Substance Use Among Patients Receiving Out- and Inpatient Dependence Care: a Prospective Norwegian Cohort Study From 2016 to 2020

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Research Article

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Abstract

Background

Continuous use of amphetamines, alcohol, benzodiazepines, cannabis, cocaine, or opioids contributes to health impairments, increased morbidity, and overdose deaths among patients with substance use disorders (SUDs). This study evaluates the impact of inpatient detoxification, specialized opioid agonist therapy (OAT), and low-threshold municipality care on substance use over time.

Methods

We used data from a cohort of SUD patients in Norway through health assessments of self-reported substance use and sociodemographic and clinical factors. A total of 881 substance use measurements, including type and amount of substances, were assessed from 708 SUD patients in 2016-2020. Substance use for individual and total substances was calculated, creating a substance use severity index (SUSI) ranging from zero (no use) to one (daily use). We defined *baseline* as the first substance use measurement when the measurements were listed chronologically. *Time* was defined as years from baseline. We used a linear mixed model to analyze associations between the SUSI and inpatient detoxification, specialized OAT compared with low-threshold municipality care, as well as the factors like injecting substance use, gender, and age, presented with coefficients and 95% confidence intervals (CI).

Results

Neither inpatient detoxification (mean SUSI change: 0.01, -0.03;0.04) nor specialized OAT (0.03, -0.09;0.14) compared with low-threshold municipality care were associated with changes in substance use over time. Patients who were over 60 years of age (mean SUSI difference: -0.06, -0.13;0.00) had a lower SUSI than those under 30 years of age, while patients who injected substances had a higher SUSI than those who did not inject substances (0.18, 0.15;0.20) at baseline. The mean SUSI for the individual substances were 0.50 (standard deviation (SD): 0.38) for cannabis, 0.40 (0.37) for benzodiazepines, 0.33 (0.34) for amphetamines and cocaine, 0.31 (0.29) for alcohol, and 0.22 (0.31) for opioids at baseline. The mean SUSI of all substances was 0.35 (0.20).

Conclusion

The present study demonstrates that neither inpatient detoxification nor specialized OAT compared to low-threshold municipality care were associated with changes in substance use over time. Future research needs to evaluate the impact on substance use and healthy survival of multiple health care interventions to this patient group.

1. Background

More than half of patients with substance use disorders (SUDs) use addictive substances continuously while enrolled in care [1, 2]. Continuous substance use diminishes treatment effects and is associated with health adversities, morbidity, and overdose deaths [2, 3]. In 2020, the European Union presented a substance strategy

for 2021–2025 to reduce the substance demand, dependence, and supply of substances and address the substance-related health and social by 2025 [4]. By this ambitious strategy, increased opioid agonist therapy (OAT) coverage is essential in preventing injecting opioid use [5], reducing premature mortality [6], and limiting illegal opioid consumption for patients with severe opioid dependence [7, 8]. However, it is highly uncertain to what extent long-term specialized OAT and other treatment approaches – such as inpatient detoxification, low-threshold municipality care, and various specialized outpatient treatments – reduce the total substance use among SUD patients.

Patients with continuous substance use suffer from multiple disease burdens, and many have physical and mental comorbidities and socioeconomic difficulties [2]. Mental comorbidities – such as personality disorders, psychotic and affective disorders – are common [9–11]. Also, there is a high prevalence of hepatitis C virus (HCV) and human immunodeficiency virus (HIV) infections, endocarditis, and bacterial abscesses, caused by injecting substance use [12–16]. A chaotic life situation is presented in many cases involving unstable housing situations, unemployment, and disrupted family and social relationships. Additionally, continuous substance use constitutes a particular risk of non-fatal and fatal overdoses [15], typically when combining opioids with other sedative substances or alcohol [17]. The European Monitoring Centre of Drug and Drug Addiction has estimated a wide variance in percentages between 11 % and 70 % of OAT patients who use other substances than opioids [2]. This is almost similar percentages for the Europeans with harmful opioid use [18].

Inpatient detoxification, specialized OAT, and low-threshold municipality care may be steps toward rehabilitation and recovery from continuous substance use. Inpatient detoxification usually involves medical and psychosocial follow-ups targeting a range of physical and mental substance withdrawal symptoms, e.g., nausea, tremors, sweating, irritability, insomnia, hallucinations, seizures, and anxiety [19]. However, studies have shown that relapse to substance use is common, and few remain long-term abstinent [20–23]. Furthermore, low-threshold municipality care and specialized OAT involving integrated and multidisciplinary teams lack evidence on their impact on substance use changes in SUD populations [24, 25].

Thus, the present study's objectives are to evaluate the continuous substance use in terms of type and amount of consumed substances, including benzodiazepines, cannabis, opioids, amphetamines and cocaine, and alcohol over time among Norwegian patients in care for substance use disorders (SUD) using a substance use severity index. In addition, we aim to assess three treatment approaches and injecting substance use and how these are associated with changes in substance use over time. More specifically, we will:

1. calculate the substance use at baseline and assess changes over time.
2. evaluate the injecting substance use, inpatient detoxification, and specialized opioid agonist therapy (OAT) compared with low-threshold municipality care's impact on the substance use.

2. Methods

2.1. Data source

We used data from a cohort nested to the INTRO-HCV study in Bergen and Stavanger, Norway [26]. Data were collected from May 2016 to July 2020, and patients were recruited from specialized OAT outpatient clinics in Bergen and Stavanger and from municipality health care clinics underlying the Bergen Municipality.

2.2. Data collections

All included patients were assessed yearly concerning physical and mental health status, current substance use, and sociodemographic and clinical data. The data were amassed in a health register using electronic data collection software (Checkware) under research nurses' supervision. All the clinical data, including OAT medication (buprenorphine- or methadone-based medication), educational level, inpatient detoxifications, specialized OAT, low-threshold municipality care, severe infectious diseases (HCV, hepatitis B virus, and HIV infections), and substance use were collected from the electronic medical record.

2.3. Study sample

We included 881 self-reported substance use measurements from 708 patients with SUDs in the study period. Of those, 171 patients had more than one substance use measurements, providing 346 repeated measurements. The median time interval between the first health assessments (baseline), and any subsequent assessments in the same patients, including substance use measurements, was 16 months (interquartile range (IQR): 13–20).

2.4. Measuring substance use

We measured substance use during the past 12 months prior to the assessments using a Likert scale ranging from zero (no use) to six points (daily use) for each substance class, including cannabis, opioids (opioids received in OAT were not included), stimulants (amphetamines or cocaine), benzodiazepines, and alcohol. The substance scores (0–5) were handled separately for each substance class and were additionally summarized as a sum score ranging from zero to 25 points (Additional File 1). Furthermore, the scores were standardized into a continuous SUSI ranging from zero (no use) to one (daily use) by dividing the total substance sum score by five (for individual substance class) or 25 (for all substance classes). The data collection software only allowed valid responses to each substance and prompted empty questions before submission to minimize missing data.

2.5. Assessing severe infectious diseases

We assessed the extent of severe infectious diseases as the markers of the study populations' comorbidities. Thus, we collected blood samples, including hepatitis B surface antigen, HIV antigens/antibodies, and HCV polymerase chain reaction, during health assessments. Blood samples were analyzed at the Department of Laboratory Medicine, Haukeland University Hospital, Bergen, Norway, and the Department of Medical Biochemistry and Microbiology, Stavanger University Hospital, Stavanger, Norway (accredited by ISO-standard 15189).

2.6. Definition of study variables

We defined baseline for patients as the first health assessment that included a substance use measurement when we listed the health assessments chronologically. The age was classified into five groups: 18–30, 30–40, 40–50, 50–60, and ≥ 60. We defined being in OAT according to whether patients received buprenorphine

or methadone (OAT opioids) or not at baseline. We set 'injecting substance use' as having injected at least once at any time during the past six months prior to the health assessment. Having chronic infectious diseases was defined as detecting HCV RNA by polymerase chain reaction, hepatitis B virus surface antigen, or HIV antigen/antibodies in the blood samples. Additionally, we defined inpatient detoxifications as being hospitalized for detoxification at least once between baseline and the last substance use measurement. The duration of inpatient detoxification was not considered. Furthermore, "specialized OAT" and "low-threshold municipality care" were defined according to the locations for the health assessments. The "low-threshold municipality care" served basal medical and psychosocial support, including activities and food supply, for marginalized SUD patients, while SUD patients with severe opioid dependence received specialized OAT involving at least weekly deliveries of OAT opioids and medical and psychosocial support performed by multidisciplinary teams, including consultant in addiction medicine, phycologist, nurses, and social workers.

2.7. Statistical analyses

We used Stata/SE 17.0 (StataCorp, TX, USA) for descriptive and linear mixed model analyses. Sankeymatic (sankeymatic.com) was used for the generation of a Sankey diagram for graphical presentation of the change in the use of substances over time. The threshold for statistical significance was set to $P < 0.05$ for all analyses unless otherwise stated. In all analyses, we defined time as years from baseline.

Linear mixed model analyses were used to investigate whether the treatment approaches, injecting substance use, age, and gender affected the SUSI at baseline and to what extent they influenced any changes in the SUSI from baseline to the following health assessments. We specified the linear mixed models as a random intercept fixed slope regression model. The estimator was set to Restricted Maximum Likelihood. The predictors were handled both as constant baseline variables and as time-varying variables over time, with the SUSI as the outcome variable. The full information maximum likelihood ensured that all available substance use measurements were used.

2.8. Ethics approval and consent to participate

The study is reviewed and approved by the Regional Ethical Committee for Health Research West, Norway (REK Vest 2017/51). Each patient provided written informed consent prior to enrolling in the study.

3. Results

3.1. Patients' characteristics at baseline

Seventy-three percent of the study sample were males, and the mean age was 43 years (standard deviation (SD): 11 years) at baseline (Table 1). Six percent had not completed primary school, and 44 % had primary school as their highest educational level. Fifty-four percent injected substances during the past six months leading up to the substance use measurement, and 20 % of patients were admitted to at least one inpatient detoxification in the time between baseline and the last health assessment. Ninety-six percent had consumed at least one substance during the past 12 months before the first health assessment.

3.2. Substance use severity index at baseline

The mean SUSI for all the substances was 0.35 (SD: 0.20) (Table 2). Cannabis was the substance most frequently used (mean score: 0.50 (0.38)), followed by benzodiazepines (0.40 (0.37)), stimulants (0.33 (0.34)), alcohol (0.31 (0.29)), and opioids (0.22 (0.31)).

3.3. The associations between the substance use severity index and treatment approaches, age, gender, and injecting substance use at baseline

Patients who received low-threshold municipality care were associated with a higher SUSI than those who received the specialized OAT (mean SUSI difference: 0.07, 95 % confidence interval: 0.04;0.10). Furthermore, patients over 60 years of age (-0.06, -0.13;0.00) had lower SUSI than those under 30 (Table 3), while patients who inject substances had a higher SUSI compared to those who did not inject (0.18, 0.15;0.20).

3.4. The associations between the substance use severity index and treatment approaches, and injecting substance use over time

No changes in the SUSI were found when comparing low-threshold municipality care with the specialized OAT from baseline until the end of the study period (mean SUSI change: 0.03, 95 % CI: -0.09;0.14). Likewise, patients admitted to the inpatient detoxification did not show changes in the SUSI over time compared with those not admitted to inpatient detoxification (0.01, -0.03;0.04). However, the SUSI increased among patients who started to inject substances from baseline compared with those who did not start to inject (0.11, 0.07;0.15). Overall, the SUSI did not change substantially over time in this SUD population (-0.02, -0.04;0.00), although some intra-individual substance use changes were found (Fig. 1).

4. Discussion

The present study has revealed considerable substance use among SUD patients enrolled in care. Patients who received low-threshold municipality care had higher substance use than those who received specialized OAT at baseline, probably because OAT opioids were not included in the SUSI. Neither inpatient detoxification nor specialized OAT compared with low-threshold municipality care were associated with changes in substance use. Patients over 60 years of age had lower substance use than patients under 30 years of age at baseline, and higher substance use was found among patients who injected substances at baseline and those who started to inject after baseline. Overall, cannabis was the most prevalent substance used, followed by alcohol, benzodiazepines, stimulants, and opioids. The adjusted SUSI remained substantially unchanged over time in this population.

The substance use levels were high among patients undergoing specialized OAT and those receiving low-threshold municipality care, with levels exceeding prevalence estimates of benzodiazepine and stimulant use in the national data on the OAT population in Norway [27]. Additionally, the benzodiazepine prevalence estimate reached the upper part of the estimates in European countries among harmful opioid users, ranging from 45 % to 70 % [18]. Higher availability of illegal substances and a consequently higher number of SUD patients in bigger cities than in other regions could be a possible reason for these findings.

There was no association between substance use before and after inpatient detoxification. This indicates that reducing substance use does not seem to be the outcome of inpatient detoxification care. However, other

indirect effects of detoxification could occur. Most SUD patients were marginalized substance users with different aspects of health and social problems, in addition to the current SUDs, which needed to be addressed during inpatient detoxification [3]. Thus, inpatient detoxification should be one of several approaches in a comprehensive treatment course for these patients. Nevertheless, reducing substance use may be difficult, and relapse to substance use may even be expected for many of these patients. A previous study found that younger patients, patients having a psychiatric diagnosis, and those receiving short-term (two-four months) compared with long-term (> six months) SUD treatment were at particular risk for relapsing after inpatient SUD treatment [20]. In the present study, many patients met at least one of these risk factors, which might be the reasons for our findings. Another factor may be that inpatient detoxifications primarily aimed to stabilize the patient and improve follow-up care without reducing substance use. If this is the case, the treatment went under the wrong heading and should instead be classified as a form of stabilization. Other outcome measures of their effectiveness may be thus needed.

The specialized OAT and the low-threshold municipality care had similar and low impacts on substance use. Although being in specialized OAT is well-documented in reducing illegal and injecting opioid use and opioid-related overdose deaths compared with it before OAT [5–8], to our knowledge, no studies have evaluated the impact of ongoing OAT on total substance use over time. Our findings showed unchanged substance use levels, which were in line with the trends of national substance use and prescribed potentially addictive substances in the OAT population during 2015–2017 [27–30]. On the other hand, the present study only included patients who had received specialized OAT over several years, which means that the substance use changes before entering specialized OAT or low-threshold municipality care were not considered. Nevertheless, identifying treatment approaches that reduce the use of other substances is essential for successful rehabilitation and for protecting against relapse to illegal opioid use for patients undergoing specialized OAT [6, 31]. Likewise, low-threshold municipality care, including medical and psychosocial follow-ups, activities, and food supply, may be essential in creating relationships between patients and health professionals to encourage substance use change and prevent fatal and non-fatal overdose deaths. The present study was not designed to demonstrate causal relationships. Evaluating new approaches – such as long-term tapering off from some substances like benzodiazepines [32] and integrated treatment care [33–35], within existing treatment approaches might be one of several keys to reduce substance use in this population in the future.

Injecting substance users showed a higher rate of substance use than those who did not inject. According to previous studies [36, 37], it is also likely that high substance use predicts injecting substance use in this population. Injecting substances are associated with dependences and a wide range of health harms [2, 38], resulting in overdoses and hospital admissions [38]. The broad range of comorbidities and complexity among injecting substance users signifies the need for coordinated medical and psychosocial health care to reduce substance use in line with the European Union's Drug Strategy for 2021–2025 [4]. Thus, various treatment approaches may be important in recovering these patients for injecting substance use and taking care of the complex medical and psychosocial comorbidities [33].

Age over 60 years was substantially associated with lower substance use than those under 30 years of age. This corresponds to previous reports [39, 40]. Older SUD patients usually have more substance-related physical and mental comorbidities than younger, placing a higher responsibility on existing health care

services. Previous observational studies have shown that receiving health services and being older were associated with more legal prescriptions of addictive medications to older patients compared to younger ones, perhaps intending to make their illegal substance use less likely [28, 41, 42]. This might explain the lower substance use among older than younger SUD patients. On the other hand, one can assume that SUD patients who have reached 60 years of age generally have fewer substance dependences and a lower risk of dying in overdose accidents. In 2017, 59 % of premature deaths from substance overdose were among those younger than 50 years globally [43], which may give evidence that those with the most extensive substance use die before reaching 60.

5. Strengths And Limitations

This study has some strengths and limitations. We have included 708 SUD patients that usually are difficult to reach in health care. Of those, 171 patients had follow-up measurements at least in one year, making longitudinal analyses possible. However, these results should be interpreted cautiously because they only represented one out of four recruited patients. Three out of four patients were mainly recruited from specialized OAT outpatient clinics, which could affect the generalizability of our results to other SUD populations. Due to clinical challenges, including systematic and patient delays, the health assessments were conducted at varying time intervals. This may slightly complicate the interpretation of the predicted substance use changes from baseline. Moreover, the duration for inpatient detoxification and the time intervals between substance use measurements and inpatient detoxification were not considered in the analyzes, which may reduce the results' generalizability. Furthermore, the substance use changes were only estimated for patients who underwent specialized OAT or low-threshold municipality care over time, which means that the impact of entering specialized OAT or low-threshold municipality care in comparison to the time before those was not considered. Furthermore, more frequent substance use measurements could have identified possible fluctuations within shorter time intervals that might not necessarily be prolonged. Still, our estimates are likely to have captured the general patterns.

6. Conclusion

Neither inpatient detoxification nor specialized OAT compared with low-threshold municipality treatment were associated with changes in substance use over time. However, reduction in substance use is only one of many goals of SUD care and treatments. Future research needs to evaluate the impact on substance use, and other key outcomes of a range of treatment approaches, including integrated methods, ideally in randomized controlled trials.

7. Abbreviations

CI: Confidence Interval

HCV: Hepatitis C Virus

HIV: Human Immunodeficiency Virus

IQR: Interquartile Range

OAT: Opioid Agonist Therapy

SD: Standard Deviation

SUSI: Substance Use Severity Index

SUD: Substance Use Disorder

8. Declaration

Ethics approval and consent to participate

The study has been reviewed and approved by the Regional Ethical Committee for Health Research (REC) West, Norway (reference number: 2017/51/REK Vest, dated 29.03.2017/20.04.2017). Each patient provided written informed consent prior to enrolling in the study.

Consent for publication

Participants have consented for publication

Availability of data and material

No additional data are available due to data protection requirements.

Competing interests

Not applicable

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Authors' contributions

JHV have led the study design, analysis, and article preparation. FC, CFA, EML, KAJ, and LTF have contributed in the article preparation. All authors have read and approved the final article.

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Tables

Table 1

Basic characteristics at baseline for all patients and for patients with more than one substance use measurement (numbers (n) and percentages (%)):

	All patients (N = 708)	**Patients with > 1 substance use measurement (N = 171)**
Age (years), n (%)		
18–30	84 (12)	11 (6)
30–40	204 (29)	43 (25)
40–50	215 (30)	57 (33)
50–60	164 (23)	47 (27)
≥ 60	41 (6)	13 (8)
Mean (SD)	43 (11)	46 (10)
Gender, n (%)		
Male	514 (73)	130 (76)
Female	194 (27)	41 (24)
Highest educational level, n (%)		
Not completed primary school	39 (6)	11 (6)
Completed primary school (9 years)	306 (44)	77 (45)
Completed high school (12 years)	277 (40)	66 (39)
≤ 3 years of college or university	58 (8)	< 15 (< 10)
> 3 years of college or university	14 (2)	< 15 (< 10)
Injected substances during the past six months, n (%)	384 (54)	82 (48)
Unstable housing situation during the past 30 days[1)], n (%)	86 (12)	5 (4)
Substance used during the past 12 months[2)], n (%)		
Alcohol	513 (72)	113 (66)

SD: Standard deviation.

[1)] An unstable housing situation was defined as living in a homeless shelter, with family or friends at any time during the past 30 days. Having owned or rented housing situation or being imprisoned were defined as a stable housing situation.

[2)] The number of patients who have used a substance at least once during the past 12 months.

	All patients (N = 708)	Patients with > 1 substance use measurement (N = 171)
Benzodiazepines	489 (69)	126 (74)
Cannabis	537 (76)	133 (78)
Opioids	344 (49)	75 (44)
Stimulants (amphetamines and cocaine)	451 (64)	103 (60)
Inpatient detoxification, n (%)	-	35 (20)
Specialized OAT, n (%)	553 (78)	166 (97)
Low-threshold municipality care, n (%)	155 (22)	5 (3)
Comorbidities, n (%)		
Hepatitis C virus infection	349 (60)	89 (57)
Hepatitis B virus infection	5 (< 1)	< 5 (< 5)
Human immunodeficiency virus	< 5 (< 5)	< 5 (< 5)

SD: Standard deviation.

[1)] An unstable housing situation was defined as living in a homeless shelter, with family or friends at any time during the past 30 days. Having owned or rented housing situation or being imprisoned were defined as a stable housing situation.

[2)] The number of patients who have used a substance at least once during the past 12 months.

Table 2

The Substance Use Severity Index (SUSI) (mean (SD)) at baseline and follow-up

	Baseline[1)] (N = 708)	**Baseline[2)] (N = 171)**	**Follow-up[3)] (N = 171)**
Alcohol	0.31 (0.29)	0.29 (0.29)	0.28 (0.27)
Cannabis	0.50 (0.38)	0.51 (0.38)	0.50 (0.40)
Benzodiazepines	0.40 (0.37)	0.42 (0.36)	0.39 (0.34)
Opioids	0.22 (0.31)	0.21 (0.31)	0.14 (0.23)
Stimulants (amphetamines and cocaine)	0.33 (0.34)	0.28 (0.31)	0.25 (0.31)
All substances	0.35 (0.20)	0.34 (0.18)	0.31 (0.18)

[1)]The SUSI for all included patients at baseline

[2)]The SUSI for patients with two or more substance use measurements at baseline

[3)]The SUSI for patients with two or more substance use measurements on the last substance use assessment during the study period.

Each substance class and the total substance use (“All substances”) are standardized using the SUSI ranging from 0 to 1, where 0 indicates no use and 1 indicates daily use of all substances (alcohol, cannabis, benzodiazepines, opioids, and stimulants). SD: standard deviation.

Table 3

Adjusted linear mixed model for the Substance Use Severity Index (SUSI)[1)] (N = 706)

	Effect estimates
	Coefficients (95 % CI)
Substance Use Severity Index (β_0)	0.27 (0.23;0.32)
Time trend	-0.02 (-0.04;0.00)
Baseline	
Female	-0.02 (-0.04;0.01)
Years of age: < 30 30–40 40–50 50–60 ≥ 60	 0.00 (ref.) -0.03 (-0.08;0.01) -0.02 (-0.06;0.02) -0.04 (-0.08;0.00) -0.06 (-0.13;0.00)
Injecting substance use	0.18 (0.15;0.20)
Treatment: Specialized OAT Low-threshold Municipality Care	 0.00 (ref.) 0.07 (0.04;0.10)
Predictors remain constant from baseline[2)]	
Injecting substance use	0.01 (-0.02;0.05)
Treatment: Specialized OAT Low-threshold Municipality Care	 0.00 (ref.) 0.03 (-0.09;0.14)
Time-varying predictors from baseline[3)]	
Inpatient detoxification	0.01 (-0.03;0.04)
Starting to inject substances	0.11 (0.07;0.15)

OAT: Opioid agonist therapy.

[1)] The SUSI is a continuous variable ranging from 0 to 1, where 0 indicates no substance use and 1 indicates daily substance use for all substances (cannabis, amphetamines, cocaine, opioids, benzodiazepines, and alcohol).

[2)] Interpretation: An estimation of the SUSI changes when the predictors remain constant from baseline (e.g., ongoing injecting substance use leads to no changes in the SUSI from baseline.)

[3)] Interpretation: An estimation of the SUSI changes when the predictors vary over time from baseline (e.g., going to inpatient detoxification or starting to inject substances from baseline).

The table displays a linear mixed model analysis (Restricted Maximum Likelihood regression) evaluating various treatment approaches, injecting substance use, age and gender's impact on the SUSI changes at baseline and over time.

Figures

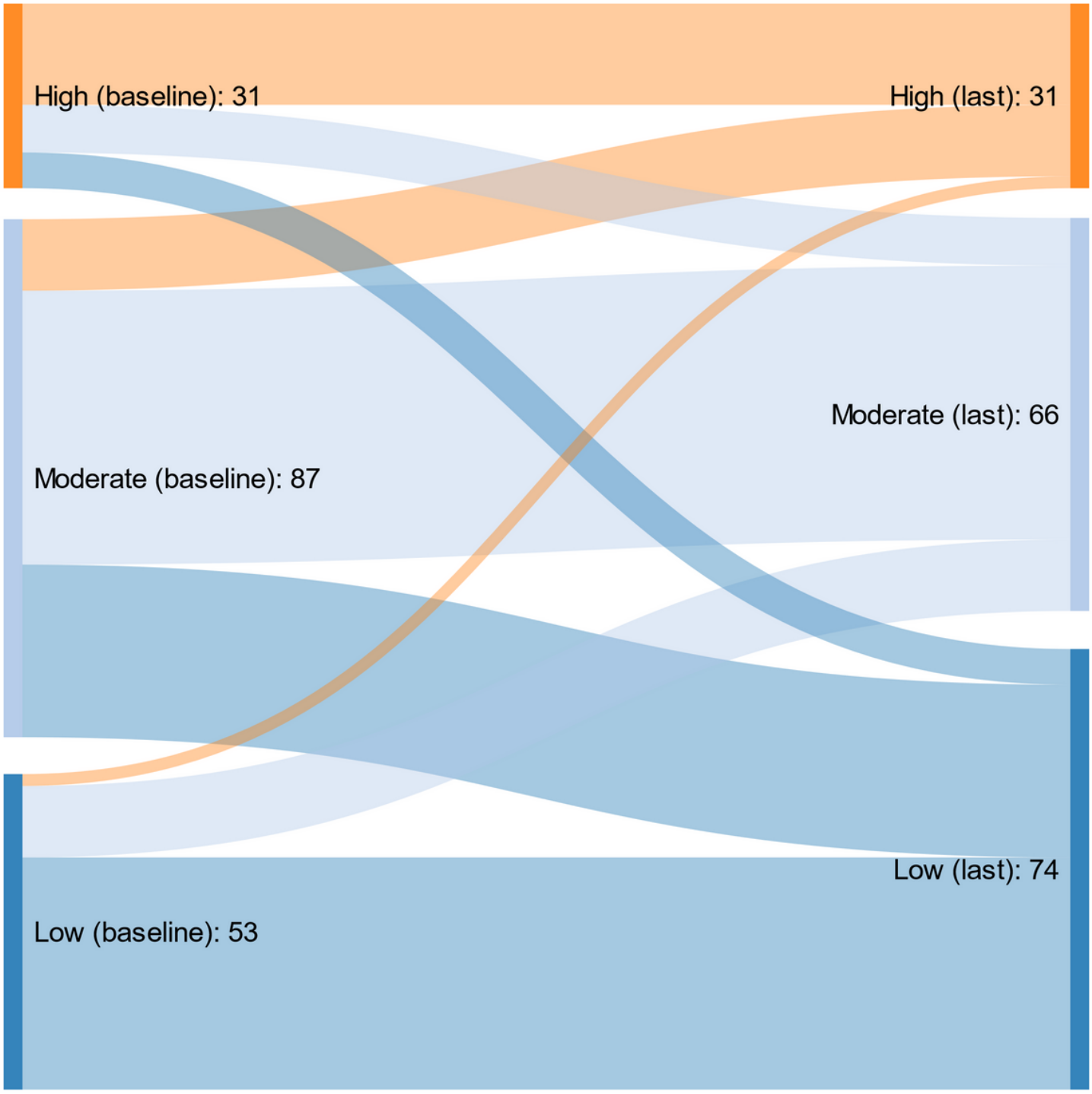

Figure 1

title: Patients' substance use severity index (SUSI) changes from baseline to the last substance use measurement (N = 171) Legends: The figure displays the SUSI changes from baseline (left (baseline)) to the last substance use measurement (right (last)) for patients with at least two substance use measurements. Patients were divided into three SUSI levels at baseline and the last substance use measurement: low (SUSI

<0.2 (dark blue)), moderate (SUSI 0.2 – 0.4 (light blue)), and high (SUSI > 0.4 (orange)). The SUSI ranges from 0 to 1, where 0 indicates no substance use and 1 indicates daily substance use for all substances (cannabis, amphetamines, cocaine, opioids, benzodiazepines, and alcohol).

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