

Guideline for Screening, Diagnosis and Treatment of ADHD in Adults with Substance Use Disorders

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Abstract Currently there is no guideline for the screening, diagnosis and treatment of adult attention deficit/hyperactivity disorder (ADHD) in patients with a substance use disorder (SUD). The aim was to develop such a guideline, starting out from a systematic review and based on the methodology of the Scottish Intercollegiate Guideline Network (SIGN). Due to the lack of scientific evidence on some of the topics, the guideline is a combination of evidence based and practice based recommendations. Given the high prevalence of ADHD in treatment seeking SUD patients and the availability of valid screening instruments, all treatment seeking SUD patients should be screened for ADHD. Diagnosis of ADHD should be based on clinical observation and history taking, including informant data. Integrated treatment of ADHD and SUD is recommended, including pharmacotherapy, psycho-education, coaching, and cognitive

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behavioral therapy (CBT). The lack of scientific data and the overall lack of expertise in the field are significant obstacles to the implementation of the guideline. Intensive training programs in the substance abuse sector need to be organized to implement these guidelines.

Keywords Guideline · Attention deficit hyperkinetic disorder · Substance use disorder · Comorbidity · Screening · Diagnosis · Treatment · ADHD

Introduction

To the best of our knowledge, no guidelines are currently available for the screening, diagnosis and treatment of adult attention deficit/hyperactivity disorder (ADHD) in patients with a substance use disorder (SUD). There are guidelines for ADHD in adults (Kendall et al. 2008; Kooij et al. 2010) and we found several expert opinions on ADHD and SUD (Kollins 2008; Levin et al. 1999; Wilens 2004a). Here we present the first guideline for this population based on scientific evidence when available, complemented with practice based information and clinical consensus. The need for guidelines on ADHD in addicted patients originated within the Forum for Addiction Medicine of the Flemish Association for Alcohol and other Drug Problems. The Vereniging voor Alcohol-en andere Drugproblemen (VAD) coordinates most of the Flemish organizations dealing with the treatment of patients with alcohol, drug, and gambling problems.

Several studies have shown that ADHD is much more common in patients with SUD opposed to the general population, and that there is a statistically significant and clinically relevant bidirectional overlap between ADHD and addiction (Arias et al. 2008; Wilens 2004a), i.e. SUD is overrepresented in patients with ADHD and ADHD is overrepresented in patients with SUD.

In a population of adults that experience ADHD, the 12 month prevalence of alcohol abuse or dependence ranges between 17 % and 45 %, whereas the prevalence of drug use disorders ranges between 9 % and 30 % (Wilens and Upadhyaya 2007). In patients with ADHD the age of onset of alcohol and drug use is lower (Wilens 2004b), the transition from regular use to more serious forms of abuse or dependence accelerates and there is a reduced probability of recovery from an individual with SUD (Wilens et al. 1997). The risk of addiction problems in adults with ADHD is four times higher than in adults from the general population (Fayyad et al. 2007). Once ADHD is accompanied with a comorbid disorder (e.g. depression, anxiety disorder, bipolar disorder), the risk of developing an SUD is even higher (Biederman et al. 1995).

In subjects with a SUD, the lifetime prevalence of adult ADHD ranges from 16 % in addicted patients not receiving treatment to 23 % in patients seeking treatment for their alcohol and/or drug use disorder (van Emmerik-van Oortmerssen et al. 2012). In a combined sample of treatment seeking and non-treatment seeking illicit psychostimulant users, 45 % screened positive for adult ADHD (Kaye et al. 2013). In the case of cocaine or heroin dependence, ADHD is also strongly associated with other comorbid disorders, such as disruptive behavior disorders, antisocial personality disorder, bipolar disorder and post-traumatic stress disorder (Arias et al. 2008). Finally, the combination of ADHD and SUD also makes ADHD symptoms more marked (Farhoodi et al. 2010; Levin et al. 2004).

Method

The guidelines were developed based on the methodology prescribed by the Scottish Intercollegiate Guidelines Network (SIGN) (Sign.ac.uk 2001). This is a recognized reference

for the development of guidelines by the Belgian branch of the Cochrane Collaboration (CEBAM) (Cebam.be 2013).

Guideline Development Group and Focus Groups

In the composition of the Guideline Development Group, we ensured participation from all relevant disciplines. The group consisted of Flemish specialists in ADHD in adults, ADHD in children, addiction medicine and addiction psychiatry both from outpatient and inpatient centers. The director of the Belgian branch of the Cochrane Collaboration, the Belgian Center for Evidence Based Medicine (CEBAM), provided methodological advice. In order to keep the content of the guideline consistent with the actual needs and obstacles perceived by therapists and patients, focus groups with patients and therapists (physicians, psychologists) were organized to gain better insight into their experiences and opinions (Fig. 1) (Matthys et al. 2013). Based on the results of these focus groups a strategy for a systematic review of evidence-based research was developed. Based on this review and clinical experience, the first version of the guideline was written and tested over a 6-month period in twelve addiction treatment centers. The final version of the guideline was documented taking their feedback into account and is electronically available: <http://fur.ly/a6h1>

Literature Search and Data Sources

The objective of the search was to reveal all relevant studies using sensitive search strategies. An initial search was performed for guidelines and systematic reviews in the Cochrane Database of Systematic Reviews, the NHS Guideline Finder, the Health Evidence Network and Pubmed. A subsequent search for other studies was carried out using Pubmed, Cinahl, Psycinfo and the Web of Science between January 1994 and April 2009. For the items on which systematic reviews were found, the subsequent search focused on studies published after the systematic review. Manual searching and checking the reference lists of selected studies enabled the inclusion of studies that were not retrieved in the initial search (Fig. 2).

Selection of Studies

Inclusion and exclusion criteria were defined before the selection procedure: adults with ADHD with SUD. In the absence of data, studies on adults with ADHD but without SUD were also included. Further selection was based on the specific questions from focus groups (Fig. 1). Only English and Dutch language studies were selected from January 2000 until April 2009. Studies were selected based on the titles and provided abstracts. Two independent assessors subsequently assessed the selected studies. Irrelevant studies were excluded and full texts were screened for the presence of answers to questions from Fig. 1. In cases of doubt, the Guideline Development Group made the decision. A flow chart of the search can be found in Fig. 2 below.

Quality Assessment

All of the selected studies were evaluated for methodological quality using checklists. For assessing guidelines, the Appraisal of Guidelines for Research and Evaluation (AGREE)

Topics from the focus groups**Diagnosis**

- a. What are the different steps in making a diagnosis of ADHD in adults with addiction problems?*
 - a.1. When can the diagnostic process be started?
 - a.2. Who is eligible to diagnose ADHD?
- b. Which specific aspects should be taken into account during the screening for ADHD in adults with addiction problems?*
 - b.1. Is systematic screening for ADHD recommended in adults with SUD and what instruments are best suited?
 - b.2. After which screening results is comprehensive diagnostic examination recommended?
- c. Which specific aspects should be taken into account when checking the current symptomatology of ADHD and during the clinical interview?*
- d. Are personal characteristics of the patient important in the diagnostic process and how can these been taken into account? (gender, socioeconomic status)*
- e. Which specific aspects are important in the supplementary examination? (comorbidity)*

Treatment

- a. What comprises good treatment of ADHD in adults with SUD?*
- b. What medication is effective for ADHD in adults with SUD and what is the effect on the use of alcohol and other drugs?*
- c. What are the risks of ADHD medication in addicts?*
- d. What psychotherapeutic treatments are effective for ADHD in adults with SUD?*

Fig. 1 Topics from the focus groups

instrument from the AGREE Collaboration (Agreecollaboration.org 2003) for assessing guidelines was used. The SIGN checklist was used for assessing systematic reviews, randomized control trials (RCTs) and cohort case studies.

Data Extraction

The data from valid studies was tabulated in evidence tables and summarized by level of evidence. In accordance with the SIGN grading system, (Sign.ac.uk 2001) (Fig. 3) our recommendations are graded from A to D. These grades match the strength of the supporting evidence from Levels of Evidence 1 to 4. If no relevant research evidence was found, recommendations were based on clinical judgment and consensus of the Guideline Development Group to what extent constitutes good practice.

Validation

The first version of the guideline was tested over a 6-month period in 12 addiction treatment centers. Physicians and psychologists gave feedback on scope, quality, clarity and usefulness. The Guideline Development Group then considered the responses. An independent expert committee, following the CEBAM external validation procedure, officially approved the final guidelines in September 2011.

Levels of Evidence

We selected 66 studies to support our recommendations, including three meta-analyses, one systematic review, 11 RCTs, 16 non-systematic reviews, 12 cohort studies, eight open trials, four case reports/series, eight cross-sectional surveys, two prevalence studies, and one study protocol.

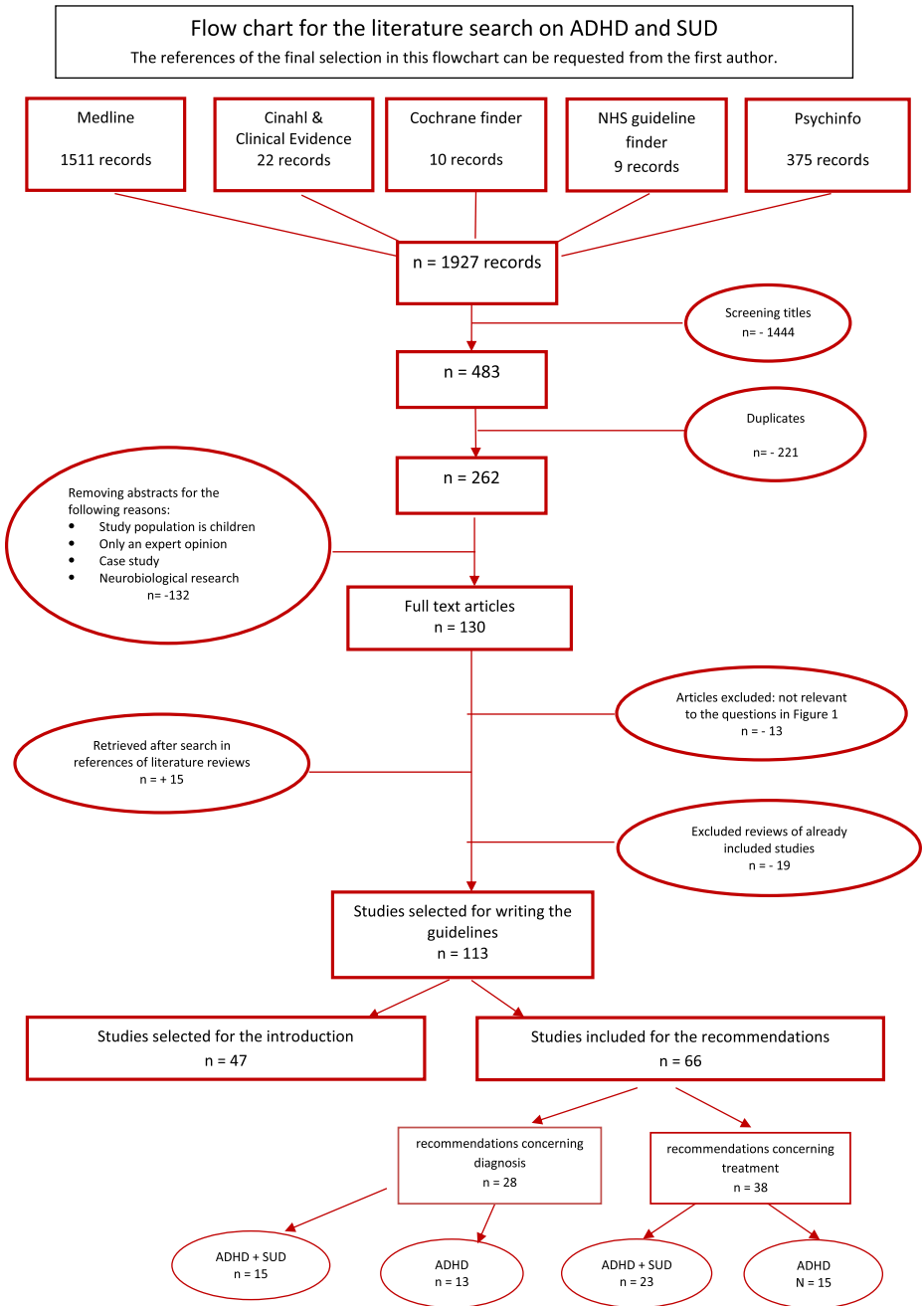


Fig. 2 Flow chart for the literature search on ADHD and SUD

Only 38 of the 66 studies contained specific information about the target group (adults with ADHD and SUD), eight of which were non-systematic literature reviews. We found no guidelines for the target group of patients with SUD and ADHD. As a consequence, some

LEVELS OF EVIDENCE

- 1++ High quality meta-analyses, systematic reviews of RCTs, or RCTs with a very low risk of bias
- 1+ Well-conducted meta-analyses, systematic reviews, or RCTs with a low risk of bias
- 1- Meta-analyses, systematic reviews, or RCTs with a high risk of bias
- 2++ High quality systematic reviews of case control or cohort studies
High quality case control or cohort studies with a very low risk of confounding or bias and a high probability that the relationship is causal
- 2+ Well-conducted case control or cohort studies with a low risk of confounding or bias and a moderate probability that the relationship is causal
- 2- Case control or cohort studies with a high risk of confounding or bias and a significant risk that the relationship is not causal
- 3 Non-analytical studies, e.g. case reports, case series
- 4 Expert opinion

GRADES OF RECOMMENDATIONS

- A** At least one meta-analysis, systematic review, or RCT rated as 1++, and directly applicable to the target population *or*
A body of evidence consisting principally of studies rated as 1+, directly applicable to the target population, and demonstrating overall consistency of results
- B** A body of evidence including studies rated as 2++, directly applicable to the target population, and demonstrating overall consistency of results *or*
Extrapolated evidence from studies rated as 1++ or 1+
- C** A body of evidence including studies rated as 2+, directly applicable to the target population and demonstrating overall consistency of results *or*
Extrapolated evidence from studies rated as 2++
- D** Evidence level 3 or 4 *or*
Extrapolated evidence from studies rated as 2+

Fig. 3 SIGN grading system

of the recommendations were derived from research in other populations, such as young people with ADHD and SUD as well as adults with ADHD but without SUD. We marked these recommendations with ^①.

Results

Findings Screening and Diagnosis

It is generally assumed that a good diagnosis comprises a number of necessary steps: mapping the current symptoms and the symptoms during childhood, family history, school and

vocational history, relationships, physical signs and investigation of comorbidity (Upadhyaya 2006) (L. Adler and Cohen 2004) ^①. **3**

Although there is no specific evidence on when the diagnostic process in individuals with an addiction problem should be started, experts mention an abstinence period of 1 month for an accurate and valid diagnosis (Wilens 2004b). Other sources argue that the patient should at least be approachable to obtain adequate information about the life course in an interview (Glind et al. 2004). Our group of experts and practitioners rejected a 1-month abstinence requirement. They concluded that this recommendation could not be generalized in view of the great variation in the history, the type of substance use and the nature of the treatment setting. In addition, it was emphasized that for a correct diagnosis of ADHD in adults with SUD, expertise with regard to both disorders is required (Glind et al. 2004). **4**

Screening

The high prevalence of ADHD in patients with SUD and the impact of ADHD on the course of SUD symptoms are important reasons for screening (West et al. 2003). **3** Early detection and treatment of ADHD in a population with SUD is significant for successful treatment of these patients (Kalbag and Levin 2005).

The screening should be done with a validated questionnaire based on the eighteen DSM-IV symptoms of ADHD. However, until recently, only one screening instrument for ADHD was tested in a population of young adults with addiction problems: Conners' Adult ADHD Rating Scale (CAARS) (Cleland et al. 2006). **2+** At the time of the development of the guideline, the Flemish version of the Adult ADHD Self-Report Scale (ASRS) had not yet been validated in this patient group. However, experts felt that the CAARS and the ASRS can be used, provided that the results are interpreted with caution. This screening gives an indication of the presence of ADHD. However, the specificity of such questionnaires is generally limited, resulting in a substantial number of false positives and thus over-diagnosis of ADHD (Upadhyaya 2006). **3**

Under-Diagnosis and Over-Diagnosis

The stringency of the DSM-IV criteria, at least six of the nine symptoms currently and the presence of symptoms before the age of seven, can complicate the diagnosis of ADHD in adults, which may lead to an under-diagnosis of ADHD in the adult population (Levin and Upadhyaya 2007). **3** It is often wrongly assumed that in the presence of anxiety disorders, depression or other psychiatric disorders, ADHD should not be diagnosed. If ADHD exists together with other axis-I disorders, all disorders should be taken into account (Kalbag and Levin 2005). Since the DSM-IV criteria was originally developed for children, the absence of age-specific symptoms can also lead to underdiagnosis. Patients with addiction problems combined with ADHD often have difficulties in recalling the presence of ADHD symptoms in childhood which is necessary for proper diagnosis (Levin and Upadhyaya 2007). Moreover, the patient may be reluctant in giving information, while the family may not be willing to cooperate either (Kalbag and Levin 2005). **3** Ultimately, if a patient with SUD is not diagnosed with ADHD as a child, it is highly unlikely that current behavioral problems will be linked to ADHD. Social problems such as poor school results, job loss, etc., are easily attributed to existing substance abuse issues. In addition, many adults with ADHD have developed compensatory strategies to mask the negative impact of their ADHD symptoms in daily functioning (Adler and Cohen 2004) (Culpepper and Mattingly 2008) ^①. **3** Therefore, if an adult with SUD is examined, it is also important to take into account the overall clinical picture and to interpret reasonably, but critically, the age limit of 7 years as well as the requirement of six of the nine symptoms. In the DSM-V, the age limit of 7 years is raised to

12 years and the number of symptoms required for the diagnosis of adult ADHD is reduced from six to five (American Psychiatric Association 2013).

Differential diagnosis with bipolar disorder or borderline personality disorder can be difficult, but should be taken seriously in order to prevent misdiagnosis. Checking the continuity of the symptoms from early childhood to adulthood and their appearance in different settings and situations can give further insights. Over-diagnosis of ADHD can also occur due to symptoms of drug dependence or drug use itself being mistaken for ADHD symptoms (Kalbag and Levin 2005; Levin and Upadhyaya 2007; Wilson and Levin 2001). **3** Therefore, it is highly recommended to consider developmental history, psychiatric comorbidity and family history of the patient while focusing on drug-free and alcohol-free episodes in the patient's life. (Sullivan & Rudnik-Levin 2001). **3** Another risk of over-diagnosis can occur when patients exaggerate experienced ADHD symptoms and try to influence the diagnosis in order to obtain stimulant medication (Upadhyaya 2006). **3**

Diagnostic Instruments

Self-report questionnaires based on the DSM-IV criteria for ADHD can be useful but are insufficient for an accurate diagnosis (Adler and Cohen 2004). However, only two instruments were tested in a population of young adults with addiction problems (Cleland et al. 2006; West et al. 2007) **2+**: CAARS and Attention Deficit Scales for Adults (ADSA). Both instruments are reliable and valid in determining which patients with addiction problems should receive a more in-depth diagnostic examination (Adler et al. 2008; West et al. 2003, 2007) **3** [Ⓛ].

In addition, there are two semi-structured diagnostic interviews for adults available to assess current and past symptoms, the Diagnostic Interview for ADHD in Adults (DIVA) (Kooij 2012) and the Conners' Adult ADHD Diagnostic Interview for the DSM-IV (CAADID) (Epstein et al. 2001). The DIVA was only available in Dutch at the time the guideline was developed and neither of the interviews had been validated in a population with ADHD and comorbid SUD.

Gender and Socio-Economic Situation

The investigator should take into account the environment of the patient. Attention deficit, impulsiveness, easy distraction, overreacting etc., can also be the result of living in a stressful and unpredictable substance abusing environment rather than being symptoms of ADHD (Gingerich et al. 1998) [Ⓛ].

The clinical appearance of ADHD may differ between men and women. Women with ADHD are more likely to suffer from mood and anxiety disorders and low self-esteem (Arcia and CONNERS 1998; Biederman et al. 2006; Katz et al. 1998) [Ⓛ]. **2** Unlike the findings from research in girls, in which the inattentive type is diagnosed more often than in boys, in a clinical trial, adult women were diagnosed more often with the combined type than men (Robison et al. 2008) [Ⓛ]. **2** Other authors suggest women with ADHD generally do not exhibit symptoms of hyperactivity, but rather less obvious symptoms such as restlessness, forgetfulness and disorganization (Quinn 2008; Waite 2007) [Ⓛ]. **3**

As in other pathologies, it is important to know the cultural background of the patient (importance of individuality, family loyalty and honor, performance orientation, etc.) in order to assess whether the behavior is abnormal. Cultural differences can have an influence on the signs and treatment access of ADHD (Rohde et al. 2005) [Ⓛ]. **1+** Although the prevalence of ADHD seems similar in different countries (Faraone et al. 2003), cross-national research shows a lower prevalence of ADHD in lower-income countries (1.9 %) compared with higher-income countries (4.2 %) (Fayyad et al. 2007). Within a population of young adults with ADHD the association between socio-economic class and comorbid

addiction problems is U-shaped, with an increased risk of substance abuse in both the highest and lowest social classes (Monuteaux et al. 2007). 2+

Comorbidity

Co-morbidity complicates the diagnosis of ADHD, because there can be an overlap in symptoms as well as associated features with SUD (Kalbag and Levin 2005), (hypo)mania (Kim and Miklowitz 2002) ^① or other axis I and axis II disorders. Moreover, the combination of ADHD and SUD is associated with an increased risk of mood and anxiety disorders (Wilens et al. 2005). 2+ Finally, intoxication and/or withdrawal from alcohol or drugs can mimic the symptoms typical associated with ADHD (Faraone et al. 2007). 2+

Recommendations Screening and Diagnosis

General Principles D

The diagnosis should not be exclusively based on self-report questionnaires and/or semi-structured interviews covering the current situation. In addition to the current symptoms, daily life observation, symptoms present in early childhood, lifetime presence of symptoms and substance abuse should also be considered. The clinician should, on an individual basis, determine the minimal duration of the abstinence needed before screening and diagnosis can be initiated, taking into account the history of the patient, the setting in which the patient is treated and the substance of abuse. Interviewing the patient and his/her family can be started even when the patient has not been fully stabilized. Any physician who has had comprehensive training in the differential diagnosis of ADHD can make the formal diagnosis of ADHD. The physician should also have sufficient experience in substance abuse treatment and with a population of young adults with ADHD.

Screening

Given the high prevalence of ADHD in patients with SUD, screening for ADHD is important. **C** Since there is no screening tool validated in Dutch, the physician will have to rely on clinical experience when choosing a valid instrument. Further diagnostic examination can be started if the screening is positive but also when the history of the patient or the clinical observation suggests that ADHD is a possible diagnosis. **D**

Diagnostic Examination

A comprehensive clinical interview with the patient and family is necessary, preventing potential over-diagnosis or under-diagnosis. **C** The use of validated questionnaires and semi-structured interviews is an ideal starting point. For the selection of diagnostic instruments, the physician should base his/her choice on his/her clinical experience. **C**

A timetable of the use of alcohol and drugs (duration, frequency and pattern of use, route of administration, type of substance) matching the appearance of ADHD symptoms can help to differentiate between ADHD symptoms and similar drug induced symptoms. Moreover, this feedback can make the patient aware of his/her problems. During the clinical interview, it is appropriate to focus on the abstinent/clean episodes in the patient's life. **D**

The involvement of the patient's parents (or siblings) is significant in collecting information about the patient's childhood, though intentionally or unintentionally, family members can underestimate or exaggerate his or her symptoms. **C** Additional observer information can be gathered from school reports (if available), with special attention to the evolution of the patient's performance and any added comments from teachers. **C**

For systematic data collection (current and childhood), diagnostic interviews such as CAADID and DIVA can be used. **D**

Gender aspects and cultural backgrounds should be included in the diagnostic assessment, as well as the socio-economic status (SES) of the patient. **C**

Most patients have more than two comorbid conditions, therefore it is important to look for other psychiatric problems in the patient's personal and family history, **D** screening for mood and anxiety disorders. **C**

In case of planning, organizational or memory dysfunctions, neuropsychological examination can be useful to determine cognitive deficits. **D**

Findings Treatment

A Complex Problem Requires Complex Treatment

Presently, there is a general consensus that proper treatment of ADHD in people with SUD comprises several components: psycho-education and medication need to conjoin with individual and/or group therapy, as well as peer support (Goossensen et al. 2006). **3** It has been indicated that combined interventions (medication + behavioral therapy) have a better outcome opposed to medication alone (Safren et al. 2005) [Ⓢ] **1** (Rostain and Ramsay 2006) [Ⓢ]. **2** Abstinence is not an absolute precondition to start treatment (Wilens 2004a) **3**, but substance use must be stabilized, e.g. occasional moderate alcohol consumption, moderate cannabis use, fixed dose methadone or buprenorphine. The treatment of ADHD should be integrated into the treatment of addiction, which is vital considering ADHD symptoms (such as impulsivity and disturbed planning and organization) may interfere with the addiction treatment (Mariani and Levin 2007). **3** There is no consensus about the order of treatment of comorbid disorders. However, researchers claim that serious psychiatric disorders that significantly affect functioning (such as psychosis or depression) should be treated first. When symptoms of an SUD are too serious or when housing is unstable, time-limited in-patient treatment is recommended (Wilens 2004b). **3**

Treat the Patient, not the Illness

Most adults with ADHD have two requests to reduce their symptoms: developing coping mechanisms to handle symptoms and a decrease of the emotional and functional problems that accompany ADHD (Ramsay and Rostain 2005). Combined with an addiction problem, there will be two additional objectives: to keep the patient in treatment and to influence the SUD in a positive way (Carpentier et al. 2012).

Most young adults with ADHD suffer from a negative self-image and low self-esteem. If the diagnosis of ADHD is first recognized and made in adulthood, patients often experience a period of anger and grief for how different the outcome of life could have been if the diagnosis had been made earlier (Murphy 2005). **3** Involving families in the treatment process is recommended: when members of the family are well informed and educated on the issue, coping mechanisms are easily developed and utilized towards the patient. Essentially, family-

patient coping strategies allow for proper supervision in medication use to avoid abuse (Wilens 2004b). **3**

Pharmacological Treatment

There is sufficient evidence about the effect of medication on ADHD in adults. In placebo-controlled trials, stimulants have larger effect-sizes than atomoxetine (Peterson et al. 2008) ^①. 1 Certain antidepressants (desipramine, a metabolite of imipramine, and bupropion) have an obvious effect on ADHD symptoms, but the effect is still smaller than that of stimulants (Maidment 2003; Verbeeck et al. 2009) ^①. 1 All products have a smaller effect in adults than in children (Mészáros et al. 2009) ^①, **1** perhaps partly due to inadequate dosing (Dodson 2005) ^①.

However, data on adult ADHD in a population of substance users is much more limited. A number of case reports and open-label investigations suggest a positive effect of medication on ADHD symptoms in addicts (Castaneda et al. 2000; Levin et al. 2009; Mann and Bitsios 2009; Riggs et al. 1998; Solhkhah et al. 2005; Somoza et al. 2004; Vaiva et al. 2002; Wilens et al. 2010; Winhusen et al. 2006). **3** However, most double-blind and placebo-controlled studies, albeit with small groups and of short duration (Upadhyaya 2006; Wilens et al. 2008), show little or no improvement in ADHD symptoms. **2** In several of the studies, however, there is an improvement in ADHD symptoms in all groups, indicating a strong placebo effect, or an effect due to the accompanying psychotherapy. In one study, the treatment of ADHD and co-occurring alcohol dependence with atomoxetine showed a significant effect on ADHD symptoms with an effect size of 0.48. This is comparable to a study with atomoxetine in adult ADHD patients without SUD (Wilens et al. 2008).

Does ADHD Treatment Decrease Substance Abuse in Comorbid Patients?

Since ADHD generally precedes SUD and since ADHD is considered a complicating factor in the treatment of addiction, it was expected that the reduction of the ADHD symptoms would make the addiction easily treatable. Initially, there was a great deal of optimism about the effects of ADHD treatment on substance abuse (Levin et al. 2002). However, optimism was based on the results from open label trials in small samples and without a control group, it could not be confirmed in RCTs (Levin et al. 2006, 2007; Szobot et al. 2008; Wilens et al. 2008). **1**

It should be noted, however, that there is hardly any evidence for a worse substance use outcome in comorbid patients treated for their addiction. ADHD is a risk factor for an earlier onset of a substance use disorder (Biederman et al. 1998) and adults with ADHD have a more prolonged course of SUD (Wilens 2004a), but severity of drug dependency seems to be a more important predictor of comorbid ADHD in patients that dropout of treatment (Levin et al. 2008). **3**

Does ADHD Treatment Prevent Substance Use Disorder?

Children with ADHD are at increased risk for developing an addiction problem. In several studies it is shown that the treatment of childhood ADHD with stimulants does not increase the risk of SUD (Faraone and Wilens 2003; Kollins 2003) (Wilson 2007). **1** Other studies show that treating childhood ADHD with stimulants results in a 50–70 % reduction of addiction (Wilens 2004b). However, a prospective study in which children with ADHD were studied for 10 years, results showed that short-term treatment with stimulants had no effect on the risk of the onset of substance abuse (Biederman et al. 2009). **2** Some authors have, therefore, concluded that stimulant treatment of childhood ADHD does not prevent the development of addiction. However, it is proposed that this is only true for short-term medical treatment and

that treatment with medicine and/or psychotherapy, should be continued until young adulthood in order to definitively prevent addiction in patients with ADHD.

Misuse of the Medication

Patients being treated for ADHD often see treatment as a sign of recognition of their problems, this further increases their treatment compliance. **4** Therefore, medication with a delayed effect (e.g. atomoxetine) often causes dropout in extremely impatient individuals. However, in addiction treatment centers there is often great concern about prescribing stimulants given their abuse potential in patients with SUD. Although methylphenidate should have less abuse potential than cocaine because of its pharmacological properties (slower uptake) when administered in therapeutic doses (Kollins 2003; Volkow and Swanson 2003), **3** it remains a product that can be abused by the patients themselves or by someone in their surroundings. In research, 16.5 % of those surveyed in an ADHD treatment center affirmed that they shared medication with others (Bright 2008). **3** Products with immediate release effects are more likely to be abused than the modified released stimulants. Modafinil can also be abused (Turner et al. 2004). Atomoxetine, on the other hand, has no abuse potential (Jasinski et al. 2008; Wilens et al. 2008), but has a delayed effect. **1**

Non-Pharmacological Treatment

There is limited evidence about the effectiveness of psychotherapeutic treatment of ADHD in adults. However, there is some evidence on a positive effect of cognitive behavioral therapy (CBT) (Rostain and Ramsay 2006; Safren et al. 2005; Virta et al. 2008) [Ⓢ] and structured skills training (Solanto et al. 2008) [Ⓢ]. There are indications of a positive effect of psycho-education and peer support (Murphy 2005) [Ⓢ], dialectical behavioral therapy (DBT) (Hesslinger et al. 2002; Philipsen et al. 2007) [Ⓢ], and mindfulness training (Zylowska et al. 2008) [Ⓢ]. Most of these methods are also part of the standard treatment in addiction and for some of them, such as cognitive behavioral therapy (CBT), considerable evidence is available (Kleber et al. 2007; Rieger 2006). There is no evidence on the effects of any of these treatments in addicted patients with ADHD. Only expert opinions are available (Goossensen et al. 2006; Levin et al. 2008). **4**

Because of the chronic nature of both ADHD and addiction, with repercussions in all life domains, combining as many interventions as possible is recommended. According to the experts in the focus groups, many therapeutic methods are appropriate for both the addiction problem and the ADHD, e.g. providing structure, teaching time management and planning and learning to cope with impulsivity and mood swings. In an inpatient program, there is sufficient time and manpower for these intensive therapies. In an outpatient setting, patient contacts are often fragmentary and too short. Yet even in this setting, a combination of individual with group-based training and peer support seems to be the best answer to the problem.

Recommendations Treatment

General Principles

The treatment of ADHD in addicts can be started when the addiction problem is stabilized. **D** Combining medication with psychotherapy **D** and using an integrated approach to substance abuse and ADHD (and to any other mental disorder present) are recommended. **C** Peer and family support enhances the effect of the treatment. **D**

Pharmacological Treatment C

Atomoxetine is preferred since it lacks abuse potential but the delayed effect can be a problem for patients that express little patience in recovering. Methylphenidate (extended release) may be prescribed, on the assumption that delivery and administration are sufficiently supervised. Imipramine and bupropion are possible alternatives for the treatment of ADHD. Due to abuse potential, methylphenidate (immediate release) only has a place in an inpatient setting and in the startup phase to assess its impact.

Extended release dexamphetamine can, in high doses, have a positive effect on cocaine use, but is not recommended at the moment. **D**

Non-Pharmacological Treatment

A multimodal treatment is preferable. The first phase consists of psycho-education. In the second phase, cognitive behavioral therapy (CBT) and skills training (individually or group-based), **C** individual coaching and peer support are recommended in addition to medication. **D** Dialectical behavior therapy (DBT) and mindfulness training can also be helpful. Relationship therapy should be considered. **D** Remaining comorbid disorders should be treated. **S**

Update

The guideline was approved by the Belgian Centre for Evidence-Based Medicine Belgian Branch of the Dutch Cochrane Centre (CEBAM) in September 2011. The literature search on which we based the development of our guidelines was completed in April 2009. In the meantime, some new research findings have been published. For this reason we carried out a new literature search with the same terms and using the same sources for the period May 2009—July 2013. Eventually we selected three studies on screening and five on pharmacological treatment trials (three RCT's and two open trials) in adults with ADHD and SUD. The data from these new studies have either confirmed or nuanced some of our findings and recommendations.

A recent paper (Dakwar et al. 2012) confirmed that various ADHD screening instruments, recommended in our guideline, have adequate sensitivity and specificity in SUD population. Especially the ASRS has been investigated in this population by several researchers (Chiasson et al. 2012; van de Glind et al. 2013), and was found to be useful with good sensitivity but limited specificity. The data of van de Glind et al. (2013) also show that there is no difference in the screening results when patients are interviewed in the withdrawal stage or after a few weeks of abstinence.

The support for the effect of medication on ADHD in patients with SUD is still limited. However, some new open trials with sustained-release bupropion and atomoxetine are promising (Wilens et al. 2010) (Adler et al. 2010). Furthermore, in an RCT with high dose osmotic release oral system methylphenidate there was a significant reduction of both ADHD-symptoms and the risk for relapse to substance use in criminal offenders with a co-diagnosis of ADHD and amphetamine dependence (Konstenius et al. 2013). In contrast, an RCT with atomoxetine in adolescents did not show any difference with the placebo group (Thurstone et al. 2010; Wilens et al. 2011).

Finally, the evidence for the effect of cognitive behavioral therapy (CBT) and dialectical behavioral therapy (DBT) in patients with ADHD (without SUD) is now stronger (Hirvikoski et al. 2011; Safren et al. 2010; Solanto et al. 2010).

Discussion

This is the first evidence-based guideline for the diagnosis and treatment of ADHD in adults with SUD. Only limited evidence was found for screening, diagnosis and treatment. When evidence was not available, our recommendations are based on expert consensus. Fear of both over-diagnosis and under-diagnosis is common. The diagnostic rules are often too strict, e.g. regarding information from early childhood and the requirement for complete abstinence. Especially in an inpatient setting observation may provide more information than self-report questionnaires and interviews. Standard neuropsychological examination may be useful to objectify and measure deficits in executive functioning.

We found strong evidence for the effect of pharmacological treatment of ADHD in adults without SUD, but not for ADHD patients with a comorbid substance use disorder. Perhaps the dosages in this population need to be increased (Konstenius et al. 2013). Considering the specific vulnerability of our patients and the misuse of medication, caution is needed when prescribing stimulants. Although there is only limited evidence for the effectiveness of non-pharmacological treatment in ADHD patients with a comorbid addiction, there are indications that the combination with the evidence-based treatments from addiction care may be effective in this population with some adaptation. However, more research is needed for the development of integrated treatments that target both ADHD and substance abuse in order to go beyond standard treatment.

Contemporary research does not lead to new conclusions. Major differences were not found between the group treated with medication and the placebo group. It was interesting to find, as it was already mentioned in our findings, that both groups (who also receive motivational intervention and cognitive behavioral treatment) have a high treatment response. We therefore look forward to the results of research into integrated cognitive behavioral therapy (CBT) for which a protocol was recently published (van Emmerik-van Oortmerssen et al. 2013).

We hope this guideline will help practitioners to make their approach more effective and will encourage the scientific community to start new research efforts in this area. A strategy should be developed to implement the guideline in treatment centers.

Weaknesses and Strengths of the Guideline

This guideline is based on a limited number of studies. A potential limitation of this review is the possibility of missing articles despite our attempt to include all pertinent articles and to be comprehensive by checking the reference lists of selected studies. Nevertheless, studies that were in a language other than English and Dutch were not reviewed. Due to the lack of scientific evidence in this patient group, the guideline is a combination of evidence-based and practice-based recommendations. Even though the evidence base was limited, the recommendations in this guideline were systematically developed.

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