

Quality of Life in Substance Use Disorder patients with and without Attention Deficit Hyperactivity Disorder 12 months after treatment: a naturalistic follow-up study

Abstract

Background. There is sparse research on quality of life (QoL) as an outcome measure in patients with substance use disorders (SUD), with or without attention deficit hyperactivity disorder (ADHD). We aimed to investigate whether SUD patients with and without ADHD (SUD+ADHD vs. SUD-ADHD) differed in QoL at baseline and at a 12-month follow-up after SUD treatment. The groups were additionally compared with data from a national population sample (NPS). *Methods.* From a sample of 16 SUD+ADHD and 87 SUD-ADHD patients originally recruited between 2010 and 2012, eight SUD+ADHD (50.0%) and 28 SUD-ADHD (32.2%) patients were reached at follow-up. QoL was measured with the short version of the World Health Organization QoL instrument (WHOQOL-BREF). Cross-sectional data on QoL from NPS was utilized. *Results.* Compared to NPS, SUD patients reported significantly lower QoL at baseline and follow-up. Furthermore, QoL was similar at baseline in SUD+ADHD and SUD-ADHD patients. At a 12-month follow-up after SUD treatment, SUD+ADHD patients' QoL had improved, however not significantly differing from SUD-ADHD patients or the NPS. SUD-ADHD patients' QoL remained significantly lower. *Conclusions.* At follow-up, SUD+ADHD patients' QoL improved nominally compared to SUD-ADHD patients, but not the NPS. The clinical and functional relevance of these findings should be investigated further.

Keywords: Substance use disorders, Attention deficit hyperactivity disorder, adult, general population, prospective, quality of life

Quality of Life in Substance Use Disorder patients with and without Attention Deficit Hyperactivity Disorder 12 months after treatment: a naturalistic follow-up study

Substance use disorders are defined by cravings, tolerance, withdrawal symptoms, and a compulsive substance seeking despite the devastating consequences at physical, psychological, interpersonal, and societal levels (American Psychiatric Association, 2013; Volkow & Baler, 2014). Adults seeking substance use disorder (SUD) treatment frequently present with attention deficit hyperactivity disorder (ADHD) as a co-occurring condition (5–31%) (van de Glind et al., 2014). ADHD is a neurodevelopmental disorder encompassing the core symptoms of inattention, hyperactivity, and impulsivity (American Psychiatric Association, 2013). Both disorders have similar difficulties, including impulsive decision-making and reward deficits (Ortal et al., 2015). In addition, individuals with SUD may present symptoms resembling those of ADHD, including states of intoxication or withdrawal (Levin, 2007). Other mental conditions in SUD (e.g., bipolar disorder, anxiety and personality disorders) may present symptoms similar to those of ADHD (Fatseas, Debrabant, & Auriacombe, 2012). Such matters make the assessment and diagnosis of ADHD difficult in SUD populations (Crunelle et al., 2018). Furthermore, individuals with SUD who have also been diagnosed with ADHD (SUD+ADHD) challenge SUD treatment because they transition more rapidly and more severely from substance use (SU) to SUD (Kim et al., 2006; Moura et al., 2013), drop-out of SUD treatment earlier (Levin et al., 2004), and are more frequently afflicted with other psychiatric disorders (van Emmerik-van Oortmerssen et al., 2014) than are SUD patients without ADHD.

Increasingly investigated as a secondary outcome measure in health care research (Brod, Johnston, Able, & Swindle, 2006; Coghill, 2010; Laudet, 2011; Picci et al., 2014), the construct of quality of life (QoL) is defined as how we experience our circumstances, goals, and interests in life, based on the value system and cultural context in which we live (The WHOQOL Group, 1998). As the complexity associated with SUD plus ADHD affects individuals in nearly all life domains (Gjervan, Torgersen, & Hjemdal, 2016; Uchida, Spencer, Faraone, & Biederman, 2015; Umar, Salihu, & Owolabi, 2017), interventions targeting this group of patients should aim to improve their QoL.

When compared cross-sectionally, SUD+ADHD and SUD-ADHD patients seem to have no differences in QoL (Kronenberg, Goossens, van Etten, van Achterberg, & van den Brink, 2015). However, to our knowledge only one study has prospectively (two months after treatment) considered the QoL of these individuals (without a comparison group) (van Emmerik-van Oortmerssen et al., 2019). That study found that the ADHD symptoms among SUD+ADHD individuals had improved but there were no changes in QoL. There is evidence that improved QoL in ADHD is associated with psychopharmacological treatment (e.g., Agarwal, Goldenberg, Perry, & IsHak, 2012). Therefore, the QoL in SUD+ADHD patients may benefit from such treatment as well. Naturalistic follow-up studies concerning QoL in SUD+ADHD patients are still scarce. Such studies may contribute to the literature by identifying factors that improve the QoL of SUD+ADHD patients, which can be integrated into SUD treatment. For these reasons we were interested in investigating the following in the present naturalistic study:

1. To compare the QoL of SUD patients at baseline and at a 12- month follow-up after SUD treatment with cross-sectional data from a national population sample.

2. To investigate whether there were differences in QoL between SUD+ADHD and SUD-ADHD patients at baseline and follow-up.

Materials and Methods

Participants

Sixteen SUD+ADHD and 87 SUD-ADHD participants signed an informed consent form at the University Hospital of Northern Norway (between February 2010 and July 2012). Ethical approval was granted by regional committees for medical and health research ethics, REK sør-øst B, 2009/1355b. Study participants were followed up at three points after SUD treatment (at three, six and 12 months, as shown in Figure 1). The present study reports on 36 SUD patients, eight SUD+ADHD patients and 28 SUD-ADHD patients (34.9% of the original sample of 103 patients), who were reached at the longest observation time available, the 12-month follow-up, (hereafter referred to as “follow-up”). This is because although some improvements in QoL have been observed as early as six months after SUD treatment (Pasareanu, Opsal, Vederhus, Kristensen, & Clausen, 2015), studies indicate that QoL reaches stability in one to two years after addiction treatment, granted considerable substance reduction or abstinence (Chou et al., 2013; Daepfen et al., 2014; Laudet, 2011). Furthermore, because psychopharmacological treatment is associated with improved QoL in ADHD (Agarwal et al., 2012), we report the psychopharmacological treatment status of SUD+ADHD individuals reached at the longest observation time. Additional information about recruitment and patient characteristics is presented in Flores-Garcia, Ytterstad, Lensing, and Eisemann (2016).

The self-reported QoL of the two SUD patient groups were compared against QoL data from a national population sample (NPS), reported in a cross-sectional study by Mathiesen and colleagues (2012). This study consisted of 1,230 randomly selected adults drawn from the Norwegian National Register.

Procedure

The study participants, all of whom had previously received detoxification treatment, were assessed during an SUD treatment of about two months. Baseline assessments were commonly completed one to three weeks after initiation of SUD treatment. Follow-ups were conducted either by outpatient services (i.e., via telephone, postal mail, home visits, or with the assistance of a contact person chosen by the participant from his/her local public support system) or by one-week inpatient readmissions. Depending on time constraints, these follow-up assessments were conducted either by the clinician with whom the study participant had collaborated most frequently or by the first author (LF). It was not always feasible for participants to adhere to the original follow-up schedule. In such cases, delays of up to two months were allowed. All participants were offered reading and writing assistance.

ADHD diagnosis and pharmacological treatment

According to the national guideline on ADHD (Norwegian Directorate for Health and Social Affairs, 2007), the assessment and diagnosis of ADHD in adults (International Classification of Diseases 10th revision, ICD-10) involves the assessment of impairment in childhood and adulthood (i.e., the extent to which the ADHD symptoms have affected functioning in the different life domains), assessment of concurrent psychopathology and differential diagnosis, and collection of collateral information from the individual’s parents and other relevant informants. This

procedure must be conducted by authorized healthcare practitioners (physicians/psychologists). Information about those participants fulfilling the criteria for an ADHD diagnosis was extracted from their medical records. The eight SUD+ADHD patients (mean age at baseline 41.5 ± 7.9 ; age range 30-50) reached at follow-up were all assessed in their adulthood (mean age at assessment 36.5 ± 11.5 , age range 18-50). The time from diagnosis to entering the study at baseline was 4.0 ± 4.4 years. At baseline, five of the eight SUD+ADHD patients had recently started psychopharmacological treatment with methylphenidate (MPH).

Baseline characteristics and re-assessment at follow-up

As previously reported, at baseline, SUD+ADHD patients were younger, showed more severe ADHD symptomatology, more amphetamine addiction and self-reported less alcohol use than SUD-ADHD patients (Flores-Garcia et al., 2016). In this study, the eight SUD+ADHD and 28 SUD-ADHD patients were compared regarding QoL, ADHD symptoms and SUD symptoms at baseline and follow-up.

Measures

At baseline, DSM-IV Axis I current comorbid disorders were assessed by the Mini International Neuropsychiatric Interview (M.I.N.I. PLUS) (Sheehan et al., 1994). Axis II disorders were assessed by the Structured Clinical Interview for DSM-IV (SCID II, First, Spitzer, Gibbon, Williams, & Benjamin, 1995), but only when the treatment staff considered it necessary.

SUD patients were assessed for QoL, ADHD symptoms and substance use at baseline and follow-up. A brief description of the instruments used is presented below.

QoL was assessed using the World Health Organization questionnaire, short version (WHOQOL-BREF), which consists of 26 items measuring four QoL domains: physical health (domain 1); psychological health (domain 2); social relationships (domain 3) and environment (domain 4) (Mathiesen et al., 2012; The WHOQOL Group, 1998). Answer alternatives are on a five-point Likert scale varying from 1 (lowest) to 5 (highest). Elevated scores indicate better QoL. In the NPS, the internal consistency reliability (Cronbach's α) ranged from 0.63 (domain 3) to 0.84 (domains 1 and 2) (Mathiesen et al., 2012). In this study, baseline Cronbach's α coefficients ranged from 0.71 (domain 3) to 0.84 (domain 4) and at follow-up from 0.68 (domain 3) to 0.89 (domain 2). A systematic review and meta-analysis showed that WHOQOL-BREF is able to detect meaningful changes in QoL across different patient populations even though when they are small (Skevington & Epton, 2018).

The adult ADHD Self-Report Scale (ASRS) measures the frequency of experiencing the core ADHD symptoms of inattention and hyperactivity/impulsivity are experienced (Kessler et al., 2005). The 18 items comprising the ASRS are divided into parts A and part B. Answer alternatives range from 0 (never) to 4 (very often). High scores indicate high symptom severity. Part A is a six-item scale that covers the most predictive symptoms of ADHD, whereas part B covers additional symptoms associated with the clinical picture of ADHD (Kessler et al., 2007; Taylor, Deb, & Unwin, 2011). The ASRS part A is frequently used in studies aiming to identify individuals who potentially have ADHD in SUD populations (e.g., van de Glind et al., 2013). In general, the cut-off score recommended to carry a full assessment of ADHD is ≥ 14 . A recent study specifically performed in SUD

populations recommended a lower cut-off score of ≥ 11 (Luderer et al., 2018) to gain adequate sensitivity for ADHD in SUD. In the present study, part A and part B of the ASRS were analyzed to elucidate changes from baseline to follow-up in the additional symptom burden of those diagnosed with SUD+ADHD, as compared to SUD-ADHD patients. Cronbach's α coefficients reported previously for part A and part B of the ASRS were 0.86 and 0.93, respectively (Flores-Garcia et al., 2016). In this study, the Cronbach's α coefficients for part A and part B were 0.86 and 0.90 at the baseline and 0.84 and 0.86 at follow-up, respectively.

Self-reported alcohol use was measured by the screening instrument Alcohol Use Disorder Identification Test (AUDIT) (Babor, Higgins-Biddle, Saunders, & Monteiro, 2001) based on the DSM-IV diagnostic criteria for SUD (American Psychiatric Association, 1994), consists of ten questions, and answer alternatives vary from 0 (never) to 4 (daily). The maximum possible score is 40. Scores >8 indicate risk of harmful drinking, scores >16 indicate medium level of drinking harmfully, and scores >20 indicate excessive drinking (Saunders, Aasland, Babor, de la Fuente, & Grant, 1993). AUDIT has previously shown an internal consistency coefficient of 0.77 (Rumpf, Wohlert, Freyer-Adam, Grothues, & Bischof, 2013), compared to 0.94 at both observation times in this study.

The screening instrument Drug Use Disorder Identification Test (DUDIT), consisting of 11 questions measured non-alcohol SU (Berman, Bergman, Palmstierna, & Schlyter, 2005). Similar to the AUDIT, the answer alternatives in the DUDIT range from 0 (never) to 4 (daily). The maximum score is 44. Scores >2 for women and >6 for men are considered problematic use, whereas scores >25 indicate substance addiction (Berman et al., 2005). The DUDIT has shown Cronbach's α coefficients of 0.90 (Hildebrand, 2015). In this study, they were 0.98 and 0.96 at the baseline and 12-month follow-up, respectively.

Statistical analyses

Survival analysis with the Cox proportional regression model was applied to all data ($n=103$) to locate possible factors explaining drop-outs at follow-up. Time in days from baseline until the date of drop-out, date of the individual 12 month follow-up appointment or death date, whichever came first, were recorded for all 103 SUD patients. Survival times for individuals not dropping out were recorded as censored, according to the terminology of survival analysis.

Non-parametric Mann-Whitney U (scale variables) and Fisher's exact tests (count variables) were chosen to compare the NPS and SUD groups due to the small size of the SUD+ADHD group. A one-sample U -test compared the SUD group with the NPS mean value, and the baseline to follow-up change. Two-sample U -test compared SUD+ADHD vs. SUD-ADHD.

Due to the many statistical tests in this study, significant results were restricted to p-values below .01, whereas results below .05 were considered tendencies. The statistical packages SPSS v.22 (IBM Corp., 2013) and the statistical computing language R (R Core Team, 2015) were used for the analyses. In particular, we utilized R-functions: `wilcox.test`, `fisher.test`, `glm`, and `coxph` in the survival-package.

Results

Sociodemographic and Clinical Characteristics at Baseline and Follow-up

Sociodemographic characteristics. The sample comprised 28 males and eight females aged between 28 and 65 (Mean age 47.5 ± 9.6 years). When comparing the SUD groups with the NPS, three out of four SUD patients were men, while the gender ratio was nearly equal in the NPS. Individuals in the NPS were more often employed than in either SUD patient group. Additionally, NPS individuals were more likely to cohabit and had more years of completed education than SUD-ADHD patients. The age differences between the NPS and SUD groups were not significant (Table 1).

From baseline to follow-up, five male SUD-ADHD patients had died, of which the majority consumed multiple substances, predominantly alcohol. None of the SUD+ADHD patients had died at follow-up. A survival analysis of all 103 SUD patients at baseline (see flow chart) revealed that younger patients and those cohabiting with a partner had an increased likelihood of dropping out at follow-up compared to older SUD individuals and those with no cohabitant (HR=1.05, $p=.001$ and HR=2.5, $p = .008$, respectively). However, there were no significant differences between SUD+ADHD and SUD-ADHD patients concerning dropping out at follow-up. In the SUD+ADHD group, 50% of the follow-up assessments were conducted through outpatient services and 50% as inpatient readmissions. In the SUD-ADHD group, the corresponding proportions were 57.7% and 42.3%, respectively.

Clinical characteristics. At baseline five SUD+ADHD patients were receiving MPH. In our previous study we reported the baseline ASRS scores of the original samples of SUD+ADHD and SUD-ADHD patients. In that study, SUD+ADHD patients showed significantly higher scores on parts A and part B of the ASRS compared to SUD-ADHD patients (Flores-Garcia et al., 2016). In the present study, we also investigated whether the eight SUD+ADHD patients showed higher baseline ASRS scores on part A and part B compared to the 28 SUD-ADHD patients. As Table 2 shows, compared to SUD-ADHD patients, SUD+ADHD patients showed baseline tendencies ($p<.05$) toward a higher ADHD symptom frequency. The recommended cut-off score for ASRS part A for a further assessment of ADHD is ≥ 14 . For SUD populations recently an ASRS part A cut-off score of ≥ 11 has been suggested (Kessler et al., 2007; Luderer et al., 2018; Taylor et al., 2011). As a reference, 75% in the SUD+ADHD group (already diagnosed as having ADHD) reported scores above the recommended cut-off score of ≥ 14 for the ASRS part A and 12.5% reported a cut-off of ≥ 11 . Among the SUD-ADHD patients, the corresponding proportions were of 32.1% and 21.4%, respectively. SUD+ADHD patients also had higher rates of amphetamine SUD ($p<.01$) and less alcohol use ($p<.05$) than SUD-ADHD patients. Neither group differed statistically in baseline non-alcohol SU, or in other clinical variables. However, psychiatric comorbidity was more frequent among SUD-ADHD patients.

At follow-up, seven of the eight SUD+ADHD patients were treated with MPH. In terms of ADHD symptomatology, no statistical differences were observed between SUD+ADHD and SUD-ADHD patients (Table 2). Furthermore, at this observation point, 37.5% of the SUD+ADHD group still reported ASRS screener scores at the cut-off of ≥ 14 and 12.5% had scores at a cut-off of ≥ 11 . In the SUD-ADHD group, the corresponding proportions were 17.8% and 28.5%, respectively. In addition, the SUD groups reported reduced alcohol use, particularly SUD-ADHD patients. The differences between SUD+ADHD and SUD-ADHD patients found at baseline ($p<0.05$), were non-significant at follow-up (see Table 2).

QoL at baseline and follow-up compared to the NPS

Preliminarily, we compared the QoL of the SUD patients who were reached at the three-month and six-month follow-ups to the NPS. This, to verify that the results from a larger sample showed trends similar to the results from the sample reached at follow-up. The results from the three- and six months follow-ups were similar to those observed at baseline (data available on request).

Comparisons in QoL between the SUD patients and the NPS are reported in Table 3 and Figure 2. SUD patients in total reported significantly lower QoL on all domains ($p < .001$) than the NPS at both observation times.

SUD+ADHD patients reported a 3.6–5.0 lower average baseline QoL on all domains compared to the NPS, but this was non-significant in domain 3 ($p=0.057$) and only tendencies in domain 1, 2 and 4 ($p=0.014$). SUD-ADHD patients had significantly lower QoL at baseline in all domains ($p < .000$) compared to the NPS.

At follow-up, score differences in QoL between SUD+ADHD patients and NPS were smaller (1.4–2.4) than those observed at baseline, and non-significant in all domains except in domain 1 physical health where there was still a tendency of lower QoL compared to NPS ($p = .016$). The QoL among SUD-ADHD patients was almost unchanged and still significantly lower than the NPS (Table 3 and Figure 2).

The two SUD groups reported similarly low QoL (0.3-1.4 point's difference) at baseline in all domains. From baseline to follow-up, only SUD+ADHD patients had a tendency of improved QoL which was present in domain 1, 2 and 4. However, the difference between the SUD groups at follow-up (0.8-1.7 point's difference) remained non significant (physical health, $p=.390$; psychological health, $p=.229$; social relations, $p=.213$; and environment, $p=.542$) (Table 3 and Figure 2).

Discussion

The aims of the present study were (1) to compare the QoL of SUD patients both at baseline and at 12-months follow-up after SUD treatment with cross-sectional data from a NPS and (2) to investigate whether there were differences in QoL between SUD+ADHD and SUD-ADHD patients at both the baseline and the follow-up.

At both observation times, the SUD patients reported significantly lower QoL (all domains) than did the NPS. This is in line with results from studies comparing individuals with SUD (Tracy et al., 2012) and ADHD (Lensing, Zeiner, Sandvik, & Opjordsmoen, 2015) to the general population. The present results seem rational because for individuals with persistent disorders, such as SUD and ADHD, reaching a similar QoL as those in good general health may take substantial efforts at different levels.

When the SUD group was investigated by ADHD status, at a tendency level ($p < .05$), SUD+ADHD patients showed improvements in QoL at follow-up. These improvements were observed specifically in domain 1 (physical health), domain 2 (psychological health) and domain 4 (environment). SUD-ADHD patients reported a nearly unchanged QoL from baseline to follow-up on all domains. Furthermore, five SUD+ADHD patients were treated with MPH at baseline and seven at follow-up. It is likely that those receiving MPH treatment at baseline would have reported a lower baseline QoL in the absence of MPH treatment, which would have meant larger differences in QoL at follow-up. However, the small sample size limited investigating this point further.

A systematic review and meta-analysis indicated that WHOQOL-BREF detects clinically meaningful changes in QoL (Skevington & Epton, 2018). Therefore, we suggest that SUD+ADHD patients' enhanced QoL is reliable and clinically relevant. Although the present study is substantially limited by its small sample sizes, particularly regarding the number of SUD+ADHD patients, it begins a discussion concerning the QoL over time of this patient group. The results may be explained either by issues specific to ADHD, such as reduced symptoms, reduced SUD symptoms or by more general issues associated with self-reporting. These possible explanations are considered in the following discussion.

There is scant research comparing the QoL of SUD+ADHD vs. SUD-ADHD populations. A longitudinal study of individuals with another complex comorbidity, bipolar disorder, both with and without SUD (Mazza et al., 2009) reported no changes in QoL in both groups a year after treatment. In addition, there is little research comparing the QoL of individuals with ADHD with and without other psychiatric disorders. A longitudinal study in adolescents showed that ADHD symptoms and co-occurrent anxiety and depression symptoms greatly affected their QoL (Pan & Yeh, 2017). Findings from these studies on SUD or ADHD plus psychiatric comorbidity conflict with the present results, which show increased QoL scores among SUD+ADHD patients at follow-up.

In the present study, most SUD+ADHD patients were diagnosed with an amphetamine SUD. Some studies of SUD+ADHD individuals with stimulant SUD have reported associations between central stimulant treatment and improved SUD and ADHD symptoms (Konstenius et al., 2014; Levin et al., 2015). Although those studies did not consider QoL, research on ADHD and SUD suggest that QoL increases as the symptoms of these disorders abate (Laudet, 2011; Picci et al., 2014). In ADHD, psychopharmacological treatment is also associated with symptom reduction and improved QoL (Agarwal et al., 2012). Based on this body of research, one interpretation of the present findings is that improvements in QoL and ADHD symptoms in SUD+ADHD patients, particularly in those with stimulant SUD, was associated with MPH treatment. Nevertheless, implying that psychopharmacological treatment reduces symptoms in SUD+ADHD individuals with a specific SUD may be an oversimplification of the complexity of SUD, as these individuals may not have a specific substance use pattern (Clure et al., 1999) or it may change over time. As for the SUD-ADHD group, the proposition that QoL changes in parallel with SUD symptoms (Laudet, 2011) is challenged by the present finding that despite reporting less SU at follow-up, SUD-ADHD patients showed almost unchanged QoL.

Studies suggest that specific ADHD symptoms are associated with QoL. For instance, severity of inattention seems to negatively affect QoL more than does hyperactivity/impulsivity (Weiss et al., 2010). Additionally, Gjervan, Torgersen, Rasmussen, and Nordahl (2014) posited that inattention was specifically related to the vitality and emotional aspects of QoL and that hyperactivity/impulsivity was related to social functioning and mental health. In the present study, SUD+ADHD patients' specific ADHD symptoms might have been associated with particular domains of QoL. However, it was not possible to test for associations between QoL and ADHD, nor could we investigate the potential effect of MPH on the QoL of SUD+ADHD patients. Such relationships should be further investigated in larger samples, using the same measurements to enable interpretation. An alternative interpretation is that because as individuals with ADHD tend to show positive appraisal bias (i.e., inflated self-perceptions) in self-

reports (Owens, Goldfine, Evangelista, Hoza, & Kaiser, 2007), it is possible that this phenomenon contributed SUD+ADHD patients' enhanced QoL evaluations. Finally, a more general interpretation of the present findings may relate to the bias implicit in prospective studies on QoL (Blome & Augustin, 2015), including recalibration (i.e., understanding the questions differently when revisited) or to social desirability (i.e., seeing one-self in a positive light and seeking acceptance from others). Social desirability has been commonly observed in the self-reports of SUD individuals (Arab et al., 2014). Accordingly, due to recalibration, SUD+ADHD patients might have interpreted their QoL differently at follow-up compared to baseline. Additionally, due to social desirability, SUD+ADHD patients may have reported better QoL, believing that they were expected to show improvements at follow-up. However, as the SUD-ADHD patients' QoL self-reports remained unchanged, it is difficult to attribute the present results to either response-shift bias or social desirability.

It was not possible to determine clearly why SUD+ADHD patients reported higher QoL scores following SUD treatment, nor how exactly these improvements were meaningful for the patients. The need to prospectively investigate what SUD+ADHD patients consider essential to enrich their QoL is highlighted by these results. Future studies should be designed to ensure inclusion of a large sample size, the use of current guidelines and recommendations to diagnose ADHD in SUD patients, and special caution in the case of naturalistic studies, because of the many uncontrolled variables inherent in these type of studies. As a suggestion for clinical practice, determining SUD+ADHD patients' baseline QoL, symptom severity, functional status, and associated goals during SUD treatment could lead to individualized interventions involving various forms of support. Subsequently, these interventions should be revisited in collaboration with the SUD+ADHD patients' support systems.

Limitations

This study has several limitations, mostly related to its small sample size, which compromised statistical inference and limited the data analysis. First, although eight out of 16 SUD+ADHD patients were reached at follow-up, overall, the retention rate was low (35%). Even though the survival analysis detected no specific variables explaining drop-out from the study by ADHD status, the samples still may have been biased. Second, women, individuals with greater symptom severity and psychiatric comorbidity, which is a characteristic consistently reported in this patient group (van Emmerik-van Oortmerssen et al., 2014) were underrepresented in the study. Consequently, the SUD+ADHD group might have had relatively better mental health than individuals in other studies. Relatedly, the findings from ASRS part A suggested some cases of subthreshold ADHD (Crunelle et al., 2018), which we did not investigate. Third, the role of MPH treatment could not be investigated further. Fourth, the study lacked information on life-productivity/functionality outcomes (e.g., employment status, functionality in everyday tasks and goals), which is important to the QoL of adults with ADHD (Brod et al., 2006). Without information on patients' functional outcomes, it was not possible to elucidate possible associations between improved QoL and functionality among SUD+ADHD patients. Fifth, in some cases, follow-ups were not conducted precisely as scheduled. Thus, the timing of the self-reported QoL was not the same for all SUD patients. Some patients might have had access to treatment for SUD/mental health problems or other types of healthcare support between discharge and follow-up. In such cases, this access may have exerted an important protective effect against

SU and may have influenced the QoL self-reports of these individuals. Conversely, we did not gather systematic information on relapse rates at follow-up, which might have affected participants' perception of QoL. Lastly, type of SUD treatment as a possible explanation for the present findings was outside the scope of the present study.

Conclusions

When assessing 12 months following treatment, SUD patients in general showed a lowered QoL compared to individuals in the general population. When divided by ADHD status, SUD+ADHD patients reported increased QoL scores from baseline to follow-up, which did not differ significantly from the NPS in most QoL domains. However, no statistical difference between SUD+ADHD vs. SUD-ADHD was observed at baseline nor at follow-up. Furthermore, SUD+ADHD patients reported a reduction (below cut-off) in ADHD symptoms as well as improvements in SUD symptoms. In spite of reporting a reduction in SUD symptoms at follow-up, SUD-ADHD patients' QoL remained unchanged, significantly differing from the NPS at both observation times. It was unclear whether factors associated with ADHD played a role in how SUD+ADHD patients evaluated their QoL. Determining whether SUD+ADHD patients' improvements in QoL are clinically meaningful should be complemented by information about patients' functional outcomes.

The authors declare no conflict of interests.

This study was funded by Northern Norway Regional Health Authority (Helse Nord RHF), research grants 3925/RUS983-10. The funding source had no role in the study design, collection, analysis or interpretation of the data, writing the manuscript, or the decision to submit the paper for publication.

References

- Agarwal, R., Goldenberg, M., Perry, R., & IsHak, W. W. (2012). The quality of life of adults with attention deficit hyperactivity disorder: a systematic review. *Innov Clin Neurosci*, 9(5-6), 10-21.
- American Psychiatric Association. (1994). *Diagnostic and statistical manual of mental disorders* (4th ed.). Washington, DC: Author.
- American Psychiatric Association. (2013). *Diagnostic and statistical manual of mental disorders* (5th ed.). Washington, DC: Author.
- Arab, M., Kohan, M., Ranjbar, H., Arab, N., Rayani, M., Mirrashidi, S. S., . . . Amiri, M. (2014). Quality of life, social desirability and their relationship in opium addicted persons in southeast of Iran. *Glob J Health Sci*, 6(3), 97-103. doi:10.5539/gjhs.v6n3p97
- Babor, T. F., Higgins-Biddle, J. C., Saunders, J. B., & Monteiro, M. G. (2001). The Alcohol Use Disorders Identification Test (AUDIT): Guidelines for use in primary care. In (2nd ed.). Geneva: World Health Organization.
- Berman, A. H., Bergman, H., Palmstierna, T., & Schlyter, F. (2005). Evaluation of the Drug Use Disorders Identification Test (DUDIT) in criminal justice and detoxification settings and in a Swedish population sample. *Eur Addict Res*, 11(1), 22-31.
- Blome, C., & Augustin, M. (2015). Measuring change in quality of life: bias in prospective and retrospective evaluation. *Value Health*, 18(1), 110-115. doi:10.1016/j.jval.2014.10.007
- Brod, M., Johnston, J., Able, S., & Swindle, R. (2006). Validation of the adult attention-deficit/hyperactivity disorder quality-of-life Scale (AAQoL): a disease-specific quality-of-life measure. *Qual Life Res*, 15(1), 117-129. doi:10.1007/s11136-005-8325-z
- Chou, Y. C., Shih, S. F., Tsai, W. D., Li, C. S., Xu, K., & Lee, T. S. (2013). Improvement of quality of life in methadone treatment patients in northern Taiwan: a follow-up study. *Bmc Psychiatry*, 13, 190. doi:10.1186/1471-244x-13-190
- Clure, C., Brady, K. T., Saladin, M. E., Johnson, D., Waid, R., & Rittenbury, M. (1999). Attention-deficit/hyperactivity disorder and substance use: symptom pattern and drug choice. *Am J Drug Alcohol Abuse e* 25(3), 441-448.
- Coghill, D. (2010). The impact of medications on quality of life in attention-deficit hyperactivity disorder: a systematic review. *CNS drugs*, 24(10), 843-866. doi:10.2165/11537450-000000000-00000
- Crunelle, C., van den Brink, W., Moggi, F., Konstenius, M., Franck, J., Levin, F. R., . . . Matthys, F. (2018). International Consensus Statement on Screening, Diagnosis and Treatment of Substance Use Disorder Patients with Comorbid Attention Deficit/Hyperactivity Disorder. *Eur Addict Res*, 24(1), 43-51. doi:10.1159/000487767
- Daepfen, J. B., Faouzi, M., Sanchez, N., Rahhali, N., Bineau, S., & Bertholet, N. (2014). Quality of life depends on the drinking pattern in alcohol-dependent patients. *Alcohol Alcohol*, 49(4), 457-465. doi:10.1093/alcalc/agu027
- Fatseas, M., Debrabant, R., & Auriacombe, M. (2012). The diagnostic accuracy of attention-deficit/hyperactivity disorder in adults with substance use disorders. *Curr Opin Psychiatry*, 25(3), 219-225.
- First, M. B., Spitzer, R. L., Gibbon, M., Williams, J. B. W., & Benjamin, L. (1995). Structured Clinical Interview for DSM-IV (SCID II). In. New York: State Psychiatric Institute.
- Flores-Garcia, L., Ytterstad, E., Lensing, M. B., & Eisemann, M. (2016). Exploring Personality and Readiness to Change in Patients With Substance Use Disorders With and Without ADHD. *J Atten Disord* doi:10.1177/1087054716677819
- Gjervan, B., Torgersen, T., Rasmussen, K., & Nordahl, H. M. (2014). ADHD symptoms are differentially related to specific aspects of quality of life. *J Atten Disord*, 18(7), 598-606.
- Gjervan, B., Torgersen, T., & Hjemdal, O. (2016). The Norwegian Translation of the Adult Attention-Deficit/Hyperactivity Disorder Quality of Life Scale: Validation and Assessment of QoL in 313 Adults With ADHD. *J Atten Disord*, doi:10.1177/1087054716640087
- Hildebrand, M. (2015). The Psychometric Properties of the Drug Use Disorders Identification Test (DUDIT): A Review of Recent Research. *J Subst Abuse Treat*, 53, 52-59.
- IBM Corp. Released 2013. IBM SPSS Statistics for Windows (Version 22.0). Armonk, NY: IBM Corp.
- Kessler, R. C., Adler, L., Ames, M., Demler, O., Faraone, S., Hiripi, E., . . . Walters, E. E. (2005). The World Health Organization Adult ADHD Self-Report Scale (ASRS): a short screening scale for use in the general population. *Psychol Med*, 35(2), 245-256.
- Kessler, R. C., Adler, L. A., Gruber, M. J., Sarawate, C. A., Spencer, T., & Van Brunt, D. L. (2007). Validity of the World Health Organization Adult ADHD Self-Report Scale (ASRS) Screener in a representative sample of health plan members. *Int J Methods Psychiatr Res*, 16(2), 52-65. doi:10.1002/mpr.208
- Kim, J. W., Park, C. S., Hwang, J. W., Shin, M. S., Hong, K. E., Cho, S. C., & Kim, B. N. (2006). Clinical and genetic characteristics of Korean male alcoholics with and without attention deficit hyperactivity disorder. *Alcohol Alcohol*, 41(4), 407-411. doi:10.1093/alcalc/agl034
- Konstenius, M., Jayaram-Lindstrom, N., Guterstam, J., Beck, O., Philips, B., & Franck, J. (2014). Methylphenidate for attention deficit hyperactivity disorder and drug relapse in criminal offenders with substance dependence: a 24-week randomized placebo-controlled trial. *Addiction*, 109(3), 440-449.
- Kronenberg, L. M., Goossens, P. J., van Etten, D. M., van Achterberg, T., & van den Brink, W. (2015). Need for care and life satisfaction in adult substance use disorder patients with and without attention deficit hyperactivity disorder (ADHD) or autism spectrum disorder (ASD). *Perspect Psychiatr Care*, 51(1), 4-15. doi:10.1111/ppc.12056
- Laudet, A. B. (2011). The case for considering quality of life in addiction research and clinical practice. *Addict Sci Clin Pract*, 6(1), 44-55.
- Lensing, M. B., Zeiner, P., Sandvik, L., & Opjordsmoen, S. (2015). Quality of life in adults aged 50+ with ADHD. *J Atten Disord*, 19(5), 405-413. doi:10.1177/1087054713480035
- Levin, F. R., Evans, S. M., Vosburg, S. K., Horton, T., Brooks, D., & Ng, J. (2004). Impact of attention-deficit hyperactivity disorder and other psychopathology on treatment retention among cocaine abusers in a therapeutic community. *Addict Behav*, 29(9), 1875-1882. doi:10.1016/j.addbeh.2004.03.041

- Levin, F. R. (2007). Diagnosing attention-deficit/hyperactivity disorder in patients with substance use disorders. *J Clin Psychiatry, 68 Suppl 11*, 9-14.
- Levin, F. R., Mariani, J. J., Specker, S., Mooney, M., Mahony, A., Brooks, D. J., . . . Grabowski, J. (2015). Extended-Release Mixed Amphetamine Salts vs Placebo for Comorbid Adult Attention-Deficit/Hyperactivity Disorder and Cocaine Use Disorder: A Randomized Clinical Trial. *JAMA Psychiatry, 72*(6), 593-602. doi:10.1001/jamapsychiatry.2015.41
- Luderer, M., Kaplan-Wickel, N., Richter, A., Reinhard, I., Kiefer, F., & Weber, T. (2018). Screening for adult attention-deficit/hyperactivity disorder in alcohol dependent patients: Underreporting of ADHD symptoms in self-report scales. *Drug Alcohol Depend, 195*, 52-58. doi:10.1016/j.drugalcdep.2018.11.020
- Mathiesen, E. F., Nome, S., Eisemann, M., & Richter, J. (2012). Drinking patterns, psychological distress and quality of life in a Norwegian general population-based sample. *Qual Life Res, 21*(9), 1527-1536. doi:10.1007/s11136-011-0080-8
- Mazza, M., Mandelli, L., Di Nicola, M., Harnic, D., Catalano, V., Tedeschi, D., . . . Janiri, L. (2009). Clinical features, response to treatment and functional outcome of bipolar disorder patients with and without co-occurring substance use disorder: 1-year follow-up. *J Affect Disord, 115*(1-2), 27-35. doi:10.1016/j.jad.2008.08.019
- Moura, H. F., Faller, S., Benzano, D., Szobot, C., von Diemen, L., Stolf, A. R., . . . Kessler, F. H. (2013). The effects of ADHD in adult substance abusers. *J Addict Dis, 32*(3), 252-262. doi:10.1080/10550887.2013.824359
- Ortal, S., van de Glind, G., Johan, F., Itai, B., Nir, Y., Iliyan, I., & van den Brink, W. (2015). The Role of Different Aspects of Impulsivity as Independent Risk Factors for Substance Use Disorders in Patients with ADHD: A Review. *Curr Drug Abuse Rev, 8*(2), 119-133.
- Owens, J. S., Goldfine, M. E., Evangelista, N. M., Hoza, B., & Kaiser, N. M. (2007). A critical review of self-perceptions and the positive illusory bias in children with ADHD. *Clin Child Fam Psychol Rev, 10*(4), 335-351. doi:10.1007/s10567-007-0027-3
- Pan, P. Y., & Yeh, C. B. (2017). Impact of depressive/anxiety symptoms on the quality of life of adolescents with ADHD: a community-based 1-year prospective follow-up study. *Eur Child Adolesc Psychiatry, 26*(6), 659-667. doi:10.1007/s00787-016-0929-z
- Pasareanu, A. R., Opsal, A., Vederhus, J. K., Kristensen, O., & Clausen, T. (2015). Quality of life improved following in-patient substance use disorder treatment. *Health Qual Life Outcomes, 13*, 35. doi:10.1186/s12955-015-0231-7
- Picci, R. L., Oliva, F., Zuffranieri, M., Vizzuso, P., Ostacoli, L., Sodano, A. J., & Furlan, P. M. (2014). Quality of life, alcohol detoxification and relapse: is quality of life a predictor of relapse or only a secondary outcome measure? *Qual Life Res, 23*(10), 2757-2767. doi:10.1007/s11136-014-0735-3
- R Core Team. (2015). R: A language and environment for statistical computing. Vienna, Austria: R Foundation for Statistical Computing. Retrieved from <https://www.R-project.org/>
- Rumpf, H. J., Wohler, T., Freyer-Adam, J., Grothues, J., & Bischof, G. (2013). Screening questionnaires for problem drinking in adolescents: performance of AUDIT, AUDIT-C, CRAFFT and POSIT. *Eur Addict Res, 19*(3), 121-127.
- Saunders, J. B., Aasland, O. G., Babor, T. F., de la Fuente, J. R., & Grant, M. (1993). Development of the Alcohol Use Disorders Identification Test (AUDIT): WHO Collaborative Project on Early Detection of Persons with Harmful Alcohol Consumption--II. *Addiction, 88*(6), 791-804.
- Sheehan, D., Janavs, J., Baker, R., Harnett-Sheehan, K., Knapp, E., & Sheehan, M. (1994). Mini International Neuropsychiatric Interview. In: University of South Florida, Tampa.
- Skevington, S. M., & Epton, T. (2018). How will the sustainable development goals deliver changes in well-being? A systematic review and meta-analysis to investigate whether WHOQOL-BREF scores respond to change. *BMJ Glob Health, 3*(Suppl 1), e000609. doi:10.1136/bmjgh-2017-000609
- Sosial-og Helsedirektoratet, 2007. Veileder i diagnostikk og behandling av AD/HD : diagnostikk og behandling av hyperkinetisk forstyrrelse/attention deficit hyperactivity disorder (AD/HD) hos barn, ungdom og voksne (IS 1244), revidert utgave ed. Sosial-og Helsedirektoratet, Oslo, Norway. [Norwegian Directorate for Health and Social Affairs, 2007. Guide to diagnosis and treatment of AD/HD: Diagnosis and treatment of hyperkinetic disorder/attention deficit hyperactivity disorder (AD/HD) in children, adolescents and adults (IS 1244)]. Oslo, Norway: Author.
- Taylor, A., Deb, S., & Unwin, G. (2011). Scales for the identification of adults with attention deficit hyperactivity disorder (ADHD): a systematic review. *Res Dev Disabil, 32*(3), 924-938. doi:10.1016/j.ridd.2010.12.036
- The WHOQOL Group. (1998). Development of the World Health Organization WHOQOL-BREF quality of life assessment. *Psychol Med, 28*(3), 551-558.
- Tracy, E. M., Laudet, A. B., Min, M. O., Kim, H., Brown, S., Jun, M. K., & Singer, L. (2012). Prospective patterns and correlates of quality of life among women in substance abuse treatment. *Drug Alcohol Depend, 124*(3), 242-249. doi:10.1016/j.drugalcdep.2012.01.010
- Uchida, M., Spencer, T. J., Faraone, S. V., & Biederman, J. (2015). Adult Outcome of ADHD: An Overview of Results From the MGH Longitudinal Family Studies of Pediatrally and Psychiatrically Referred Youth With and Without ADHD of Both Sexes. *J Atten Disord, 19*(10), 1177-1187. doi:10.1177/1087054715604360
- Umar, M. U., Salihu, A. S., & Owolabi, S. D. (2017). Prevalence and correlates of ADHD in individuals with substance use disorder in Nigeria. *Atten Defic Hyperact Disord, 9*(3), 189-198. doi:10.1007/s12402-017-0218-9
- van de Glind, G., van den Brink, W., Koeter, M. W. J., Carpentier, P.-J., van Emmerik-van Oortmerssen, K., Kaye, S., . . . Levin, F. R. (2013). Validity of the Adult ADHD Self-Report Scale (ASRS) as a screener for adult ADHD in treatment seeking substance use disorder patients. *Drug Alcohol Depend, 132*(3), 587-596.
- van de Glind, G., Konstenius, M., Koeter, M. W. J., van Emmerik-van Oortmerssen, K., Carpentier, P.-J., Kaye, S., . . . Young, J. (2014). 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. *Drug Alcohol Depend, 134*, 158-166.
- van Emmerik-van Oortmerssen, K., van de Glind, G., Koeter, M. W. J., Allsop, S., Auriacombe, M., Barta, C., . . . Young, J. T. (2014). Psychiatric comorbidity in treatment-seeking substance use disorder patients with and

- without attention deficit hyperactivity disorder: results of the IASP study. *Addiction*, *109*(2), 262-272. doi:10.1111/add.12370
- van Emmerik-van Oortmerssen, K., Vedel, E., Kramer, F. J., Blankers, M., Dekker, J. J. M., van den Brink, W., & Schoevers, R. A. (2019). Integrated cognitive behavioral therapy for ADHD in adult substance use disorder patients: Results of a randomized clinical trial. *Drug Alcohol Depend*, *197*, 28-36. doi:10.1016/j.drugalcdep.2018.12.023
- Volkow, N. D., & Baler, R. D. (2014). Addiction science: Uncovering neurobiological complexity. *Neuropharmacology*, *76 Pt B*, 235-249.
- Weiss, M. D., Gibbins, C., Goodman, D. W., Hodgkins, P. S., Landgraf, J. M., & Faraone, S. V. (2010). Moderators and mediators of symptoms and quality of life outcomes in an open-label study of adults treated for attention-deficit/hyperactivity disorder. *J Clin Psychiatry*, *71*(4), 381-390. doi:10.4088/JCP.08m04709pur
- World Health Organization: (1992). *The ICD-10 classification of mental and behavioural disorders: Clinical descriptions and diagnostic guidelines*. Geneva, Switzerland: Author.