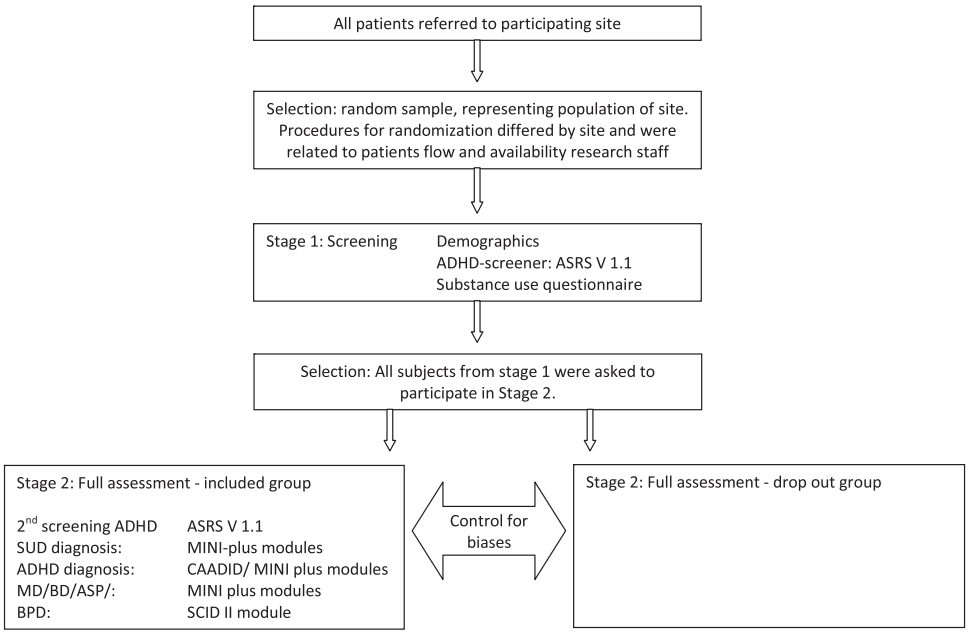

Figure 1. Design of the study.

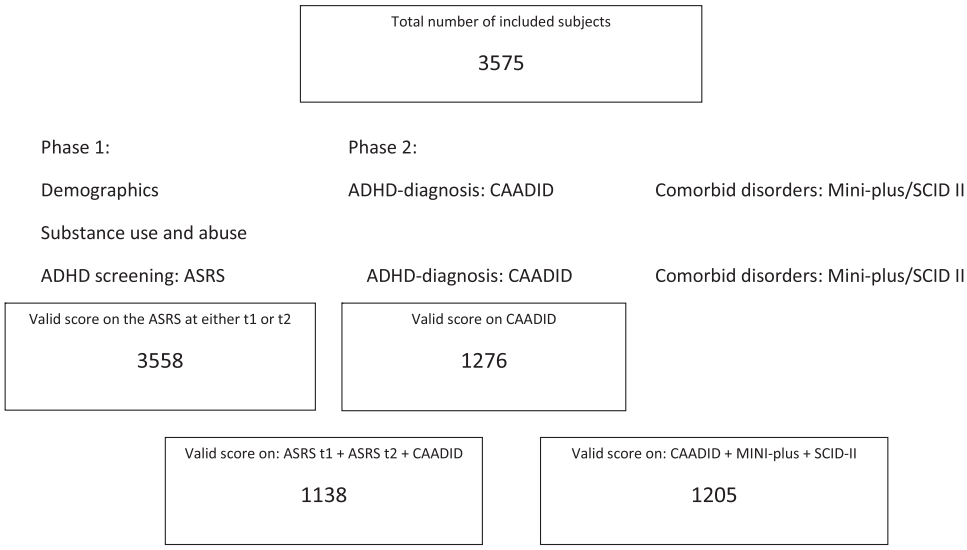

Figure 2. Numbers of subjects in the IASP study.

only patients with alcohol use disorders, only patients with (certain) drug use disorders, and settings dedicated to the treatment of a mixed population of patients with alcohol and/or drug use disorders.

The only exclusion criteria used were related to practical problems interfering with participation such as the incapacity to fill out the screening questionnaire (e.g. due to limited literacy and/or cognitive impairment), the inability to participate due to substance intoxication, or the presence of acute psychiatric crisis (e.g. an acute psychotic or manic episode) and/or severe somatic problems (efforts were made to include these subjects at a later stage in their treatment), and unwillingness to sign informed consent.

Abstinence was not a prerequisite for the screening phase and subjects were to participate in the screening "*as they came in*". However, the full assessment phase was preferably performed in conditions of abstinence at which time the screening for ADHD was to be repeated in order to document the influence of recent drug use and the possible consequences of withdrawal on the reliability and validity of the screening instrument (ASRS). Full and sustained abstinence as a mandatory rule for inclusion in the full assessment phase would probably lead to more reliable results in individual subjects, but at the cost of drop out of subjects who would not be able to obtain full and sustained abstinence.

Instruments

In the screening phase a short questionnaire about sociodemographic variables and substance use (age of onset, years of use, current use) was administered. For the screening of adult ADHD, the ASRS was used. The ASRS (Kessler *et al.*, 2005, 2007) is an 18 item self-report questionnaire. The first six items are decisive for the presence of adult ADHD. If four or more of the six items are scored positive, further diagnostic assessment is indicated. The ASRS V 1.1 was estimated to have a sensitivity of 68.7% and specificity of 99.5% evaluated using population survey data (Kessler *et al.*, 2005). The ASRS has demonstrated high internal consistency (Adler et al., 2009) and good test–retest reliability (Matza *et al.*, 2011). Studies on validation of ASRS, or on any ADHD screening instrument in SUD populations are limited with conflicting results. Daigre Blanco *et al.* (2009) reported a sensitivity of 87.5 % and a specificity of 68.6% in a study on primarily drug dependent patients. Good results also were reported in a Spanish study by Pérez Pedrero and García (2007). A third study in similar studies found a positive predictive value of 57.6, comparable to that observed in the managed care sample described earlier (Adler *et al.*, 2009). However, Chiasson *et al.* (2011) reported that in SUD patients scoring ADHD positive on the ASRS-V 1.1 the ADHD diagnosis could only be confirmed in 26% of the sample by an expert psychiatrist.

The full assessment phase started with a repeated administration of the ASRS in order to learn more about the influence of substance use and withdrawal on the reliability, stability and validity (sensitivity and specificity) of the instrument in the population of treatment seeking SUD patients.

During the full assessment phase, ADHD diagnoses were established with two instruments: the ADHD module of the fifth version of the Mini International Neuropsychiatric Interview (MINI-plus 5.0: Sheehan *et al.*, 1998; Lecrubier *et al.*, 1997) and the Conners' Adult ADHD

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Table 1. Number of sites per country, sort of setting and respondents self reported most problematic substance of abuse/dependence

	France ($n=216$)	Hungary ($n=343$)	Netherlands ($n=403$)	Norway ($n=487$)	Spain ($n=432$)	Sweden ($n=325$)	Switzerland ($n=389$)	USA ($n=130$)	Belgium ($n=371$)	Australia ($n=462$)	Total ($n=3558$)
Number of sites	1	2	1	11	1	10	3	1	3	14	47
Setting	Out pt.	In pt.	Out pt.	Mixed	Out pt.	Out pt.	In pt.	Out pt.	Out pt.	Mixed	Mixed
Main problem (n)	216	343	403	214	428	319	385	129	369	462	3269[1]
Alcohol (%)	46.3	73.8	59.3	31.8	22.4	50.2	96.1	29.2	68.0	39.0	53.7
Drugs (%)	53.7	26.2	40.7	68.3	77.6	49.8	3.9	70.8	31.8	61.0	46.3
Opiods (%)	12.0	5.0	2.0	17.3	19.4	24.5	1.3	17.7	7.9	24.9	12.9
Stimulants (%)	7.9	5.8	14.1	26.6	39.0	10.0	0.5	6.2	11.9	17.5	14.8
Cannabis (%)	22.2	2.3	19.9	14.0	13.6	7.2	0.5	6.9	6.5	8.9	9.9
Other drugs (%)	11.6	13.1	4.7	10.3	5.6	8.2	1.6	40.0	5.7	9.7	8.7

[1]More than half of the Norwegian sample was drawn from another local study using the same methods. However in this study they did not ask for the self reported main problem substance.

Diagnostic Interview for DSM-IV (CAADID) (Epstein & Kollins, 2006).

CAADID is one of the most frequently used semi-structured diagnostic interviews for the assessment of adult ADHD (Arcos-Burgos *et al.*, 2010; Daigre Blanco *et al.*, 2009; Epstein *et al.*, 2001; Epstein & Kollins, 2006; Medori *et al.*, 2008; Ribasés *et al.*, 2009). Part 1 of CAADID consists of a questionnaire investigating a subjects history related to gestational, delivery, temperamental, developmental, environmental, medical history and family history risk factors. Furthermore, school and academic, psychiatric, occupational, social/interpersonal, health and adult psychological/psychiatric history is investigated. In this study, part 1 of CAADID was used as a self report questionnaire. Part II of CAADID is a semi-structured interview, focused on determining the presence or absence of the five DSM-IV-TR criteria: (1) number of symptoms, (2) age of onset, (3) pervasiveness, (4) level of impairment and finally (5) whether or not the symptoms can be better explained by another psychiatric disorder. In a recent case control study among 691 patients referred to a specialized clinic for the treatment of ADHD, Ramos-Quiroga *et al.* (2012a) concluded that the CAADID is a valid and useful tool for the diagnosis of adult ADHD. More importantly, a case control study among patients with SUD also showed promising results for the validity of the CAADID. In a comparison between the CAADID and the Psychiatric Research Interview for Substance and Mental (PRISM) disorders, the sensitivity was 78% and the specificity 88% (Ramos-Quiroga *et al.*, 2012b).

SUD diagnoses were obtained in the full assessment phase using the Alcohol Module and the Non-alcohol Substance Modules of the MINI-plus 5.0 (Sheehan *et al.*, 1998; Lecrubier *et al.*, 1997). In order to also establish the prevalence of mental disorders with ADHD-like symptoms, to determine prevalence rates of these disorders in subjects with and without ADHD, and to examine the effects of the presence of these disorders on the performance of the ASRS, the following DSM-IV disorders were assessed: antisocial personality disorder (ASP), borderline personality disorder (BPD) and bipolar disorder (BD). To better understand the data on BD it was decided to also evaluate the presence of major depression (MD). ASP, BD and MD were evaluated using MINI-plus 5.0 modules. BPD was evaluated using the Structured Clinical Interview for DSM-IV Axis II Disorders (SCID-II) Borderline module (Williams *et al.*, 1992; Massoubre *et al.*, 2009). Psychometric features of MINI-plus and SCID-II from prior research will be documented in subsequent publications reporting on the results of these instruments in the IASP study.

Translation of the instruments

Permission regarding the use of the CAADID was obtained from the license holding company, Multi Health System (MHS). If not yet available in the necessary languages, instruments were translated. The CAADID was used as the gold standard for diagnosing ADHD and therefore regarded as the key instrument for this study. For the CAADID we therefore applied the World Health Organization (WHO) standards for translation of research instruments (WHO, 2012), including forward translation, expert panel, back-translation, pre-testing and cognitive interviewing and the construction of a final version based on the previous steps. In addition, two harmonizing meetings for the CAADID were organized following the WHO translating procedure. The participating countries were divided in two groups. The local project leaders and the first author (VdG G.) were present during these meetings. The specific difficulties of diagnosing ADHD in adults were discussed, and the CAADID items were discussed in English. This procedure ensured that each question and each item of the CAADID was translated in the best possible way.

Training of interviewers

The first author (VdG G.) visited all participating sites and provided a one day training course for interviewers. During the morning session, the ASRS, MINI plus and SCID modules were discussed. In the afternoon session, the CAADID was discussed, based on the CAADID Technical Manual (Epstein *et al.*, 2001). It was required that interviewers had knowledge and experience in diagnosing patients with psychiatric disorders.

Ethics

All of the participating institutes received formal approval of their medical ethical committees for participating in the IASP, and for storage and analyses of the data via the central data base of the IASP at the University of Amsterdam. All of the participating subjects gave informed consent. The informed consent forms are stored according to the procedures for the local medical ethical committees.

Quality of the data

The system used for data collection and storage, Oracle Clinical©, fits within the rules and regulations for Good Clinical Practice (GCP; European Medicines Agency, 2002). It features various automatic checks on data entry errors and an audit trail in which changes in the data are registered. In addition, all sites participating in the full assessment were asked to take a random sample of 40 subjects and control for data entry mistakes. The results from this exercise for the CAADID part II, the ASRS, MINI plus and SCID-II (borderline module) indicate that data entry was performed very accurately. Mistakes occurred in less than 4% of the variables, which is expected and acceptable. For the CAADID part II, however, this level of accuracy is not good enough, because a diagnosis of ADHD requires all five DSM criteria (minimum of six symptoms; age of onset before seven years; pervasiveness, impairment, not better accounted for by another disorder) to be present, resulting in many key variables that might be decisive on an ADHD diagnosis being present or absent. This means that any mistake on these key variables could potentially result in a wrong conclusion on the presence or absence of the ADHD diagnosis. We therefore decided to perform a second data entry of all key variables of the CAADID part II. Apart from Norway, all sites participating in the full assessment performed this second data entry and the results were compared with the original data using SPSS. Discrepancies were indicated and sent back to the institutes in order to correct the data.

Statistical analysis

The prevalence of ADHD in these treatment seeking SUD populations may differ for many reasons: (a) differences in ADHD prevalence in the general populations of participating countries (e.g. DuPaul *et al.*, 2001; Fayyad *et al.*, 2007); (b) differences in referral procedures of patients ADHD and patients with ADHD with SUD and comorbid psychiatric disorders: in some countries these patients might be referred to mental health institutes rather than to addiction treatment centres (e.g. Fayyad *et al.*, 2007); (c) differences in the availability and legal status of specific substances in regions and/or countries; (d) differences in the organizational structure of mental health and addiction treatment within and between countries. Given these national and regional differences we do not expect to find similar prevalence rates of ADHD in the different countries and treatment centres in the current study. Therefore, this study is more likely to provide an estimate of the range of prevalence rates of ADHD in treatment seeking SUD patients in different countries and continents rather than a single overall prevalence estimate for ADHD in treatment seeking SUD patients. For the statistical analyses needed to answer the other research questions, we will always consider to perform analyses stratified by country and or site or to use multi-level analyses with country and/or site as separate levels.

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First results

A total of 3558 subjects were screened and the number of participants per country varied from 130 (USA) to 487 (Norway). Three countries were not able to participating in the full assessment due to lack of funding. Together these countries contributed 963 screenings: USA (130), Belgium (371), and Australia (462). The other seven countries (France, Hungary, the Netherlands, Norway, Spain, Sweden, Switzerland) participated both in the screening (2595) and in the full assessment phase (1276: ranging from 129 in the Netherlands to 226 in Hungary). Table 2 shows the distribution of subjects over the participating institutes and the study.

All subjects participating in stage 1 were also asked for stage 2. Unfortunately, this procedure resulted in substantial drop-out. Possible selection bias was therefore investigated by comparing stage 2 participants with stage 2 drop outs on key demographic and clinical variables (see Table 3). We tested, using *t*-test and chi-squared test, for significant differences on potential confounding variables like ASRS-screen results, age, gender, primary substance of abuse, and variables indicating severity of SUD and other issues such as employment, social status and housing. The data showed no significant ($p < 0.001$) differences between the cases included in the full assessment sample and the ones that dropped out. With two exceptions: 1)the mean age in Norway and Spain was significantly higher for phase 2 clients than for drop outs and 2) both the overall difference and the in-countries difference between phase 1 and phase 2 rate of ASRS positive/negative was significant. The latter differences are taken into account by the fact that in additional papers prevalence estimates will be weighted by the differential sampling fractions from the ASRS+ and ASRS- phase 1 samples. Table 3 also shows that, on average 40.9% of the subjects were screened positive for ADHD. This prevalence varied between 20.1% (Switzerland) and 60.0% (Norway) for different countries.

Discussion

The main advantage of this study over previous research is the use of the same sample procedure and the use of the same instruments and analysis methods over a wide range of countries, institutes and cases. This provides a good picture of the prevalence of ADHD in the participating institutes. Information on the generalizability of the findings will be published in subsequent papers. The high numbers of both alcohol use disorder (AUD) subjects and drug use disorder (DUD) subjects will allow us to provide substance specific prevalence ADHD estimates.

Table 2. Respondent flow stratified by country

	France	Hungary	Netherlands	Norway	Spain	Sweden	Switzerland	USA	Belgium	Australia	Total
Screened	216	343	403	487	432	325	389	130	371	462	3558
Positive on ASRS t1[1]	38.9%	21.3%	38.7%	60.0%	38.4%	43.1%	20.1%	56.2%	32.9%	58.4%	40.9%
Drop out for stage 2	59	117	274	267	210	157	235	NA (130)	NA (371)	NA (462)	2282[2]
Full assessment (*n*)[3]	157	226	129	220	222	168	154	NA	NA	NA	1276
Full assessment (%)	72.7%	65.9%	32.0%	45.2%	51.4%	51.7%	39.6%	NA	NA	NA	35.9%

Note: NA = not applicable: sites only participated in the screening phase of the project.
[1]Cases who did not have a score on t1 (screening stage) on the ASRS, but did have a score on the ASRS at t2 (full assessment stage), the t2 score was imputed. This concerned 126 cases.
[2]Total number of drop outs (missed full assessment) and cases from countries that did not participate in the full assessment stage (not applicable, NA) (USA, Belgium, Australia).
[3]Number of subjects that participated in the CAADID interview for diagnosing adult ADHD.

Table 3. Potential selection bias due to drop out between screening and full assessment

	France		Hungary		Netherlands		Norway		Spain		Sweden		Switzerland		Total		
	A	B	A	B	A	B	A	B	A	B	A	B	A	B	A	B	C
Number of subjects (*n*)	59	157	117	226	274	129	267	220	210	222	157	168	235	154	1319	1276	
Age (mean)	34.0	36.8	40.6	43.1	39.3	40.4	33.9	38.1	33.8	37.0	40.1	42.6	44.1	42.6	38.2	40.0	5
Female (%)	30.5	28.0	30.8	24.3	26.3	17.3	34.5	31.4	21.0	20.7	35.0	31.0	34.9	33.6	30.3	26.7	2
Employed (%)	44.1	32.5	20.5	24.0	46.3	53.1	17.4	26.4	35.9	36.7	23.5	35.9	20.2	13.4	29.4	31.0	94
Homeless (%)	1.7	2.5	3.7	5.4	3.7	4.7	?	4.5	3.4	3.6	7.2	4.3	7.7	5.3	4.9	4.3	336
Married/living with partner	22.1	22.3	34.1	31.7	27.2	23.3	?	18.1	29.0	26.4	27.4	28.7	28.9	30.9	28.6	25.9	300
Main substance[1]																	
Missing on main substance	0	0	0	0	0	0	267	6	3	1	3	3	2	2	275	12	287
Alcohol (%)	35.6	50.3	71.8	74.8	58.4	61.2	?	31.8	18.8	25.8	44.2	55.8	96.1	96.1	57.1	54.6	
Opioids (%)	18.6	9.6	7.7	3.5	2.6	0.8	?	17.3	21.3	17.6	27.9	21.2	1.3	1.3	11.2	10.8	
Stimulants (%)	11.9	6.4	6.0	5.8	16.4	9.3	?	26.6	41.5	36.7	10.4	9.7	0.0	1.3	15.4	15.1	
Cannabis (%)	27.1	20.4	3.4	1.8	17.9	24.0	?	14.0	13.5	13.6	8.4	6.1	0.9	0.0	10.7	10.8	
Other (%)	6.8	13.4	11.1	14.2	4.7	4.7	?	10.3	4.8	6.3	9.1	7.3	1.7	1.3	5.7	8.6	
ASRS case (%)	35.6	40.1	22.2	20.8	31.8	53.5	55.1	65.9	41.4	35.6	49.0	37.5	14.5	28.6	36.3	40.0	0

Note: with the exception of Norway the number of persons with missing data on main problem substance was small: France (A=; B=). A = drop outs after screening; B = full assessment stage; C = number missing. More than half of the Norwegian sample was drawn from another local study using the same methods. However in this study they did not ask about housing, social status and self reported main problem substance. This explains the high numbers of missing cases in these categories.
[1]Main problem substance based on self report at the screening stage.

The psychometric features of the ASRS and other ADHD screening instruments have been scarcely examined in SUD treatment seeking populations (Adler *et al.*, 2009; Daigre Blanco *et al.*, 2009; Pérez Pedrero & García, 2007; Chiasson *et al.*, 2011). The inclusion of both ASRS positive and ASRS negative cases in the full assessment sample allows us to analyse the sensitivity and specificity of the ASRS. The overall rate of screen positive cases in this population was 40.9%. and is comparable to results in other studies that have used the ASRS in SUD populations (Adler *et al.*, 2009; Daigre Blanco *et al.*, 2009; Chiasson *et al.*, 2011). The differences in the percentage of screen positive cases between the several countries, 20.1% (Switzerland) to 60.0% (Norway) need further analysis, but these preliminary data suggest that countries/centres with high rates of alcohol as the primary substance of abuse (Hungary, Switzerland) have lower rates of ASRS positives compared to countries with low rates of AUDs (Norway, Spain). To what extent the differences in ADHD-screening results can be explained by the simultaneous presence of MD, BD, BPD or ASP is beyond the scope of this methods paper and will be analysed and discussed in subsequent papers.

Although the number of included subjects is impressive, this study has several limitations. The first is the lack of information about the initial number of referred patients and the drop-out rates in some countries. Added to the number of subjects that refused to participate or left before they were asked to participate, it remains unclear to what extent the included subjects are a representative sample of the total group of referred patients. Although, the patients that dropped out from the study were very similar to those that participated in many aspects (see Table 3), it can not be excluded that drop-outs are different from participants in other important aspects related to the presence of ADHD in these SUD patients leading to an under- or over-estimation of the prevalence.

It is also unclear to what extend the participating institutes represent a balanced picture of addiction treatment services. Although we speak of countries in our population sample, the level of generalizability of finding over the countries remains uncertain.

The third limitation is the cross-sectional/retrospective design of the study. The diagnosis of adult ADHD requires a retrospectively drawn conclusion on presence of childhood ADHD, possibly leading to an under-estimation of the prevalence (Barkley *et al.*, 2008).

Because requiring sustained abstinence as a criterion for inclusion may have resulted in the exclusion of the more severely dependent subjects and an under-estimation of the prevalence of ADHD (Wilens, 2004), we dropped this inclusion criterion, resulting in the fourth limitation of this study. In order to compensate for the risk of invalid data, we decided to ask the interviewer to judge the reliability of the answers during the full assessment. If the answers were judged to be reliable, inclusion in the full assessment phase was allowed even in the presence of recent substance use.

Finally, for diagnosing ADHD it is recommended to use information from persons knowing the patient in childhood (parent, sibling, friend). It has been reported that adults with ADHD tend to under-estimate the presence of their symptoms (Barkley *et al.*, 2008). We hypothesized that in our sample many subjects, and most probably even more those having ADHD, would not be able to have informants participating in the diagnostic procedure. Hence, making the recommended use of informants mandatory would lead to high drop-out rates with potentially unrepresentative results. The lack of informant participation in the diagnostic procedure may have led to an under-estimation of the presence of ADHD in this population.

To our knowledge, this is the first time that a study of this scale has been undertaken without prior funding. It reflects the sense of urgency felt by the participating institutes related to the growing awareness of ADHD as an important factor in the onset and persistence of addiction. The number of participating countries will balance the documented presence of American studies on this topic (Van Emmerik-van Oortmerssen *et al.*, 2011). The size and quality of the study sample will provide a unique contribution to the body of knowledge on several aspects of the linkage between ADHD and SUD.

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The first two authors contributed equally to this publication.

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The ICASA Network developed the IASP study, and arranged with its participating institutes that each of these institutes would seek funding for their regional process and data sampling efforts. The ICASA Network would seek funding for the central organization costs. These central costs included:

- Organizing meetings for the network;
  Site visits for training and monitoring (The first author (VdG G) visited all of the institutes at least once, the European institutes were visited twice);

Building a data base fit for remote data storage at the University of Amsterdam;
- Obtaining the right for use of the CAADID interview;
- Translating the instrument in the necessary languages;
- Cleaning the data;
- Analysing the study results and coordinating publishing.

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Declaration of interest statement

G. Van de Glind was on one occasion consultant for Shire, for which he refused payment. Apart from the funding resources mentioned in the acknowledgement section he declares no conflicts of interest.

J. A. Ramos-Quiroga and W. van den Brink declare, apart from the funding resources mentioned in the acknowledgement section, no other conflicts of interest.

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Conflict of Interest

The other authors did not report any conflict of interest.

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