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CLINICAL PSYCHOLOGY & NEUROPSYCHOLOGY | RESEARCH ARTICLE

Predictors of problematic substance use 18 years after treatment: a longitudinal cohort study of persons with substance use disorders

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Abstract: Objective: To examine the extent of substance use and explore which baseline factors predicted current problematic substance use 18 years after treatment in surviving patients. **Methods**: This longitudinal cohort study used a mailed self-report questionnaire on a group of patients with long-term problematic substance use, and high psychiatric comorbidity, 18 years after they received treatment for substance use disorders. A consecutive sample of patients with substance use disorders (*n* = 287, mean age 38.6 years, 72% male; 45% alcohol use disorder only and 55% other substance use disorders) was recruited in 1997 and 1998. Baseline measurements included the Composite International Diagnostic Interview, the Millon Clinical Multiaxial Inventory II, the Hopkins Symptom Checklist 25 and demographic data. In the 18-year follow-up study (*n* = 91), the Alcohol Use Disorders Identification Test and the Drug Use Disorders Identification Test were used. A multivariate logistic regression analysis was used to identify predictors of having current problematic substance use 18 years after treatment for participants with full data collection at baseline (*n* = 75). **Results**: Of the 91 participants who responded at the 18-year follow-up study, 47 (52%) had no current problematic substance use and 44 (48%) had current problematic substance use during the past 12 months. Of participants with no current problematic

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PUBLIC INTEREST STATEMENT

Most persons with severe substance use disorders also have mental disorders. This comorbidity makes treatment complex and is associated with poor outcomes for both disorders, leading to poor quality of life and high costs for society. Finding early risk-factors for poor long-term outcomes is important for the development of tailored effective treatment programs. The knowledge on the long-term course of substance use in persons with comorbid substance use and mental disorders is limited. We have done a follow-up study on patients with substance use disorders and mental disorders who entered specialized treatment for substance use problems 18 years ago. We examined the extent of substance use, and explored if there were risk-factors for having problematic substance use 18 years after treatment. Close to half of the patients still had problematic substance use, and high mental distress at baseline predicted having problematic substance use 18 years later.

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substance use, 17 (36%) reported total abstinence from alcohol, illicit substances and misuse of pharmaceuticals during the past 5 years. Mental distress measured with the Hopkins Symptom Checklist 25 at baseline predicted having current problematic substance use 18 years after treatment (*n* = 75). **Conclusions**: In a group of patients with long lasting substance use disorders and high psychiatric comorbidity that entered treatment, close to half of those participating at a follow-up study had current problematic substance use during the past 12 months 18 years later. Mental distress at baseline predicted having current problematic substance use 18 years after treatment, adjusted for other factors. Self-reported general mental health symptoms can be a relevant predictor of the long-term course of substance use disorders.

1. Introduction

Remission and relapse rates over time vary between substances and subgroups of persons with substance use disorders (SUDs), and persons can fluctuate between periods of problematic use, nonproblematic use and abstinence (Heyman, 2013). The literature on predictors of outcome of SUDs is inconsistent, but emphasized general factors are: age of SUD onset (Landheim, Bakken, & Vaglum, 2006), SUD severity and type or number of substances used, psychiatric comorbidity, psychological factors such as negative affective states, coping skills and motivation, length of treatment, sleep, and genetic and socioeconomic factors (Ciraulo, Piechniczek-Buczek, & Iscan, 2003). There are few longitudinal studies on outcome predictors in patients with polysubstance use (Andreas, Lauritzen, & Nordfjaern, 2015), but we have previously shown in a clinical cohort of patients with different SUDs that lifetime major depressive disorder is a predictor of having problematic substance use 6 years after entering SUD-treatment (Landheim et al., 2006). Examples of outcome predictors on specific SUDs show that for patients with alcohol use disorder (AUD) low self-efficacy and avoidant coping-strategies are predictors of alcohol use relapse 16 years later (Moos & Moos, 2006), while, surprisingly, childhood psychological vulnerabilities do not predict long-term alcohol use relapse (Valliant, 1995). For opioid dependence high self-efficacy and low psychological distress predict stable recovery 10 years later (Hser, 2007), while exposure to physical or sexual abuse and comorbid mental disorders predict continued opioid use (Hser, Evans, Grella, Ling, & Anglin, 2015).

Different aspects of mental health, including mental disorders, appear relevant for understanding substance use relapse and the long-term course of SUDs. High comorbidity between SUDs and mental disorders is well documented (Lai, Cleary, Sitharthan, & Hunt, 2015; Landheim, Bakken, & Vaglum, 2002; Regier et al., 1990). This comorbidity reduces quality of life (Colpaert, De Maeyer, Broekaert, & Vanderplasschen, 2012) and leads to lower treatment adherence (Weiss, Smith, Hull, Piper, & Huppert, 2002) and poorer treatment outcome (Bahorik, Newhill, & Eack, 2013), including increased SUD severity and more frequent relapses and hospitalizations (Morisano, Babor, & Robaina, 2014). The relationships, including the causal direction, between different types and levels of SUDs and various mental health problems continue to be debated (Kessler, 2004; Swendsen et al., 2010). Research on clinical cohorts with severe SUDs is demanding and complex, and there is a paucity of longitudinal studies, especially of polysubstance use and predictors of outcomes and the severity of long-term SUDs. Progress in understanding the long-term course of SUDs will require prospective studies with long observational times on heterogeneous clinical

cohorts. Improved understanding is important for the development of tailored effective prevention and treatment programs for a diverse group of patients.

The current study examined a heterogeneous cohort of patients with long lasting problematic use of various substances when entering specialized treatments for substance abuse 18 years ago. The cohort had high comorbidity with lifetime mental disorders assessed at baseline. The aims were to examine the extent of substance use, and explore which baseline factors predicted the presence of problematic substance use 18 years after treatment in surviving participants.

2. Methods

2.1. Design
This was a longitudinal cohort study with an observation period of 18 years. Patients entering specialized treatment for SUDs in public facilities in two Norwegian counties in 1997 and 1998 were invited to participate in the study (baseline). A follow-up study was conducted by questionnaire to living participants approximately 18 years later (the 18-year follow-up study). The study protocol was reviewed and approved at baseline and the 18-year follow-up by the Regional Committee for Medical and Health Research Ethics, Health Region South-East (ID 2014/1936 C). All participants gave their written consent before taking part in the study, and to be contacted for follow-up studies.

2.2. Sample
At baseline, 287 patients with SUDs (mean age 38.6 years ± standard deviation [SD] 11.3 years, 72% male) were recruited. Among these patients 130 (45%) had only AUD and 157 (55%) other SUDs, 166 (58%) came from six inpatient units and 121 (42%) from three outpatient units. At baseline, the prevalence of lifetime mental disorders (other than SUDs and personality disorders) in the sample was 91%; 83% had lifetime anxiety disorder, 65% had lifetime affective disorder, and 63% had three or more lifetime mental disorders (Landheim et al., 2002). The most prevalent lifetime mental disorders at baseline (other than SUD and personality disorders) was agoraphobia with or without panic (48%), social phobia (47%), specific phobia (46%) and major depressive disorder (44%). The mean duration since first onset SUD at baseline was 13.8 years (SD 8.8 years) and 46% had SUD onset before the age of 18 years. Among the patients with other SUDs than only AUD; 53% had lifetime opioid dependence, 50% stimulant dependence, 50% sedative, hypnotic or anxiolytic dependence, 42% cannabis dependence and 66% also had lifetime alcohol dependence. Among the patients with other SUDs than only AUD, the mean number of lifetime SUDs was 3.6 (SD = 2.0). Sampling, subjects and methods at baseline have been previously described more extensively (Landheim, Bakken, & Vaglum, 2003; Landheim et al., 2006). Compared with a national sample (*n* = 5000) of patients in facilities for specialized treatment for SUD in Norway in the same period, our sample was skewed toward having older patients with a longer duration of SUD and a higher frequency of AUD (Landheim et al., 2003).

The 18-year follow-up study was conducted between October 2015 and March 2016 by a mailed by post questionnaire to living participants, approximately 18 years after entering treatment. The questionnaire included a return-envelope with postage paid, a general description of the study, a form to decline participation, and an offer that participants who answered and returned the questionnaire within approximately 3 weeks, would receive 400 Norwegian kroner (~ 43 euros in 2016) to their reported bank account. Participants were informed that estimated time to fill out the questionnaire was between 30 and 60 minutes. There was no means to monitor when, how or where participants answered the questionnaire. The questionnaire was sent out a second time to participants who did not respond the first time. Those still not responding were contacted once by telephone to confirm that they had received the questionnaire. In the 18-year follow-up study, 91 (32%) subjects participated (mean age 54.9 ± 10.0 years, 70% male), 93 (32%) subjects were deceased (mean age 53.5 ± 11.7 years at time of death, 80% male) and 103 (36%) did not participate (mean age 53.2 ± 10.9 years, 67% male (21 declined, 10 were not located and 72 did not respond)).

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2.3. Measurements

Baseline: For all measurements in the study, the Norwegian versions used in clinical practice and research were used. The Composite International Diagnostic Interview (CIDI), Norwegian computer version, a structured personal psychiatric interview based on DSM-IV criteria and the corresponding lifetime nonhierarchical diagnoses in the ICD-10 (Robins et al., 1988) were used. The reliability of the CIDI has been demonstrated to be excellent, and the validity to be adequate (Andrews & Peters, 1998). The Millon Clinical Multiaxial Inventory II (MCMI-II), a self-report psychiatric diagnostic (DSM-III-R) inventory (Choca, Shanley, & Van Denburg, 1992) was used to measure current personality disorders. The manual states that the MCMI-II has acceptable test-retest reliability, good internal consistency, and generally acceptable levels of validity (Millon, 1987), but there has also been raised concerns about insufficient stability (Zimmerman, 1994), and overdiagnosis among persons with SUDs (Flynn, McCann, & Fairbank, 1995) for the personality disorders. Personality disorder diagnoses were given using a cutoff base-rate score of 85 or higher. The Hopkins Symptom Checklist-25 (HSCL-25), a self-report instrument consisting of 25 items on a four-point scale, mainly anxiety and depression symptoms, was used to measure mental distress during the last week (Derogatis, Lipman, Rickels, Uhlenhuth, & Covi, 1974). The HSCL-25 has proved satisfactory validity and reliability as a measure of mental distress (Strand, Dalgard, Tambs, & Rognerud, 2003). The Norwegian National Client Assessment form (Gerdts & Iversen, 2000) which covers information on sociodemographics and treatment history was also used.

The 18-year follow-up: the Alcohol Use Disorders Identification Test (AUDIT) (Saunders, Aasland, Babor, De la Fuente, & Grant, 1993) and the Drug Use Disorders Identification Test (DUDIT) (Berman, Bergman, Palmstierna, & Schlyter, 2004), both self-report screening instruments for identifying problematic use of substances during the past 12 months were also used. The AUDIT consists of 10 items and a cutoff score of 8 or more for men and 6 or more for women was used. A review concluded that the AUDIT is psychometrically sound and that research on validity consistently confirms sensitivities and specificities comparable to and generally exceeding those of other alcohol use screening methods (Reinert & Allen, 2007). The DUDIT has 11 items and a cutoff score of 6 or more for men and 2 or more for women was used. A review concluded that the DUDIT yields satisfactory measures of reliability and validity for use as a clinical or research tool (Hildebrand, 2015). Questions on use of alcohol, illicit substances, and misuse of pharmaceuticals during the last 5 years were also included in the questionnaire. Participants in the 18-year follow-up study were divided into those with "no current problematic substance use" (AUDIT < cutoff and DUDIT < cutoff during the past 12 months at the 18-year follow-up) and participants with "current problematic substance use" (AUDIT ≥ cutoff and/or DUDIT ≥ cutoff during the past 12 months at the 18-year follow-up).

The HSCL-25 was not answered at baseline by 13 of the participants in the 18-year follow-up study, and the MCMI-II was not answered at baseline by 8 of the participants in the 18-year follow-up study. There were no missing items on AUDIT, DUDIT or other relevant measurements in the 18-year follow-up study.

Figure 1 shows a flow diagram illustrating participation and loss of participants during the study, and the foundation for analyzed data.

Table 1 provides characteristics as age, gender and selected factors regarding substance use and mental health measured at baseline for participants (*n* = 91), nonparticipants (*n* = 103) and deceased (*n* = 93) in the 18-year follow-up study. A comparison with bivariate simple statistical tests between participants and nonparticipants showed no significant differences (Table 1). We also compared the participants in the 18-year follow-up study with complete data collection at baseline (*n* = 75) with nonparticipants (*n* = 103) and still did not find significant differences between the groups. A comparison between the participants (*n* = 91) and the deceased (*n* = 93) in the 18-year follow-up study, displayed in Table 1, showed that the deceased were older, more seldom had onset first SUD before age 18 years, shorter duration

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Figure 1. Flow diagram; partici-pants, data collection and ana-lyzed data during the study.
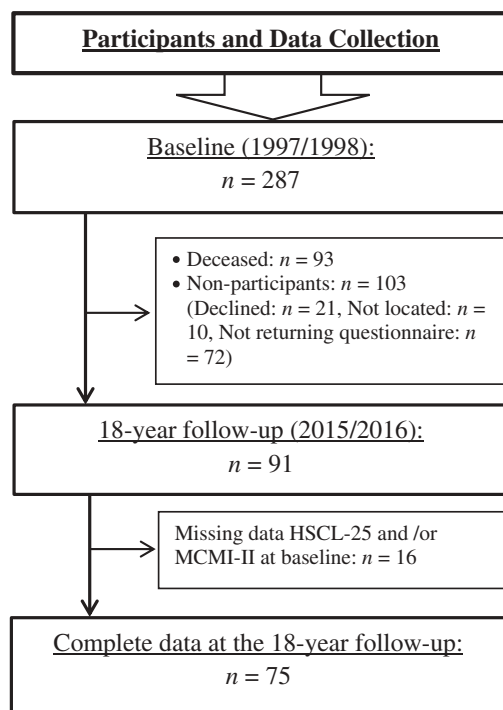
since first onset SUD, more often had only AUD, more seldom had lifetime affective disorder and more often received inpatient treatment at baseline (all *p* < 0.05).

2.4. Statistical analysis

Participants were compared with nonparticipants and deceased, and participants with no current problematic substance use were compared with participants with current problematic substance use at the time of the 18-year follow-up study using demographic variables, mental disorders, mental distress and substance use variables measured at baseline with simple statistical tests: χ2-test for categorical variables, and t-tests and Mann–Whitney *U* tests for continuous variables. Because of restricted sample size in the 18-year follow-up study, separate mental disorders at baseline were clustered into lifetime affective disorders, lifetime anxiety disorders, and current personality disorders.

A logistic regression model giving odds ratios (OR) and 95% confidence intervals (95% CI) of having current problematic substance use at the time of the 18-year follow-up study was con-structed for participants with complete data collection at baseline and at the 18-year follow-up study (*n* = 75). All covariates with *p* < 0.2 (Hosmer & Lemeshow, 2000) from the unadjusted analysis, plus age and gender, were included in a multivariate analysis. All correlations between covariates were < 0.7. In the multivariate model, *p* < 0.05 was considered significant and defined "predictor".

All analyses were conducted using IBM SPSS Statistics for Windows (version 23.0; IBM Corp., Armonk, NY).

3. Results

In the 18 year follow-up, 47 (52%) participants had no current problematic substance use and 44 (48%) had current problematic substance use during the past 12 months. Among the participants with no current problematic substance use at the 18-year follow-up, 26 (55%) reported no use of alcohol or illicit substances, while 21 (45%) used alcohol or illicit substances, or both, under the cutoff values during the past 12 months. During the 5 years immediately preceding the 18-year follow-up study, 17 (36%) of the participants with no current problematic substance use reported

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Table 1. Characteristics of participants, nonparticipants and deceased in the follow-up 18 years after treatment

		Participants (*n* = 91)	Nonparticipants (*n* = 103)	*p*[a]	Deceased (*n* = 93)	*p*[b]
Gender (male)	*n* (%)	64 (70)	69 (67)	0.617[c]	74 (80)	0.148[c]
Age, years at baseline	mean (SD)	36.5 (10.1)	34.7 (10.8)	0.218[d]	44.2 (11.1)	<0.001[d]
Onset SUD before age 18 years	*n* (%)	50 (55)	46 (45)	0.153[c]	35 (38)	0.019[c]
Duration since first SUD, years at baseline	mean (SD)	13.5 (8.3)	11.7 (8.0)	0.111[d]	16.2 (9.6)	0.047
Only AUD (vs.other SUDs) baseline	*n* (%)	36 (40)	34 (33)	0.343[c]	60 (65)	0.001[c]
Lifetime affective disorders baseline	*n* (%)	63 (72)	69 (68)	0.556[c]	47 (51)	0.004[c]
Lifetime anxiety disorders baseline	*n* (%)	74 (82)	83 (84)	0.767[c]	72 (80)	0.703[c]
Number of personality disorders baseline	mean (SD)	2.8 (2.5)	2.7 (2.8)	0.595[d]	2.7 (2.8)	0.407[d]
HSCL–25 baseline	mean (SD)	2.14 (0.57)	2.02 (0.63)	0.134[d]	1.97 (0.54)	0.060[d]
Inpatient treatment at baseline	*n* (%)	44 (48)	59 (57)	0.214[c]	63 (68)	0.008[d]

[a]Comparison between participants and nonparticipants

[b]Comparison between participants and deceased

[c] χ2-test

[d]Mann-Whitney *U* test

SUD = Substance Use Disorder

AUD = Alcohol Use Disorder

HSCL-25 = Hopkins Symptom Check List 25

SD = Standard Deviation

total abstinence from any substance use (alcohol, illicit substances, and misuse of pharmaceuticals). For the participants with current problematic substance use at the 18-year follow-up, the mean score on the AUDIT was 13.8 (SD = 11.4) and that on the DUDIT was 12.1 (SD = 11.8).

Table 2 shows a comparison for participants with complete data collection (*n* = 75) between those with no current problematic substance use (52%) and those with current problematic substance use (48%) at the time of the 18-year follow-up using selected demographic, mental health, and substance use variables. We found no differences between the groups on gender, age, status as married/cohabiting, educational level, having full-time ordinary work at baseline, lifetime affective or anxiety disorders, number of mental disorders, number of SUDs or having only AUD at baseline (all *p* > 0.05). Participants with current problematic substance use had more personality disorders at baseline (3.69 vs. 2.28, *p* = 0.013), scored higher on mental distress measured by the HSCL-25 at baseline (mean score 2.34 vs. 1.98, *p* = 0.006) and were younger at first onset of SUD (19.3 vs. 22.5 years, *p* = 0.035) compared to those with no current problematic substance use. Although the subgroups were small, we also compared the groups on specific lifetime mental disorders instead of clustered lifetime affective or anxiety disorders (not shown in the table). Participants with current problematic substance use more often had lifetime agoraphobia with or without panic disorder at baseline than participants with no current problematic substance use (60% vs. 36%, *p* = 0.038), while there were no differences between the groups for lifetime major depressive (50% vs. 54%, *p* = 0.729), specific phobia (47% vs. 40%, *p* = 0.501), social phobia (49% vs. 46%, *p* = 0.844), post-traumatic stress (14% vs. 23%, *p* = 0.308), and somatization (25% vs. 29%, *p* = 0.702) disorder at baseline.

Table 3 shows the results from a logistic regression model (*n* = 75) using selected predictors, based on results presented in Table 2, of having current problematic substance use at the time of the 18-year follow-up study. HSCL-25 mean score at baseline was a significant predictor of having current problematic substance use at the time of the 18-year follow-up study (OR = 3.24, 95% CI 1.08–9.68, *p* = 0.035), when adjusted for gender, age, number of personality disorders at baseline, and age at onset first SUD.

4. Discussion

In a group of patients with long-term problematic substance use and high psychiatric comorbidity that entered SUD treatment, close to half of those participating in a follow-up study had current problematic substance use 18 years later. Only one-fifth reported total abstinence during the 5 years preceding the 18-year follow-up. Mental distress at baseline was a predictor of having current problematic substance use at the time of the 18-year follow-up study, and also when adjusted for other factors. Various demographic factors, lifetime mental disorders, personality disorders, and substance use factors at baseline were not found to be predictors of having current problematic substance use 18 years after treatment.

Despite the high extent of substance use, there was a decrease over time. All participants had one or several SUDs at baseline and only about half of the participants had current problematic substance use at the 18-year follow-up. At the time of the 6-year follow-up study of this cohort (Landheim et al., 2006), more than two thirds of the participants at the 18-year follow-up had current problematic substance use, indicating a gradual decrease in problematic substance use over time. This finding is consistent with a review on the long-term course of opioid addiction in clinical samples (Hser et al., 2015), and a general decrease in problematic substance use over time found in several longitudinal clinical dual-diagnosis studies (Drake et al., 2006; Xie, Drake, McHugo, Xie, & Mohandas, 2010) and epidemiological studies (Heyman, 2013). In our cohort participants had high psychiatric comorbidity with long duration and high severity of SUD, which are features often associated with poor outcomes (Ciraulo et al., 2003; Morisano et al., 2014). Prognosis for the long-term course of SUD will probably be better in cohorts with a shorter duration of SUD and lower psychiatric comorbidity.

Mental distress measured at baseline was found to be a predictor of having current problematic substance use at the time of the 18-year follow-up study. Negative affective states are a known

Table 2. Comparison between participants with no current problematic substance use and current problematic substance use 18 years after treatment.*

		No current problematic substance use (n = 39)	Current problematic substance use (n = 36)	p
Demographics				
Gender, male	n (%)	27 (69)	28 (78)	0.403[a]
Age, years at the 18-year follow-up study	mean (SD)	56.5(10.9)	53.6(8.6)	0.212[c]
Married or cohabitant at baseline	n (%)	13 (34)	16 (44)	0.367[a]
Completed upper secondary school at baseline	n (%)	19 (51)	18 (50)	0.908[a]
Full-time ordinary work at baseline	n (%)	8 (21)	9 (25)	0.687[a]
Mental health				
Diagnoses CIDI nonhierarchical lifetime at baseline				
Affective disorder	n (%)	29 (76)	26 (74)	0.841[a]
Anxiety disorder	n (%)	31 (80)	38 (89)	0.290[a]
Number of mental disorders (minus SUD and personality disorders)	mean (SD)	3.67 (2.68)	3.75 (2.35)	0.668[b]
Personality disorders MCMI-II at baseline				
Number of personality disorders	mean (SD)	2.28 (2.43)	3.69 (2.51)	0.013[b]
Mental distress				
HSCL-25 at baseline	mean (SD)	1.98 (0.49)	2.34 (0.59)	0.006[c]
Substance use				
Number of SUDs at baseline	mean (SD)	2.46 (1.83)	2.72(2.15)	0.827[b]
Age onset SUD	mean (SD)	22.5 (9.7)	19.3 (8.5)	0.035[b]
Only AUD (vs. other SUDs) at baseline	n (%)	17 (44)	16 (44)	0.941[a]

*Participants with complete data collection at baseline and the 18-year follow-up study (n = 75)

[a]χ2-test.

[b]Mann-Whitney U test.

[c]Independent samples t-test.

CIDI = Composite International Diagnostic Interview

SUD = Substance Use Disorder

MCMI-II = The Millon Clinical Multiaxial Inventory II

HSCL-25 = Hopkins Symptom Check List 25

AUD = Alcohol Use Disorder

SD = Standard Deviation

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Table 3. Bivariate and multivariate logistic regression analysis of having current problematic substance use 18 years after treatment

		Logistic regression model (*n* = 75)					
		Bivariate[a]			**Multivariate[b,c]**		
	n (%)/mean (SD)	**OR**	**95% CI**	**p**	**OR**	**95% CI**	**p**
Demographics							
Gender (male)	55 (73)	0.64	0.23–1.82	0.405	0.69	0.21–2.24	0.536
Age	55.1 (9.9)	0.97	0.93–1.02	0.210	0.98	0.92–1.05	0.629
Mental health at baseline							
Number of personality disorders	3.0 (2.5)	1.26	1.04–1.53	0.019	1.09	0.86 – 1.38	0.479
HSCL–25 mean score	2.15 (0.57)	3.40	1.37–8.49	0.009	3.24	1.08–9.68	0.035
Substance use at baseline							
Age onset SUD	21.0 (9.2)	0.96	0.91–1.01	0.142	0.96	0.90–1.04	0.335

[a]Bivariate unadjusted analysis for having current problematic substance use at the 18-year follow-up study

[b]Multivariate adjusted analysis for having current problematic substance use at the 18-year follow-up study, with all covariates that reached p < 0.2, plus gender and age, in the bivariate analysis.

[c]Nagelkerke`s R[2] for the multivariate analysis was 0.210 and the Hosmer-Lemeshow goodness of fit test was χ2- = 3.134, df = 7, p = 0.872.

HSCL–25 = Hopkins Symptom Check List 25

SUD = Substance Use Disorder

SD = Standard Deviation

OR = Odds Ratio

CI = Confidence Interval

predictor of SUD relapse (Ciraulo et al., 2003), and our results are consistent with earlier findings that psychological distress predicted substance use 10 years later in a clinical cohort with opioid dependence (Hser, 2007). An association between mental distress measured by the HSCL-25 and the long-term course of SUD has also been reported (Andreas et al., 2015). Our multivariate analysis has substantial unexplained variance and several potential predictors (e.g. treatment after baseline, genetic or biological variables) were not adjusted for. It is likely that mental distress and SUDs have a bidirectional relationship over time, and have shared genetic predisposition (Kendler, Prescott, Myers, & Neale, 2003).

Psychiatric diagnoses were not found to predict current problematic substance use at the 18-year follow-up, which differs from findings in a review on relapse among individuals diagnosed with co-occurring mental health and substance use disorders (Bradizza, Stasiewicz, & Paas, 2006). It also differs from the 6-year follow-up of the same cohort where lifetime major depressive disorder at baseline was a predictor of having current problematic substance use (Landheim et al., 2006). This could be an effect of differences between participants at the 6-year and 18-year follow-up studies because of loss of participants to death and nonparticipation, although statistical comparisons do not support this interpretation. Negative results on diagnoses may be related to clustering single diagnoses into "affective" or anxiety "disorders", or sample size limitations on single diagnoses, but secondary bivariate or multivariate statistical analysis do not support such effects. High baseline prevalence of both affective and anxiety disorders in the cohort can make differences difficult to detect (cf. Berkson`s fallacy (Sackett, 1979)). At baseline psychiatric diagnosis was measured as lifetime instead of current diagnosis. This does not likely explain the negative result for psychiatric diagnoses, because analyzing diagnosis during the previous 12 months at baseline gave the same results as lifetime diagnosis. Negative findings for psychiatric diagnoses could also be related to differences between results for structured diagnostic interviews, as we used, compared with diagnoses set by clinical experts, who likely set fewer diagnoses (Andrews & Peters, 1998). Another interpretation could be that measures from self-administered continuous symptom items yield better predictive results for the long-term course of substance use than responses to dichotomous diagnostic items in personal interviews. If these results are valid, one interpretation may be that predictors of substance use relapse change over time. This seems to be the case when we compare results for, for example, mental distress and lifetime major depressive disorders at baseline as predictors of having current problematic substance use at 6-year follow-up versus 18-year follow-up. Psychiatric diagnoses with defined clusters of symptoms may be better short-term predictors, while general mental health symptoms may be more relevant predictors of the long-term course of SUDs. Studies that find mental disorders as predictors of substance use relapse typically have shorter observation times than 18 years (Bradizza et al., 2006).

At the 6-year follow-up study on this cohort, early onset of SUD was a predictor of having current problematic substance use (Landheim et al., 2006), but age at onset SUD was not found to be a predictor in the 18-year follow-up study. This negative finding for early onset SUD can be an effect of the cohort being skewed toward higher frequency of AUD and older patients at baseline and loss of participants to death and nonparticipation in the 18-year follow-up study.

4.1. Limitations
Our cohort with long lasting SUDs and high psychiatric comorbidity at baseline, is clearly vulnerable to selection bias (Sackett, 1979). A substantial decrease of participants because of mortality and nonparticipation is inevitable in such a cohort, and may lead to attrition bias. As shown in Table 1, there were differences in baseline characteristics as age, onset, duration and type of SUD, affective disorders or type of treatment received at baseline between participants and deceased at the 18-year follow-up that may have influenced the results. Although we found no differences in baseline characteristics between participants and nonparticipants, there may be systematic differences between the groups. Few participants and small subgroups, especially on specific psychiatric diagnosis, at the 18-year follow-up can possibly cause type-II statistical errors (Liebert & Liebert, 1995).

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Current substance use and mental distress may influence participation and the proportions of participants with or without current problematic substance use at the 18-year follow-up study. There can also be problems in measuring lifetime mental disorders at baseline in temporal proximity to substance abuse. Especially the MCMI-II can generate false-positive personality disorder diagnoses (Flynn, 1995) and lack stability (Samuel et al., 2011; Zimmerman, 1994). Also, it is not optimal that the personality disorder diagnoses correspond to the DSM-III-R which is older and somewhat different to the DSM-IV and ICD-10 which are used for the other diagnoses from CIDI in the study. All data at the time of the 18-year follow-up study were self-reported and can be prone to recall bias (Coughlin, 1990) and skewed self-presentation (Mortel, 2008), which may lead to both under- or over reporting of substance use depending of subjects` current state while filling out the questionnaire. There was no monitoring of the self-reported data, so we do not know number of sessions or time used to answer the questions, issues which may affect the quality of the data.

The main strengths of the study were the 18-year observation time, a heterogeneous clinical cohort with long-term problematic substance use and a thorough diagnostic investigation with structured personal interviews at baseline. Despite possible limitations, this study provides useful unique data on the long-term course of SUDs and may help to direct future research.

4.2. Conclusions

In a group of patients with long lasting SUDs and high psychiatric comorbidity who entered SUD treatment, close to half of those participating in a follow-up study had current problematic substance use 18 years later. Mental distress at baseline was a predictor of having current problematic substance use 18 years after treatment, adjusted for other factors. Self-reported general mental health symptoms can be a relevant predictor of the long-term course of SUDs. To prevent prolonged problematic substance use after SUD treatment, it is important to investigate and treat mental health symptoms.

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