PROFILING PATIENTS WITH SUBSTANCE USE DISORDERS AND THEIR CARE UTILIZATION IN ADDICTION TREATMENT

Ruud Rutten

DONDERS
SERIES

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Door de bomen het bos
De bomen verschillend
Als de mensen

Contents

1. General introduction

Almost one-third of the global disease burden from mental health problems is caused by alcohol and drug related disorders (WHO, 2022). In the Netherlands, there is a lifetime prevalence of 16.7% substance use disorder (SUD) and a 12 months prevalence of 7.1% (Ten Have, et al., 2022). SUDs are conditions where a problematic pattern of substance use leads to clinical significant impairment or distress, as manifested by at least two of the following symptoms, occurring within a 12-month period:

1. Use of larger amounts or over longer period than was intended.
2. There is a persistent desire or unsuccessful efforts to cut down or control use.
3. A great deal of time is spent in activities necessary to obtain substances, use them and recover from their effect.
4. Craving, or a strong desire or urge to use the substance(s).
5. Recurrent substance use resulting in a failure to fulfill major obligations at work, school, or home.
6. Continued substance use despite having persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of the used substance.
7. Important social, occupational, or recreational activities are given up or reduced because of substance use.
8. Recurrent substance use in situations in which it is physically hazardous.
9. Substance use is continued despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to be caused by that substance.
10. Tolerance, as defined by either of the following:
    a. A need for markedly increased amounts of the substance to achieve intoxication or desired effect.
    b. A markedly diminished effect with continued use of the same amount of the substance.
11. Withdrawal, as manifested by either of the following:
    a. The characteristic withdrawal syndrome for the used substance.
    b. The substance (or a closely related substance) is taken to relieve or avoid withdrawal symptoms.

(American Psychiatric Association, 2013)

1.1 Patient heterogeneity

Patients with SUD are a heterogeneous group, with various sources of variation, including biological, psychological and social variance (West, 2013). On the neuropsychological level differences are caused by differences in heritability and early developmental factors, including childbirth traumas. These factors may lead to different neuropsychological challenges, which in turn might contribute to the vulnerability to develop SUD. On the psychological level they differ in personality, coping styles, self-efficacy, talents, and resilience. Patients' social networks also differ, as well as their level of social support and the limitations in social functioning they experience. Related to that, a variety of psychiatric co-morbid diseases occur in patients with SUD. The political and cultural circumstances also are of influence, especially when it comes to for instance the supply market of substances. Whether a substance is freely assessable and its use widely accepted, or limited available in an illegal market with high prices, causes great differences in the circumstances and the scene people use in. Also the substances used are different, to the extent that they are addictive and cause craving and withdrawal. Patients also differ in the amount of use of the different substances, the history and the patterns and the way of use. Patients also show different stages or levels of severity, and differ in levels of therapy readiness and motivation for change.

All these factors influence each other, resulting in a heterogenous picture of different patterns and levels of SUD symptoms. The clinical heterogeneity calls for a broad differentiated field of care and cure interventions to meet the needs of patients.

1.2 Treatment variation

In the Netherlands professional treatment of SUDs is commonly delivered in relatively large, regional treatment organizations. Reimbursements for addiction treatment by either municipalities, health insurance or the Ministry of Justice and Security, ensures that treatment is easily accessible to every citizen. These treatment organizations offer a broad spectrum of treatment, varying from short term assessment and advise to long-term inpatient treatment for up to 6 months or longer. Medical/pharmacological treatments, as well as motivational enhancement, cognitive behavioral therapy, E-health, and recovery support are applied, next to treatment of co-occurring psychological/psychiatric problems and social support. In selected treatment centers, coercive treatment, both from forensic and mental health perspective, next to probation, are also available. All these services differ widely in applied methods and disciplines deployed, and even more so in intensity, duration and therefore in costs. Some of these regional treatment centers are embedded in larger mental health treatment organizations, others are not. In the debate which form is favorable, we did not find that the data did support one in favor (Rutten & Schippers, 2013).

Taken together, the heterogeneity of SUD patients is answered by a broad variety of treatment possibilities. This situation offers the opportunity to match the offered treatment with the individual needs of a specific patient. It is a major clinical challenge to match patients' needs to the diverse landscape of interventions and treatment facilities.

1.3 Patient-treatment matching

Treatment organizations generally prefer working with evidence-based methods. There is a broad variety of evidence based treatments available, ranging from psychotherapy to pharmacological treatment (Miller & Carroll, 2006; Miller, 2009) that are overall moderately effective (Howick et al., 2022). There is also a large heterogeneity in treatment response. As a result, research focus shifted from 'which treatment works and which does not', to 'which treatment works for whom' (Project MATCH Research Group, 1997; ASAM; Mee-Lee, 2001). Patient-treatment matching in every day practice is mostly based on practical experience and common sense (Gastfriend, 1997; McGee, 1997; Kersten, 1998). For instance, the more severe patients' problems are, the more intensive the treatment should be. The worser the prognosis, the more treatment should shift from cure to care. Similarly, the more danger is involved for a patient or his surroundings as a consequence of substance use, the more coercion is justified.

Despite a large body of research and meta-analyses supporting treatment effectiveness in addiction care, evidence available to support the clinical decision-making process is still limited (McKay et al., 1997; Gastfriend et al., 2003; Project MATCH Research Group, 1998; Merkx et al., 2013; Kramer-Schmidt et al., 2017). There are several reasons to improve this situation. First, people who suffer from a SUD receive less often treatment than people who suffer from other psychiatric diagnosis (Nemesis-3). Treatment is also limited by availability of resources as personal and finance. So ineffective or inefficient treatment should be avoided. Treatment organizations are held accountable for the care they provide. In 2001 the National Institute on Healthcare in the United States put the 'Quality Chiasm', the balance between available and needed amount and quality of prevention and treatment facilities, high on the agenda in the US (Institute of Medicine, 2001).

1.4 Focus on quality improvement

In the course of time the research on patient-treatment matching in the addictions focused more on quality improvement. As part of mental healthcare quality improvement initiatives, the National Institute on Healthcare recommended to implement the use of valid and reliable patient reported measures to routinely and systematically assess the progress and outcomes of treatment (Institute of Medicine, 2006). Using these measures should fuel continuous efforts for quality improvement of the care provided. Many initiatives focused on improving treatment participation and retention and minimalizing drop-out by improving quality of programs (McCarty, 2007; Hoffman et al., 2012; Hunter et al., 2014; Simpson, 2010; Allsop, 2018), adding specific aid for specific patient needs (Humphreys & McLellan, 2011) and addressing non-specific treatment factors (Wild & Wolfe, 2009; Miller, 2008).

In the Netherlands, in 1998, a nationwide quality improvement program started, named 'Scoring Results' (Rutten et al., 2010). Within this program a structured assessment interview was developed, called Measurement in the Addictions for Triage and Evaluation (MATE) (Schippers et al., 2011, 2012). The MATE made it possible to collect Patient Routine Outcome Measurement (PROM) data nationwide. Given the richness of data collected using the MATE in real practice, this holds promise to explore clinical heterogeneity as it occurs in addiction care. Furthermore, these data could add to the knowledge based on randomized clinical trials (RCT), since clinical trials commonly investigate efficacy in highly selected populations (Kostis & Dobrzynski, 2020). As a result, many patients in real practice do not resemble those included in these trials, and randomized trials cannot covert the diversity of patients encountered in addiction care (Susukida et al., 2020). In the current thesis we explored alternative ways to investigate clinical heterogeneity and patient-treatment matching, using large datasets from everyday clinical practice. An inspiring example of this kind of approach comes from another field of medicine: oncology. For example: Eddes et al. (2020) reported on the added value of installing a temporary stoma in oncological bowel surgery. Analyzing clinical data of large groups of patients in real practice, using clinically reported outcome measures showed that there was no difference in recovery and complications between the group with and without the temporary stoma. Resulting in the guideline to skip this stressful intermediate step. Even if the routine assessment of data is established, acquiring knowledge from the data that is instrumental for the practice of treatment meets a lot of challenges. Challenges are privacy legislation, lack of commitment of practitioners, but most of all the complexity of safely exchanging and processing data. As a result, systematic use of the collected data is still sparce, especially in everyday practice.

1.5 Present thesis

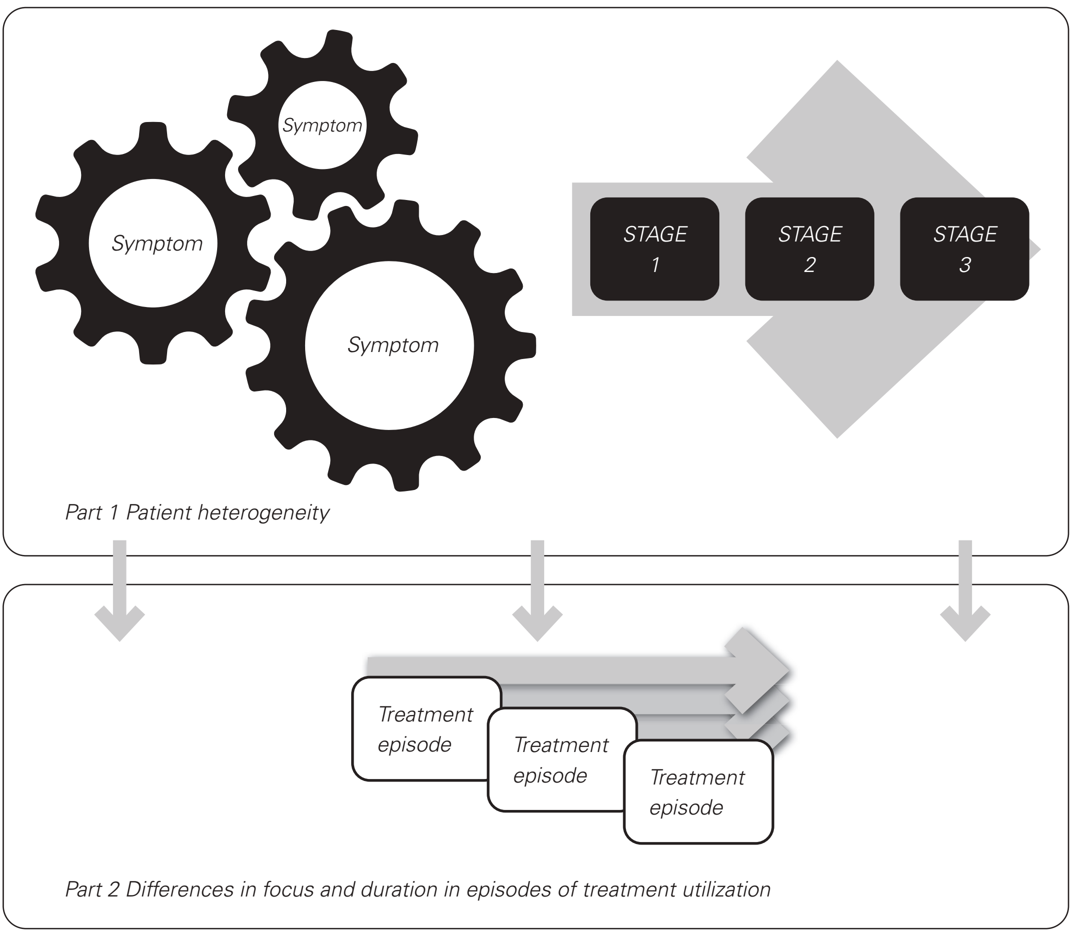
With the focus on quality improvement in addiction care, the implementation of routine clinical assessment using the MATE provides the unique opportunity to investigate clinical heterogeneity in real practice, based on large scale databases. The aim of this thesis is to explore data driven, clinical heterogeneity in addiction care in a large set of naturalistic patient and treatment data. Specifically, we aimed at answering the following questions:

Part I

1. Can clinical heterogeneity be clarified by looking at the symptoms of SUD in their interrelationship?
2. Can we define stages in the course of a SUD?

Part II

3. Can the amount and focus of treatment episodes be related to patient characteristics?



Part 1 Patient heterogeneity

Part 2 Differences in focus and duration in episodes of treatment utilization

With this endeavor, we wish to contribute to the clinical decision-making process of patients and practitioners in every day practice of addiction treatment programs. We think that investigation of large clinical datasets can also contribute to efficient treatment planning and management of addiction care and the development of patient placement guidelines. Efficient and effective healthcare planning is of the utmost importance because of a growing need to balance treatment offered with limited availability of resources, both in terms of financial and human capital. For these studies we used date from a large regional Dutch addiction treatment center TACTUS addiction care (see text frame). We used routinely collected data at intake using the MATE.

Part I: Heterogeneity of treatment-seeking SUD patients

In the first part of this thesis we did two studies that explored the heterogeneity of SUD patients (research question 1 & 2).

Chapter 2

SUD symptoms interact with each other in different ways. In this study we used the network approach of psychopathology to capture clinical heterogeneity (Borsboom & Cramer, 2013). The network model considers mental disorders as complex dynamic systems of interacting symptoms. First, we explored the overall symptom network of the cohort, calculating global strength, strength of the symptoms, and the weights of the symptom-to-symptom connections. Second, we tested whether networks differed between the most prevalent substances in addiction care (i.e., alcohol, cannabis, opioids, cocaine, and other stimulants). Finally we compared the networks based on DSM-IV and on DSM-5 SUD criteria.

Chapter 3

Patients show different stages or levels of severity in the course of their disease. A staging model could be useful to differentiate treatment needs among treatment-seeking SUD patients. A staging model, analogous to the Tumor-Nodes-Metastasis model in oncology (Van den Brink & Schippers, 2012) is tested in this study. The proposed model distinguishes the following stages of addiction: (0) addicted, but not severely; (1) severely addicted, but without psychiatric co-morbidity or social disintegration; (2) severely addicted with psychiatric co-morbidity, but with no social disintegration; and (3) severely addicted in combination with psychiatric co-morbidity and social disintegration. The objectives of this study were twofold: first to examine to what extend the proposed stages occur in a cross-sectional sample of treatment seeking SUD patients, and second to assess whether the model is invariant across subgroups (age, gender and primary substance of misuse), and whether there are certain subgroups for which the model does not apply.

Part II: Heterogeneity of addiction care offered to SUD patients

In the second part, we describe clinical heterogeneity at the level of the care provided to patients in addiction care, also at Tactus treatment center. We combined routinely collected data at intake using the MATE with health insurance claims data (study 3) and actual utilized treatment in (outpatient) hours and (inpatient) days (study 4).

Chapter 4

In a third study, we investigated the way patient characteristics correlate with the level of care they use. On behalf of umbrella organizations of mental health organizations and of the insurance companies in the Netherlands, a first model for mental health care utilization was developed (mental health care utilization model 1.0), and tested on the relatively restricted number of variables that were available in their data (Werkgroep zorgvraagzwaarte GGZ, 2013). This allowed us to test whether the more detailed data for SUD patients that we gathered, were able to improve the prediction off the amount of care consumed for our treatment domain.

Chapter 5

In a fourth study, we developed a model for service utilization in addiction care, trough cluster analyses of the actual care and cure services used. The objective of the study was to investigate clinical heterogeneity in service use in addiction care. We aimed to 1) identify service use patterns of SUD patients, and 2) explore differences in patient characteristics between these service use clusters.

Chapter 6

In the general discussion we will sum up the results of our studies and outline and elaborate conclusions and limitations, as well as our suggestions for further research.

Tactus Centre for Addiction Treatment

Tactus Centre for Addiction Treatment is a treatment and care center in the central east part of the Netherlands, covering the provinces Gelderland, Overijsel, and Flevoland, with a total population of 2,5 million people. Tactus is a broad-spectrum treatment center providing prevention, treatment, care, and probation programs.

Prevention activities ranges from alcohol and drug education in schools for both children and their parents, to focused prevention and early interventions in organizations for childcare, care for intellectual disabled, and general practitioners practices.

Treatment varies from minimal interventions and advice to coercive clinical treatment, both in the healthcare system and in the forensic system.

Care programs vary from self-help groups and aftercare to intensive, sometime lifelong social help for patients who can't stop their substance use, like opioid maintenance programs, hostels, walk-in centers and outreached support for many aspects of everyday life.

Probation varies from court advices to judicial supervision, short treatment interventions and learn and work punishments.

Tactus provides her prevention, care, treatment, and probation from seven inpatient clinics, seven hostels and 20 outpatient centers. Tactus has a yearly budget of 100 million euro's, 1,500 employees, 1,300 probation clients and 5,000 patients a year.

Tactus has also joint ventures with other treatment organizations:
- Amethist, a treatment organization with GGz Centraal, with a clinic and several outpatient facilities.
- Basalt, a forensic clinic with Oostvaarders clinics with 24 inpatient places.
- Omnizorg, a large care facility with two other organizations in sheltered housing and social care, Riwis and Iriszorg.

Research samples and data

For the studies presented in this thesis, we used routine assessment data at intake, using using the structured clinical interview Measurement of Addictions for Triage and Evaluation (MATE 2.1; Schippers et al., 2011, 2010). Patients provided informed consent based on opt out for scientific analyses of their medical files by the treatment center, according the ethical and privacy rules of the treatment institute and approved by the internal ethical board. The table underneath shows the number of patients in de samples used in the different studies.

Study	Sample size
1	10.832
2	6.602
3	3.434
4	9.841

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Part I:

HETEROGENEITY OF TREATMENT-SEEKING SUD PATIENTS

2. Symptom networks in patients with substance use disorders

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Abstract

Background

Reciprocity between symptoms of psychiatric disorders is increasingly recognized to contribute to their chronicity. In substance use disorders (SUD) little is known on reciprocal interactions between symptoms. We applied network analyses to study these interactions.

Methods

We analyzed 11 DSM-IV / DSM-5 criteria for SUD for the most prevalent substances in addiction care (alcohol, cannabis, cocaine, stimulants, and opioids) in a sample of 10,832 SUD patients in treatment. First, we estimated an overall symptom network. Second, we compared symptom networks between the different substances. Finally, we tested differences in symptom networks between DSM-IV and DSM-5.

Results

In the overall symptom network for SUD patients the most central symptom was: "spending substantial amount of the day obtaining, using, or recovering from substance use". The symptoms "giving up or cutting back on important activities because of use" and "repeated usage causes or contributes to an inability to meet important obligations", were the symptoms that influenced each other the most. Networks differed between substances both in global strength and structure, especially regarding the position of "use despite health or interpersonal problems". Networks based on DSM-5 criteria differed moderately from DSM-IV, mainly because "craving" was more central in the DSM-5 network than "legal problems" in DSM-IV.

Conclusions

Network analyses can identify core symptoms of SUD that could maintain the disease processes in SUD. Future studies should address whether targeting these core symptoms with precedence, might help to break through the addictive process.

2.1 Introduction

Almost a quarter (24%) of the global mental disease burden is caused by alcohol and drug related disorders, with about 35 million people suffering from a substance use disorder (SUD) (Degenhardt et al., 2018). SUD are conditions where causes, consequences, and symptoms interact, and individual symptoms influence each other (West, 2013). For instance, drinking more and longer than intended leads to neglect of important activities and social obligations, which leads to social conflict, which can again lead to more drinking. More insight in the strengths and dynamics of the various SUD-symptoms can help to depict which of these symptoms play a key role in causing and maintaining the disease processes, contributing to chronicity. The most central symptoms may be most crucial to address in treatment (Borsboom and Cramer, 2013).

In recent years there is a growing interest in a network approach of psychopathology, which considers mental disorders as complex dynamic systems of interacting symptoms. In the traditional approach to mental disorders, the strengths, and relations between symptoms are mostly expected to be depending on an underlying disease, abnormality, or predisposition. In contrast, the network approach assumes that disorders arise from direct interactions between the symptoms. Factors that normally are interpreted as causal, are in the network approach merely seen as triggers that provoke changes in a network of symptoms, resulting in a specific condition. The extent to which the symptoms relate to each other are thought to determine the persistence of the disorder. A disorder can therefore be understood as a relatively stable state of strongly connected symptoms (Borsboom and Cramer, 2013).

The network approach has been used to investigate various psychiatric disorders, including major depression, anxiety disorder, autism spectrum disorder, personality disorders, and schizophrenia (Van Borkulo et al., 2015; Epskamp et al., 2018; Fried et al., 2016; Fried et al., 2018). In general, these studies have shown that network analyses can help to understand how psychiatric symptoms are related. The application of network analyses in SUD is still limited (Contreras et al., 2019). Recently, Wasil et al. (2020) studied DSM symptom networks of SUD and major depression disorder, and Lin et al. (2019) studied the influence of Life stress on DSM symptom networks of SUD. These two studies however, were not primarily focused on the relationships between the SUD symptoms within the networks. Hoffman et al. (2019) studied networks of SUD criteria for alcohol use disorder in a general population sample. Their primary goal was to study the influence of sample selection on the network structure of alcohol users and showed that when asymptomatic individuals are systematically culled from the sample, the estimated pairwise relations in networks are often significantly affected.

The most extensive study of networks in symptoms of SUD is by Rhemtulla et al. (2016). They studied a sub-sample of a general population twin study, who used at least one drug (out of six drug classes) more than 6 times lifetime. 'Using more and longer than intended' was identified as the most central symptom over all drug classes. They also observed relevant differences between substance classes. For example, they observed differences in strength of the symptom's withdrawal and tolerance. Moreover, the connections between symptoms, especially those involving connections with hazardous use and legal problems because of use, showed differences between substance classes.

The studies of Hoffman et al. (2019) and Rhemtulla et al. (2016) however, were done in non-clinical population samples, not fulfilling the criteria of SUD. It remains to be studied therefore, whether these findings also hold for patients seeking treatment. Recent developments in the field of network analyses provide the opportunity to analyze accuracy of network parameters in more detail, and to test differences within (Epskamp et al., 2018) and between networks (van Borkulo et al., 2019). In addition, Rhemtulla et al. (2016) used DSM-IV criteria (American Psychiatric Association, 1994), whereas the introduction of DSM-5 in 2013 (American Psychiatric Association, 2013) brought some prominent changes in the classifications of SUD.

In this study we analyzed the interaction between SUD symptoms through network analyses in a large cohort of SUD patients in the first phase of treatment. First, we explored the overall symptom network of the cohort, calculating global strength, strength of the symptoms, and the weights of the symptom-to-symptom connections. Second, we tested whether networks differed between the most prevalent substances in addiction care (i.e., alcohol, cannabis, cocaine, opioids, other stimulants). Finally, we compared the networks based on DSM-IV and on DSM-5 SUD criteria.

2.2 Method

2.2.1 Design

In a cross-sectional observational design, routine intake data were extracted from electronic patient files. Patients provided informed consent based on opt out for scientific analyses of their medical files by the treatment center, according the ethical and privacy rules of the treatment institute and approved by the internal ethical board.

2.2.2 Sample

The sample included SUD patients who signed up for treatment at Tactus Addiction Care, a regional Dutch addiction treatment center, in a semi-rural area with a population of 2.5 million people. Between 2011-2016, 27,770 SUD patients entered treatment, of whom 15,588 had regular intake-assessments and 12,182 had another intake procedure because they were juveniles or received low intensity community help (daycare, housing etc.).

Complete records were available for 14.622 (94%) patients. In line with Rhemtulla et al. (2016) we selected cases with a primary problem substance (PPS) being alcohol, cannabis, cocaine, stimulants, opioids, hallucinogens, or sedatives, resulting in 12,813 assessments. At the time, treatment for tobacco use disorder was not available in our treatment center. Therefore, tobacco use disorder is not analyzed separately. Because of limited numbers, patients with hallucinogens (n = 2) and sedatives (n = 116) as PPS, were left out of the analyses, resulting in 12,695 assessments. To avoid more than one assessment for the same patient, we further selected only the first intake-assessment for a patient in that period, ending up with a final cohort of 10,832 patients (See supplementary Figure 1). For 184 patients one or more DSM- item was missing, so the network analyses sample was 10,648 patients.

2.2.3 Measures

SUD criteria were assessed using the structured clinical interview Measurement of Addictions for Triage and Evaluation (MATE 2.1; Schippers et al., 2011, 2010). The MATE is designed for use in routine practice for treatment allocation and evaluation of patients with SUD. The MATE has 10 modules. In this study we used the 11 DSM-IV items of Module 4 for substance abuse and dependence of the PPS. The items of Module 4 are binary items (No/Yes, scored as 0/1). We used the sums core on an abridged 5-item version of the Obsessive-Compulsive Drinking Scale to assess craving (Module Q1) (Anton et al., 1996; De Wildt et al., 2005). The MATE-Y(outh) has a DSM-5 craving item. A treatment seeking population study with the MATE-Y made it posible to calibrate the OCDS on the frequency of endorsement of this item (82%). This resulted in the dichotomized score SQ1.1d [Craving]: 0 = score 0-2, and 1 = score 3-20 (Broekman and Schippers, 2017).

2.2.4 Analyses

i.Network estimation

The SUD symptom networks were constructed using the Ising model for binary variables as implemented by Van Borkulo et al. (2015) in the IsingFit package similar to Rhemtulla et al. (2016). The model estimates the unique connections between two variables. It uses l1-regularized (lasso) logistic regressions for each symptom on all the other symptoms with standard maximal 100 iterations with a regularization parameter lambda (λ)[1]. The extended Bayesian Information Criterion (EBIC) is used to choose from these the best set of variables and coefficients for the regression equation that constrains many of the small regression coefficients to zero. So, for every variable a regression equation with an intercept and a set of non-zero regression weights for all or a selection of the other variables is obtained.

Networks consist of nodes (symptoms) and connecting edges. The weight of an edge indicates the strength of the connection between two symptoms. In the undirected Ising model the weight of the edge between two nodes is the mean of the two regression coefficients of each node on the other. Edge weights can be positive or negative and are in the Ising model not restricted to 1 or -1. The absolute sum of the weights of all the edges from one node (symptom) is defined as the node strength. Node strength is a measure for the centrality of a node in a network: the higher the strength, the more central the role of that node in the network. The global strength of a network is defined as the absolute sum of all the edge weights in the whole network.

ii.Statistical analysis

Within networks

To test if two node-strengths or two edge-weights within a network differed, we used the Bootstrapped Difference Test (Epskamp, 2019; Epskamp et al., 2018). This test computes difference scores for all bootstrap values, constructs a bootstrapped confidence interval (CI) around these scores, and checks if zero is in the bootstrapped CI. For our DSM-IV networks, this resulted in 55 node test statistics and maximum 1,485 edge weight test statistics per substance. For all analyses we used the bootstrap with 2,500 samples. To group nodes with comparable strength, we ordered them, starting from the strongest node and find the first significant different node, the nodes from start to this point form a group. We repeated this starting with the next node, etc. A significance level of .025 resulted in unambiguous group classification.

1 Because the obtained λ (and thus the regression equation) depends on the sample size, a lower bound to lambda can be set in the IsingFit package in case of comparison of networks based on different sample size. The manual advises to choose as lower bound for λ $\sqrt{\log (p)/n}$, where p is the number of nodes and n the sample size. This was for our smallest network 0.07. This turned out to be a too restrictive value, because it made the network for the smallest sample much sparser than when estimated based on EBIC alone. So, we chose to set the lower bound for λ to the mean of the 11 lambda's of the smallest sample which was 0.025.

Between networks

To investigate the differences between networks we use the Network Comparison Test (NCT; van Borkulo et al., 2019). It can test differences in the structure (M) and global strength (Gs), as well as node strengths and edge weights between two networks. NCT is a permutation test in which a reference sampling distribution of the relevant difference statistic between two networks is created, based on permuted data in which group membership is repeatedly rearranged. This distribution is used to test whether the observed difference is likely under the null hypothesis. For the difference in structure (M) the test uses the largest difference in all edge-weight differences between the two networks as the test statistic. We used the NCT to compare a) the different substances with each other, and b) the DSM-IV and DSM-5 networks for the different substances. For the DSM-IV networks this resulted for each comparison (10 in total) between two substance networks in one test statistic for structure (M), one for global strength (Gs), 11 for differences in node strength, and maximum of 55 for edge weights. For all analysis we used 2,500 permutations.

Network stability

To assess stability of the network node strengths and edges, we computed the correlation stability coefficients for each network, which represents the maximum proportion of cases that can be dropped such that with 95% probability the correlation between the node strengths and edges of the original network and the sampled networks is at least 0.7. Correlation stability coefficients (CS (cor = 0.7) should not be below 0.25, and preferably above 0.5 (Epskamp et al., 2018)

i i i.Visualization

For the visualization of the networks, we used the R-package qgraph (Epskamp et al., 2018). Nodes were depicted as circles of varying scale indicating the strength, and edges as lines of varying thickness, indicating the weight of the edge. We colorized the nodes using the same color for nodes with comparable strength. To ensure comparable thickness of the edge weights, we set the maximum edge weight =1.66 for all graphs. We replicated the layout of Rhemtulla et al. (2016) to facilitate visual comparison of the networks.

2.3 Results

2.3.1 Demographics

In total, 56.5% of the sample (n = 6,125) used alcohol as PPS, 22.1% cannabis (n = 2,396), 12.1% cocaine (n = 1,307), 4.6% opioids (n = 499), and 4.7% stimulants (n = 505). The majority was male (73.3%); the average age was 39.1, and varied from 28.4 years for cannabis patients to 45.4 years for alcohol patients, see Table 1. Average lifetime use varied from 8.1 years for cocaine to 16.2 years for alcohol. The average score on the 11 DSM items was 6.39 for the DSM-IV and 6.98 for DSM5.

Table 1

Patients demographics and DSM-IV and DSM-5 total scores

	Alcohol (*n* = 6,125)	Cannabis (*n* = 2,396)	Cocaine (*n* = 1,307)	Opioids (*n* = 499)	Stimulants (*n* = 505)	Total (*n* = 10,832)
Male	4,489 (73.3%)	1,926 (80.4%)	1,155 (88.4%)	397 (79.6%)	404 (80.0%)	8,371 (77.3%)
Age, yrs: *M (SD)*	45.08 (13.07)	28.03 (8.87)	33.88 (8.30)	42.17 (9.84)	28.98 (8.03)	39.07 (13.62)
Lifetime regular use of Primary Problem Substance, yrs: *M (SD)*)	16.16 (12.51)	10.40 (7.38)	8.17 (6.95)	12.62 (10.00)	7.90 (6.43)	13.41 (11.15)
DSM-IV Total score (0-11): *M (SD)*	6.39 (2.64)	6.71 (2.57)	6.88 (2.87)	6.47 (3.24)	6.86 (2.76)	6.55 (2.69)
DSM-5 Total score (0-11): *M (SD)*	6.98 (2.72)	7.49 (2.62)	7.44 (2.88)	7.14 (3.23)	7.39 (2.84)	7.17 (2.76)

Network stability

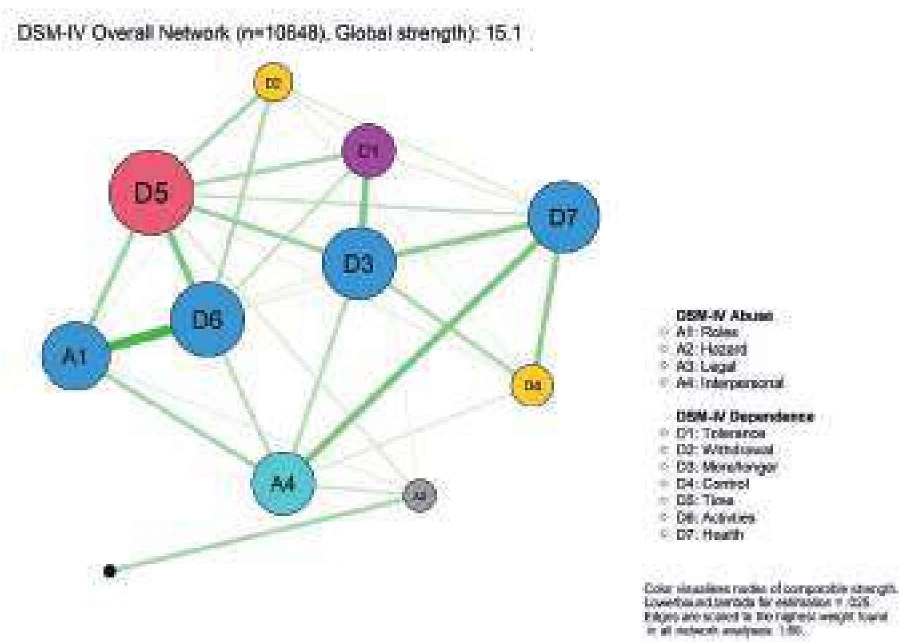
For all networks, the correlation stability coefficients CS (cor = 0.7) for the node strengths and edges were greater than the recommended value of 0.5 (range: 0.52 (Opioids) to 0.75, which is the maximum obtainable value of the correlation stability coefficients), see supplementary Table 2.

2.3.2 Overall network

In Figure 1 we present the overall DSM-IV symptoms network. The network had 40 non-zero edges (out of 55 possible edges), which were all positive, resulting in a global strength of 15.1. The strongest node was D5 [Time] (Ns = 4.2). After that, in order of strength, but not significantly different: D6 [Activities] (Ns = 3.7), D3 [More/longer] (Ns = 3.6), D7 [Health] (Ns = 3.5), and A1 [Roles] (Ns = 3.4). The nodes A3 [Legal] and A2 [Hazard] had low strength.

The edge with the highest weight was that between A1 [Roles]-D6 [Activities] (Ew = 1.28), and after that A4 [Interpersonal]-D7 [Health] (Ew = .88), but not significantly different from D5 [Time]-D6 [Activities] (Ew = .83), D1 [Tolerance]-D3 [More/longer] (Ew = .82), D3 [More/longer]-D7 [Health] (Ew = .74), and D4 [Control]-D7 [Health] (Ew = .73), see supplementary Figure 2.

Figure 1
Overall DSM-IV symptoms network (alcohol, cannabis, cocaine, stimulants, opioids)



2.3.3 Substance networks

The DSM-IV networks per substance (alcohol, cannabis, cocaine, stimulants, and opioids) are displayed in Figure 2.

For **alcohol**, the global strength was 15.6, and D5 [Time] (Ns = 4.2) was the strongest node. Nodes with comparable strength were D7 [Health] (Ns = 3.8), and D6 [Activities] (Ns = 3.8). The least strong node was A3 [Legal] (Ns = .84). The strongest edge was between A1 [Roles] and D6 [Activities] (Ew = 1.26). This edge had a significantly higher weight than all the other edges.

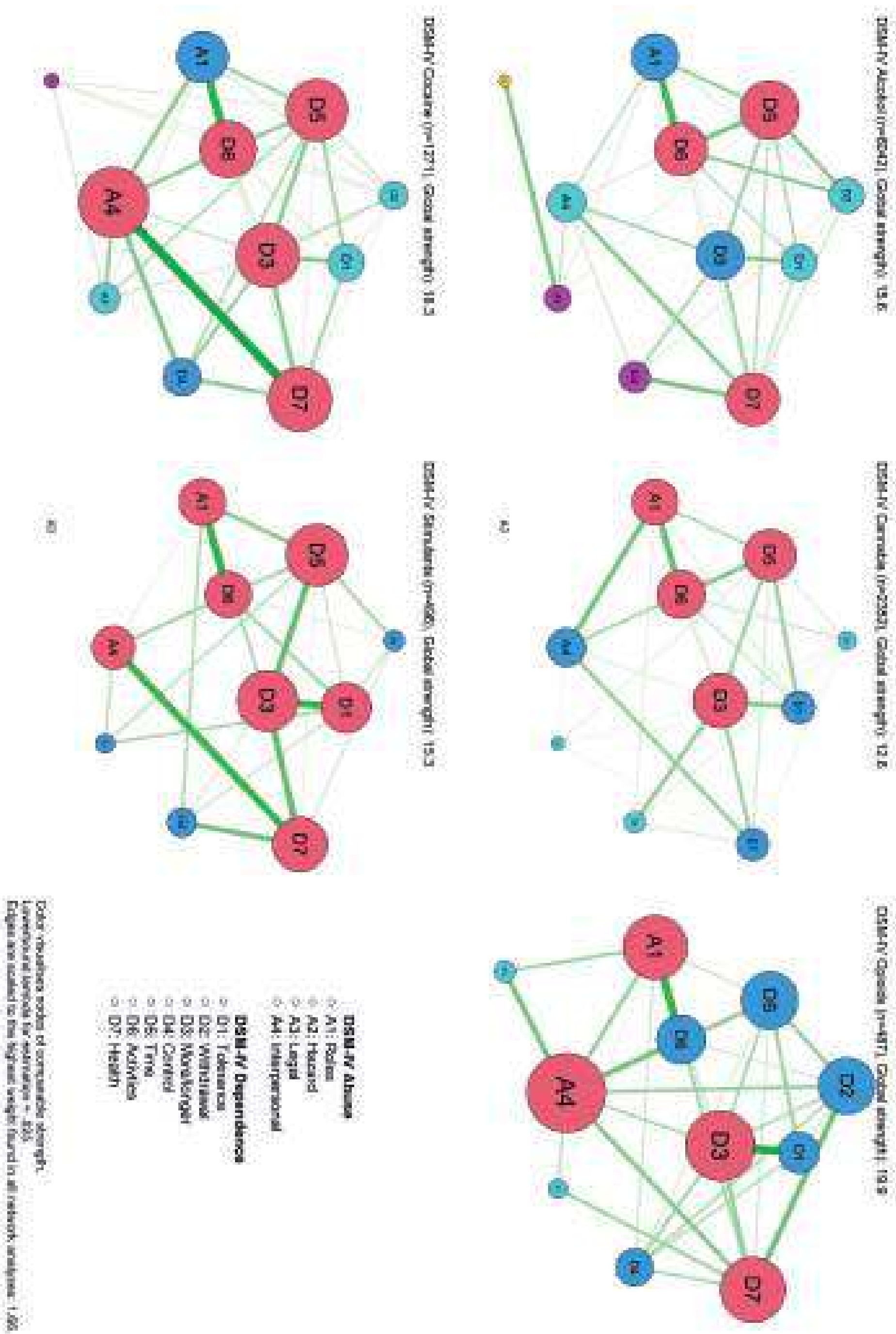
For **cannabis**, the global strength was 12.6 and D3 [More/longer] (Ns = 3.8) was the strongest node. Nodes with comparable strength were D5 [Time](Ns = 3.7), D6 [Activities](Ns = 3.4), and A1 [Roles] (Ns = 3.3). In this network A3 [Legal] had zero strength. The strongest edges, in order of strength, but not significantly different from each other, were: A1 [Roles]-D6 [Activities] (Ew = 1.06), A1 [Roles]-A4 [Interpersonal] (Ew = .91), D1 [Tolerance]-D3 [More/longer] (Ew = .80), and D5 [Time]-D6 [Activities] (Ew = .79).

For **Cocaine**, the global strength was 18.3, with six nodes with comparable high strength: A4 [Interpersonal] (Ns = 5.0), D7 [Health] (Ns = 4.6), D3 [More/longer] (Ns = 4.5), D5 [Time] (Ns = 4.4), and D6 [Activities] (Ns = 4.1). Again, A3 [Legal] (Ns = 1.0) was the node with the least strength. The strongest edges were: A4 [Interpersonal]-D7 [Health] (Ew = 1.66) and A1 [Roles]-D6 [Activities] (Ew = 1.43).

The global strength for **stimulants** was 15.3. Seven nodes with the highest strength were: D5 [Time] (Ns = 4.4), D3 [More/longer] (Ns = 4.3), D7 [Health] (Ns = 3.9), D1 [Tolerance] (Ns = 3.6), A1 [Roles] (Ns = 3.3), D6 [Activities] (Ns = 3.3), and A4 [Interpersonal] (Ns = 3.0). Here A3 [Legal] had zero strength. The strongest edge was D1 [Tolerance]-D3 [More/longer] (Ew = 1.38.).

The **opioids** network had a global strength of 19.9. The nodes with high strength were: A4 [Interpersonal] (Ns = 5.6), D3 [More/longer] (Ns = 5.0), D7 [Health] (Ns = 4.6), and A1 [Roles] (Ns = 4.6). The least strong node was A2 [Hazard] The strongest edge was D1 [Tolerance]-D3 [More/longer] (Ew = 1.53). (Diagrams of all the Bootstrapped Difference Tests are available in the supplement, Tables 3a and 3b).

Figure 2 DSM-IV substance networks for individual substances (alcohol, cannabis, cocaine, stimulants, and opioids)



2.3.4 Differences between the substance networks

The substance networks differed in global strength. The opioids network had the highest strength, followed by cocaine, then alcohol, and stimulants. The cannabis network had the lowest global strength. In the opioids and cocaine networks D7 [Health] was stronger than in the other networks. The cannabis network was the only one where A4 [Interpersonal] was not strong. NCT results of the comparison of global strength, structure and most different nodes and edges between the 5 substance networks are shown in Table 2, and supplementary Tables 4a, 4b, and 4c.

Table 2 Differences in global strength (Δ Gs), nodes differing significantly between networks (N) structure (Δ M), largest edge weight difference (E)°

Compared networks	Δ Gs	N	Δ M (p)	E
alcohol - cannabis	2.93*	D7 D2 A2 A3 D4	.84*	A2 [Hazard]-A3 [Legal]
alcohol - cocaine	-2.76*	-A4 -D3	.90*	A4 [Interpersonal]-D7 [Health]
alcohol - stimulants	.24	A3	.84	A2 [Hazard]-A3 [Legal]
alcohol - opioids	-4.28**	-A4-D2-D3	.90**	A3 [Legal]-A4 [Interpersonal]
cannabis - cocaine	-5.69*	-A4 -D7 -A2 -D4 -A3-D2	.99*	A4 [Interpersonal]-D7 [Health]
cannabis - stimulants	-2.69	-D1	.72	A1 [Activities]-A4 [Interpersonal]
cannabis - opioids	-7.22*	-A4-D2-D7-A3	.90**	A3 [Legal]-A4 [Interpersonal]
cocaine - stimulants	3.0	D4 A3	.85	A4 [Interpersonal]-D4 [Control]
cocaine - opioids	-1.53	-D2	.90	A3 [Legal]-A4 [Interpersonal]
stimulants - opioids	-4.53**	-D2 -A4 -A2	.90	A3 [Legal]-A4 [Interpersonal]

(-) means the first in the comparison is the less strong
(*) significant different p .00
(**) significant different .01 ≥ p ≤ .03
(°) Network Comparison test (NCT) (van Borkulo et al., 2019)

The global strength of the opioids and cocaine networks was higher (Figure 2) than of the other networks. Similarly, the alcohol network was stronger than that of cannabis. The strength of the symptoms A4 *[Interpersonal]* was higher in the opioids and cocaine networks than in the other networks. This was also true for the low strength for *D7 [Health]* in the cannabis network. Except for the difference between stimulants and opioids, in all cases where the global strength was different, also the structure differed significantly. In the case of alcohol versus cannabis this was caused by the higher weight for the edge A2 *[Hazard]-A3 [Legal]*. For the difference between alcohol and cocaine and for cannabis and cocaine this was because of the difference in the edge A4 *[Interpersonal]-D7 [Health]* and between Alcohol and opioids because of the edge A3 *[Legal]-A4 [Interpersonal]*.

2.3.5 DSM-IV versus DSM-5 networks

The overall DSM-5 network had a higher global strength than the DSM-IV network (ΔGs = .62, p = .02), see supplementary figure 5. The strength of *SQ1.1d [Craving]* was higher than of *A3 [Legal]* (ΔNs = .91, p = .00). *A2 [Hazard]* had lower strength in DSM-5 than in DSM-IV(ΔNs = .60, p = .00). Furthermore, the network structures differed between DSM-IV and DSM-5 (ΔM = .55, p = .00), due to the replacement of *A3 [Legal]* by *SQ1.1d [Craving]A2 [Hazard]*. The prevalence of craving was also higher (83%), than that for *A3 [Legal]* (21%).

The global strength in the DSM-5 symptom network was higher for cannabis compared to that of the DSM-IV (ΔGs = 1.28, p = .04). The network structure differed only for alcohol (ΔM = .84, p = .00).

The strength of *SQ1.1d [Craving]* was higher than of *A3 [Legal]* for alcohol (ΔNs = .72, p = .00), cannabis (ΔNs = 1.32, p = .00), and stimulants (ΔNs = .50, p = .05). For alcohol also *A2 [Hazard]* had higher strength (ΔNs = .84, p = .00) in the DSM-5 network, compared to the DSM-IV network. All edges that differed significantly were between *A3 [Legal]/SQ1.1d [Craving]* and other nodes, see supplement.

2.4 Discussion

The network analyses presented here are, to our knowledge, the first network analyses applied to a large clinical sample of SUD patients. The SUD symptom networks showed strong connections between the symptoms, resulting in high global strength. In the overall SUD network, the symptom: "Spending substantial amount of the day obtaining, using, or recovering from substance use" (D5 [Time]) had the highest strength. The symptoms "giving up or cutting back on important social, professional, or leisure activities because of use" D6 [Activities], and "repeated usage causes or contributes to an inability to meet important social, or professional obligations" (A1 [Roles]), were the symptoms that influenced each other most.

Between substances, networks differed in global strength and structure. The networks of patients with opioids or cocaine use as their PPS had the highest global strength, and the most central symptoms were: "persistent or recurrent social or interpersonal problems because of use" (A4 [Interpersonal]) and "persistent use despite the user's awareness that the substance is causing or at least worsening a physical or mental health problem" (D7 [Health]). For patients with alcohol as PPS, interpersonal problems were less central. The cannabis network had the lowest global strength and lowest strength for both health and interpersonal problems related to use, suggesting that cannabis shows a somewhat different profile in health and social consequences.

Finally, we observed a slightly higher strength of the overall network when using the criteria for DSM-5 in comparison to DSM-IV. This was caused by craving having higher strength than legal problems, although also craving had low strength. All significant differences between both networks were related to this change.

The symptoms D1 [Tolerance] and D2 [Withdrawal] were less central, compared to the symptom networks previously observed in a community sample (Rhemtulla et al., 2016). In addition, the symptoms A4 [Interpersonal] and D7 [Health] were more central in our SUD sample. The findings of Hoffman et al. (2019) in the community sample of people using alcohol, when the sample selection was restricted to individuals who met at least one DSM criterium for SUD, are in line with our findings: high centrality for A1 [Roles], D5 [Time], D6 [Activities], and D7 [Health]. On a substantially large sample, the current findings might not generalize to other SUD populations, given the sociocultural differences between regions and countries, and its potential impact on SUD symptoms. It would be of interest for future studies to compare SUD symptom networks between patients with different sociocultural backgrounds.
Our findings suggest that for SUD patients that seek help, health and social relations problems are more central. This difference might be explained by differences between stages in the development of SUDs, with substance users in the general population representing early stages of substance use, and our sample representing advanced stages of SUD (Buu et al., 2012; Neven et al., 2018; Rutten et al., 2017; Van Den Brink and Schippers, 2012).

The global strength was the lowest for cannabis, and the highest for opioids, suggesting that the opioid network is more stable and might be less easy to change (Borsboom and Cramer, 2013; van Borkulo, 2018). In DSM-5 the criteria count is considered an indication of disease severity, in line with a latent trait model of disease, where more positive scores on criteria indicate higher severity (Hasin et al., 2012; Usselman et al., 2015). In our sample, the cannabis patients had a higher total score on DSM-criteria than the opioid patients (7.49 for DSM-5 and 6.71 for DSM-IV for cannabis, and 6.47 and 7.14 for opioids). This all suggests that further exploration of the relation between the latent trait and the Ising network model is needed (MacCoun, 2013; Martin, 2013; Marsman et al., 2018). Also the concept of centrality in psychological symptom networks is less obvious than in social networks, were the network concept was first introduced. When interpreting centrality measures in psychological networks, the theoretical framework behind the concept of the nodes needs to be taken into consideration, as pointed out by Bringman et al. (2019).

A symptom network ideally consists of directly observable behaviors or measurable characteristics in real life, while edges describe the relation between those symptoms. However, DSM criteria are a summary of one-year occurrence and are context dependent, i.e. conditional on use (van Borkulo 2018). Use of network analysis in clinical practice, should use direct and frequent measurements of actual behavior at an individual level at a given point in time, known as ecological momentary assessment (EMA) (Wray et al., 2014). Future studies should investigate the difference between such an approach, and the use of DSM-criteria. Given the strength and weight differences we found within and between networks, future studies should explore whether targeting the most central symptom in a network offers opportunities for personalized treatment and could increase effectiveness.

When interpreting our findings, there are several considerations to take into account. First, for the estimation of the overall networks we did not weigh the data, and therefore the different substances influence the overall network proportional to their frequency. We did so, in order to create representative overall networks for the SUD patient population in addiction care. Second, differences between substances are potentially caused by confounding factors like age, psychiatric comorbidity or stage of the disorder. For instance, experiencing less interpersonal and health problems in the cannabis group might be due to the younger age and/or an earlier stage in the course of SUD in the cannabis group. Therefore, no causal inferences can be made concerning differences between substance groups. Furthermore, the DSM-5 criterium craving was not measured directly but constructed from OCDS-scores. Another important limitation of our findings is the use of cross-sectional data. Longitudinal data may shed more light on the dynamics in the symptom networks over time, and provide useful insight in the stages during the development of SUD.

In sum we observed that 1) spending a substantial amount of the day obtaining, using, or recovering from substances, is the most central symptom in SUD patients, 2) the centrality of continued use in spite of health and interpersonal problems differs across substances, and 3) DSM-5 criteria form a denser network than DSM-IV SUD criteria. Future studies should investigate the clinical relevance of these core SUD symptoms as treatment targets to help break the addiction cycle.

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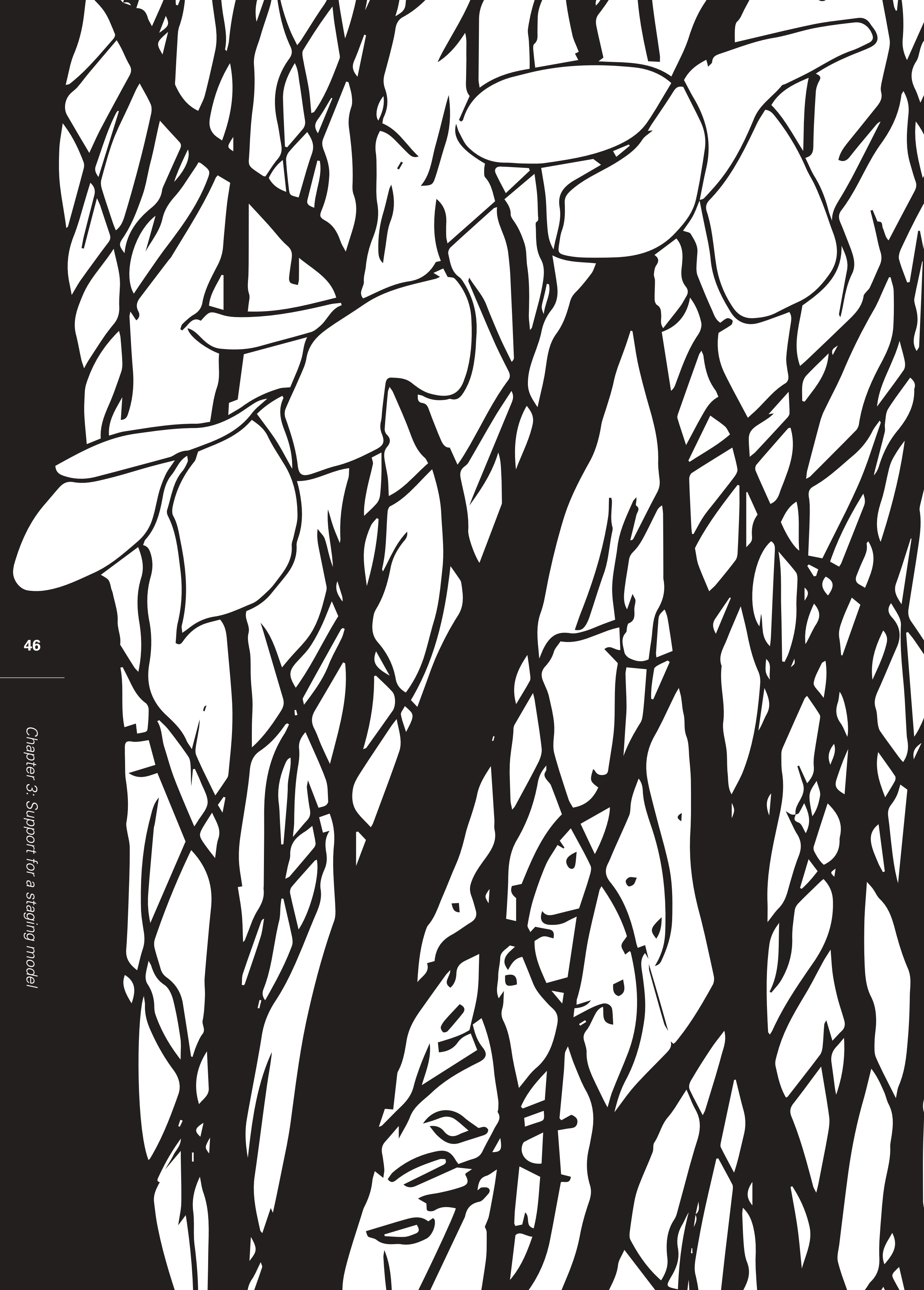

3. Differentiating treatment-seeking substance-use disordered patients:

Support for a staging model

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Abstract

Background and Aims

Profiling according to a staging model could be useful for differentiating among the heterogeneous group of treatment-seeking substance use disorder (SUD) patients. The staging model that was evaluated in this study is analogous to the hierarchical Tumor-Nodes-Metastasis (TNM) model in oncology. The proposed model distinguishes profiles derived from the following stages of addiction: (0) addicted, but not severely; (1) severely addicted, but without psychiatric comorbidity or social disintegration; (2) severely addicted with psychiatric comorbidity, but with no social disintegration; and (3) severely addicted in combination with psychiatric comorbidity and social disintegration.

Methods

We tested whether subgroups suggested by the staging model for SUDs could be identified among Dutch treatment-seeking SUD patients (N = 6,602).
Results The profile of 5,153 patients (80.9%) fitted the staging model, and the model was invariant for age, sex, and primary substance of abuse. The majority of the patients not fitting the model (N = 906 of 1,202; 75.4%) were not severely addicted but were in treatment or had recently been treated for a comorbid psychiatric disorder. When psychiatric treatment was removed as an indicator for the presence of psychiatric comorbidity, the fit increased to 87.1%.

Conclusions

These results support the validity of the hierarchical staging model, which may be used to match patients to specific treatment regimens.

3.1 Introduction

People who seek treatment for a substance-use problem differ widely in the severity of their addiction, psychiatric and physical comorbidity, social problems, motivation for change, and acceptance of the role of patient. This is true for alcohol dependence (Epstein, Labouvie, McCrady, Jensen, & Hayaki, 2002), drug dependence (Basu, Ball, Feinn, Gelernter, & Kranzler, 2004), and the combination of both alcohol and drug dependence (Harrington et al., 2012; Kirisci, Vanyukov, Dunn, & Tarter, 2002). A similar heterogeneity is found among people with alcohol dependence (De Bruijn, Van den Brink, De Graaf, & Vollebergh, 2006; Moss, Chen, & Yi, 2010; Woicik, Stewart, Pihl, & Conrod, 2009) or drug dependence (Chan, Gelernter, Oslin, Farrer, & Kranzler, 2011; Kranzler et al., 2008) in the general population. It is generally assumed that these differences reflect different treatment needs and that they are associated with different responses to treatment. Diagnostic systems, such as the Diagnostic and Statistical Manual of Mental Disorders (DSM), do not combine patients with similar symptoms based on aetiology or pathogenesis into a single category. As a consequence, DSM classifications are of limited use for predicting the course of the disorder or for allocating patients to specific treatments (Lilienfeld, 2014).

Recently, models have been proposed for the staging and profiling of psychiatric disorders (McGorry, 2010). According to these models, major psychiatric illnesses develop in stages. During the early stages, as with many somatic illnesses (e.g. cancer), symptoms are more general (de Haan et al., 2012) and relatively simple treatments can be effective, whereas during later stages as symptoms become more specific, and comorbidity and social consequences more severe, treatment needs to be more comprehensive and individualized. However, guidelines (De Wildt, Schramade, Boonstra, & Bachrach, 2002; McKay, Cacciola, McLellan, Alterman, & Wirtz, 1997; Melnick, De Leon, Thomas, & Kressel, 2001) for matching specific patients to specific treatments and levels of care, like the American Society of Addiction Medicine (ASAM) patient placement criteria (Mee-Lee, Shulman, Fishman, Gastfriend, & Griffith, 2001), lack empirical support (Merkx et al., 2013; Project Match Research Group, 1998), although it is generally accepted that professional care systems should be built, among other things, on such treatment allocation guidelines (Insitute of Medicine, 1990). A patient-treatment allocation model, based on disease stages could be helpful in the search for empirical support for these guidelines.

Some years ago, we proposed a staging model for addiction based on an analogy between addiction and cancer (Van den Brink & Schippers, 2012). In oncology, the Tumour-Nodes-Metastasis (TNM) staging model of solid tumours is based on tumour size

(T), the degree of growth in adjacent tissue (positive lymph nodes; N), and the presence and number of metastases (M). This model has helped greatly to reduce the heterogeneity of clinical presentations and has helped to refine and improve treatment allocation and long-term outcomes in oncology (Janssen-Heijnen et al., 2005). Inspired by this development, a model for staging addictive disorders has been suggested (Van den Brink & Schippers, 2012) with four levels of addiction severity (A), five levels of comorbidity (P) and two levels of social disintegration (S), leading to five stages: four for addiction and one for people who are at risk for addiction. These three domains are parallel to, respectively, tumour size (T), problems in adjacent tissue (N), and metastases (M) and are based on studies on the literature of factors with evidential influence on treatment outcomes (Pedersen & Hesse, 2009; Schippers, 2002).

Table 1 Adaptation of the TNM model for use in addiction and corresponding MATE dimension scores

Adaptation of the TNM model for use in addiction (Van den Brink & Schippers, 2012, fig 2).				Corresponding MATE dimensions and scores	
	Meaning	Variable	Meaning	MATE dimension	MATE dimension score
A	Addiction	A0	Asymptomatic use + risk factors (e.g. start use at young age)	Severity of addiction	0: Not high
		A-is (in situ)	Frequent binge drinking, not reaching DSM abuse criteria		
		A1	Pattern of abuse		
		A2	Dependence with symptoms of craving and tolerance/withd-rawal		1: High
		A3	Addiction with com-pulsive use and loss of positive experiences		

Adaptation of the TNM model for use in addiction (Van den Brink & Schippers, 2012, fig 2).				Corresponding MATE dimensions and scores	
	Meaning	Variable	Meaning	MATE dimension	MATE dimension score
P	Comorbidity	P0	No psychiatric or physical comorbidity	Severity of psychiatric comorbidity[1]	0: Not high
		P1	Mild psychiatric (e.g. depression) or physical comorbidity		
		P2	Moderate psychiatric (e.g. ADHD) or physical (e.g. HIV positive) comorbidity		1: High
		P3	Severe psychiatric (e.g. psychosis) or physical (e.g. cirrhosis) comorbidity		
		P4	Very severe psychi-atric (e.g. dementia) or terminal physical disease		
S	Social disintegration	S0	No social limitations or mild ones	Severity of social disintegration	0: Not high
		S1	Moderate or severe social problems		1: High
	Stage	0	A0/P>0/S0: treatment of risk factors	Not addicted	0000
		I	Ais-1/N0/S0: E-health or treatment by a GP	Addicted not severely	1000
		II	A1-2/P1-2/S0: brief treatment (with or without medication)	Addicted severely	1100
		III	A3/P2-3/S0: regular outpatient treatment (including medication)	Addicted severely, and severe psychiatric comorbidity	1110
		IV	A3/P2-3/S1: intensive treatment (inpatient or long-term outpatient)	Addicted severe, and severe psychiatric comorbidity and severe social disintegration	1111

1 The MATE dimension for comorbidity does not include physical comorbidity

To test the proposed model we used the three domains as they are applied in Dutch substance abuse treatment practices (De Wildt et al., 2002; Merkx et al., 2011, 2013). In the treatment allocation algorithm, the levels of addiction severity and comorbidity are dichotomized and comorbidity is limited to psychiatric comorbidity.

To the best of our knowledge this is the first staging model of addiction that is operationalized and tested empirically. Both the original and the tested model are presented in Table 1.

The general assumption of the APS-model is that addictive disorders develop in the following sequential stages: experimental and normal use of a substance, excessive and problematic use, severe addiction without psychiatric comorbidity, severe addiction with psychiatric complications, and severe addiction with both psychiatric comorbidity and social disintegration. We assigned the following numerical values to the four stages:

I = addicted, but not severely;
II = severely addicted, but no severe psychiatric comorbidity and no severe social disintegration;
III = severely addicted with severe psychiatric comorbidity but no severe social disintegration;
IV = severely addicted with both severe psychiatric comorbidity and severe |social disintegration.

People for example who suffer from a bipolar or borderline personality disorder and who are abusing alcohol and drugs at the same time, might subsequently develop alcohol or drug dependence and not fit in this model. They might fit better in a staging model for bipolar or borderline personality disorder. We expect this group to be bigger in a general psychiatric population. This study focuses on patients who seek treatment for their addiction. Another group of patients that would not fit the current model would be a group with social disintegrate directly related to the severity of their addiction, i.e. without developing psychiatric comorbidity. We expect this to be a rather small group. This counts also for the group that has no severe addiction and still disintegrates socially, with or without other psychiatric comorbidity. Those groups do violate the suggested model.

Without longitudinal observations, a staging model cannot be fully evaluated. However, in a cross-sectional study, the proportion of patients with characteristics in accordance with the proposed stages can indicate the validity of the model. The purpose of this study was twofold: first to examine to what extend the proposed stages occur in a cross-sectional sample of treatment seeking SUD patients, and second to assess whether the model is invariant across subgroups (age, gender and primary substance of misuse), and whether there are certain subgroups for which the model does not apply.

3.2 Methods

3.2.1 Design and sample

The sample included individuals who had signed up for treatment at the Tactus Addiction Care Centre, a regional Dutch treatment centre, which provides a broad range of treatment and other care programs in a semirural area with a population of 2.5 million people. Patient characteristics were assessed at intake using a structured assessment interview called Measurement in the Addictions for Triage and Evaluation (MATE) (Schippers, Broekman, & Buchholz, 2011a, 2011b; Schippers, Broekman, Buchholz, Koeter, & Van Den Brink, 2010). In the period 2008-2011, the MATE was administered to an unselected group of 7,039 patients. Only patients with a DSM-IV diagnosis of a SUD were included in the present study (N = 6,602). Data are collected during regular intake under an already existing general informed consent.

3.2.2 Measures

The MATE was designed for use in routine practice for treatment allocation and evaluation. It is based on the biopsychosocial disease model of the World Health Organisation, which comprises the International Classification of Diseases (ICD) and the International Classification of Functioning, Disability, and Health (ICF). The MATE has 10 modules: (1) substance use; (2) substance abuse and dependence; (3) craving; (4) depression, anxiety, and stress; (5) indicators of the need for psychiatric or medical consultation; (6) personality disorders; (7) physical complaints; (8) personal and social functioning, activities and participation, care, support and needs; (9) environmental factors that can influence recovery; and (10) history of treatment for a substance-use disorder. The MATE yields 20 scores. The MATE was developed as a triage instrument. Thus, it assigns patients to appropriate levels of care according to a patient-allocation algorithm that was developed by De Wildt et al. in 2002. Since then, the algorithm has been routinely applied in almost all addiction treatment centres in the Netherlands (Merkx et al., 2007, 2013; Schippers, Broekman, Koeter, & Van den Brink, 2004). In the algorithm, patients are allocated to levels of care according to their scores on the MATE. These scores and patients' treatment history are also used in the staging model. The MATE scores were operationalised by considering cut-offs that were available in the literature, pragmatic arguments, and opinions of experts in the field (Schippers et al., 2010).

Based on seven of the MATE scores and patients' data on substance use from MATE Module 1, dichotomous scores on the three aspects of the staging model (i.e. addiction severity, psychiatric comorbidity, and social disintegration) were computed and used for analysis in this study.

Patients were considered to be severely addicted if they had any one (or more than one) of the following: (a) eight or nine DSM-IV abuse/dependence symptoms (but excluding tolerance and legal problems; based on Langenbucher et al.'s (2004) suggestions), (b) a high level of craving (score ≥ 12 on an abridged version of the Obsessive Compulsive Drinking Scale (De Wildt et al., 2005), (c) a high level of substance use. The level of substance use was calculated from patients' data on their alcohol, nicotine, cannabis, opiates, and cocaine/other stimulant use as assessed by the MATE. For each of the five substances, a score of 0 or 1 was assigned, indicating that the level of use was either not high or high. The cutoffs for the different substances were: alcohol: > 240 units of alcohol drunk in the past 30 days; nicotine: > 600 cigarettes smoked in the past 30 days; cannabis: at least weekly use for at least more than one year and use on more than 28 days in the past 30 days; opioids: at least weekly use for at least one year and use on more than one day in the past 30 days; cocaine/other stimulants: the same criteria as for opiates. The five scores were summed, and the total score could range from 0 to 5. A cut-off of 3 was considered a high level of substance use.

Patients were considered to have psychiatric comorbidity if any one (or more than one) of the following criteria was met: (a) current or recent treatment for a psychiatric or a psychological problem and current use of psychotropic medication, (b) presence of acute psychiatric symptoms such as suicidality or psychosis, and (c) a score ≥ 60 on the depression, anxiety, and stress module of the MATE (Depression, Anxiety, Stress Scales; range 0-126; Lovibond & Lovibond, 1995).

Patients were considered to be socially disintegrated if any one of the following criteria was met: (a) a score ≥ 12 on MATE S7.1 Limitations—Basic (range 0-32), which is part of the MATE-ICN module on activities and participation, and (b) a score ≥ 12 on MATE S8.2 Negative External Influences (range 0-20), which is part of the MATE-ICN module on environmental factors.

3.2.3 Modelling

Combining the dichotomous scores on the four aspects (a) addicted, (b) severely addicted, (c) psychiatric comorbidity, and (d) social disintegration results in four combinations that fit the staging model and four combinations that do not fit the model (see Table 2).

Table 2 Combinations of dimensions in the four-stages model of addiction.

Stages	Addicted	Severely addicted	Psychiatric comorbidity	Social disintegration	Pattern
	Combinations that fit the staging model				
I	yes (1)	no (0)	no (0)	no (0)	1000
II	yes (1)	yes (1)	no (0)	no (0)	1100
III	yes (1)	yes (1)	yes (1)	no (0)	1110
IV	yes (1)	yes (1)	yes (1)	yes (1)	1111
	Combinations that do not fit the staging model				
	yes (1)	no (0)	no (0)	yes (1)	1001
	yes (1)	no (0)	yes (1)	no (0)	1010
	yes (1)	no (0)	yes (1)	yes (1)	1011
	yes (1)	yes (1)	no (0)	yes (1)	1101

3.2.4 Analysis

We calculated the percentage of patients with characteristics that fit the staging model (accuracy of the fit of the model). Because the sample of patients was drawn from only one population, we have no other statistics on the goodness of fit of the model. To check consistency of the fit in different subgroups of patients, we also compared the accuracy of the fit separately for men and women, for different age groups, and for patients with different primary substances of abuse. To determine whether the model should be adapted or the applicability should be narrowed, we further compared the characteristics of patients who did and those who did not fit the staging model.

Because of the large sample size, even small differences would yield significant p-values; thus, we also report effect sizes. Frequency tables were analyzed using chi-square analysis and p-values for significance and Cramer's V for effect sizes. The latter are interpreted as follows: small: .10, medium: .30, large: .50 (Cohen, 1988). Differences in symptom severity between adjacent groups were analyzed as trends using the generalized linear model (GLM) procedure and reporting p-values for significance and partial η^2 for effect sizes. The latter were interpreted as follows: small: .01, medium: .06, large: .14 (Cohen, 1988). All analyses were conducted using IBM SPSS Statistics for Windows, Version 23.0.

3.3 Results

Patients' characteristics are shown in Table 3. Of the 6,602 patients, 77.9% (n = 5,141) were males with a mean age of 36.4 years (sd = 13.8); 36.1% (n = 2,382) were younger than 30 years; 52.2% (n = 3,447) were 30 to 55 years of age; and 11.7% (n = 773) were older than 55 years. Participants' primary substance of abuse was as follows: alcohol (53.0%), cannabis (25.9%), stimulants (14.9%), and opioids (6.2%). The distribution of patients across the possible combinations of the three aspects of the staging model is also presented in Table 3: 80.9% of the patients fit the model, and 19.1% did not fit the model.

The majority (74.6%) of the patients who did not conform to the model were those with psychiatric comorbidity, but who were not severely addicted (Pattern 1010; n = 906; 14.2% of the total cohort). The second largest group of patients who did not fit were those exhibiting Pattern 1101 (n = 141; 2.2% of the total cohort), i.e., those who were socially disintegrated, but who did not have psychiatric comorbidity. The other two groups not fitting the model each constituted only 1.3% of the total sample.

Table 3 also shows the fit to the model in the different subgroups. The fit was higher for those ≤ 30 years (84.3%) than for those > 30 years (79.1%) [χ^2 (1, N = 6367) = 26.76, p < .001, Cramer's V = .065], and higher for men (81.9%) than for women (77.5%) [χ^2 (1, N = 6367) = 14.25, p < .001, Cramer's V = .047)], and the fit somewhat varied among patients with different primary substances of abuse: opioid users (84.4%), cannabis users (84.0%), alcohol abusers (79.2%), and stimulant users (80.4%) [χ^2 (3, N = 6367) = 19.20, p < .001, Cramer's V = .055]. However, the magnitude of all these differences was small; all Cramer's Vs were less than .10.

Table 3 Matches and mismatches with the staging model of addiction

		Total		Age group			Sex		Primary substance of abuse			
				- 30	30-55	55+	M	F	Alcohol	Opioids	Stimulants	Cannabis
		N	%	%	%	%	%	%	%	%	%	%
pattern	**According to model**	**5153**	**80.9**	**84.3**	**79.0**	**79.3**	**81.9**	**77.5**	**79.2**	**84.4**	**80.4**	**84.0**
	1000	2703	42.5	44.5	37.8	56.9	43.6	38.5	46.8	26.0	34.9	41.6
	1100	1108	17.4	19.0	17.9	10.2	18.5	13.6	14.3	29.4	19.1	20.1
	1110	1044	16.4	16.9	17.6	9.6	15.1	20.9	13.9	20.7	18.9	19.1
	1111	298	4.7	3.9	5.7	2.5	4.8	4.4	4.2	8.2	7.4	3.2
	Not according to model	**1214**	**19.1**	**15.7**	**21.0**	**20.7**	**18.1**	**22.5**	**20.8**	**15.6**	**19.6**	**16.0**
	1010	906	14.2	12.0	15.0	17.4	12.9	18.7	16.3	5.8	12.6	12.7
	1011	82	1.3	.8	1.7	.9	1.3	1.3	1.5	1.3	1.6	.7
	1101	141	2.2	1.7	2.7	1.3	2.5	1.2	1.9	6.4	2.9	1.5
	1001	85	1.3	1.0	1.6	1.1	1.3	1.3	1.0	2.1	2.5	1.2
	Total	6367	100	100	100	100	100	100	100	100	100	100

**For 235 patients, a pattern could not be derived because of missing data in the MATE.*

To better understand why some patients did not fit the staging model, we compared the characteristics of the largest group of non-fitting patients, i.e. patients with the Pattern 1010 (those with psychiatric comorbidity but who were not severely addicted) with the characteristics of the patients in the closest adjacent groups who did fit the model, i.e. those with the Pattern 1000 (who neither had psychiatric comorbidity nor were severely addicted), and with those with the 1110 Pattern (who both had psychiatric comorbidity and were severely addicted). Table 4 shows that overall the group of non-fitting Pattern 1010 patients had higher MATE scores than the Pattern 1000 patients and lower MATE scores than the Pattern 1110 patients. For all of the scores this linear trend was significant, and except for negative external influences [S8.2], all of the effect sizes were large (partial $\eta2 > .20$). However, for undergoing psychiatric or psychological treatment [S2.2], the mean of the non-fitting group was higher than it was for the Pattern 1110 group (1.46 vs 1.14). This is reflected in a quadratic trend with a large effect size (partial $\eta2 = .16$). Although the other scores also had significant quadratic trends, their effect sizes were small (partial $\eta2 = 0$) to medium (partial $\eta2 = .07$).

Table 4 MATE scores, including means, SDs, and linear and quadratic trends for patterns 1000, 1010, and 1110

	Stage Profile			Linear Trend		Quadratic Trend	
MATE Score (range)	1000 (n=2,703)	1010 (n=906)	1110 (n=1,044)	p	Partial η2	p	Partial η2
[S2.2] Undergoing psychiatric or psychological treatment (0-2)	0.32 (0.47)	1.46 (0.8)	1.14 (0.88)	<.0001	0.20	<.0001	0.16
[S2.3] Psychiatric co-morbidity (0-5)	0.11 (0.31)	0.82 (1.05)	1.05 (1.14)	<.0001	0.20	<.0001	0.02
[S4.3] Severity of dependence/ abuse (0-9)	4.75 (1.69)	5.31 (1.54)	7.61 (1.45)	<.0001	0.34	<.0001	0.04
[S7.2] Limitations - Basic (0-32)	2.26 (2.61)	3.3 (2.88)	5.19 (3.16)	<.0001	0.15	<.0001	0.00
[S8.2] Negative external influences (0-20)	2.66 (2.31)	3.54 (2.53)	3.92 (2.56)	<.0001	0.04	0.006	0.00
[SQ1.1] Craving (0-20)	5.01 (3.11)	5.98 (3.21)	11.8 (4.5)	<.0001	0.38	<.0001	0.07
[SQ2.4] Depression Anxiety Stress - Total (0-126)	20.34 (15.3)	43.1 (25.87)	62.98 (24.24)	<.0001	0.42	0.057	0.00

On the basis of these findings, we performed a post-hoc analysis in which we excluded undergoing psychiatric or psychological treatment [S2.2] as an indicator of psychiatric comorbidity, i.e. patients with few or relatively mild symptoms and who were not in treatment or were not receiving medication, were regarded as not having psychiatric comorbidity (N = 670).

Table 5 Matches and mismatches according to the adjusted staging model

		N	%
pattern	**According to model**	**5,537**	**87.1**
	1000	3,121	49.1
	1100	1,318	20.7
	1110	828	13.0
	1111	270	4.2
	Not according to model	**817**	**12.9**
	1010	483	7.6
	1011	66	1.0
	1101	167	2.6
	1001	101	1.6
	Total	6,354	100

When we applied this adapted model to the present cohort, the number of patients that did not fit the model diminished by 6.2% from 19.1% to 12.9%, resulting in an increase in accuracy from 80.9% to 87.1% (see Table 5).

3.4 Discussion

This study was a first step in the evaluation of the validity of a staging model for addiction that is analogous to the TNM staging model for cancer. We found that 80.9% of the patients fitted the model. Importantly, the results were robust for age, sex, and the primary substance of abuse. These results support a model in which there is a progressive development of the disorder over time: in most cases, addiction becomes more severe and is then followed by psychiatric complications and, without successful treatment, progresses into social disintegration.

In most cases not fitting the model, the addiction was not considered severe, but the patient had recently been or was currently in treatment for a comorbid psychiatric or psychological problem, without the presence of acute psychiatric symptoms or severe symptoms of depression, anxiety, or stress. May be this intermediate (non-fitting) group of patients had suffered from psychiatric or psychological problems, for which they had to some extent been successfully treated. The use of current treatment as the indicator for psychiatric comorbidity could be questioned. By removing it and only using acute psychiatric symptoms or high score on depression, anxiety and stress as indicators for psychiatric comorbidity, the APS model fit increased to 87.1%. It should be noted, however, that this improvement was based on a post-hoc analysis, and these results should thus be confirmed in an independent sample of patients.

This also makes clear that the fit of the model is highly dependent on the operationalization and measurement of the clinical aspects included in the model: addiction severity, psychiatric comorbidity, and social disintegration. A more lenient operationalization of the severity of the addiction, for example, would by definition reduce the number of violations, and a stricter operationalization would by definition increase the number of violations. In addition, patient factors such as genetics, biochemistry, life events, personality, and intelligence could be added to further profile patients and obtain better efficacy and efficiency (Beekman, van Os, van Marle, & van Harten, 2012). Staging and profiling used together could help in developing more precision in predicting the course of the illness and the treatment outcome (van der Stel, 2015).

The current study has both strengths and limitations. It's the first time a staging model for addiction is tested. On the one hand, the large sample size and the standardized assessment are among the most important strengths. On the other hand, the outcome depends on the chosen operationalization. In addition, further studies should also include physical comorbidity. We also limited this study to treatment-seeking patients. The most important limitation is, however, that all analyses were based on cross-sectional data. In order to investigate if the fitting profiles are stages in a fixed sequence (model), a prospective follow-up study is needed. A complicating factor is of course the fact that addiction is not a one-way street and that different directions are possible. Here, we tested a staging model for addiction as the primary disorder and not as a comorbid disorder for other psychiatric disorders.

In conclusion, the current study shows that the profile of the vast majority of treatment-seeking SUD patients fit the suggested staging model. The profile included the severity of the addiction and whether or not a comorbid psychiatric disorder and subsequent social problems were present. Future studies should investigate the predictive power of this model for triage, treatment allocation, and patient-treatment matching.

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Part II:

HETEROGENEITY OF ADDICTION CARE OFFERED TO SUD PATIENTS

4. Prediction of healthcare utilization in addiction care*

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Abstract

Background

The ability to predict the level of healthcare utilization of patients suffering from a substance use disorder (SUD) on the basis of patient characteristics is important both for treatment planning and for the funding of mental healthcare. In The Netherlands, health insurers have proposed a simple level of care demand model, whereas clinicians use more extensive routine assessment. Direct comparison of the predictive value of these models is lacking.

Method

To explore the predictive ability of a simple model for the level of care demand, and of a model based on more detailed patient characteristics. Data were extracted from a large database of patient characteristics collected during intakes to a large regional addiction care facility in the Netherlands at the beginning of an addiction treatment episode. Two regression models were tested comparing a prediction of healthcare utilization based on a simple level of care demand model, and a prediction based on more detailed patient characteristics.

Results

We found an explained variance of healthcare utilization according to the level of care demand model of 5.4% for alcohol and 3.4% for other substances. Using more extensive routine intake data, the explained variance rose for alcohol to 13.8% and for other substances to 10.0%.

Conclusion

Prediction of healthcare utilization during an addiction treatment episode using a level of care demand model can be enhanced by applying more detailed patient data. However, the predictive value of these models limits their use in financial management.

4.1 Introduction

Patients with substance use disorder (SUD) are a heterogeneous population, with a broad variation at the biological, psychological and social level (West,2013). Despite a large body of research supporting the effectiveness of addiction treatment, evidence available to support clinical decision-making regarding personalized patient-treatment matching is sparce (McKay et al., 1997; Gastfriend et al., 2003; Project MATCH Research Group, 1998; Merkx et al., 2013; Kramer-Schmidt et al., 2017; Broekman & Schippers, 2017). Nonetheless, predicting the required treatment is important for both organizing and financing care so that patients can be well informed about their treatment, and practitioners and healthcare institutions can plan care trajectories by using, for example, care pathways (Vanhaecht & Sermeus, 2003; Huiskens & Schrijvers, 2010; Joosten, 2012).

The course of treatment is subject to certain influencing factors. The extent to which the patient is ready for therapy and motivated (Prochaska et al., 1992), therapist- and organizational factors (Norcross & Wampold, 2011; Deneckere et al., 2013), and the practical and social condition of the client (Van Os et al., 2018; Van Os, 2018) are at least as important as the combination of diagnosis and treatment. For this reason, Van Os (2014) suggested that data obtained from extensive measurements and interviews may explain a maximum of 20% of the variance of care utilized.

Good health care is expensive, and resources are always limited. Governments, insurance companies, treatment centers and practitioners hold each other accountable for optimal use of these resources. Despite the complexity and the disappointing results in predictive research so far, efforts to implement prediction tools in clinical practice continue. In order to develop a new model for the funding of mental health care, the Dutch Healthcare Authority (Nederlandse Zorg Autoriteit, NZA) proposed the so-called 'English care cluster model' (Brief minister VWS [Letter of the secretary of Health], 2015; NZA, 2016). In this model, the healthcare utilization of patients is combined in clusters of care that are supposed to meet the needs of a specific patient profile.

In March 2013, a first model for healthcare utilization in mental health (Care Cluster Model 1.0) was commissioned by the national umbrella organizations of mental health care organizations (GGZ Nederland) and the Dutch health insurance companies (Zorgverzekeraars Nederland, ZN), and tested on available data. In addition, the term level of care demand was used to indicate the patient characteristics that are predictive for the treatment utilization (duration, setting, and treatment minutes) and the care costs at registration/intake (Werkgroep zorgvraagzwaarte GGZ [Workgroup on level of care demand], 2013, p. 11). The following predictor characteristics were included: nature of the disorder (clinical judgment and severity score), existence of comorbidity (yes or no), , psychosocial factors, and the GAF-score (score for overall functioning in the DSM-IV). These predictors explained about 6.5% of the variance in treatment minutes and inpatient days. A second research phase added the following clinical data in an effort to increase the explained variance: treatment history (obtained from Vektis, the organization that collects all Dutch care claims and stores them in a data warehouse), and more detailed severity data from Routine Outcome Measurement begin scores. However, the explained variance only slightly increased. This was seen as disappointing, but could be expected given the quite restricted data that were available to test the model.

Detailed data on patient characteristics are often collected in clinical practice. In the past decades, Dutch SUD treatment incorporated the routine assessment of standardized patient characteristics for triage and indication using the Measurement in the Addictions for Triage and Evaluation (MATE version 2.1; Schippers et al., 2011). A better prediction of healthcare utilization may be possible through application of this routine data collection. The aim of this study is to investigate whether the data collected at intake in an addiction treatment facility better explains the variance in level of care demand than the generic level of care demand 1.0.

4.2 Method

4.2.1 Sample

The research cohort consisted of patients from Tactus, an addiction care institution serving the Dutch provinces of Overijssel, Gelderland and Flevoland. Standard intake data were collected during 2008 to 2011 from 7,039 patients. This concerns 43% of all registrations. We only included regularly closed trajectories (n = 3,913), which is in accordance with the analyses of the Workgroup on level of care demand (Werkgroep zorgvraagzwaarde GGZ, 2013). The forensic trajectories (n = 342) were excluded because the number of inpatient days were to a large extent determined by judicial factors. Of the remaining 3,571 trajectories, 3,434 were analysed due to a number of trajectories with missing data. Of these, 1,864 patients had received a DSM-diagnosis of alcohol use disorder whilst 1,570 were diagnosed with another substance use disorder.

4.2.2 Healthcare utilization

Healthcare utilization was observed for all cohort patients in the year following the day the MATE was completed. Two scores were calculated based on contact and admission registrations: the total contact time in hours and the number of inpatient days. These scores were then combined into a single score, with one day being counted as one contact hour. The correlation between the number of hours and the number of days with the total healthcare utilization was 0.90 and 0.86, respectively. The root of the sum was used as a measure of healthcare utilization because the total healthcare utilization was strongly skewed to the right. Patients analyzed utilized healthcare for an average of 32.47 hours over the year (sd:57.9; extremes: 0.75-836). When expressed as a root this average was 4.7 (sd:3.2; extremes: 0.87-28.9).

Level of care demand model 1.0

The Level of Care Demand model 1.0 utilizes the patient characteristics at entry/intake to predict healthcare utilization and healthcare costs. This prediction is expressed in a number from 1 to 7.

The independent variables utilized in the model are:

- DSM IV diagnosis axis 1 or 2, severity level 1 (light), 2 (medium, changeable, unclear) or 3 (severe)
- Limitations DSM IV GAF score 0 = 61, or 1 = 41 - 60, 2 = 40
- Secondary DSM IV as I of II diagnosis/diagnoses, 0 = no, 1 = yes
- Psycho-social complicating factors, 0 = no, 1 = yes

Dependent variables applied are:

- Contact hours, inpatient days and costs

Patient characteristics

Patient characteristics were recorded at intake with the MATE, a modular tool that elucidates the use of psychoactive substances and the addiction history, the diagnoses of dependence and abuse according to the DSM-IV, and the strength of craving for psychoactive substances. In addition, the MATE assesses the extent to which a person is active and participates in society, the external factors that influence this and their care needs. Furthermore, the MATE measures levels of anxiety and depression, personality problems, and data on physical complaints. Finally, the treatment history is assessed. The MATE has in 20 severity scores. All sections are based on previously validated questionnaires (Schippers et al., 2010, 2011), except for the WHO-ICF. These two modules were shown to have acceptable psychometric qualities in a heterogeneous SUD population (Schippers et al., 2010; Rutten et al., 2016; Oudejans et al., 2020).

Analyses

Firstly, we calculated the explained variance in health care utilization by patients with an alcohol or drug use disorder using the level of care demand model 1.0 (by the Werkgroep zorgvraagzwaarte GGZ [Workgroup on level of care demand], 2013). Secondly, we calculated the explained variance in health care utilization based on MATE scores using linear regression. Initially, all MATE scores were tested in four models that examined alcohol, opioids, stimulants and cannabis. MATE variables were included in the final model if the predictor achieved $p < 0.10$ in at least one of the four initial regression analyses. These subgroup regressions were performed with a bootstrap procedure in which 1,000 samples were simulated. Because the two models did not have the same number of predictors, we reported the corrected R2 as a measure of the explained variance; that is the R2 with a correction factor for the number of predictors. The analyses were done with SPSS 24.0.

In addition to the 20 MATE scores, the MATE also scores the patient's addiction treatment history. This characteristic was not included in the MATE analyses to allow for a fairer comparison with the level of care demand model 1.0, which does not include data on treatment history.

4.2.3 Results

The demographics of the Tactus sample are presented in Table 1. The average age was 38 years, 75% was male and 72% used alcohol as their primary problem substance (PPS). The percentage explained variance in healthcare utilization according to the level of care demand Model 1.0 in the Tactus research cohort was 5.4 for Disorder in the use of alcohol, and 3.4 for Disorder in the use of other substances (Table 2).

Of the 20 MATE subscale-scores, ten scores contributed ($p < 0.10$) to healthcare utilization (Table 3). These ten MATE scores were used for the prediction model based on the MATE. Table 4 shows the percentage explained variance in healthcare utilization derived from the MATE scores: 13.8 for Disorder in the use of alcohol, and 10.0 for Disorder in the use of other substances. The percentage explained variance was 24.7 for Disorder in the use of opioids, and 9.1 for both stimulant and cannabis. The MATE model explained a higher percentage variance of healthcare utilization than the level of care demand model 1.0. In fact, the percentage variance explained by the MATE model was almost three times higher for alcohol, and for other substances just over three times higher.

Table 1 Demographics of the Tactus sample

Characteristic	n	Overall, n = 3,434[1]	Alcohol, n = 1,864[1]	Opioids, n = 305[1]	Stimulants, n = 471[1]	Cannabis, n = 794[1]
Sex		3,43				
M		2,588 (75%)	1,343 (72%)	246 (81%)	380 (81%)	619 (78%)
F		846 (25%)	521 (28%)	59 (19%)	91 (19%)	175 (22%)
Age	3,434	38 (14)	45 (13)	42 (9)	31 (9)	24 (9)
S4.3 Ernst afhankelijkheid/misbruik [0-9]	3,434	5.73 (2.30)	5.61 (2.27)	5.30 (2.71)	6.12 (2.22)	5.92 (2.19)
[1] n (%); Mean (SD)						

Table 2 Explained variance in healthcare utilization for the groups with alcohol use disorder and other substance use disorders, using the Level of Care Demand model

Diagnosis	n	Variance in % (Adjusted R Squared)
Disorder in the use of alcohol	1,864	5.4
Disorder in the use of other substances	1,570	3.4

Table 3 MATE-scores that contribute significantly to variance in healthcare utilization per drug

MATE-scores	Substance				
	Alcohol	Opioids	Stimulants	Cannabis	Total
S2.2 Under psychiatric or psychological treatment	X			X	2
S4.3 Severity of dependence and misuse	X			X	2
S5.1 Physical complaints	X				1
S7.2 Limitations - Basic	X	X		X	3
S7.3 Limitations - Relational	X	X	X		3
S8.3 Care needs	X	X	X		3
SQ1.1 Craving	X			X	2
SQ2.1 Depression	X				1
SQ2.2 Anxiety	X				1
SQ2.3 Stress	X				2

Table 4 Explained variance in healthcare utilization for the groups with alcohol use disorder and other substance use disorders, using the MATE

Diagnosis	n	Variance in % (Adjusted R Squared)
Disorder in the use of alcohol	1.864	13.8
Disorder in the use of other substances	1.570	10.0
Opioids	305	24.7
Stimulants	471	9.1
Cannabis	794	8.8

4.4 Discussion

At a large regional addiction care facility in the Netherlands, the level of care demand model 1.0 explained 5.4% and 3.4% of health care utilization in a cohort of SUD patients in treatment for alcohol and other SUDs respectively. A model with more detailed clinical data derived from the MATE explained 13.8% and 10% of the variance in healthcare utilization for both treatment groups respectively. Despite both models reaching statistical significance, with the more detailed model explaining more of the variance, these data indicate that prediction of health care utilization using baseline clinical data has limited clinical relevance.

We applied disorder in the use of alcohol and disorder in the use of other substances in our analyses reflecting the working methods of the Workgroup on level of care demand. However, our analyses shows that the explained variance differs substantially between substances.
Our analyses show that routine intake data derived during admission for SUD treatment in the Netherland can be used for the prediction of healthcare utilization. This highlights the advantages of using extensive clinical data for modelling purposes. Our analyses also show that further development in modelling and data collection is required to reach explained variances that have true clinical value (Van Os, 2014). The application of models for staging and profiling of psychiatric syndromes may offer more opportunities for future progress, as they have done in oncology (see Beekman et al. 2012; Boonzaaijer et al. 2015). In past analyses of the Tactus dataset applied here, we indeed found indications for staging in the course of addiction (Rutten et al. 2017). This bodes well for the future.

Progress in modelling and predicting health care utilization may also be made when, besides the diagnosis (DSM-5 and ICD-11), also diagnosis specific symptoms (Van Os, 2013; Van Os et al. 2014), and general functioning (WHO, 2001; Hopfe et al. 2015) are taken into account. Furthermore, the dimensions of personal recovery, recovery strength and recovery-oriented diagnostic data may offer avenues for improvement (Van Hoof et al. 2014). We expect that the further development of such models will enhance the power of prediction of disease course and treatment effects, and identify different patient profiles in the different phases of their condition.

Accurate prediction of healthcare utilization on the basis of patient characteristics to improve care planning and evaluate health care costs is a legitimate goal. However, expectations for the rapid development of predictive models should be tempered given our results and the known complexities of patient characteristics, and variations in disease course and recovery. Efforts should focus on the development of methods for gathering and analyzing big data on patient characteristics, courses of illness and recovery, and healthcare utilization. Sophisticated approaches, for example, artificial intelligence, are required for both retrospective and prospective longitudinal analyses. On the long run this can lead to information that patients and practitioners can use to optimize personalized treatment with information.

The application of comprehensive clinical data allows the prediction of healthcare utilization by patients in SUD treatment. However, the variance explained by these models remains limited. This limits the applicability of such models in the guidance of healthcare utilization reimbursement. Future studies that make use of big data and sophisticated analysis techniques such as artificial intelligence, may, in addition to the prediction of financial reimbursement, facilitate personalized addiction medicine and support shared decision-making in the consulting room.

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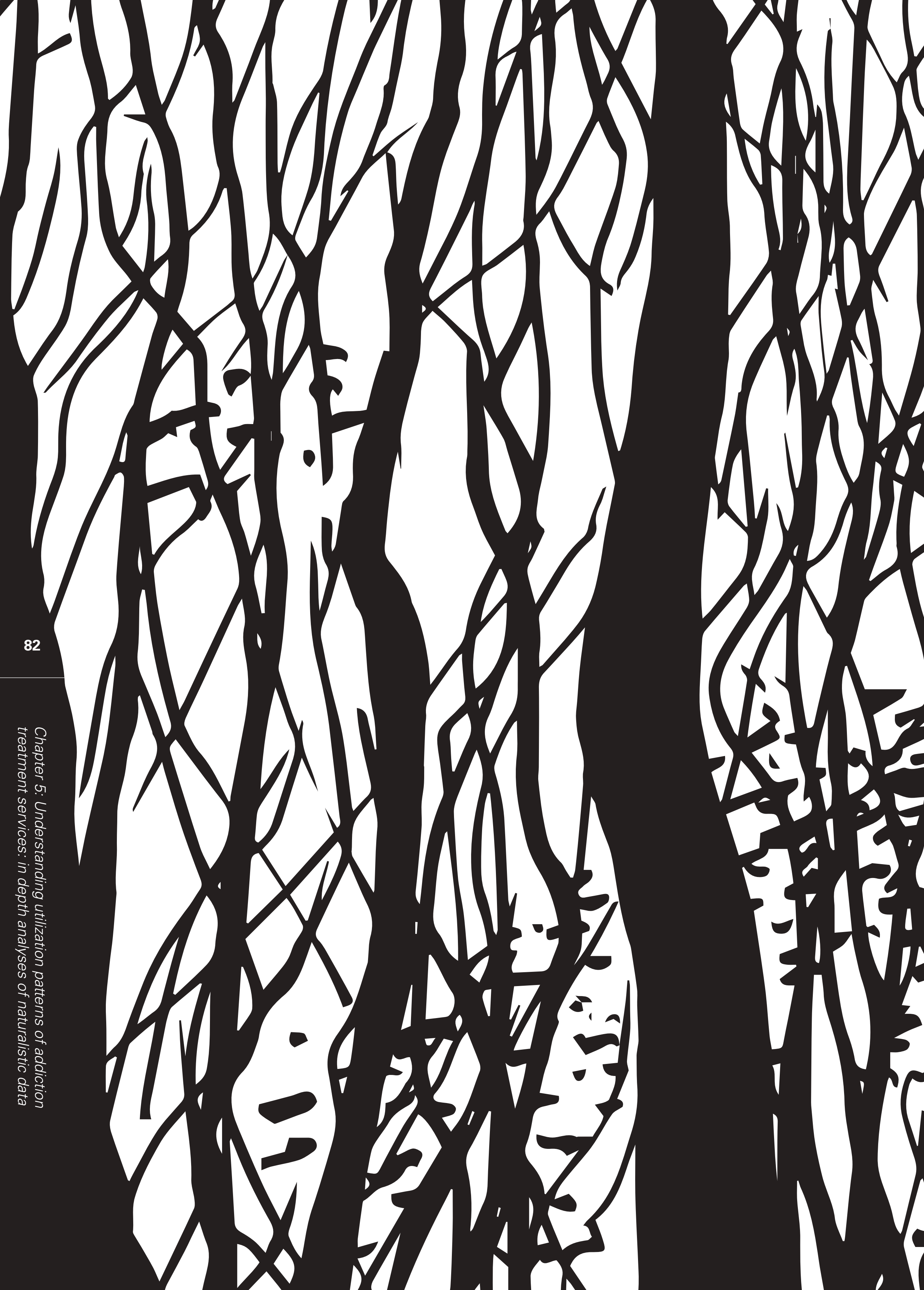

5. Understanding utilization patterns of addiction treatment services: in depth analyses of naturalistic data

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Abstract

Introduction

Patients with substance use disorders show a broad variety of clinical characteristics. This heterogeneity calls for a broad range of treatment interventions varying in intensity, duration and aims. However, knowledge of variations in service utilization in addiction treatment as a result of these differing clinical characteristics is limited. This study aims to: 1) identify service utilization clusters in addiction treatment, and 2) explore differences in patient characteristics between these service utilization clusters.

Methods

The addiction treatment services utilized by 9,841 patients spanning one year in a Dutch addiction treatment were grouped according to 'care', 'cure', and 'general' treatment categories. Total inpatient days and outpatient treatment hours were calculated per category and cluster analysis was used to identify service utilization clusters. Patients in the resulting service utilization clusters were analyzed according to age, sex, primary problem substance, and 21 severity scores, measured at intake.

Results

Ten service utilization clusters were identified that varied according to treatment amount and focus. Patients differed between these clusters according to primary problem substance, limitations in general functioning, care need, depression, anxiety, stress, craving, treatment history and addiction severity.

Conclusions

There is considerable variation in service utilization in addiction treatment. Patients undergoing addiction treatment vary in their service utilization relating to their characteristics at intake. This finding warrants further research on service utilization related to different patient profiles to improve treatment planning and patient placement in addiction treatment.

5.1 Introduction

Substance Use Disorders (SUDs) are globally highly prevalent, contributing to 5.4 % of the total burden of disease worldwide (WHO, 2010). Individuals diagnosed with SUD use different types of substances in different amounts and patterns of use over time, and SUDs develop over different stages of severity and chronicity of the addiction cycle (Moos & Moos, 2006; Hser et al., 2015; Gardner, 2011; Wise & Koob, 2014; Rutten et al., 2017). Furthermore, comorbid somatic and psychiatric conditions, as well as socioeconomic differences, social participation and support, and financial and housing problems further contribute to the observed heterogeneity in patients with SUDs (Mee-Lee et al., 2012; West, 2013). Patients also differ in their treatment goals, reflecting their individual needs and potential (Moos & Moos, 2006; Dennis et al., 2005).

This heterogeneity calls for a broad variety of cure and care interventions (Institute of Medicine, 2006). An improved understanding of service utilization by SUD patients will enable personalized treatment planning based on patient characteristics that leads to improved patient outcomes and efficiency. However, our knowledge of patient placement and treatment matching is still limited (Merkx et al, 2013). To address this, the American Society of Addiction Medicine (ASAM; Mee-Lee, 2001) developed the Patient Placement Criteria (PPC) tool for patient placement. Unfortunately, there is limited data supporting the validity of this approach (McKay et al., 1997; Gastfriend et al., 2003; Sharon et al., 2003). Studies on outpatients with alcohol use disorder (Project MATCH Research Group, 1997, 1998; Kramer-Schmidt et al., 2017), and inpatients with alcohol and drug use disorders (Ouimette et al., 1999a, 1999b; Kadden et al., 2001), showed no matching effects of patient characteristics with type of outpatient treatment (Twelve-Step Facilitation Therapy, Motivational Enhancement Therapy, and Cognitive Behavioral Therapy). Merkx et al. (2013) also found no matching effect using a matching algorithm in patients with alcohol use disorder, but did observe that longer treatment or adding extra medical support to detoxification services improved treatment results (Merkx et al., 2014). Some longitudinal drug treatment studies also show positive effects of Time spent In Program (TIP) (Zhang et al., 2003; Hser et al., 2015). Finally, several studies showed some beneficial effects of, for instance, stepped care approaches on reducing drinking (Morgenstern et al., 2021) or cost saving (Drummond et al., 2009).

The availability of electronic patient records makes the investigation of service use and links with patient characteristics easier. Such a practice-based approach may have some advantages over more pre-structured designs such as randomized clinical trials since these data may be more generalizable and representative for the clinical heterogeneity of the SUD treatment population (Kostis & Dobrzynski, 2020; Susukida et al., 2020; McCarty et al., 2020). Service use analysis and the linking of service use profiles with patient characteristics has previously been undertaken. For example, patients with heart failure were analyzed by Kim et al. (2020) and armed forces veterans with PTSD by Roughead et al. (2021). The latter showed highly heterogeneous service use. A potential explanation for this heterogeneity was the variation in physical and psychiatric co-morbidities in patients between utilization clusters (Roughead et al., 2021).

In addiction care, Vandivort et al. (2009) used health insurance claims to elucidate differences in service utilization between patients younger than 65 years and older. Younger patients had a higher number of co-occurring mental disorders, underwent more detoxification treatments, and utilized more rehabilitation services in the 30 days following detoxification. Huỳnh at al. (2016) investigated service use within a single addiction rehabilitation center by merging the data from four administrative databases. Three patient profile clusters were defined and classified according to service use. Patients without formal diagnoses used the least services. Patients with one psychiatric diagnosis, but not of SUD, and patients with dual diagnoses, using the most services. Crable et al. (2022) investigated service use by SUD patients over a period of five years in a hospital that provides both in and outpatient SUD services. In this study five service use clusters were found: disengaged (42%), substance use services (7%), mental health services (13%), primary care (25%) and other specialty services (13%). The authors concluded that the analyses could contribute to the development of treatment engagement strategies.

The abovementioned studies provide valuable insight in general service use by SUD patients. However, knowledge of service utilization in relation to patient characteristics within addiction care is currently lacking. Furthermore, most studies are hindered by limited data on patient characteristics or service utilization. In the Netherlands, addiction treatment is mainly provided by large, regional addiction treatment centers, offering a broad range of addiction treatment services (e.g., prevention, outpatient, inpatient, opioid-maintenance and care programs as well as forensic treatment and probation).

The objective of the current study was to investigate heterogeneity in service utilization in addiction treatment, using a detailed database from a large representative regional addiction care facility in the Netherlands. The aims of the study are to 1) identify service utilization clusters (SUCs) in addiction treatment and determine how often SUD patients make use of these clusters, and 2) explore differences in patient characteristics between these service utilization clusters.

5.2 Method

5.2.1 Design

Routinely collected data on patient characteristics and service utilization were extracted from electronic patient records in a cross-sectional observational study. A treatment observation period of one year was applied because the majority of episodes fitted into this timeframe. Patients provided informed consent for scientific analyses of their records by the treatment center based on an opt out procedure and approved by the internal ethical board.

5.2.2 Sample

The sample included patients with a substance use disorder (SUD) who received treatment in the period 2011-2016 at Tactus Addiction Care. Tactus Addiction Care is a regional treatment center, based in the Netherlands, that provides a broad range of treatment programs. Patients are drawn from a semi-rural area with a population of 2.5 million people. There were 16,602 patients in treatment and a total of 19,756 treatment episodes carried out in the observation period. We selected 13,226 patients with alcohol, cannabis, stimulants, or opioids as their primary problem substance (PPS). Patients were excluded if their primary problem was the use of other substances or they suffered primarily from behavioral addictions. This was because no Routine Outcome Measures were available for these disorders (see below). Of the selected patients, 10,728 (81%) completed all routine assessments, covering 12,306 treatment episodes. If a patient received multiple treatment episodes within the observation period, the treatment episode with the most Routine Outcome Measurement data available was included. We excluded patients who received coercive interventions as part of forensic treatment (8,3%) from the patients identified with the above criteria. This was because such mandated treatment influences decisions on treatment duration and intensity beyond that of problem severity and symptoms at the start as well as during treatment. We excluded patients who underwent forensic inpatient days and those patients who received 50% voluntary treatment hours and 50% voluntary treatment duration. The final sample consisted of 9,841 patients. A flowchart that illustrates the sample selection process is available in the supplement (Supplement Fig. 1).

5.2.3 Measures

Treatment episode and Treatment activities:

With the assistance of treatment and registration experts, we divided different types of activities from the electronic patient records into 12 categories based on their treatment function (Table 1). These 12 categories were then further classified as 'general', cure', or 'care', depending on their main focus. General treatment activities included, for example, detoxification, emergency aid and general support (Table 1). Cure activities are generally time limited and focus on change of substance use. For instance, cognitive behavioral therapy (CBT) and community reinforcement approach (CRA) treatments are both categorized as addiction treatments. Both these treatments, together with e.g., family therapy and psychiatric treatment, are categorized as 'cure'. Care activities, on the other hand, focus on long-term support. For instance, methadone maintenance, user rooms and walk-in day care (Table 1). General and cure activities include inpatient activities measured in days, or outpatient activities measured in hours of service.

Table 1 Service use activity categories General, Cure and Care; and total amount of service use in hours and days in the whole sample

Focus	Activity categories	Category definition	Hours	Days
General	General support 1	General support in the field of hobby, work, finance.	23108	
	General support 2	More intensive support in the fields of assisted or sheltered living, daytime activities.	13283	8640
	Medical treatment	Treatment of physical comorbidity	16973	
	Detox	Detoxification treatment	5083	10818
	Diagnostics	All intake and diagnostic activities	67999	17679
	Family and relation therapy	Family and partner education and therapy without identified patient	907	
	Emergency aid	Acute crisis interventions	6816	11190
Cure	Addiction treatment	All forms of pharmacological and behavioral treatment to control addictive behavior.	215428	90804
	Psychiatric treatment	Treatment of psychiatric comorbidity	16271	
	Aftercare	Supporting maintenance and self-control	2915	
Care	Addiction care	All forms of medical and social care to cope with ongoing use, for example methadone maintenance, heroine supply treatment, and user rooms	80525	
	Case management	Intensive support in more domains with practical short-term goals	38075	
	Total		487383	139131

Patient characteristics

Patients were assessed at intake using the structured clinical interview 'Measurement in the Addictions for Triage and Evaluation' (MATE 2.1) (Schippers et al., 2010, 2011). The MATE was designed for use in routine practice for treatment allocation and evaluation of patients with substance use disorders. Two modules of the MATE were newly developed and not based on previously validated questionnaires (S.7 and 8). These two modules were shown to have acceptable psychometric qualities and it was concluded that the MATE is a comprehensive flexible measurement tool that can be practically applied and is well suited for use in a heterogeneous population (Schippers et al., 2010; Rutten et al., 2016; Oudejans et al., 2020).

The MATE includes the following 21 scores

- ***Characteristics of physical comorbidity [S2.1].*** The score is calculated on the basis of whether or not the person clearly gives the impression of being physically unhealthy, exhibits symptoms of intoxication or withdrawal, has an acute or contagious disease, or (if female) is pregnant.

- ***Undergoing psychiatric or psychological treatment [S2.2].*** The score is based on whether or not the person has been prescribed psychiatric medication or is receiving psychological or psychiatric treatment.

- ***Characteristics of psychiatric comorbidity [S2.3].*** The score is based on the presence or absence of the following symptoms: suicidal tendencies, hallucinations, delusions, and confusion. The score is calculated from the number of symptoms, with double weighting given to having a suicidal plan.

- ***History of treatment for substance use disorders [S3.1]***. The square root of the number of previous inpatient or outpatient treatments for SUD in the past 5 years.

- ***Dependence [S4.1].*** Based on the DSM IV (American Psychiatric Association, 1994), the criterion for substance dependence is met if at least three of the first seven items are met.

- ***Abuse [S4.2].*** Based on the DSM IV (American Psychiatric Association, 1994), the criterion for substance abuse is met if at least one of the last four items in the CIDI is answered affirmatively.

- ***Severity of dependence/abuse [S4.3].*** Scored using the number of affirmative answers to Items 2 to 9, and 11, not using items for tolerance and legal problems, according to items response analyses of Langenbucher et al. (2004).

• ***Physical complaints [S5.1].*** Scored using the sum of responses to 14 items, based on the Maudsley Addiction Profile-Health Symptom Scale (Marsden et al., 1998), exploring the need for psychiatric or medical consultation, medication use relating to addiction, physical symptoms and conditions, intoxication, severe withdrawal, or pregnancy.

• ***Personality [S6.1].*** Scored using the number of affirmative answers to the items of the Standardized assessment of Personality Abbreviated Scale (Germans et al., 2008). The cutoff point of four (out of eight) indicates the presence of a personality disorder.

• ***Limitations -Total [S7.1].*** Scored using the sum of the responses to 19 items based on the International Classification of Functioning (ICF) (WHO, 2001), with two subscales: the score of ***Limitations - Basic [S7.2].*** With eight items, and the score of ***Limitations - Relationships [S7.3]*** with five items.

• ***Positive external influences [S8.1].*** Scored using the sum of the responses to three items (based on ICF).

• ***Negative external influences [S8.2].*** Scored using the sum of the responses to five items (based on ICF).

• ***Care and support [S7.4].*** Scored using the sum of eight items.

• ***Need for care [S8.3].*** Scored using the sum of the affirmative answers to the questions relating to need for care as perceived by either the assessor or the person being assessed.

• ***Craving [SQ1.1].*** Scored using the sum of the responses to five items, based on the Obsessive-Compulsive Drinking Scale (OCDS) (Anton et al. 1996), translated and validated for the Dutch situation (DeWildt et al., 2005).

• ***Depression Anxiety Stress -Total [SQ2.4].*** Scored using the sum of the scores on the 21-item version of the Depression Anxiety Stress Scales 2.0 (DASS)(Lovibond & Lovibond, 1995). Furthermore, the DASS has three subscales. Depression [SQ2.1]. The score is the sum of the responses to the seven DASS-items related to depression multiplied by 2. A score of 21 is the cut off point for severe depressive symptoms (Lovibond & Lovibond, 1995). Anxiety [SQ2.2]. The score is the sum (multiplied by 2) of the responses to the seven DASS-items. A score of 15 is the cut off point for severe anxiety symptoms. *Stress [SQ2.3].* The score is the sum of the responses to the seven DASS-items relating to stress multiplied by 2. A score of 26 is the cut off point for severe stress symptoms.

Besides the MATE-scores, age, gender, PPS were analyzed. In addition, treatment episodes were classified according to whether they were ongoing (still in treatment after the observation period ended) or completed; or whether they were prematurely ended (patients dropped out, were detained, deceased etc.).

5.2.4 Analysis

Objective 1: Identification of service use clusters (SUCs)

We computed five service use indexes for each patient: totals of (1) general hours, (2) cure hours, (3) care hours (4) general days, and (5) days cure. These indexes were right skewed so their square roots were used for the cluster analyses. To elucidate SUCs, we performed cluster analyses using the Partitioning Around Medoids (PAM) algorithm, a more robust version of the K-means cluster algorithm. PAM uses actual data to identify the center of a cluster, instead of averages of distances between points in the sample. PAM is implemented in the R package cluster (Maechler et al., 2021). This package computes five gap statistics that can help derive the number of clusters. We found the Tibs2001SEmax to be most appropriate because other methods the number of clusters SUCs was too high in our view, namely 14. This made the SUCs smaller and clinically less, recognizable and differences between SUCs less well defined. Treatment episodes that were prematurely ended were associated with a lower frequency of service use. For this reason, we performed separate cluster analyses on the whole sample, the ongoing and completed episodes and the prematurely ended episodes.

Objective 2: Association of baseline patient characteristics with service use clusters

To assess the association of patient characteristics with SUC, we performed linear regressions for age and each of the MATE-scores as dependent variables and the SUC as a categorical independent variable. We used multinomial logistic regression for the categorical variables PPS and gender. We computed coefficients of determination for all models: R2 for the linear regressions, and Cramér's V for the multinomials. The coefficients of SUCs are relative to SUC "Intake only" as a reference category and was assigned coefficient 0. We computed marginal means and compared these for all SUCs within the model. In the figures the means that do not differ significantly between SUCs are denoted by same-colored dots. We used R packages performance (Lüdecke et al., 2021), effect size (Ben-Shachar et al., 2020), and emmanns (Lent et al., 2022) for these calculations. All analyses were performed with R 4.1.1 (R Core Team, 2021), Rstudio (Rstudio Team, 2021) and the tidyverse packages (Wickham et al., 2019).

5.3 Results

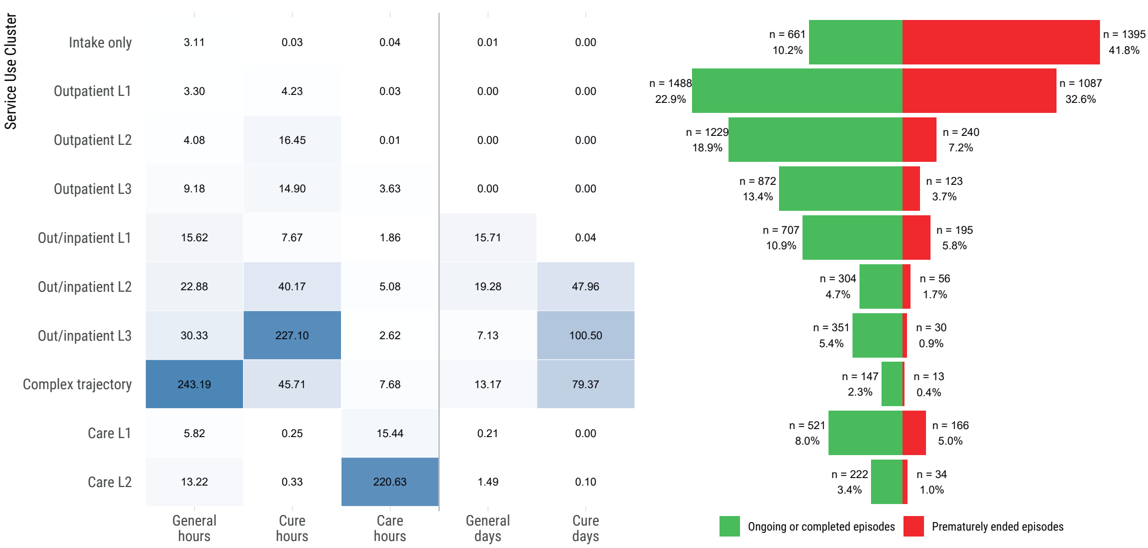
5.3.1 Demographics

Of the 9,841 unique patients included, the mean age was 39.7 years, and 76% were male. The PPS was for 59% of the patient's alcohol, 21% cannabis, 15% stimulants and 5% opioids. From these patients, 6,502 (66.1 percent) had an ongoing or completed treatment episode. 3,339 patients had a prematurely ended treatment episode, mostly because of either a unilateral decision by the patient or related to no show for appointments.

5.3.2 Service utilization clusters (SUCs)

We found 10 different distinctive SUCs based on the analysis of the ongoing or completed episode sample and the Tibs2001SEmax. Fig. 1 shows the means of the indexes for the 10 SUCs from the total sample on the left side and the distribution of the ongoing and completed, and the prematurely ended episodes.

Figure 1 Service use clusters Index mean scores and distribution by Ongoing or completed episodes vs Prematurely ended episodes



The largest cluster was *Outpatient Level 1*, n=2575 (26%). The second largest was Intake only, n=2056, (21%). Of all the prematurely ended episodes, 74.3% were classified in these two clusters. The smallest cluster was *Complex*, n=160 (1.6%). 18.3% of patients sampled were classified in SUCs with inpatient days.

One cluster consisted of a small number of mainly general activities, most likely intake activities. We labeled this *Intake only*. Three clusters consisted of outpatient visits only and were defined dominantly by cure activities. We labeled these *Outpatient L1, 2 and 3* in order of number of hours. Four clusters consisted of both outpatient and inpatient activities. Three of these clusters were labeled *Out/inpatient L1, L2, L3*. One cluster was labeled Complex because of a relatively large amount of general outpatient hours, indicating a large amount of diagnostic and/or emergency activity. With the exception of *Intake only*, all these SUCs were primarily cure oriented. Two other SUCs consisted of different levels of primarily care activities. These were labeled *Care L1 and Care L2*.

Six of the seven cure SUCs were characterized by increasing mean hours and days spent, in the order of general outpatient, cure outpatient, care outpatient, general inpatient and cure inpatient. Besides a number of 'general' hours, *Outpatient L*1 consisted of an average of 4.23 cure hours. *Outpatient L*2 consisted of more cure hours (16.45). In addition, *Outpatient L3* had also 3.6 care hours. Out/inpatient L1 featured, besides cure and care hours, 15.62 general hours and 15.9 general days (detox, diagnostics, emergency aid). *Out/inpatient L2* had 47.96 cure days, and *Out/inpatient L3* 100.6 cure days. The cluster Complex featured 243.19 general hours, and was otherwise comparable with *Out/inpatient L2*. The two care clusters had averages of 15.44 versus 220.63 care hours (Fig. 1).

The gap statistic Tibs2001SEmax estimated the number of clusters to be eight when performing cluster analyses on the total sample (i.e., including treatment episodes that ended with non-compliance). The most important difference between the 10 cluster and eight cluster solutions in the sample of ongoing and completed episodes, was that *Out/inpatient L2, Out/inpatient L3* and *Complex* were grouped into one cluster in the eight-cluster solution. A figure showing the eight- cluster solution for the whole sample is available in the supplement, Fig. 2.

5.3.3 *Linking service use clusters with patient characteristics*

We compared the SUCs with PPS, gender, age and the 21 MATE scores for the whole sample, the ongoing and completed, and the prematurely ended episodes. In Table 2 we present all the coefficients of determination of all the variables.

SUC was only associated with one categorical variable: PPS. The highest ranking R^2 values derived for the continuous variables were in descending order: limitations total (limitations total score includes the 8 limitations basic items, the 5 limitations relational items, and the remaining 6 items), need for care, depression/anxiety/stress, craving, history of treatment and severity of dependence/abuse. The difference between dependence R^2 = .054 and severity dependence/abuse R2 = .053 was small. We chose to show the latter in Fig. 2 because the DSM-5 no longer distinguishes between dependence and abuse (American Psychiatric Association, 2013).

Positive external influence, age, psychiatric treatment and personality differed only by a small degree across service clusters. Fig. 2 shows the seven variables with the highest coefficients of determination in more detail.

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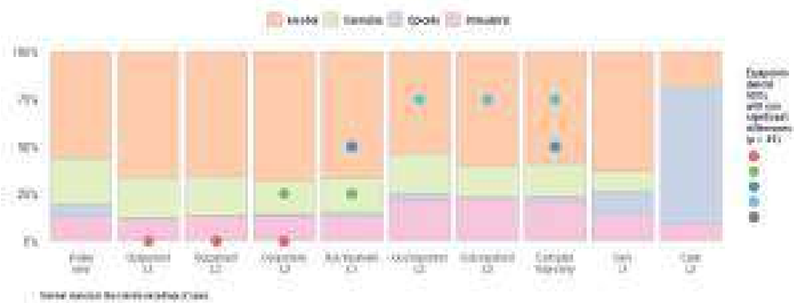
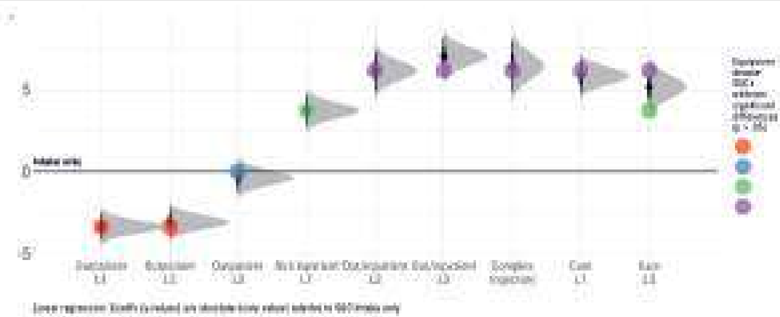
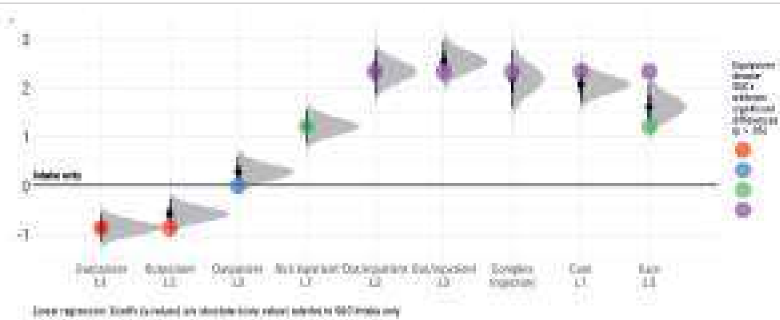
Table 2 Cramér's V and R^2 coefficients of determination for PPS, Gender, Age and MATE-scores by Service Use Cluster

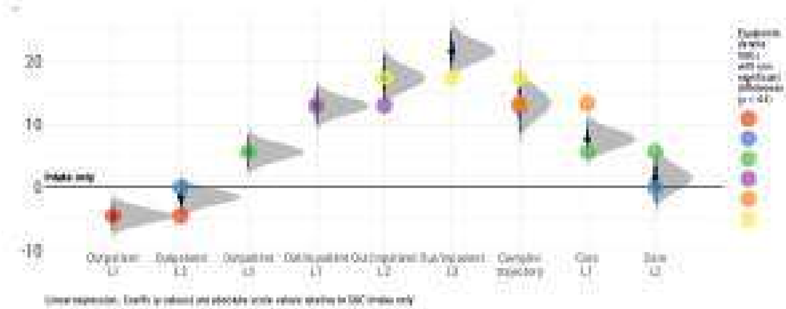
Variable	Ongoing and completed episodes	Prematurely ended episodes	Combined
Categorical variables: Cramér's V			
PPS	0.35	0.27	0.33
Gender	0.09	0.06	0.09
Continuous variables: R^2			
Age	0.01	0.01	0.02
S2.1 Characteristics of physical comorbidity [0-4]	0.04	0.02	0.03
S2.2 In psychiatric or psychological treatment [0-2]	0.02	0.01	0.02
S2.3 Characteristics of psychiatric comorbidity [0-5]	0.04	0.02	0.03
S3.1 History of treatment for substance use disorders - SQRT(n)	0.08	0.05	0.07
S4.1 Dependence [0-7]	0.08	0.02	0.05
S4.2 Abuse [0-4]	0.04	0.02	0.03
S4.3 Severity dependence/abuse [0-9]	0.08	0.03	0.05
S5.1 Physical complaints [0-40]	0.06	0.03	0.05
S6.1 Personality [0-8]	0.02	0.01	0.02
S7.1 Limitations - Total [0-76]	0.16	0.08	0.13
S7.2 Limitations - Basic [0-32]	0.15	0.09	0.13
S7.3 Limitations - Relational [0-20]	0.05	0.02	0.04
S7.4 Care & support [0-32]	0.05	0.04	0.05
S8.1 Positive external influence [0-12]	0.01	0.00	0.00
S8.2 Negative external influence [0-20]	0.04	0.02	0.03
S8.3 Need for care [0-20]	0.12	0.06	0.10
SQ1.1 Craving [0-20]	0.08	0.02	0.06
SQ2.1 Depression [0-42]	0.08	0.02	0.06
SQ2.2 Anxiety [0-42]	0.06	0.02	0.05
SQ2.3 Stress [0-42]	0.06	0.02	0.04
SQ2.4 Depression Anxiety Stress - Total [0-126]	0.09	0.03	

Figure 2. Ongoing or completed episodes. Cramér's V and R^2 coefficients of determination for the dependent variables PPS, S7.1 Limitations - Total, S8.3 Need for care, SQ2.4 Depression Anxiety Stress - Total, SQ1.1 Craving, S3.1 History of treatment for addiction disorder - SQRT(n), S4.3 Severity dependence/abuse and the independent variable Service Use Cluster

Dependent variable	Coefficient	Service Use Cluster (percent stacked bars / or coefficients). Equipoints (colored circles) denote nonsignificant difference between SUCs
PPS n = 6433	Cramér's V 0.350	
S7.1 Limitations - Total [0-76] n = 6388	R^2 0.164	
S8.3 Need for care [0-20] n = 6398	R^2 0.119	

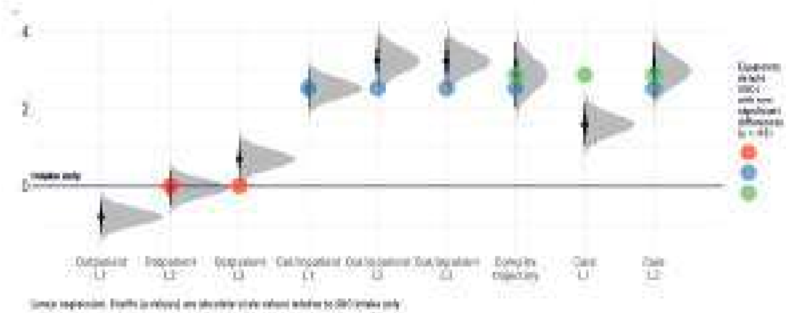
SQ2.4 Depression Anxiety Stress - Total
[0-126]
n = 6375

R^2
0.086



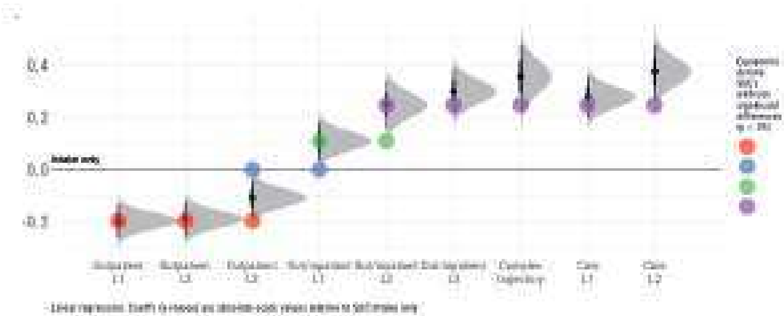
SQ1.1 Craving
[0-20]
n = 6379

R^2
0.084



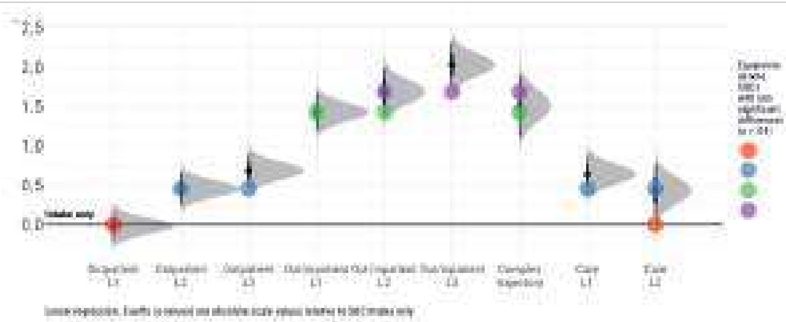
S3.1 History of treatment for addiction disorder - SQRT(n)
[0-6]
n = 6411

R^2
0.077



S4.3 Severity dependence/abuse
[0-9]
n = 6415

R^2
0.077



Analyses of all variables for the total sample and for the prematurely ended sample are available in the supplementary information Fig. 3A, 3B, and 3C. Descriptives of all scores are available in the supplementary information Table 1A, 1B, and 1C.

PPS differed from all other clusters in Intake only, Care L1, and Care L2. In Care L2, opioids were the dominant PPS, while this was alcohol in all other clusters. Out L1 featured the lowest problem severity scores of all continuous variables. Out L2 scored higher for craving and severity dependence/abuse. When compared to both Out L1 and Out L2, Intake only scored higher for limitations, need for care and history. Intake only scored lower for severity dependence/abuse in comparison to Out L2. Out L3 scored higher for depression/anxiety/stress than Intake only, Care L1, and Care L2. Out/in L1 scored higher than Out L3, Intake only, Care L1 and Care L2. Out/in L2 scored higher than Out/in L1 for limitations, and need for care. There were no differences in patient characteristics between Out/in L2 and Out/in L3, and Complex. The scores for limitations and need for care in Care L1, and Care L2 are comparable with SUCs featuring inpatient days. Scores for depression/anxiety/stress however were lower, and comparable with the cure outpatient SUCs. Craving scores, on the other hand, were for care comparable with the SUCs with inpatient days.

5.4 Discussion

Analyzing service utilization in addiction treatment in a large sample of SUD patients resulted in a model of ten SUCs that differed in focus and amount of services provided, and in the number of hours and days of services that were utilized by patients. The SUC featuring the least intensive utilization consisted of only a few general service hours, while the most intensively utilized SUC consisted of more than 260 service hours and 108 inpatient treatment days. SUCs with a high service utilization served smaller numbers of patients. Three SUCs were characterized as outpatient cure SUCs, four combined out/inpatient SUCs, and two care SUCs. The care SUCs featured only a few inpatient days. Overall, the higher the utilization intensity of the SUC the higher the patient severity scores, with limitations in general functioning and need for care showing the strongest association with SUCs.

Most patients were classified to the two SUCs with the lowest intensity of services utilization. Almost three-quarters of all prematurely ended treatment episodes were classified in these two least intensive SUCs. Treatment episodes featuring non-compliance are generally related to treatment phase to a lesser degree than personal characteristics and applied treatment methods (Brorson et al., 2013; Dalton et al., 2021). Patients with prematurely ended endings in the low intensity service clusters may have needed limited further support to reach their treatment goals. Although, these patients might also have been less motivated for treatment, leading to early termination of services without achieving treatment aims or complying to the treatment plan. Improving treatment engagement during intake and early treatment seems especially helpful for these patients. Studies suggest that motivational interventions (Miller & Rose, 2009; Smedslund et al., 2011), and offering more limited interventions such as short e-health counseling and education (Postel et al.,2010), or 'specific for alcohol use disorder' brief interventions (Kaner et al., 2019) might be helpful in this respect. This matter needs further investigation.

Although the identified SUCs are clearly distinguishable and clinically recognizable, future studies examining different SUD populations and/or treatment centers should apply the same methodology to further assess their validity and generalizability. Furthermore, it has yet to be established how useful these SUCs are for analyzing service providers and treatment planning in addiction treatment. For instance, future studies on SUCs could predict the required treatment capacity for different regions and populations, or compare practice variation based on SUCs.

Higher intensity SUCs are associated with higher baseline patient severity scores suggesting that professionals and SUD patients seem to plan interventions in line with the paradigm that patients with the highest needs also receive the most intensive treatment. This concept of patient treatment matching is in line with other practice-based literature, showing that time in programs contributes to treatment effects (Zhang et al., 2003; Hser et al., 2015; Merkx et al.,2014). However, support in other scientific literature is limited (Merkx et al., 2013; Kramer-Schmidt et al., 2017; Howick et al., 2022).

Our data do not provide an insight into the decision-making process that plays out between patient and professional. As a result, it remains unclear which patient characteristics and preferences were most relevant for patient-treatment matching. Furthermore, the process of shared decision making, where both patient and professional influence the treatment selection process, remains unclear. Though studies do support that shared decision-making might improve treatment outcomes in addiction care (Joosten et al., 2008), its effect on service utilization has hardly been studied. Further research is required to explore this process in more detail and contribute to further improvements in the clinical decision-making process.

The mean severity scores differed between the outpatient cure SUCs, between outpatient and out/inpatient SUCs, and between the care SUCs. However, no differences in patient characteristics were observed between the different Out/inpatient SUCs in spite of substantial variation in number of inpatient days between these SUCs. Apparently, there are other factors associated with the utilization of inpatient services apart from the patient characteristics measured at intake. Service utilization is not only determined as part of patient placement after intake, but results from an ongoing dynamic process of decision-making between patients and practitioners during treatment. An important factor affecting service utilization may, therefore, be related to variation in outcomes during treatment that lead to either shorter or longer inpatient treatment.

Remarkably, patients in the two care SUCs had relatively low scores for mood symptoms and SUD severity. Furthermore, the care clusters featured a relatively high number of patients with opioids as PPS compared to other SUCs. This is in line with literature that shows that a large proportion of opioid patients receive long-term opioid agonist treatment (Wisselink et al., 2016; Hser et al. 2004). These findings further support evidence for the effectiveness of such approaches, as indicated by the low scores on mood symptoms and SUD severity, despite a long treatment history and care approach.

The main strength of our analysis is the application of a large database of patient records, with comprehensive data of patient monitoring and treatment information in clinical practice. Our study also has some limitations. Firstly, we used one treatment episode per patient with a maximum duration of one year. Following patients over several years and multiple treatment episodes would provide more insight, especially for those with chronic addiction. Furthermore, we investigated the service utilization of one addiction treatment center only. The Inclusion of other treatment services, such as those provided by hospitals and general practitioners, would give a more comprehensive insight into the health services that patients use and how the use of multiple services influences each other. A further limitation is that only substance use disorders were analyzed despite behavioral addictions becoming an increasingly common reason to seek treatment (Stevens et al, 2021; Subramaniam et al., 2015; Bijker et al., 2022). Future studies should add behavioral addictions to their analyses.

SUD patients vary in their use of addiction treatment services. We identified ten addiction service utilization clusters that differed in treatment intensity and focus. These clusters were associated with the severity of the SUDs analyzed and particularly to limitations in functioning as measured at intake. Future studies should examine the prospective planning of patient treatment based on clinical data and relate this to treatment outcome. Such data analyses may contribute to improvements in patient placement and support shared decision-making in individual service planning, as well as improve treatment planning at the treatment center level.

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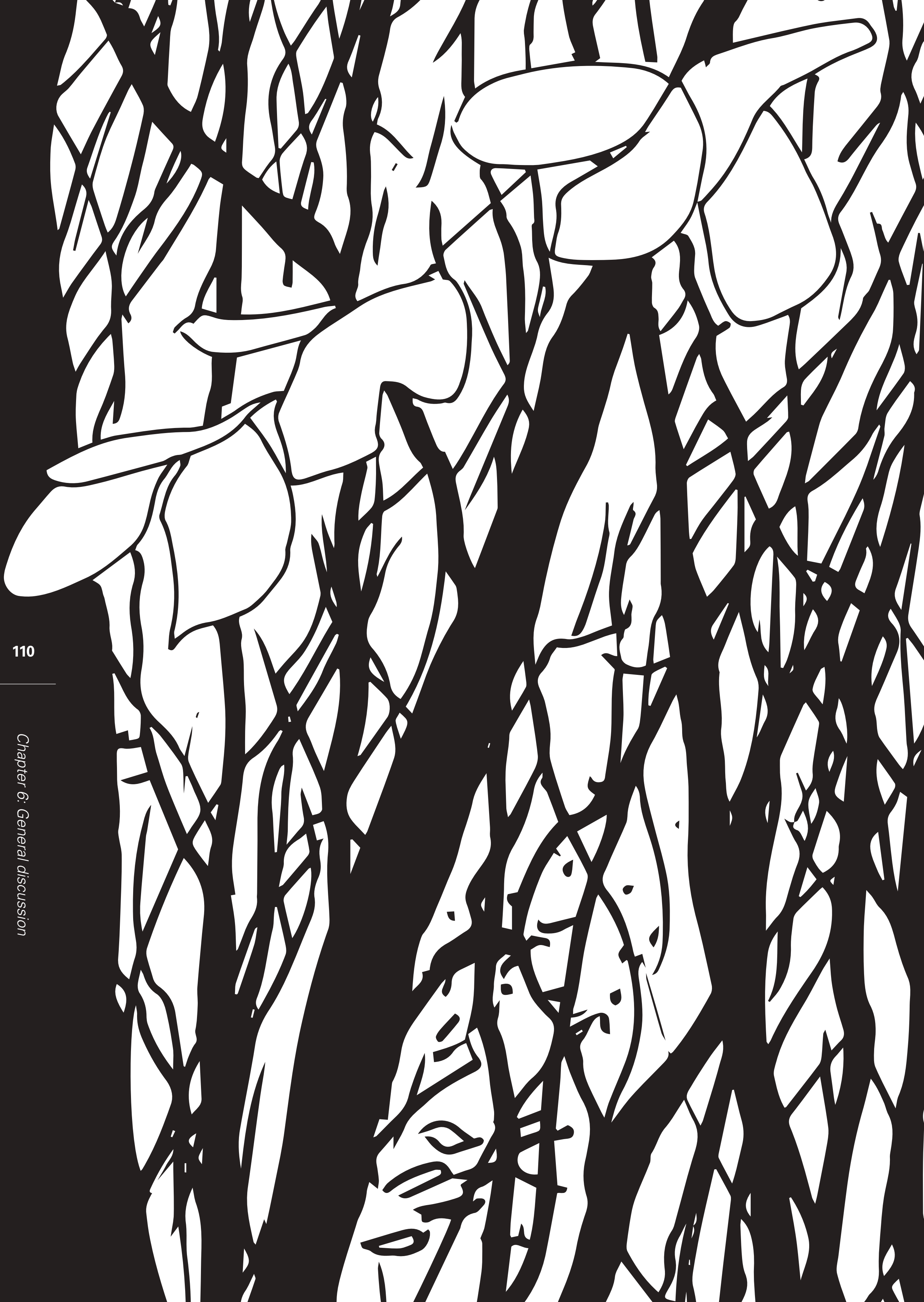

6. General discussion

The aim of this thesis is to explore clinical heterogeneity in addiction care through explorations of a large set of naturalistic patient and treatment data. Specifically, we aimed to explore heterogeneity at the level of the patient and at the level of the treatment offered. In this chapter I will first summarize our key findings. Then I will discuss practical and policy consequences, and finally give methodological considerations and suggestions for future research.

Part I: Heterogeneity of treatment-seeking SUD patients

In Chapter 2, we investigated how SUD symptoms interconnect, using the network approach of psychopathology (Borsboom & Cramer, 2013). We analyzed the interaction between SUD symptoms in nearly four thousand patients in the first phase of their treatment. First, we explored the overall symptom network of the cohort, calculating global strength, strength of the symptoms, and the weights of the symptomto-symptom connections. Second, we tested whether networks differed between the most prevalent substances in addiction care (i.e., alcohol, cannabis, cocaine, opioids, other stimulants). Finally, we compared the networks based on DSM-IV and on DSM-5 SUD criteria.

The SUD symptom networks showed strong connections between the symptoms, resulting in high global strength. In the overall SUD network, the symptom: 'Spending substantial amount of the day obtaining, using, or recovering from substance use' had the highest strength. The symptoms 'giving up or cutting back on important social, professional, or leisure activities because of use' and 'repeated usage causes or contributes to an inability to meet important social, or professional obligations', were the symptoms that influenced each other most.

Between substances, networks differed in global strength and structure. The networks of patients with opioids or cocaine use as their primary problem substance (PPS) had the highest global strength. Finally, we observed a slightly higher strength of the overall network when using the criteria for DSM-5, in comparison to DSM-IV.

Compared to previous network analyses on SUD in the general population (Rhemtulla et al., 2016), SUD patients in our sample showed health and social relations problems to be more central. Furthermore, 'using more than anticipated' was the strongest symptom in the general population, whereas 'needing more time to use and to recover from use' was the most central symptom in our SUD sample. These differences might be explained by differences between stages in the development of SUDs, with substance users in the general population representing early stages of substance use, and our sample representing advanced stages of SUD (Buu et al., 2012; Neven et al., 2018; Van Den Brink & Schippers, 2012).

In Chapter 3 we applied a staging model using a progressive development of SUD over time. We assessed, whether a staging model, where first addiction becomes more severe, and is then followed by psychiatric complications and, without successful treatment, progresses into social disintegration, could be observed in our cross-sectional sample of treatment seeking SUD patients. We found that between 80.9 and 87.1% of the patients fitted the model, depending on criteria for psychiatric problems, and that the results were robust for age, sex, and PPS. We concluded that the profile of the vast majority of treatment-seeking SUD patients fitted the suggested staging model.

Part II: Heterogeneity of addiction care offered to SUD patients

In Chapter 4, we tested two prediction models for addiction healthcare consumption using 1) a generic mental health model for predicting care consumption, introduced and tested in the Netherlands to support insurers in the reimbursement process, and 2) an enriched model, based on more detailed intake data. Predictors in the generic model were: nature of the disorder (clinical judgment and severity score), existence of comorbidity (yes or no), psychosocial factors (yes or no), and the GAF score (score for general functioning in the DSM-IV). The explained variance of health care utilization for SUD patients was 5.3% for patients with primary alcohol use disorder, and 3.4% for patients with primary drug use disorder. Using an enriched model, based on clinical intake data (MATE-scores), the explained variances were higher; for alcohol 13.8% and for drugs 10.0%. Though this clearly is an improvement, this level of explained variance is still too low for prediction purposes and financial reimbursement planning.

In Chapter 5, we identified service utilization clusters in addiction care and subsequently explored differences in characteristics of the patients treated within these service utilization clusters.

We first identified ten Service Utilization Clusters (SUCs), differing in focus and amount of care, after categorizing all activities into ‘care’, ‘cure’, and ‘general service’. The SUC of lowest intensity consisted of only a few general service hours, while the most intensive SUC consisted of more than 260 outpatient general service and treatment hours and 108 inpatient general and treatment days. Most patients were treated within the two SUCs with the lowest intensity of services utilization. Almost threequarter of all nonregular endings of treatment episodes could be observed in these two least intensive SUCs. SUCs with a high intensity of service utilization served smaller numbers of patients.

We also found that the higher the intensity of the SUC, the higher the severity scores of the patients, with ‘limitations in functioning’ and ‘need for care’ showing the strongest associations. The mean severity scores differed between the different outpatient cure SUCs, between outpatient and out/inpatient, and between care and cure. In spite of the substantial variation of inpatient days, we found no significant difference in patient characteristics between SUCs that had inpatient days. This needs closer investigation using other patient characteristics than collected at intake, for instance progress made during the inpatient treatment. Patients in the two care SUCs had relatively low scores for mood symptoms and SUD severity. Furthermore, the care clusters had a relatively high number of patients with opioids as PPS.

We concluded that this kind of big data research on service utilization related to different patient profiles, can further our understanding of clinical practice of treatment allocation in addiction care. Such an approach could contribute to the improvement of treatment planning and patient placement in addiction treatment in future.

Taken together, these studies show that SUD patients in a in large, regional addiction treatment organization show a differentiated severity profile at intake and are offered differentiated treatment. In the Netherlands, addiction care has a broad, varied programmatic approach, which fits in well with our observations. The more severe patients’ problems are, the more treatment they consume. So overall, we found that patients and practitioners seem to make rational use of the broad-spectrum treatment facilities available in the Netherlands.

Practical Implications

The lack of convincing support for differentiated patient placement or patient-treatment matching in addiction care in the literature might suggest that a onesizefitsall approach in addiction care is appropriate. However, our findings show huge heterogeneity in clinical practice, both at the level of the patient and the treatment provided. Furthermore, the observed association between these two sources of clinical heterogeneity advocates a more personalized treatment approach.

The general perception, among care professionals as well in the public, that only more severe patients with chronic and complex co-morbid illness history, are treated in specialized treatment centers, needs correction. Based on the data from one of these centers, it seems that such centers do also serve large groups of less severely afflicted patients, who, correspondingly, receive short and low intensity treatment. This general misperception might be caused by the fact that the more severe patients receive more intense and long treatment trajectories. As a result, clinicians are more often and more repeatedly confronted with these patients.

The patients that utilize the low intensive SUC's are in fact the largest group of patients in addiction care. These patients are also responsible for three quarters of all the prematurely ended treatment episodes. Generally, these patients have lower addiction severity, less co-morbid symptoms, and less limitations. They might on the one hand need less treatment, after quick first improvements. On the other hand, they might also be less motivated for (longer) treatment. Future studies may address reasons for premature treatment ending, in order to reduce unwarranted treatment drop-out, and also include the outcome of these prematurely ended treatment episodes.

Though these low severity patients might need specialized treatment and advise, this could be organized easier accessible and with lower thresholds, for instance starting with short interventions (Morgenstern et al., 2021) or (more anonymous) e-health treatment (Postel et al., 2010). This might enhance treatment retention in this group of patients. Furthermore, starting with extensive assessment and diagnostics in these patients, might for many of them be counterproductive, not necessary, and time-consuming. A more stepped care assessment, starting with a simpler triage might be more appropriate and efficient for this group.

On the other side of the spectrum, our findings show a relatively small group receiving care trajectories, mainly patients with opioid use disorder (OUD). Patients with OUD also showed the strongest symptom networks, suggesting that opioid addiction is relatively harder to cure than the other addictions because the symptom network is harder to change. This might explain the overrepresentation of patients with opioids as PPS in the care SUC's. In line with a large body of literature, this group of patients is probably a group in long-term harm reduction treatment (Loth, et al., 2012; Van Den Brink et al., 2003, 2013; Wisselink et al., 2016). As the severity of their conditions seems relatively low, this might indicate successful harm-reduction. In many cases, care will lead to a better health and social functioning, for instance preventing unemployment, malnutrition, physical illness, loneliness, and homelessness, while treatment to reach abstinence might lead to more disappointments and demoralization (Van Den Brink et al., 2013).

From the broad variation of patients' problems and their variation in severity, limitations in functioning is the most relevant symptom for differentiation in the intensity of health care utilization. If we just look at people suffering from alcohol use disorder, nearly 30% suffer from neurological/brain abnormalities (Bruijnen et al., 2019). Furthermore, people who are intellectually challenged are overrepresented in addiction care (Didden et al., 2020). Assessment of limitations is however not part of established assessment instruments in addiction care, and more instruments to measure limitations are still in development (Schellekens, et al., 2023). First of all, assessment of these possible limitations should be standard of care to differentiate in patients' needs for treatment, but more comprehensive assessment is needed for patients that enter more intensive SUC's.

Policy implications

Every professional treatment costs money, and there is always a shortage of well-trained staff. Policy makers that want to take generic cost saving measures, should be aware that most patients with SUD don't receive treatment at all, and that of those in treatment, the majority utilizes low intensity SUC's. This is in line with other illnesses, like post-traumatic stress syndrome (PTSS) (Roughead et al.,2021), and cardiovascular diseases (Kim et al.,2020). Sometimes, access to professional help should have appropriate thresholds, in order to avoid medicalization and unnecessary spending of health care budget. In other cases, early detection and treatment will in the end save costs and suffering. Substance use is worldwide responsible for one third of health loss by mental illness (WHO, 2010), while SUD is the mental illness with the lowest treatment rate in psychiatry (Ten Have, et al., 2022). For some mental illnesses there might be overconsumption of expensive professional help (Denys, 2020). For other illnesses, like SUD, service utilization is relatively low, while costs rise enormously when the illness develops to more severe stages. For SUD patients, the risk of undertreatment is bigger than that of overtreatment.

Early detection of SUD is crucial, because SUDs usually start at young age. Most diseases, like cancer and cardiovascular disease, lead to more impairments and loss of health years by advancing age. Most mental illnesses, on the other hand, develop early in life, at age 10 to 24, and incidence rates peak between age 20 and 40 (Murray, 2012). Broad spectrum treatment organizations deliver the whole chain of treatment interventions in a so-called (patient) value driven supply chain with the least organizational and funding limits (Porter & Teisberg, 2006). They can change within their own supply chain, stimulate prevention and early detection instead of focusing on intensive treatments, and even profit from that change by better service to their patients and financers: not more help than needed, not less than warranted. Our results support the recent Dutch healthcare policy, as stipulated in the so-called 'Integraal zorgakkoord' [Integral care agreement] (2022), which aims to direct the care system more to prevention and early detection, and low and easily accessible (community) care where possible, and more intensive care when needed.

Our studies show the importance of good data collection. In the early 90s, adopting digital patient files in everyday practice, was expected to have predictive models soon available to help managing waiting lists and therapy planning for patients. Two decades later we can perform evidence-based digital treatments for SUD patients, including psychoeducation, motivational process and assessment, and after care (Postel et al., 2010). However, managing waiting lists and treatment capacity hasn't really changed overtime.

Data collection and software developments have focused more on organizational, and policy needs than on the treatment process itself. To contribute more directly to better and more efficient healthcare, data collection and software developments should focus more on the treatment process itself, and collect and use data of patient profiles, disease courses, treatment delivery, and treatment history. Too much focus on policy goals, like financial accountability, or local team performance, will not lead to quicker recoveries, prevention of complications, stimulate treatment innovation, personalized treatment, and patient satisfaction. Data collection should primarily serve goals that create value for patients, and lead to enduring results and knowledge.

Big data research can link evidence-based medicine with well-organized (efficient and affordable) personalized medicine. An important condition is that the collected data are of value for patients and practitioners, and are standardized enough to be of value for big data analyses. Data on Health Care Utilization (HCU) are available in patient files, with minimal additional registration burden. Although often hindered by privacy legislations and software compatibility problems, addiction care in the Netherlands has a long tradition in collectively collecting intake, outcome, and patient satisfaction data. A next step is to make better use of these data, by sharing data and making them available for research, in order to contribute to care quality improvement.

Methodological considerations and Implications for further research

Patients are far more than their disease, even more so in psychiatry. The symptoms of a mental illness and their consequences are present in every aspect of the patient's life; in their everyday functioning, thoughts, feelings, and hopes. Capturing all these aspects in experimental research is impossible. Patients in randomized clinical research are generally not representative for patients in clinical practice (Kostis & Dobrzynski, 2020; Susukida et al., 2020; McCarty et al., 2020). Therefore, scaling up naturalistic observations with long-term follow-up is crucial to explore treatment processes and their results in real life.

For our studies we used real-life observational data from one treatment center, and data were collected within a time frame of six years. Data on service utilization were limited to one treatment episode, one year after intake. So first of all, replication of our findings in other regions/organizations and time periods is necessary. Patients also change over time, use multiple treatment episodes or make use of ongoing care (Wisselink et al., 2016). This type of data collection and analyses can, once implemented, relatively easily be expanded to a longer period of time and to ongoing measurements. Furthermore, service utilization in addiction treatment might influence healthcare use elsewhere and vice versa, which makes analysis of healthcare utilization across healthcare services useful. Finally, the combination with result and satisfaction measurements is desirable. With the Dutch tradition of data collection in addiction care, this ideal is within reach.

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Dutch summary / Nederlandse samenvatting

Het doel van deze these is te komen tot een nadere profilering van SUD patiënten en hun behandeling. Die profilering is wenselijk gezien de heterogeniteit van patiënten en hun behandeling in de dagelijkse behandelpraktijk. SUD patiënten verschillen biologisch, psychologisch en sociaal van elkaar, maar ook door het soort drug dat zij gebruiken en de verschillende stadia van hun SUD. Tot slot verschillen ze ook in de mate waarin ze klaar zijn voor behandeling en daarmee het doorbreken van hun verslaving.

In Nederland kennen we een breed spectrum aan behandel- en zorgmodaliteiten, variërend van een kort advies en educatie, tot aan intensieve klinische behandeling, inclusief forensische behandelingen, dubbeldiagnose behandelingen en behandelingen in het kader van de Wet Verplichte Geestelijke Gezondheidszorg (WVggz). Veruit de meeste behandelsettingen werken volgen de principes van evidence-based treatment en passen systematische assessments toe bij de toeleiding naar zorg. Die behandelingen verschillen sterk in doel en intensiteit. Het ontbreekt echter nog goeddeels aan wetenschappelijk onderbouwde richtlijnen voor het nader indiceren van zorg en behandeling.

Door het gebruik van elektronische patiëntendossiers en het toepassen van een systematisch assessment met behulp van de MATE (Measurement in the Addictions for Triage and Evaluation) (Schippers et al. 2011, 2012), beschikken we over een grote hoeveelheid data. Deze data worden echter nog weinig gebruikt ten behoeve van profilering van patiënten en hoe die patiënten in de dagelijkse praktijk te matchen en te plannen zijn in het brede aanbod aan interventies en behandelingen.

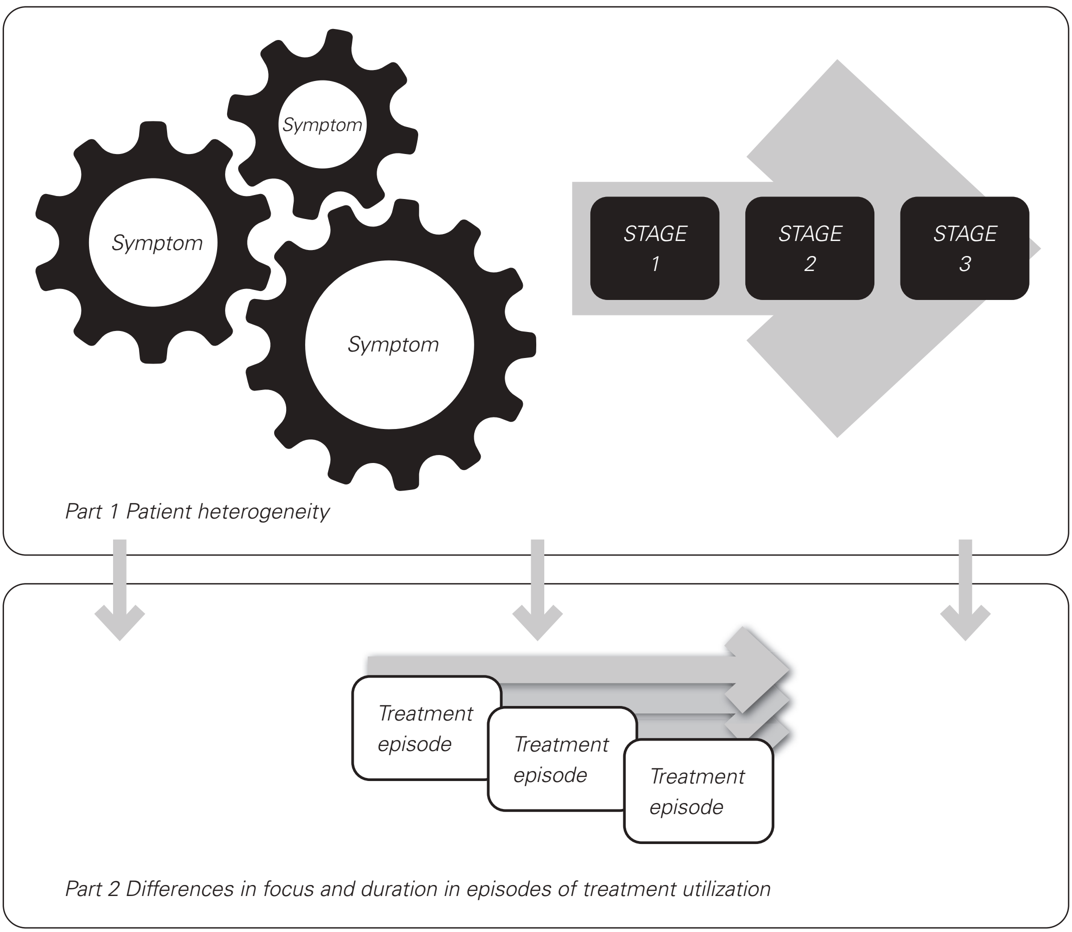
Het doel van deze these is deze data te exploreren, specifiek om de volgende vragen te beantwoorden:

1. Kan klinische heterogeniteit worden verhelderd door de onderlinge samenhang van SUD symptomen te analyseren?
2. Kunnen we stadia onderkennen in de ontwikkeling van een SUD?
3. Kunnen we hoeveelheid en focus van behandelepisodes in de praktijk relateren aan patiëntkenmerken?

Daarmee valt deze these in twee delen uiteen: ten eerste onderzoek naar de heterogeniteit onder SUD patiënten in behandeling en ten tweede naar de heterogeniteit in de verslavingszorg die die patiënten aan wordt aangeboden.

De onderstaande tabel laat de omvang van de studiecohorten van de vier studies zien.

Study	Sample size
1	10.832
2	6.602
3	3.434
4	9.841



In hoofdstuk 1 wordt de achtergrond en de vraagstelling nader geschetst en worden de vier uitgevoerde studies ingeleid.

Deel 1
Heterogeniteit onder SUD patiënten in behandeling

Hoofdstuk 2 bevat een studie naar de samenhang tussen SUD symptomen met behulp van het model voor netwerkanalyse van psychopathologische symptomen (Borsboom & Cramer, 2013). Allereerst hebben we een symptoomnetwerk van de hele onderzoekspopulatie berekend en de totale sterkte van dit netwerk, de sterkte van de verschillende symptomen en de gewichten (relatieve correlatie) van de verschillende onderlinge symptoomrelaties. Vervolgens hebben we de verschillen onderzocht tussen de netwerken van de meest voorkomende middelen: alcohol, cannabis, cocaïne, opioïden en andere stimulantia. Tot slot hebben we de symptoomnetwerken gebaseerd op de DSMIV vergeleken met die gebaseerd op de DSM-5.

De netwerken van SUD symptomen vertonen sterke connecties, resulterend in hoge globale sterktes. In het netwerk van de totale onderzoekspopulatie was het symptoom 'Veel tijd wordt besteed aan activiteiten die nodig zijn om aan middelen te komen, te gebruiken, of te herstellen van de effecten ervan' het sterkst. De symptomen met de onderling sterkste correlatie waren 'Belangrijke sociale, beroepsmatige of vrijetijdsactiviteiten zijn opgegeven of verminderd door het gebruik' en 'Terugkerend middelengebruik dat resulteert in het niet nakomen van belangrijke verplichtingen op het werk, op school of thuis.'.

Tussen de netwerken van gebruikers van verschillende middelen waren duidelijke verschillen. De netwerken van cocaïne en opioïde gebruikers hadden de hoogste globale sterkte. De globale sterkte van de DSM-5 criteria was iets hoger dan die van de DSM-IV.

Vergeleken met eerdere netwerkanalyses van mensen met SUD in de algemene populatie (Rhemtulla et al., 2016) liet de patiëntenpopulatie meer centraliteit van gezondheids- en sociale problemen zien. In de algemene populatie stond 'Er wordt vaak gebruikt in grotere hoeveelheden of langduriger dan de bedoeling was' centraal, terwijl in de patiëntgroep 'Veel tijd wordt besteed aan activiteiten die nodig zijn om aan middelen te komen, te gebruiken, of te herstellen van de effecten ervan' centraal stond. Dit kan er op wijzen dat gebruikers in de algemene populatie vroegere stadia van gebruik representeren, terwijl in de patiëntengroep meer sprake is van latere stadia (Buu et al., 2012; Neven et al., 2018; Van Den Brink & Schippers, 2012).

Hoofdstuk 3 bevat een studie naar toepassing van een progressief stageringsmodel voor SUD, waarbij verslaving eerst ernstiger wordt, waarna psychiatrische complicatie optreden en bij onvoldoende behandeleffect uiteindelijk ook sociale- en maatschappelijke desintegratie volgt. We onderzochten de mate waarin deze stadiakenmerken gerepresenteerd werden in een crosssectioneel onderzoek van een behandelpopulatie. We vonden dat 80,9 tot 87,1% van de patiënten binnen dit model paste, afhankelijk van welke criteria we hanteerden voor psychiatrische complicaties. Deze resultaten waren robuust voor leeftijd, sekse en middel. We concludeerden dat een grote meerderheid patiënten in dit stageringsmodel paste.

Deel 2
Heterogeniteit in de verslavingszorg die aan patiënten wordt aangeboden

Hoofdstuk 4 bevat de vergelijking van voorspellende waarden van twee modellen voor zorgvraagtypering voor het in de Nederlandse praktijk toegepaste zorgclustermodel (Werkgroep zorgvraagzwaarte GGZ, 2013). Het eerste model betreft de eerste versie van het generieke zorgvraagzwaartemodel 1.0, in Nederland geïntroduceerd en getest om zorgverzekeraars te ondersteunen in het zorginkoopproces. Het tweede betreft een op basis van meer intake data verrijkt model. De voorspellende variabelen van het zorgvraagzwaartemodel 1.0 waren: de aard van het stoornis, aanwezigheid van psychiatrische co-morbiditeit, aanwezigheid van psychosociale problematiek en de GAF-score van de DSM-IV. De verklarende variantie was bij dit model 5.3% voor mensen met een stoornis in het gebruik van alcohol en 3.4% voor mensen met een stoornis in het gebruik van drugs. Met het verrijkte model op basis van de klinische intake data (MATE-scores) was de verklarende variantie substantieel hoger: 13.8% voor alcohol en 10.0% voor drugs. Een duidelijke verbetering, maar nog steeds niet genoeg voor toepassing in de financiering van de zorg.

In hoofdstuk 5 wordt een studie gepresenteerd naar clusters van daadwerkelijk zorggebruik en de mate waarin deze samenhangen met patiëntkenmerken. Hiervoor hebben we eerst door middel van een clusteranalyse clusters van zorggebruik berekend die verschillen in focus en in hoeveelheid zorg. Hiertoe hebben we alle zorgactiviteiten gelabeld als primair 'care', 'cure' en 'algemene activiteit'. Het zorggebruik-cluster met de minste zorg bestond slechts uit enkele uren algemene hulp, zoals bijvoorbeeld een intake. Het meest intensieve cluster bestond uit gemiddeld 260 algemene en cureuren en 108 dagen klinisch verblijf. In de lage zorggebruikclusters zaten de grootste groepen patiënten. In die clusters zat ook driekwart van de patiënten die de onderzochte behandelepisode van maximaal één jaar na intake, niet regulier beëindigden. De intensive zorggebruik-clusters bedienden kleinere groepen patiënten. Verder vonden we dat naarmate het zorggebruik hoger was, patiënten hogere ernstscores hadden, met op de eerste plaats beperkingen in het functioneren en behoefte aan zorg. De gemiddelde ernstscores verschilden tussen de verschillende ambulante zorgclusters, tussen care en cure en tussen clusters met en zonder klinische opnames. Tussen de clusters met opname waren de verschillen in ernstscores niet significant. Dit vraagt om nader onderzoek, bijvoorbeeld naar vooruitgang tijdens de opnames. In de careclusters hadden mensen relatief lage scores voor angst- en stemmingsklachten en ernst van de verslaving. Verder waren hier hogere aantallen patiënten die primair opiaten gebruikten.

Samengevat: de studies laten zien dat in een grote regionale verslavingszorginstelling een brede variëteit aan verslavingsernst voorkomt bij intake en dat er eveneens een breed aanbod is aan behandel en zorgfocus en intensiteit. Hoe ernstiger de problematiek, hoe meer zorg en behandeling patiënten krijgen. Het lijkt erop dat patiënten en hun behandelaren op een doelmatige manier gebruik maken van de behandel- en zorgmogelijkheden.

Praktische implicaties

Het gebrek aan wetenschappelijke evidentie voor gedifferentieerde indicatiestelling zou kunnen impliceren dat een one-size-fits-all benadering afdoende zou kunnen zijn. De samenhang die wij vonden tussen heterogeniteit en behandeldifferentiatie bij patiënten suggereert eerder de wenselijkheid van een meer gepersonaliseerde aanpak.

De zowel in het algemeen als ook bij professionals levende vooronderstelling dat bij dit soort grote regionale verslavingszorginstellingen voornamelijk ernstige en chronisch patiënten in zorg zijn, dient bijgesteld te worden. Deze misperceptie kan het gevolg zijn van het feit dat patiënten met meer ernstige problematiek nu eenmaal veel meer en langer gebruik maken van de geleverde zorg. De patiënten die veel minder gebruik maken van de zorg vormen echter in aantallen de grootste groep. Bij deze patiënten vindt tevens driekwart van het totaal van de niet regulier geëindigde behandelepisodes plaats. Het dient nader onderzocht te worden in hoeverre dit komt door snelle resultaten, door minder motivatie of om andere redenen. Een meer voor deze groep passend aanbod ontwikkelen kan hier wellicht de behandelretentie versterken.

Aan de andere zijde van het spectrum, in het intensieve care-cluster, zien we vooral patiënten met een stoornis in het gebruik van opioïden. Deze patiënten hebben ook het sterkste symptoomnetwerk, hetgeen erop wijst dat het doorbreken van de elkaar versterkende samenhang tussen symptomen moeilijker is. Het feit dat hun verslavingsproblematiek relatief laag is kan het gevolg zijn van de succesvolle harm-reduction in dit cluster.

Van de brede variatie in ernstscores, zijn beperkingen in het functioneren het meest relevant voor de differentiatie in het zorggebruik. Assessment van beperkingen moet dan ook standaard worden toegepast, qua omgang en diepgang passend bij de zorgvraag van patiënten. Met name bij patiënten in de intensieve zorg-clusters is uitvoeriger onderzoek nodig dan bij de grote groep met een beperkte zorgvraag.

Beleidsimplicaties

Gezien de hoge kosten van zorg en de nijpende personeelstekorten is doelmatig gebruik van zorg een hoge prioriteit. SUDs zijn niet alleen veel voorkomende stoornissen, met grote persoonlijke en maatschappelijke consequenties (WHO, 2010), het zijn ook de stoornissen met de laagste behandelgraad (Ten Have, et al., 2022). Gezien het beperkte gebruik van zorg door SUD patiënten, ook in de gespecialiseerde verslavingszorg, is het risico van onderbehandeling groter dan dat van overbehandeling. Bovendien is de beweging naar preventie en vroegsingnalering belangrijk gezien de vaak jonge leeftijd waarop psychische stoornissen in het algemeen en SUDs in het bijzonder ontstaan (Murray, 2012). De organisatie van verslavingszorg in ketens van zorg voor specifieke doelgroepen, van preventie tot aan gespecialiseerde intensieve zorg, sluit hier goed op aan.

Traditioneel zijn dataverzameling en softwareontwikkeling in de zorg vooral gericht op beleidsmatige en beheersmatige doelen. Het is echter wenselijk om dataverzameling en -analyse primair te richten op ziekteverloop en het de zorgproces zelf. Alleen dan kan het haar doel dienen en waardevol zijn voor patiënten, waardevolle kennis genereren en op die manier bijdragen aan kostenbeheersing. Het analyseren en gebruiken van Big data uit de feitelijke zorgverlening is een zinvolle aanvulling op resultaten van meer traditioneel wetenschappelijk onderzoek en kan bijdragen aan goedgeorganiseerde gepersonaliseerde zorg. Bovendien zijn die data al in patiëntendossiers aanwezig en kunnen administratieve lasten voorkomen worden. De Nederlandse verslavingszorg heeft een lange traditie in het verzamelen van deze gegevens. Een volgende stap is deze data meer en beter te gebruiken en ze beschikbaar te maken voor onderzoek.

Methodologische overwegingen en advies voor verder onderzoek

Het is onmogelijk de complexiteit van psychische stoornissen te representeren in gerandomiseerde studies. Dataanalyse van grote datasets van naturalistische data uit de behandelpraktijk zijn dan ook van grote aanvullende waarde.

De hier gepresenteerde studies zijn gedaan in één behandelcentrum en de data zijn verzameld in een periode van zes jaar. De zorgdata beperken zich tot behandelepisode van één jaar na intake. Op de eerste plaats is replicatie nodig in verschillende centra en periodes. Ook is het zinvol patiënten langduriger over meerdere behandelepisodes te meten en ook zorggebruik bij andere zorgverleners te includeren, om zo het totale zorggebruik te meten. Tot slot is de combinatie met resultaat- en satisfactie metingen wenselijk. Met de Nederlandse traditie van data verzameling in de verslavingszorg is dit binnen handbereik.

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Research data management

This research followed al the applicable laws and ethical guidelines for data management and research.

Ethics

This thesis is based on Big date research with data drawn from regular electronic patient files and are anonymized. Data selection follows informed consent on the basis of an opt out procedure, following the privacy and safety regulations of the Tactus board and the Tactus scientific committee. This is in accordance with the Dutch General Data Protection Regulation (AVG) and Medical Treatment Act (WGBO).

Funding

There is no funding involved in this thesis. The research was financially and practically supported by Tactus addiction care.

Accessibility

Data are not publicly available. The research data of these studies are extracted from the Tactus patient files and are stored on a separate server to which only the researcher involved has access. The research data can only be used with explicit permission of the Tactus board, after consulting and approval of the first author. The researcher has no access to the full Tactus patient files (Chinese wall).

Curriculum vitae

Ruud Rutten is geboren op 6 februari in het dorpje Beek in de westelijke mijnstreek in Zuid-Limburg. Toen hij 10 jaar oud was verhuisde het gezin naar het naburige industriestadje Geleen onder de rook van de DSM. Daar doorliep hij ook de middelbare school, zonder veel belangstelling en inspanning voor het onderwijs dat daar werd gegeven. Dat veranderde toen hij op zijn achttiende naar Nijmegen vertrok om een van de eerste jaargangen van toen net gestarte Hogere Beroepsopleiding voor Verpleegkundigen te doorlopen. Hij genoot van het studentenleven in Nijmegen, maar ook van de studie. Aan alle vakken en stagerichtingen beleefde hij plezier, maar de psychiatrie fascineerde hem het meest. Na een aantal stages op de afdeling psychiatrie in het Radboudziekenhuis ging hij daar in 1979 werken. Een jaar later ging hij naast deze baan pedagogiek studeren.

In 1984 maakte hij de overstap naar het Johannes Wier-huis in Rekken, een kleine, jonge afkickkliniek, voortgekomen uit de TBR-kliniek Oldenkotte. Ruud werd daar afdelingshoofd en na het bereiken van zijn Bachelor pedagogiek stapte hij over naar de doctoraal studie Arbeid en Organisatie psychologie, waar hij afstudeerde op het thema: de modernisering van de professionele bureaucratie.

Door de jaren heen gaf hij mede vorm aan en leidde uiteindelijk een vijftal fusies, die leiden tot Instituut Verslavingszorg Oost-Nederland (IVON), de ontwikkeling van forensische verslavingszorg, en uiteindelijk het huidige Tactus verslavingszorg. In 1987 werd hij adjunct-directeur, daarna directeur behandelzaken, lid van de Raad van Bestuur en in 2001 Voorzitter van de Raad van Bestuur.

Hij vervulde vele landelijke bestuurlijke rollen in de Nederlandse ggz, Verslavingskunde Nederland en de Stichting Verslavingsreclassering GGZ. Ook stond hij mede aan de wieg van Resultaten Scoren, Verslavingskunde Nederland, Kwaliteitsprogramma Forensische Zorg en het Nijmegen Institute for Scientist-Practitioners in Addiction. Ook werkte hij door de jaren heen als redacteur en auteur aan diverse publicaties over verslavingszorg.

Recent is hij toegetreden tot de Raad van Toezicht van IVZ, een organisatie op het gebied van zorgregistraties, o.a. het Landelijk Alcohol en Drugs Informatie Systeem.

De tijd die rest na gezin, familie, vrienden en werk, besteedt Ruud aan concerten en tentoonstellingen bezoeken, reizen en gaat hij zelf aan de slag met camera, penseel en potlood.
Hij hoopt dat de komende tijd veel meer te gaan doen, want op 30 november a.s. viert hij zijn pensionering.

Dankwoord

Toen ik een keer mijn dankbaarheid uitte over een medeauteur zei Arnt spontaan: ‘Publiceren is een groepsprestatie’. Zo is het maar net. Al hetgeen in dit proefschrift staat, wat er aan onderzoek parallel aan liep en er aan publicaties aan vooraf ging, het was allemaal teamwork. Dus heb ik mij mogen verheugen in de samenwerking, de hulp en steun van velen.

Allereerst en bovenal dank ik mijn beide promotoren. Gerard, we kennen elkaar al lang. Onze samenwerking begint al in de tijd bij het door jouw opgerichte UNRAB (University of Nijmegen Research group on Addictive Behaviors). Daarna, tot aan jouw vertrek naar Amsterdam, was jij als toezichthouder en ik directeur bij het IVON (Instituut Verslavingszorg Oost-Nederland) actief. Daarna jarenlang bij Resultaten Scoren, alsmaar op zoek naar ontwikkeling van de verslavingszorg in Nederland. Uiteindelijk wilde ik toch een promotietraject doorzetten en was jij bereid mij daarbij te helpen. Het werd een lang traject waarbij ik vaak een groot beroep heb gedaan op je geduld en je begrip. Bestuurder zijn met ook nog vele landelijke nevenfuncties en klinisch onderzoek doen vormen in tijd, mentaliteit en focus geen natuurlijke harmonie. Maar je bleef van tijd tot tijd kritisch, maar vooral steunend en helpend tot aan het einde. Dank voor je vriendschap, je loyaliteit, je deskundigheid en je hulp.

Arnt, wat waren wij blij met jouw komst als hoogleraar bij NISPA en bij het Radboudumc/Donders Instituut. Ik was blij dat ook jij, van een hele nieuwe generatie verslavingswetenschappers, mijn promotor wilde zijn. Briljant, vriendelijk, kritisch en bovenal positief, al wat een promovendus nodig heeft in de tweede helft.

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Dank ook de vele collega's bij Tactus die meehielpen: Irene en Judith bij de data-extracties, Lotte en Erna bij de dataverzameling en Trudy voor de hulp bij zowel de dataverzameling als bij de analyse van het zorgaanbod. Liesbeth en Joseph voor het regelen en bewaken van de dataveiligheid en privacy, maar ook voor mijn persoonlijke ondersteuning als bestuurder, waardoor ik dit onderzoek kon doen. Dat laatste geldt zeker ook voor Heidi en Riëlle. Jeannette, dank voor alle hulp aan het einde van het traject, van drukwerk tot receptie en alles wat daar tussen zit.

Conny, mijn persoonlijke assistente, mijn steun en toeverlaat. Ik kan je niet beter danken dan door te zeggen dat ik zonder jou dit werk in de verslavingszorg en voor Tactus niet op deze manier en in deze omvang had kunnen doen. Laat staan om daarnaast ook nog eens met een proefschrift te schrijven. Dank ook voor de hulp bij het regelmatig, last minute, manuscripten gereed krijgen.

Tot slot mijn gezin, familie en vrienden: dank voor jullie begrip en geduld als ik weer eens te druk en te verstrooid was. Dank ook voor alle steun en alle oprechte interesse die ik zo vaak voelde.

Mijn kleindochters Bodi en Charlie: jullie tilden met jullie komst mijn leven in liefde op. Jullie zijn nog klein en boeken vergaan. Stiekem hoop ik echter dat jullie dit proefschrift later, als jullie ouder zijn, nog eens ergens op een zolder of in een oude boekenkast zullen vinden. Dat jullie het dan inkijken en dit dankwoord vinden en zullen lezen dat ik het op een bepaalde manier eigenlijk ook allemaal voor jullie deed.

Maar mijn leven werd al eerder in liefde opgetild, toen jullie kwamen, Rob, Ronna en Romy. Alles krijgt zin door jullie. Vol liefde en trots ben ik wanneer ik naar jullie kijk en aan jullie denk. Dank ook dat jullie Luca, Berry en Bart in ons leven brachten.
Dan die eerste keer, Resi…

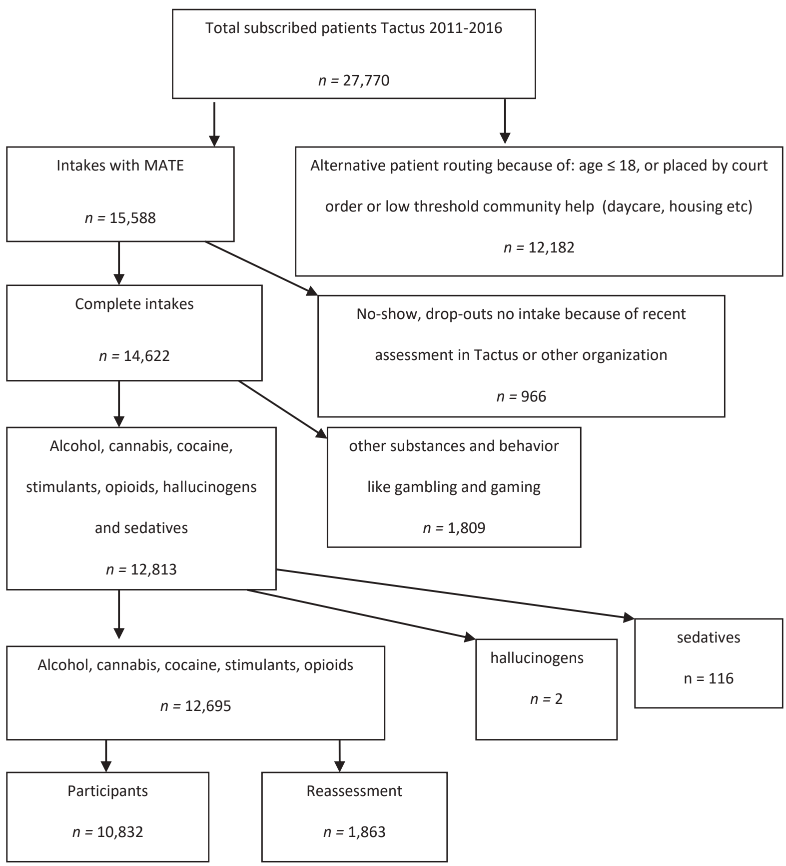
Een loopbaan als bestuurder is genoeg uitdaging voor een huwelijk. Als er dan ook nog een proefschrift bij komt, is dat de ultieme relatietest. Maar het is toch uiteindelijk telkens weer, en nog altijd, mét jou, dóór jou en vóór jou…

Appendix 1
Supplement to chapter 2

Supplementary Table 1. SUD criteria in DSM-IV and DSM-5

Code	Critirion	DSM
A1 [Roles]	Giving up or cutting back on important social, professional, or leisure activities because of use	IV/5
A2 [Hazard]	Using in physically hazardous situations, or usage causing physical or mental harm	IV/5
A3 [Legal]	Use related legal problems	IV
A4 [Interpersonal]	persistent or recurrent social or interpersonal problems because of use	IV/5
D1 [Tolerance]	Tolerance: needing to use increasing amounts of a substance to obtain its desired effects	IV/5
D2 [Withdrawal]	Withdrawal: characteristic group of physical effects or symptoms that emerge as amount of substance in the body decreases	IV/5
D3 [More/longer]	Using more of a substance than planned, or using a substance for a longer interval than desired	IV/5
D4 [Control]	Inability to cut down despite desire to do so	IV/5
D5 [Time]	Spending substantial amount of the day obtaining, using, or recovering from substance use	IV/5
D6 [Activities]	Repeated usage causes or contributes to an inability to meet important social, or professional obligations	IV/5
D7 [Health]	Persistent use despite the user's awareness that the substance is causing or at least worsening a physical or mental problem	IV/5
SQ1.1D [Craving]	Cravings or intense urges to use	5

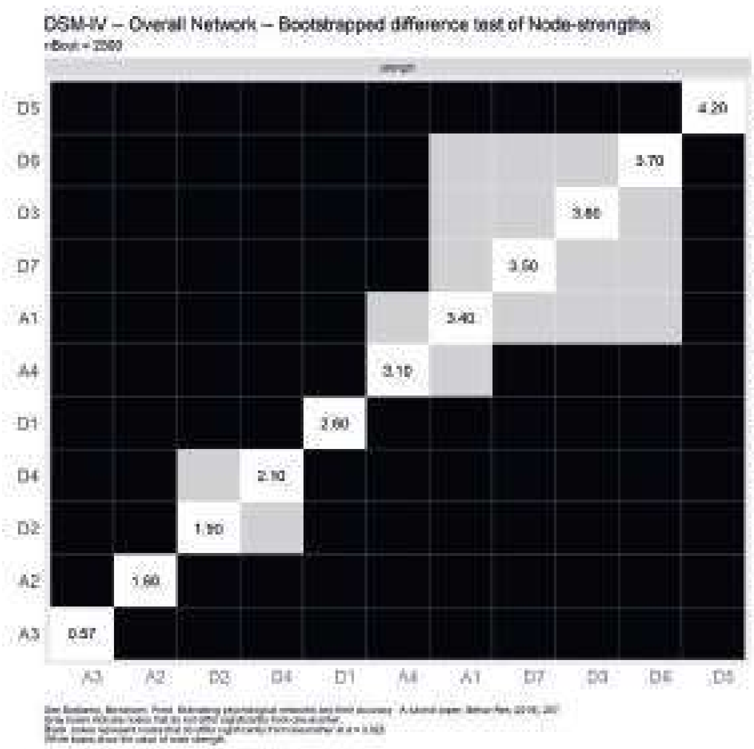
Supplementary Figure 1. Flow-chart of participants



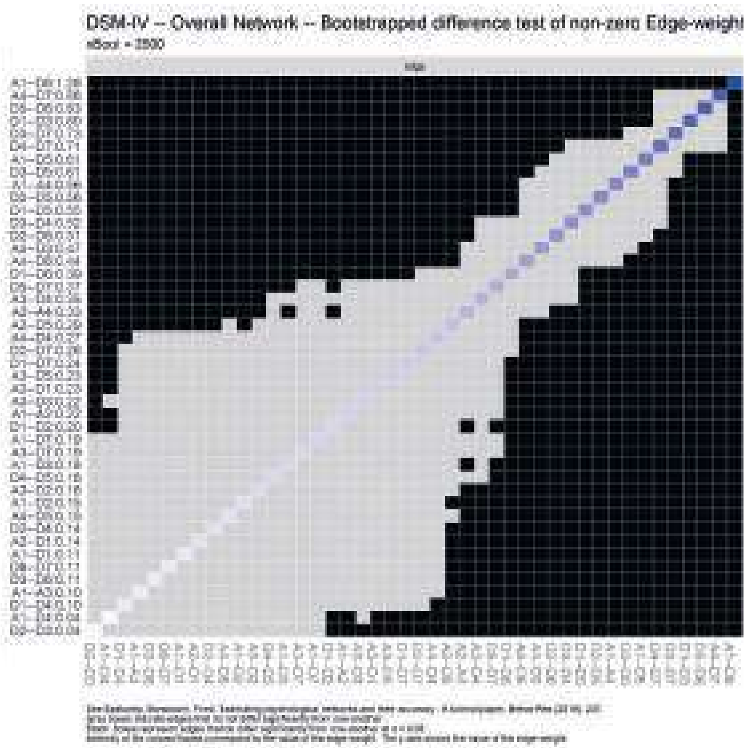
Supplementary Table 2. Correlation Stability coefficents CS(cor=.07) of nodes and edge for DSM-IV and DSM-5 Overall and substance class networks

DSM	Substance class	n	Nodes	Edges
DSM-IV	Overall	10648	0.75	0.75
DSM-IV	Alcohol	6042	0.75	0.75
DSM-IV	Cannabis	2352	0.75	0.75
DSM-IV	Cocaine	1271	0.75	0.75
DSM-IV	Stimulants	496	0.67	0.59
DSM-IV	Opioids	487	0.59	0.52
DSM5	Overall	10648	0.75	0.75
DSM5	Alcohol	6042	0.75	0.75
DSM5	Cannabis	2352	0.75	0.75
DSM5	Cocaine	1271	0.75	0.67
DSM5	Stimulants	496	0.59	0.52
DSM5	Opioids	487	0.52	0.52

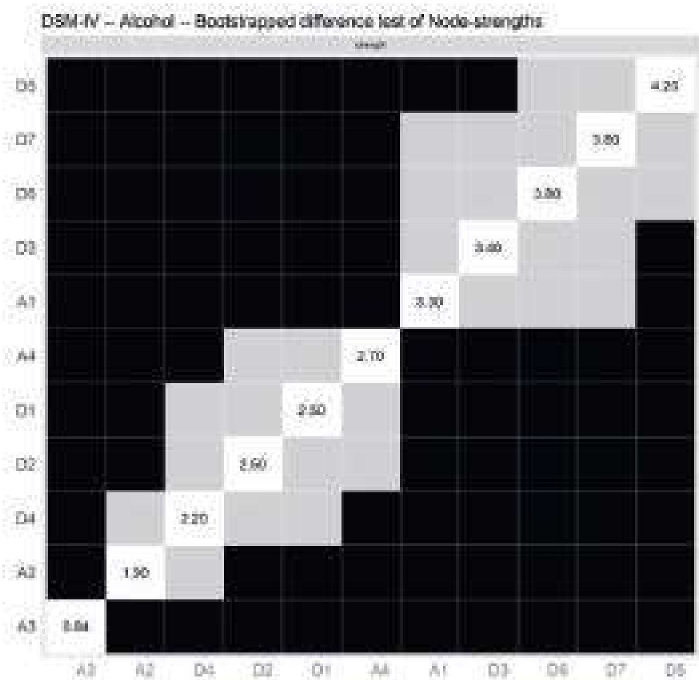
Supplementary Figure 2. DSM-IV -- Overall -- Bootstrapped difference test



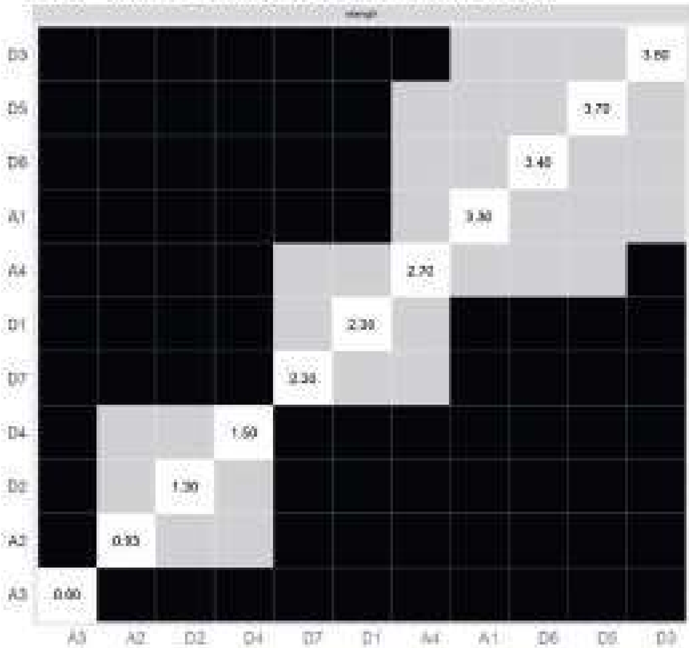
Supplementary Figure 2. DSM-IV -- Overall -- Bootstrapped difference test



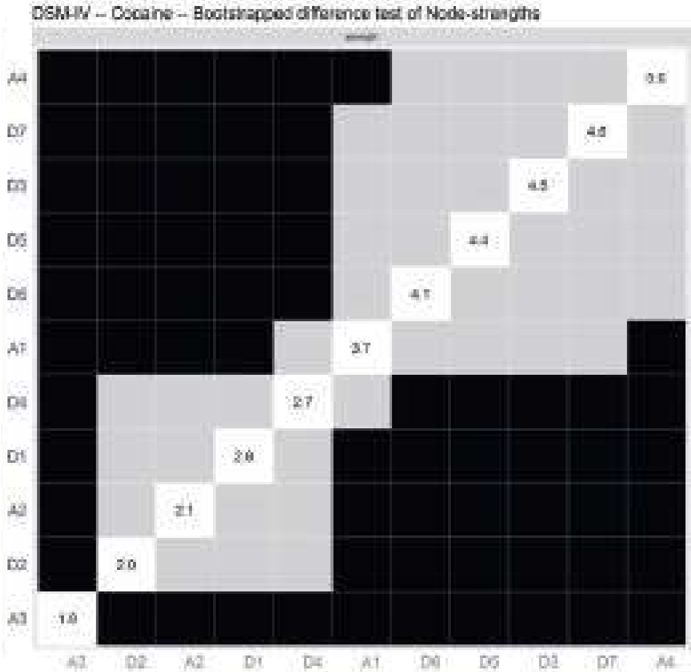
Supplementary Figure 3a.
DSM-IV -- Substance class Networks -- Bootstrapped difference test of Node-strengths



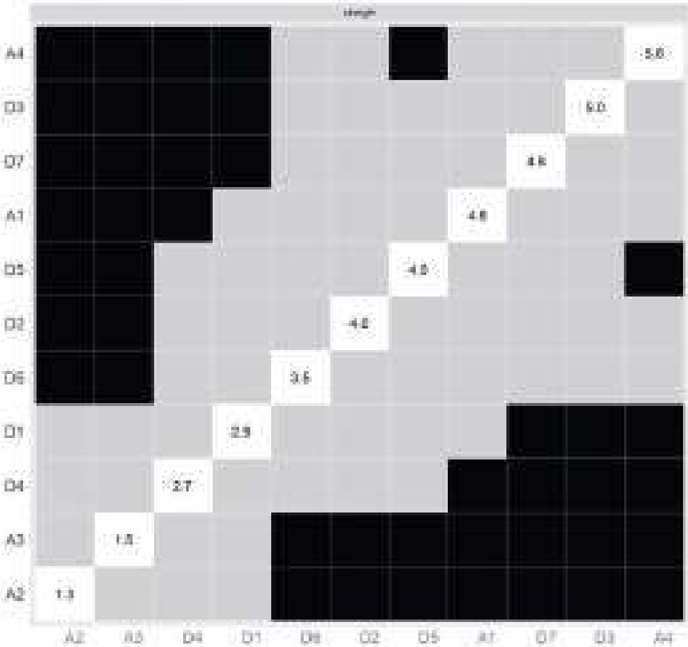
DSM-IV -- Cannabis -- Bootstrapped difference test of Node-strengths



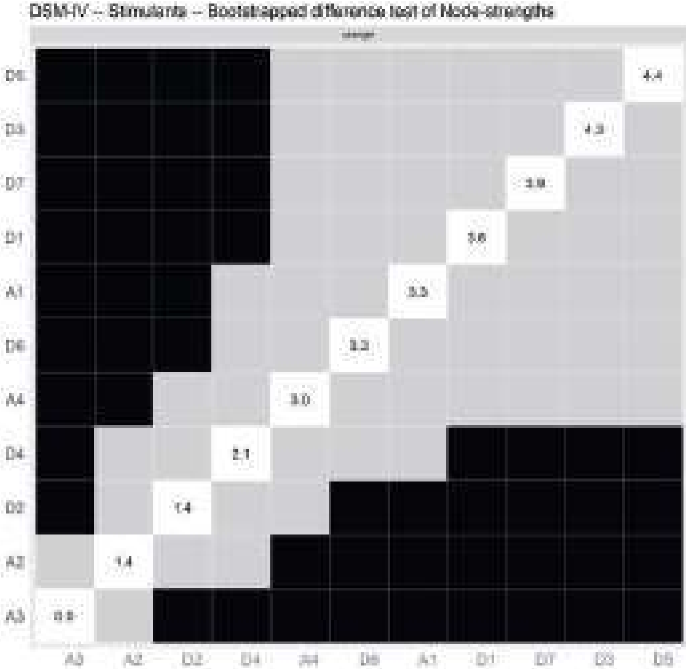
DSM-IV -- Cocaine -- Bootstrapped difference test of Node-strengths



DSM-IV – Opioids – Bootstrapped difference test of Node-strengths



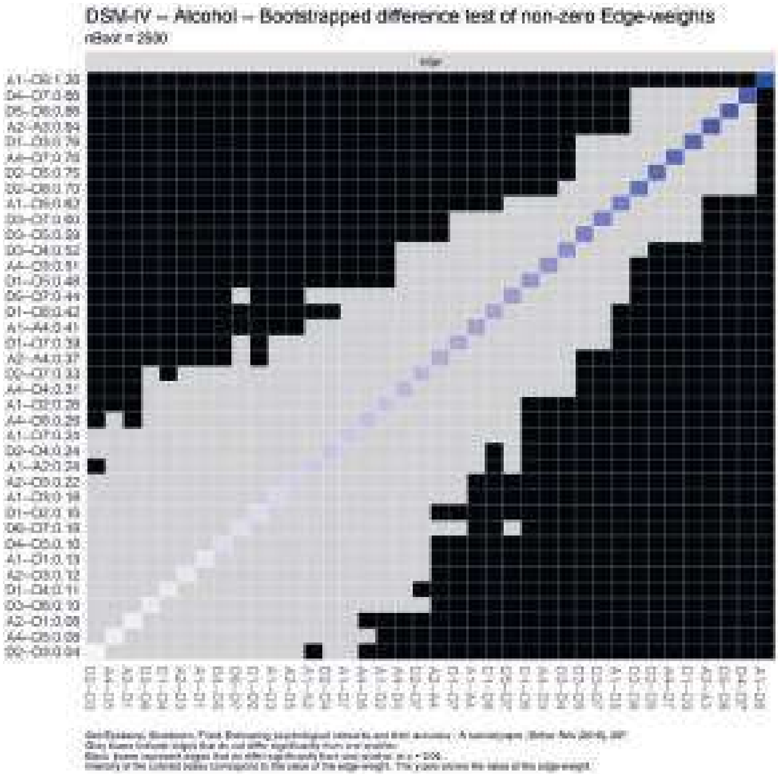
DSM-IV – Stimulants – Bootstrapped difference test of Node-strengths

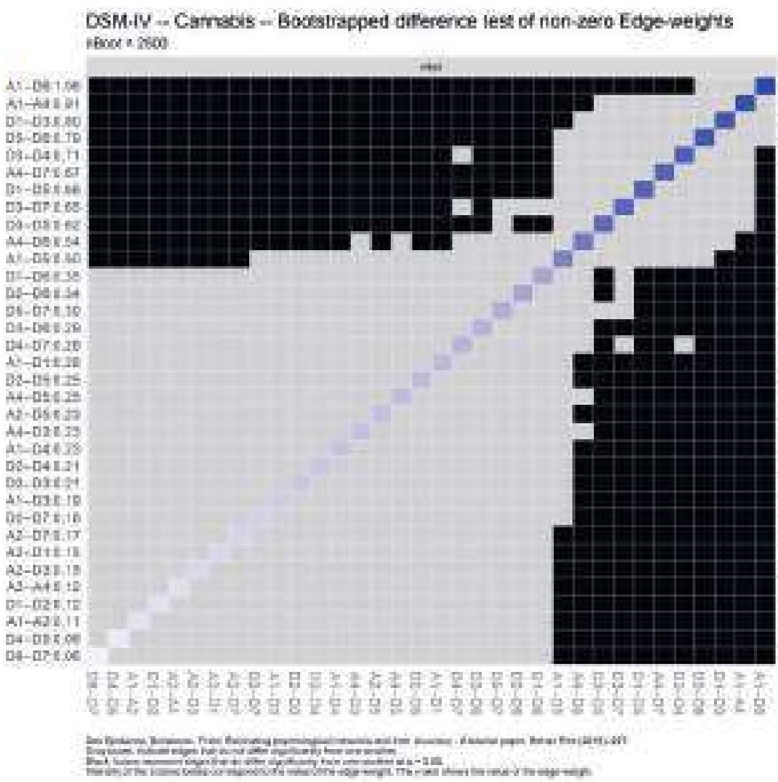


See Epskamp, Borsboom, Fried. Estimating psychological networks and their accuracy - A tutorial paper. Behav Res (2018), 207.
Gray boxes indicate nodes that do not differ significantly from one-another.
Black boxes represent nodes that do differ significantly from oneanother at α = 0.025.
White boxes show the value of node strength.

Supplementary Figure 3b.

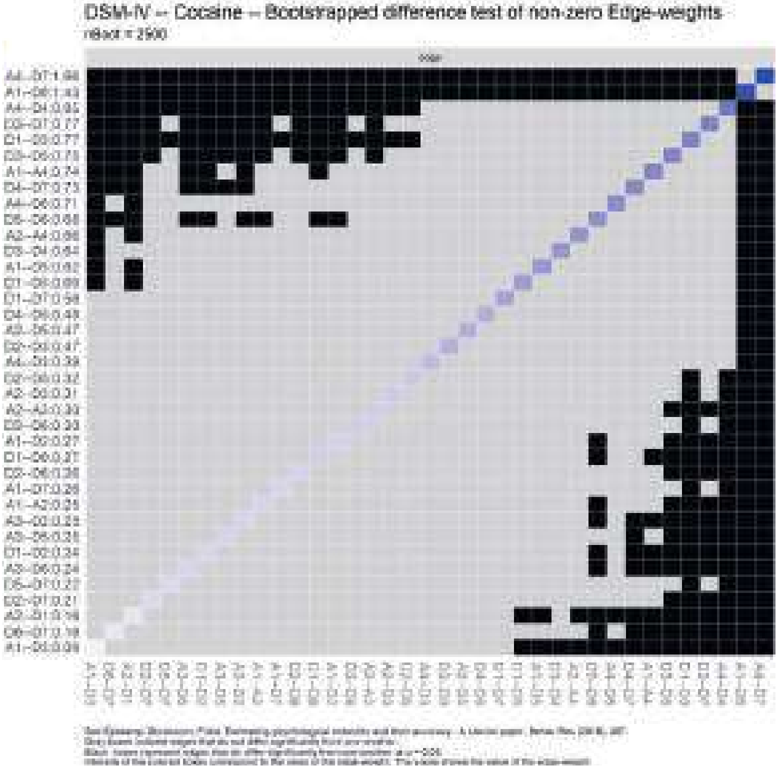
DSM-IV -- Substance class Networks -- Bootstrapped difference test of non-zero Edge-weights

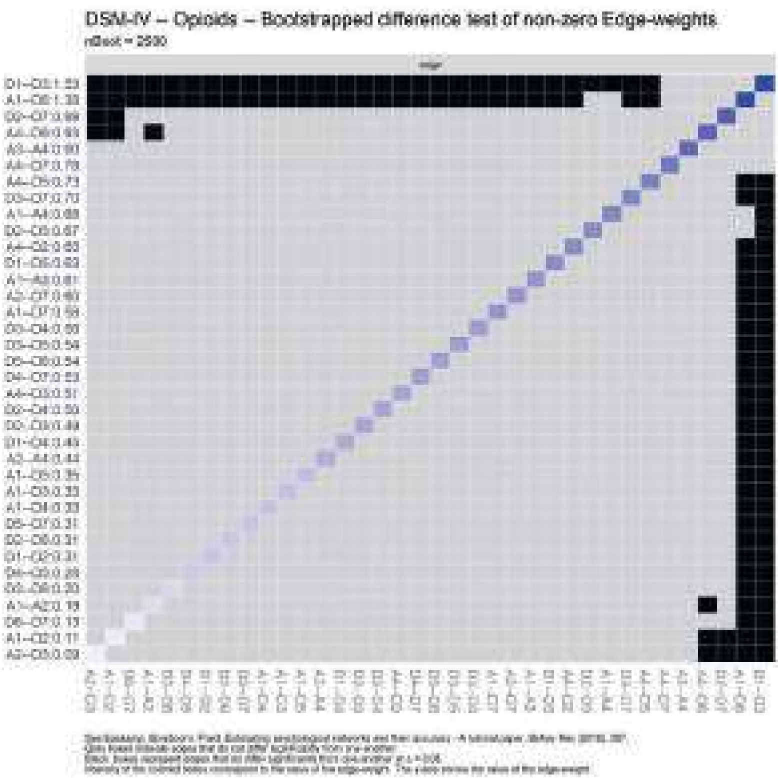


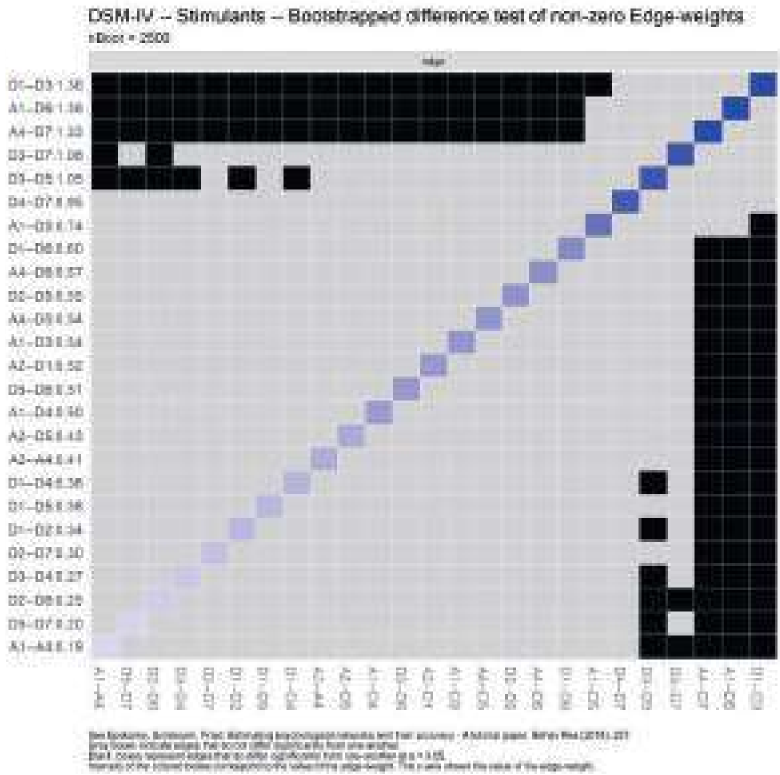


Supplementary Figure 3b.

DSM-IV -- Substance class Networks -- Bootstrapped difference test of non-zero Edge-weights

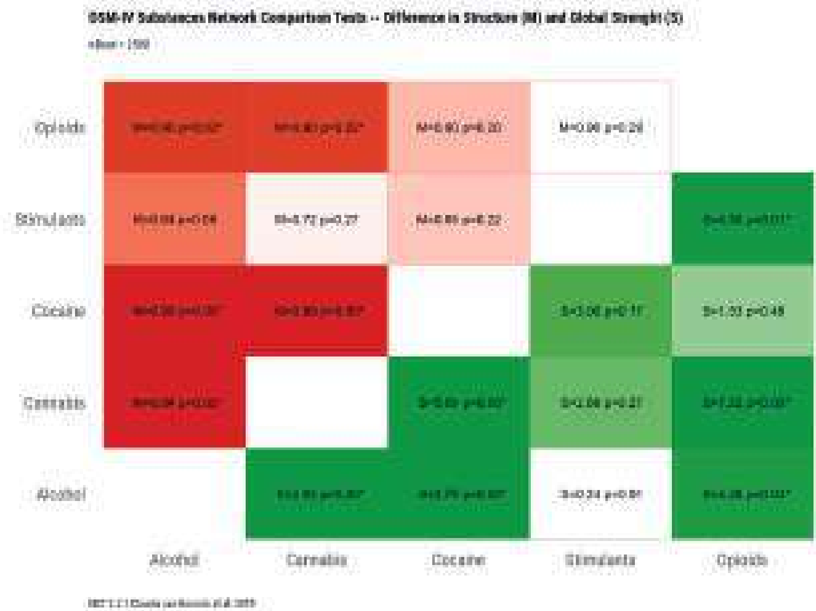




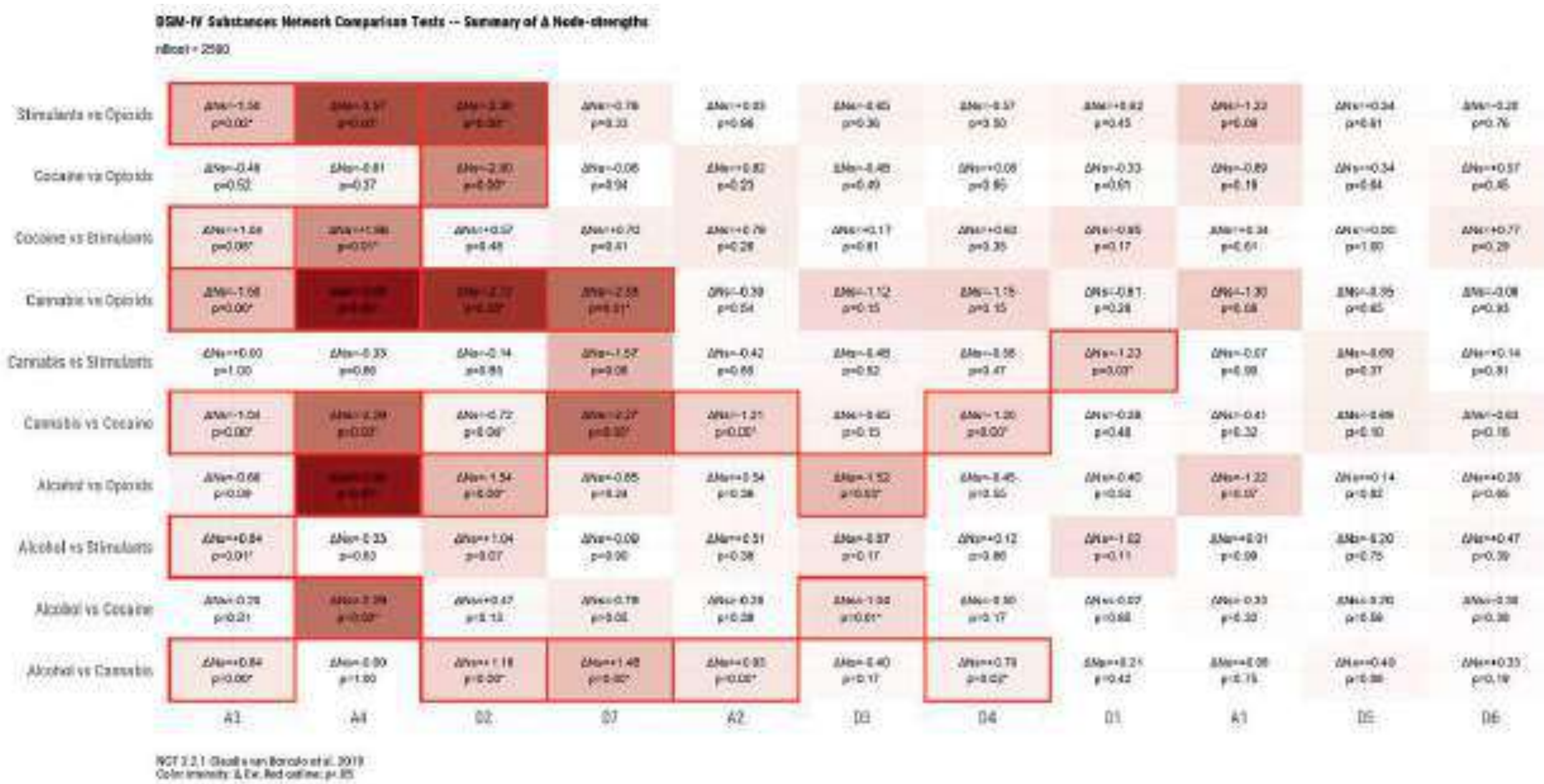


psychological networks and their accuracy - A tutorial paper, Behav Res (2018), 207.
Gray boxes indicate edges that do not differ significantly from one-another.
Black boxes represent edges that do differ significantly from one-another at α = 0.05.
Intensity of the colored boxes correspond to the value of the edge-weight.
The y-axis shows the value of the edge-weight.
nBoot = 2500

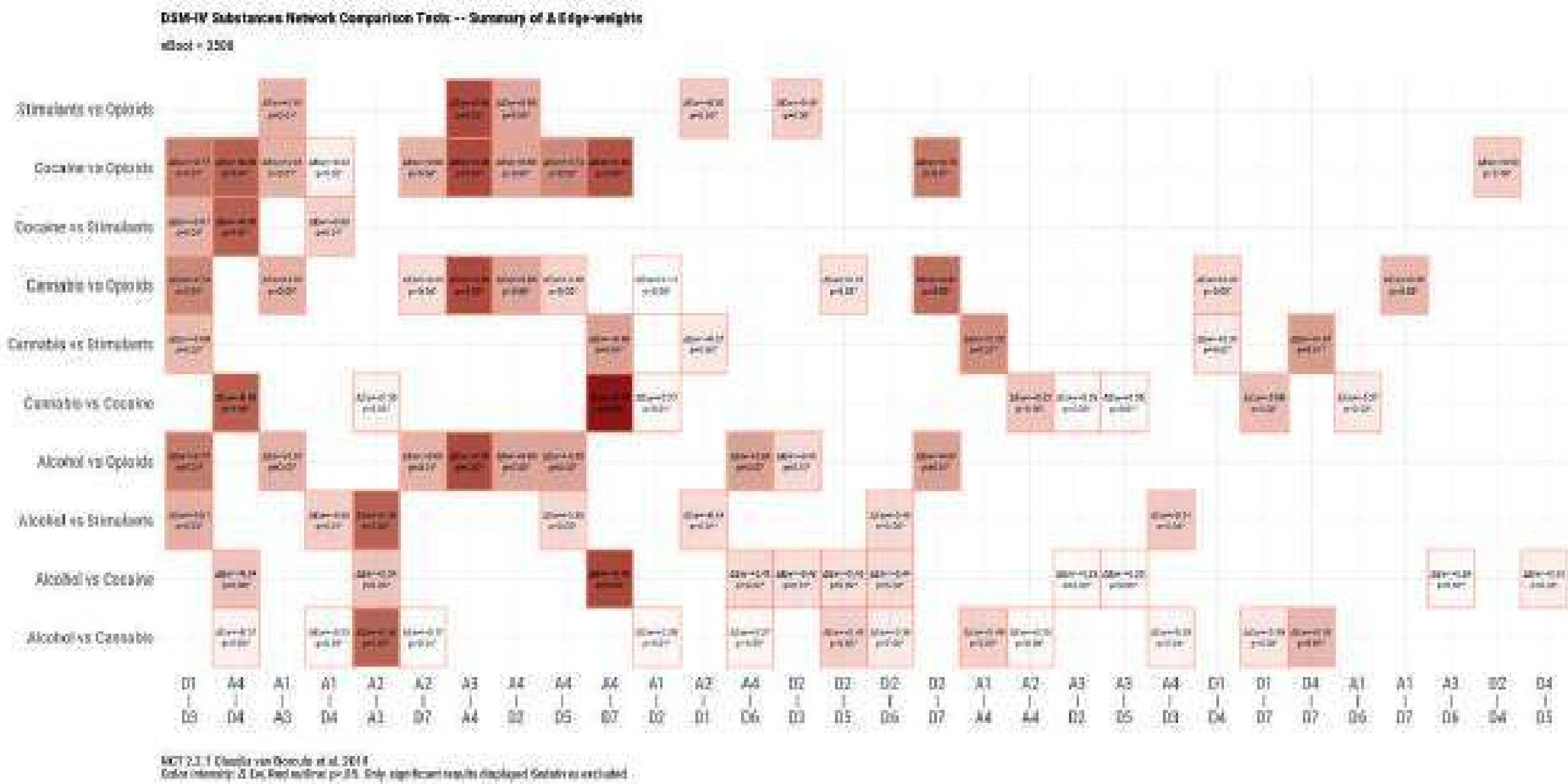
Supplementary Figure 4a. DSM-IV -- Substance class Networks
Network Comparison Tests -- Difference in Structure (M) and Global Strenght (S)



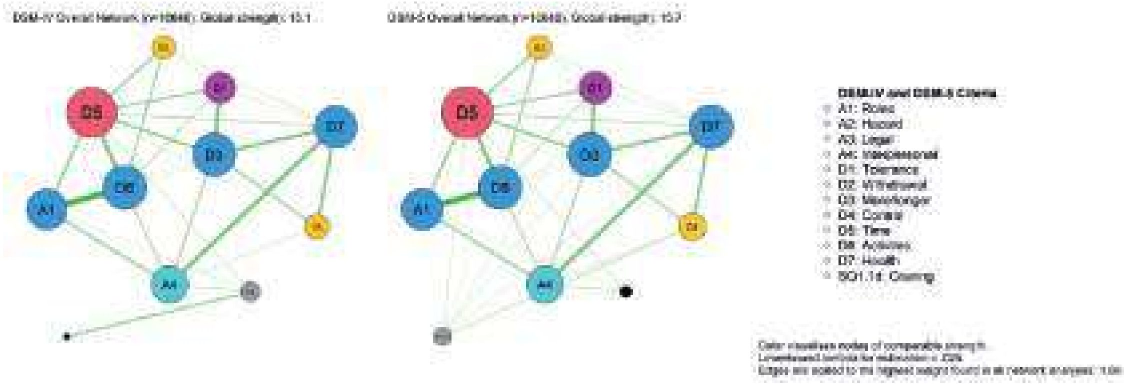
Supplementary Figure 4b. DSM-IV -- Substance class Networks -- Network Comparison Tests
Summary of DELTA Node-strengths



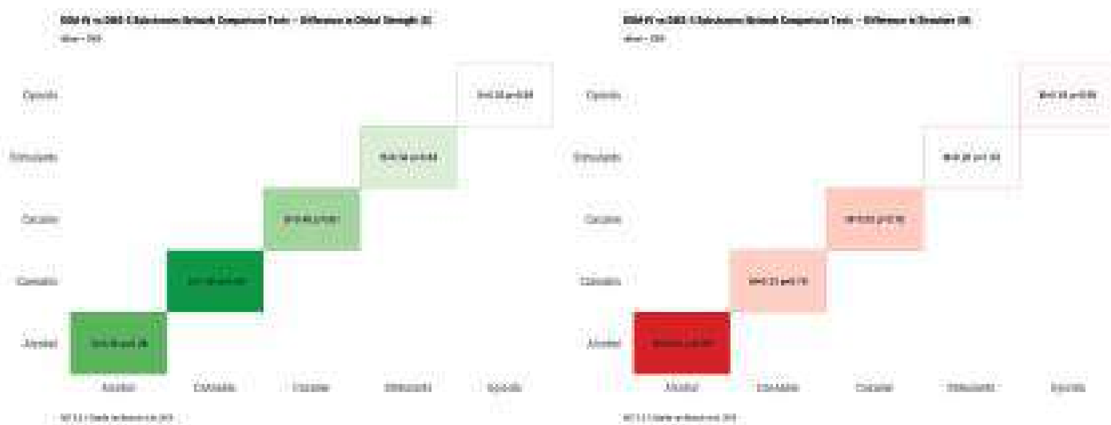
Supplementary Figure 4c. DSM-IV -- Substance class Networks -- Network Comparison Tests
Summary of DELTA Edge-weights



Supplementary Figure 5. DSM-IV vs DSM-5 -- Overall -- Networks

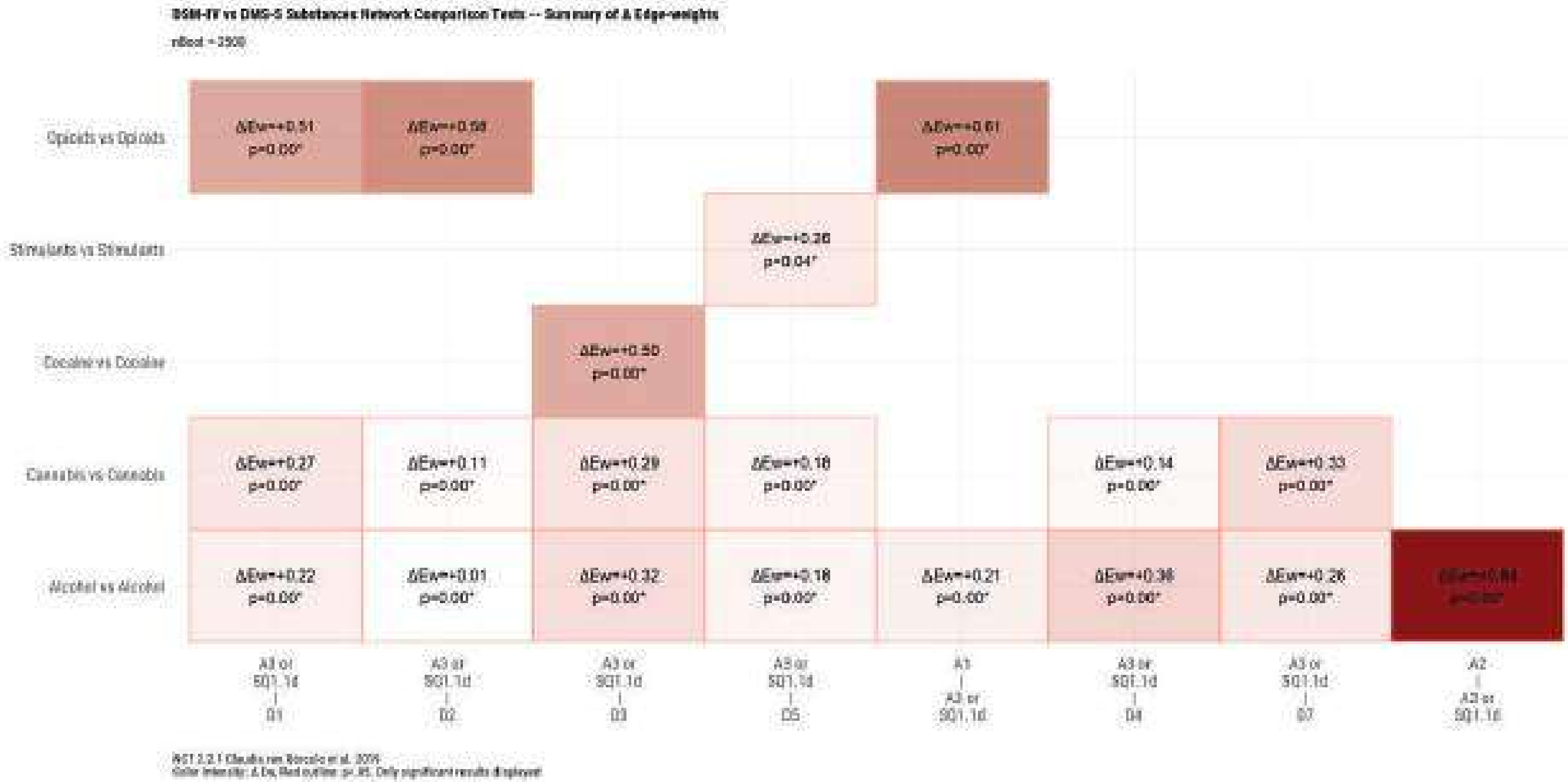


Supplementary Figure 6a.
DSM-IV vs DMS-5 -- Network Comparison Tests -- Difference in Structure (M) and Global Strenght (S)



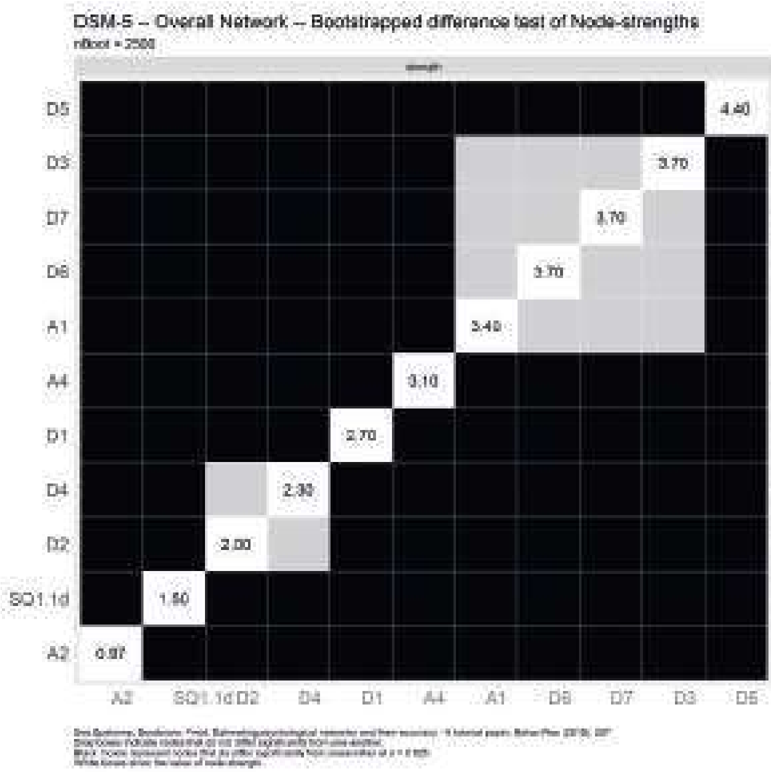
Supplementary Figure 6b. DSM-IV vs DMS-5 -- Network Comparison Tests
Summary of DELTA Node-strengths

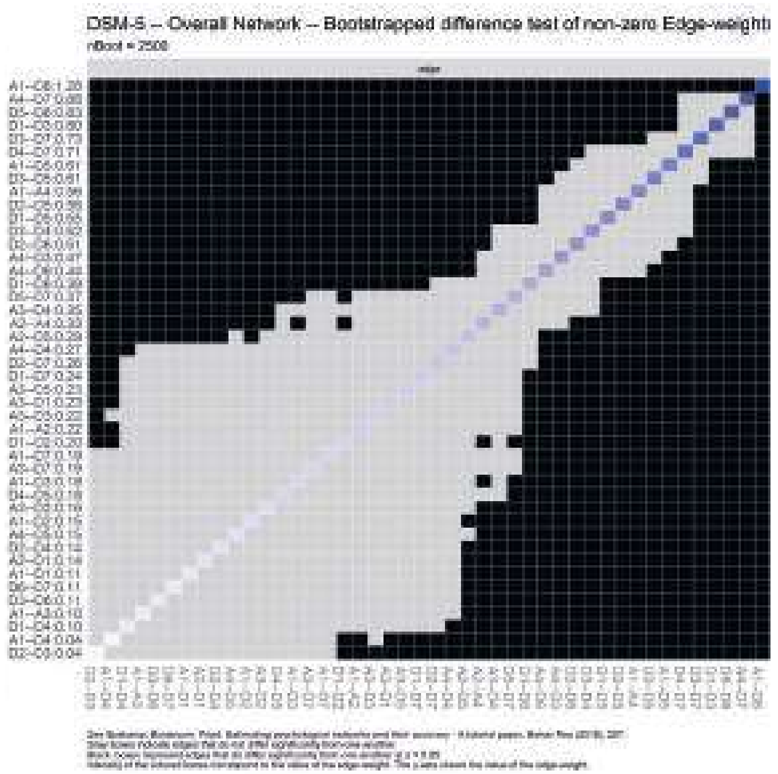
Supplementary Figure 6c. DSM-IV vs DMS-5 -- Network Comparison Tests Summary of DELTA Edge-weights



Supplementary Figure 7.

DSM-5 -- Overall -- Bootstrapped difference test

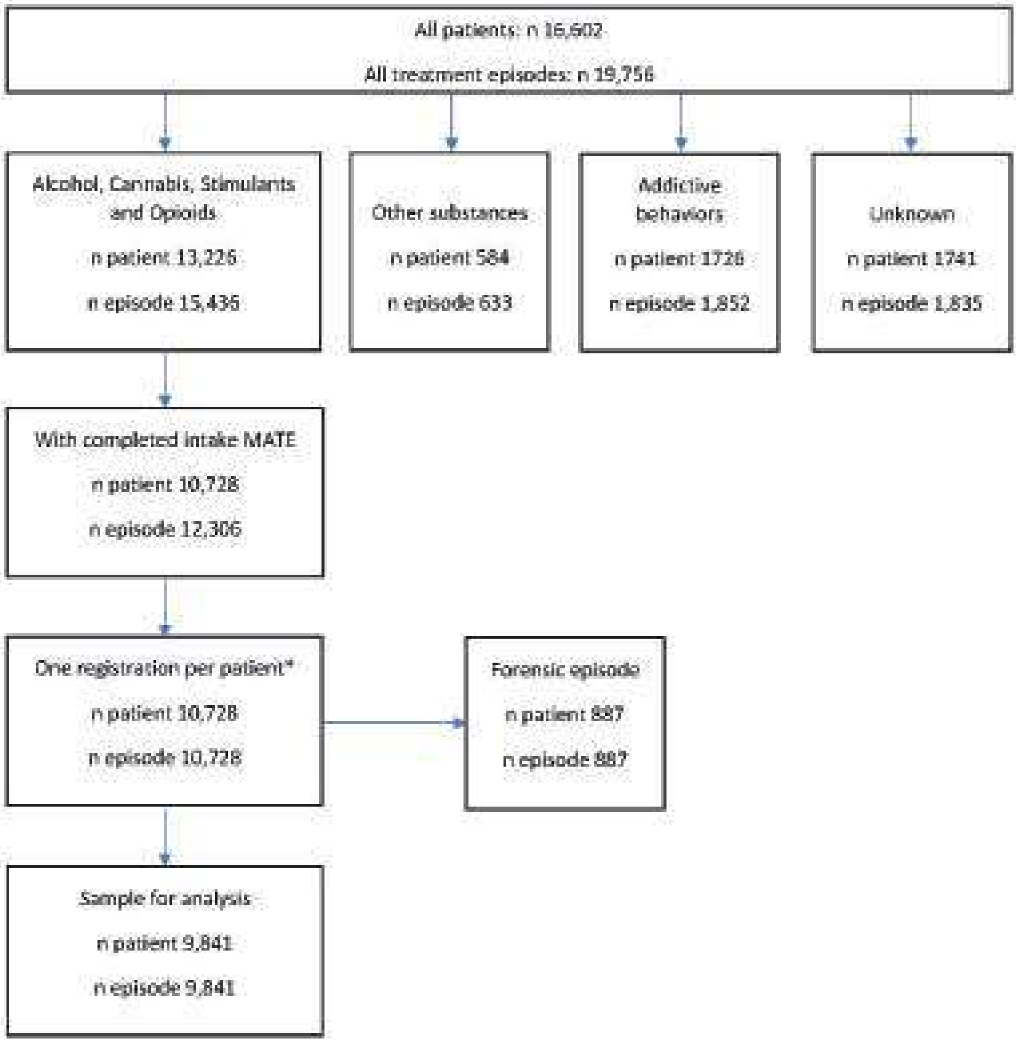




Appendix 2
Supplement to chapter 5

Supplementary Figure 1.

Flowchart. Patients and treatment episodes 2011-2016



*In the case of multiiple episodes, we chose the episode with the most MATE measurements.

Supplementary Figure 2.

Service Use Clusters: medoids for the 10 cluster solution of Ongoing or completed episodes and for the 8 cluster solution of All episodes

Supplementary Figure 2. Service Use Clusters: medoids for the 10 cluster solution of Ongoing or completed episodes and for the 8 cluster solution of All episodes

Ongoing or completed episodes

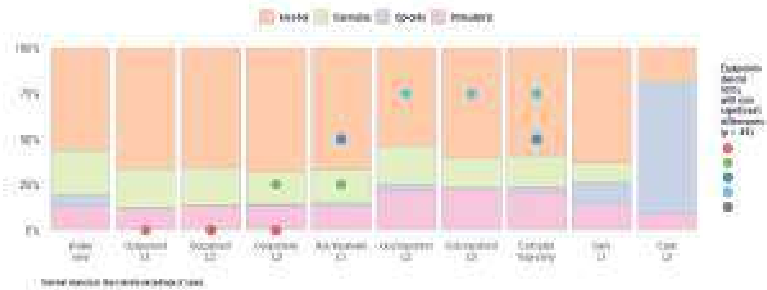
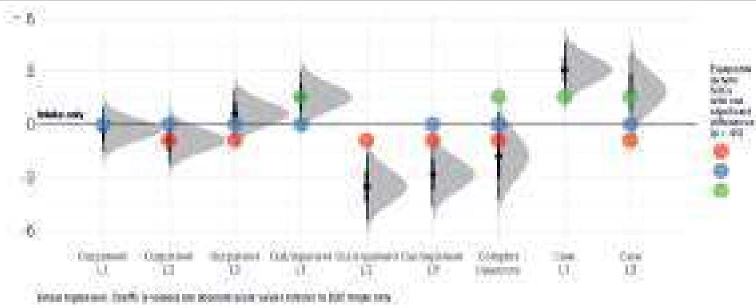
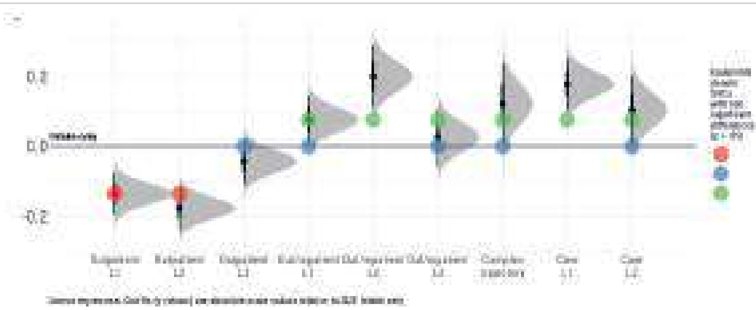
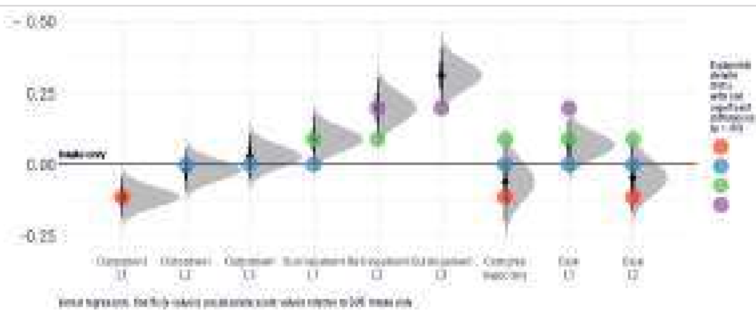
Service Use Cluster	p	n	General hhSQRT	Cure hhSQRT	Care hhSQRT	General dysSQRT	Cure dysSQRT
Intake only	10%	661	1.73	0.00	0.00	0.00	0.00
Outpatient L1	23%	1488	1.73	2.20	0.00	0.00	0.00
Outpatient L2	19%	1229	1.89	3.86	0.00	0.00	0.00
Outpatient L3	13%	872	2.83	3.71	1.80	0.00	0.00
Out/inpatient L1	11%	707	3.87	3.17	0.87	3.74	0.00
Out/inpatient L2	5%	304	4.92	5.75	2.56	5.20	6.48
Out/inpatient L3	5%	351	5.78	15.36	1.74	2.83	10.25
Complex trajectory	2%	147	14.02	6.84	2.42	3.46	9.90
Care L1	8%	521	2.29	0.65	3.50	0.00	0.00
Care L2	3%	222	2.21	0.00	14.06	0.00	0.00

All episodes

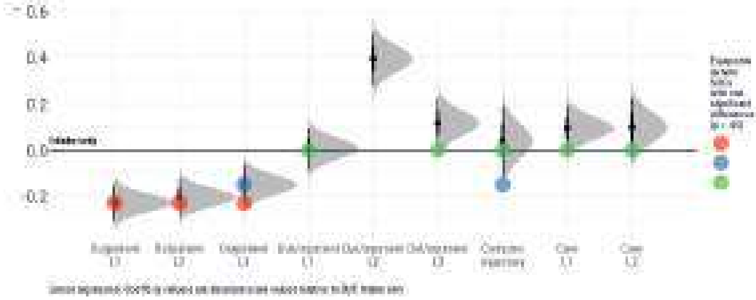
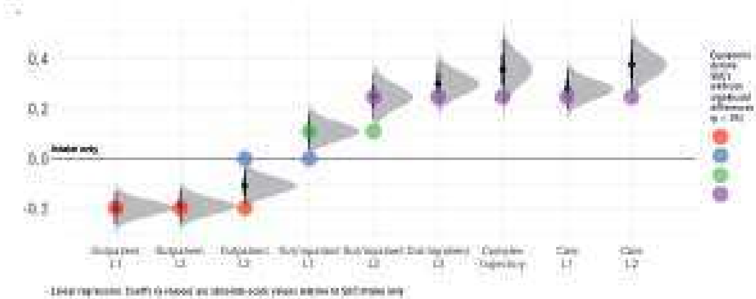
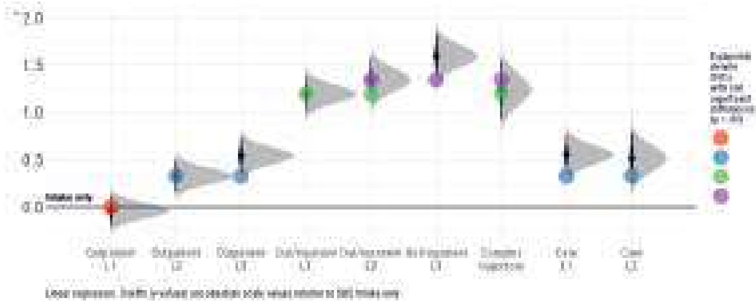
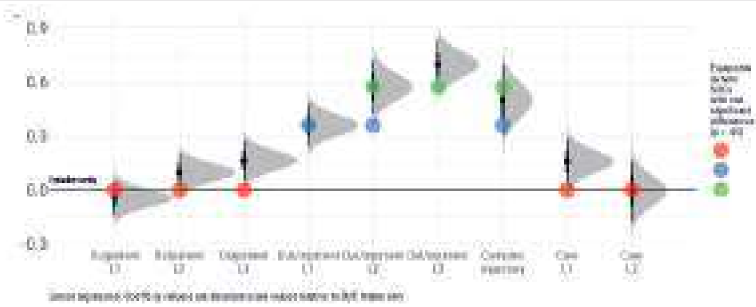
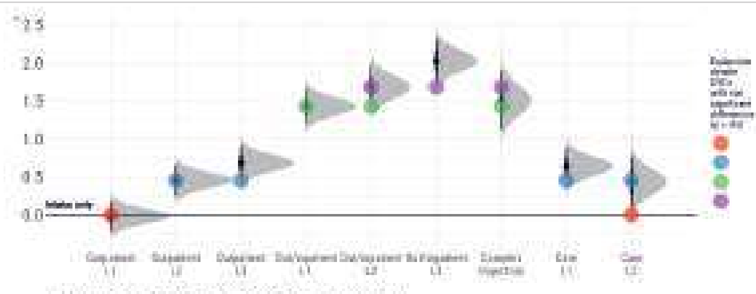
Service Use Cluster	p	n	General hhSQRT	Cure hhSQRT	Care hhSQRT	General dysSQRT	Cure dysSQRT
Intake only	19%	1871	1.58	0.00	0.00	0.00	0.00
Outpatient L1	23%	2227	1.66	1.87	0.00	0.00	0.00
Outpatient L2	18%	1810	1.80	3.40	0.00	0.00	0.00
Outpatient L3	12%	1168	3.19	3.57	1.58	0.00	0.00
Out/inpatient L1	11%	1072	3.09	2.31	1.29	3.61	0.00
Out/inpatient L2							
Out/inpatient L3	8%	772	6.60	10.96	2.96	2.83	8.25
Complex trajectory							
Care L1	6%	630	2.29	0.65	3.50	0.00	0.00
Care L2	3%	291	1.83	0.00	12.51	0.00	0.00

Indexes

Supplementary Figure 3a. Ongoing or completed episodes. Cramér's V and R^2 coefficients of determination for the dependent variables PPS, Sex, Age and MATE-scores and the independent variable Service Use Cluster

Dependent variable	**Coefficient**	**Service Use Cluster (percent stacked bars / or coefficients). Equipoints (colored circles) denote nonsignificant difference between SUCs**
PPS n = 6433	Cramér's V 0.350	
Sex n = 6502	Cramér's V 0.092	
Age n = 6433	R^2 0.013	
S2.1 Characteristics of physical comorbidity [0-4] n = 6383	R^2 0.036	
S2.2 In psychiatric or psychological treatment [0-2] n = 6386	R^2 0.019	

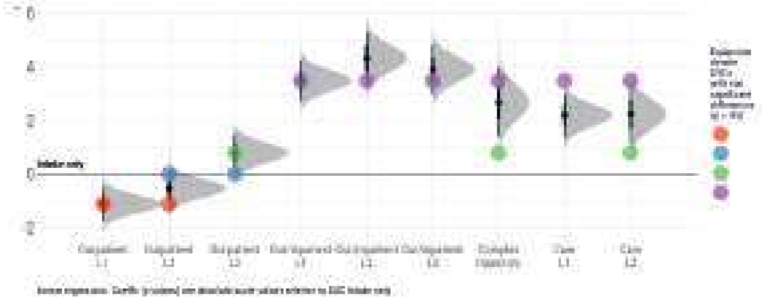
Supplementary Figure 3a. Ongoing or completed episodes. Cramér's V and R^2 coefficients of determination for the dependent variables PPS, Sex, Age and MATE-scores and the independent variable Service Use Cluster

S2.3 Characteristics of psychiatric comorbidity [0-5] n = 6381	R^2 0.037	
S3.1 History of treatment for addiction disorder - SQRT(n) [0-6] n = 6411	R^2 0.077	
S4.1 Dependence [0-7] n = 6415	R^2 0.078	
S4.2 Abuse [0-4] n = 6415	R^2 0.036	
S4.3 Severity dependence/abuse [0-9] n = 6415	R^2 0.077	

Supplementary Figure 3a. Ongoing or completed episodes. Cramér's V and R^2 coefficients of determination for the dependent variables PPS, Sex, Age and MATE-scores and the independent variable Service Use Cluster

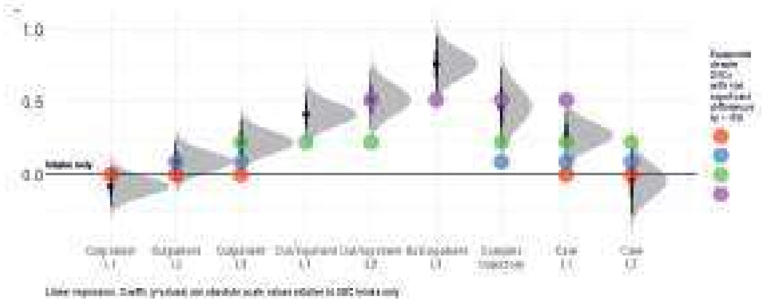
S5.1 Physical complaints
[0-40]
n = 6423

R^2
0.063



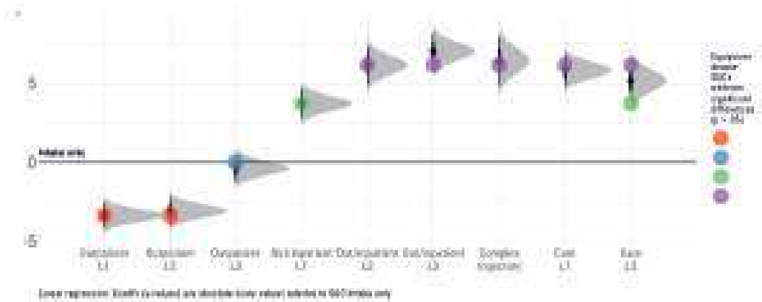
S6.1 Personality
[0-8]
n = 6339

R^2
0.024



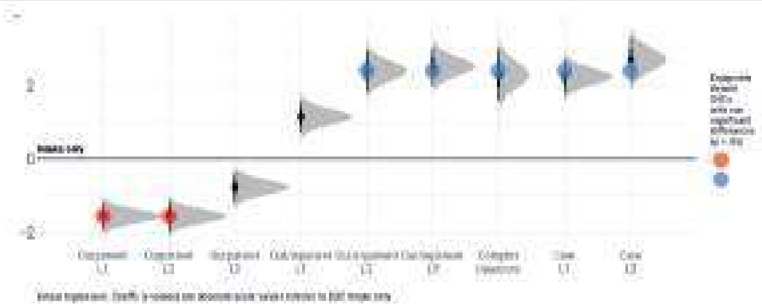
S7.1 Limitations - Total
[0-76]
n = 6388

R^2
0.164



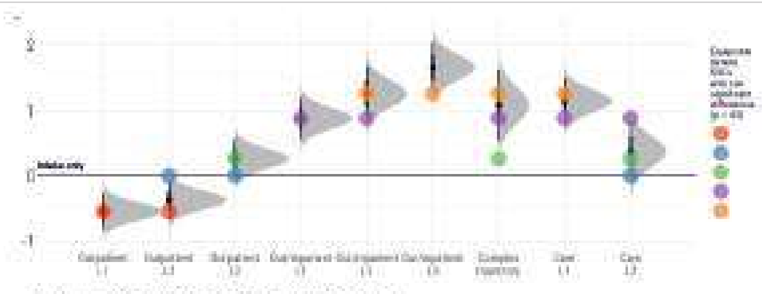
S7.2 Limitations - Basic
[0-32]
n = 6389

R^2
0.145



S7.3 Limitations - Relational
[0-20]
n = 6397

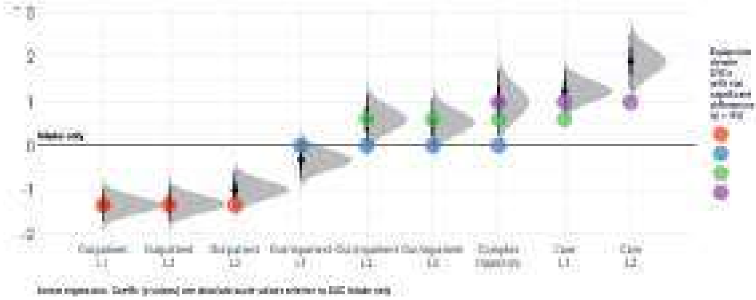
R^2
0.053



Supplementary Figure 3a. Ongoing or completed episodes. Cramér's V and R^2 coefficients of determination for the dependent variables PPS, Sex, Age and MATE-scores and the independent variable Service Use Cluster

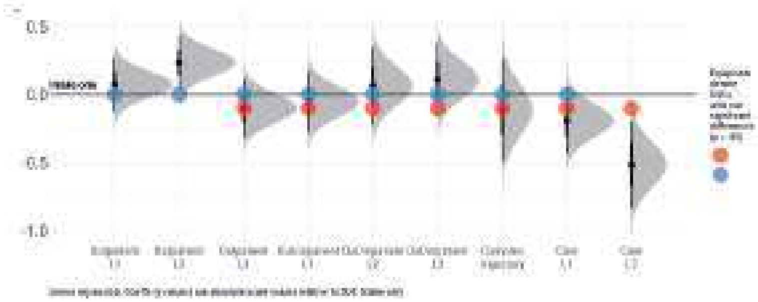
S7.4 Care & support
[0-32]
n = 6389

R^2
0.053



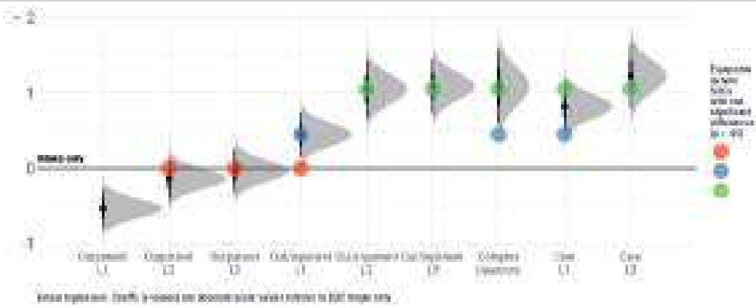
S8.1 Positive external influence
[0-12]
n = 6313

R^2
0.006



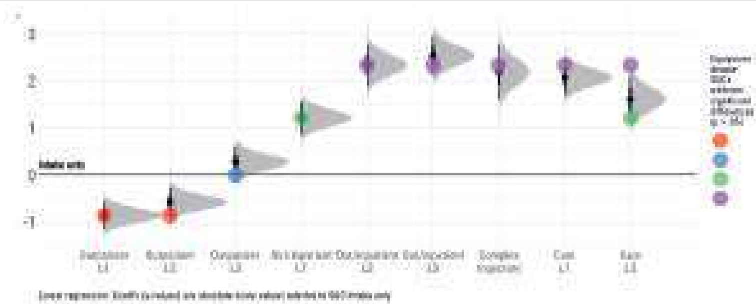
S8.2 Negative external influence
[0-20]
n = 6314

R^2
0.041



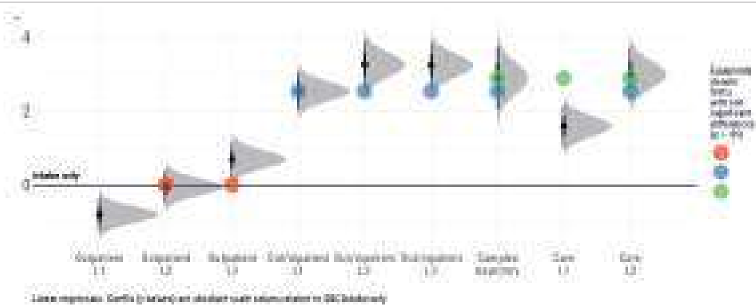
S8.3 Need for care
[0-20]
n = 6398

R^2
0.119



SQ1.1 Craving
[0-20]
n = 6379

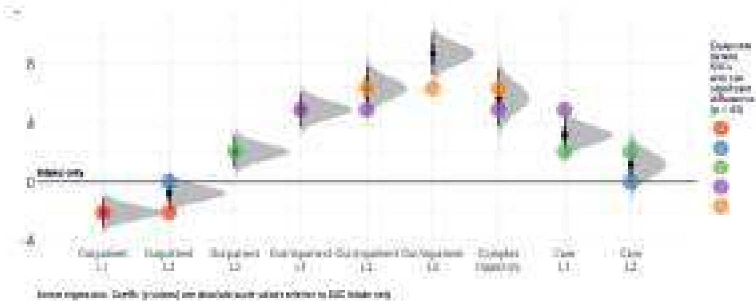
R^2
0.084



Supplementary Figure 3a. Ongoing or completed episodes. Cramér's V and R^2 coefficients of determination for the dependent variables PPS, Sex, Age and MATE-scores and the independent variable Service Use Cluster

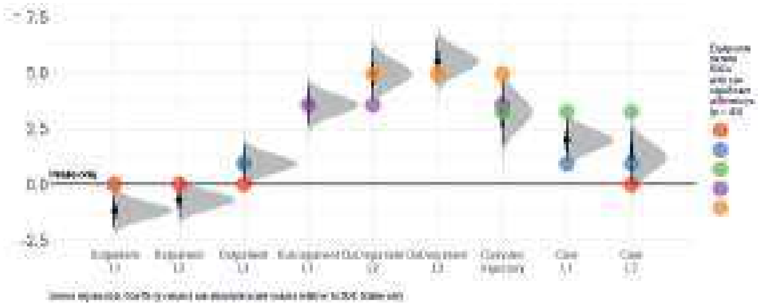
SQ2.1 Depression
[0-42]
n = 6375

R^2
0.079



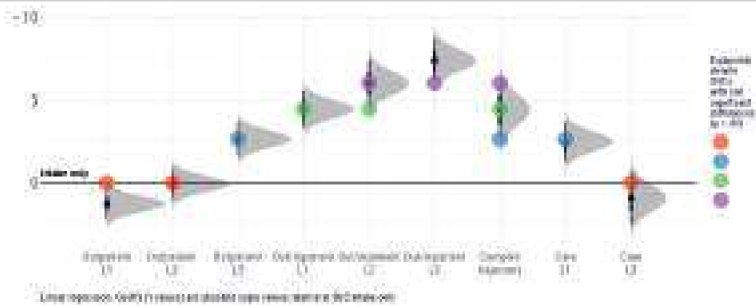
SQ2.2 Anxiety
[0-42]
n = 6377

R^2
0.062



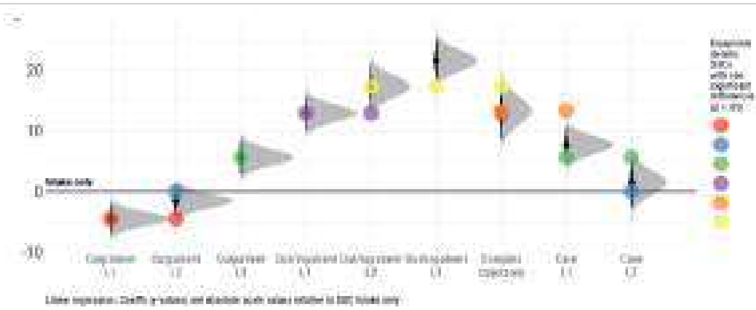
SQ2.3 Stress
[0-42]
n = 6377

R^2
0.063

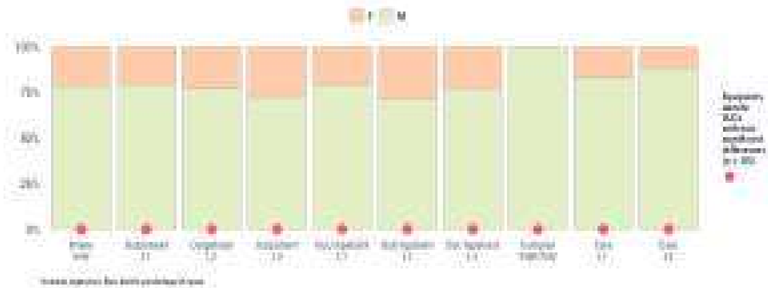
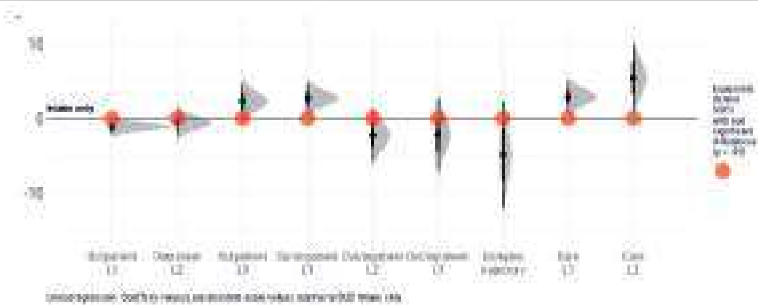
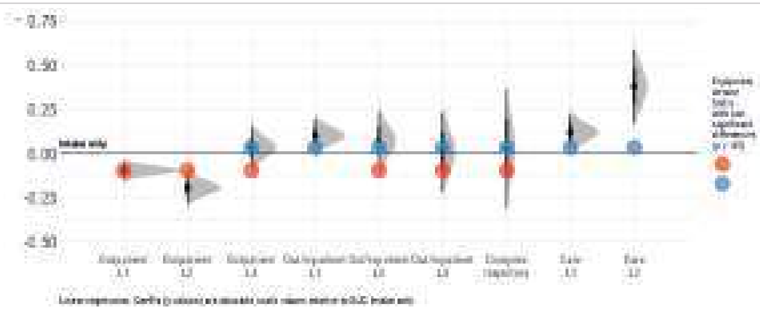
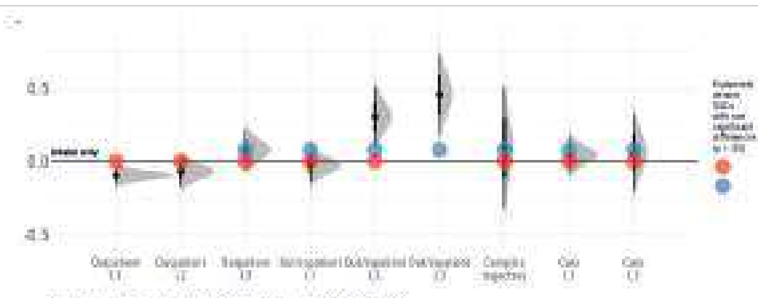


SQ2.4 Depression Anxiety Stress - Total
[0-126]
n = 6375

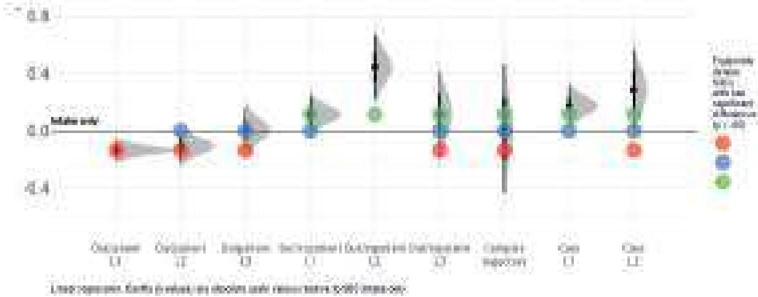
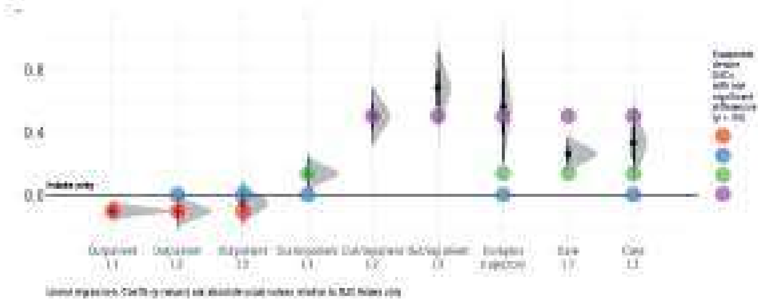
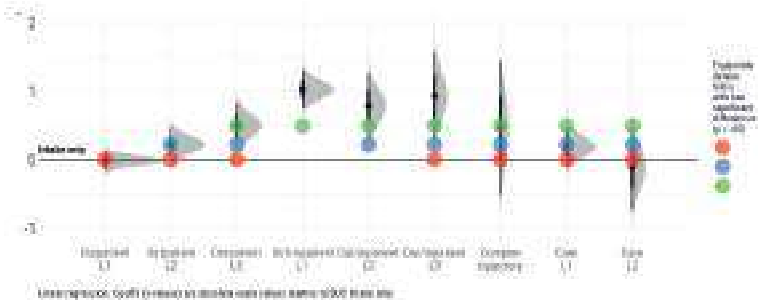
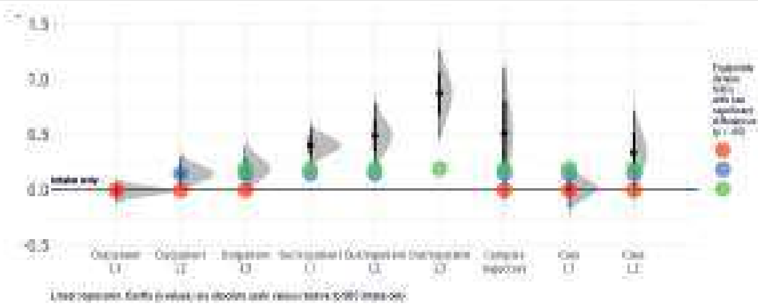
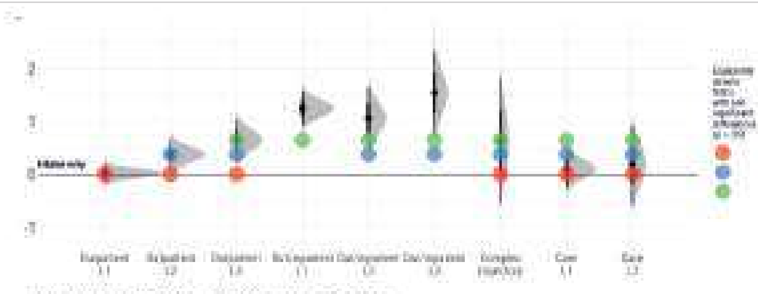
R^2
0.086



Supplementary Figure 3b. Prematurely ended episodes. Cramér's V and R^2 coefficients of determination for the dependent variables PPS, Sex, Age and MATE-scores and the independent variable Service Use Cluster

Dependent variable	**Coefficient**	**Service Use Cluster (percent stacked bars / or coefficients). Equipoints (colored circles) denote nonsignificant difference between SUCs**
PPS n = 3284	Cramér's V 0.274	
Sex n = 3339	Cramér's V 0.063	
Age n = 3284	R^2 0.011	
S2.1 Characteristics of physical comorbidity [0-4] n = 3259	R^2 0.021	
S2.2 In psychiatric or psychological treatment [0-2] n = 3262	R^2 0.011	

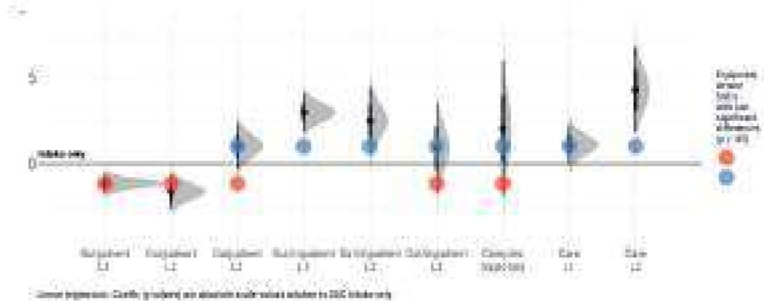
Supplementary Figure 3b. Prematurely ended episodes. Cramér's V and R^2 coefficients of determination for the dependent variables PPS, Sex, Age and MATE-scores and the independent variable Service Use Cluster

S2.3 Characteristics of psychiatric comorbidity [0-5] n = 3259	R^2 0.019	
S3.1 History of treatment for addiction disorder - SQRT(n) [0-6] n = 3275	R^2 0.045	
S4.1 Dependence [0-7] n = 3273	R^2 0.024	
S4.2 Abuse [0-4] n = 3272	R^2 0.018	
S4.3 Severity dependence/abuse [0-9] n = 3272	R^2 0.027	

Supplementary Figure 3b. Prematurely ended episodes. Cramér's V and R^2 coefficients of determination for the dependent variables PPS, Sex, Age and MATE-scores and the independent variable Service Use Cluster

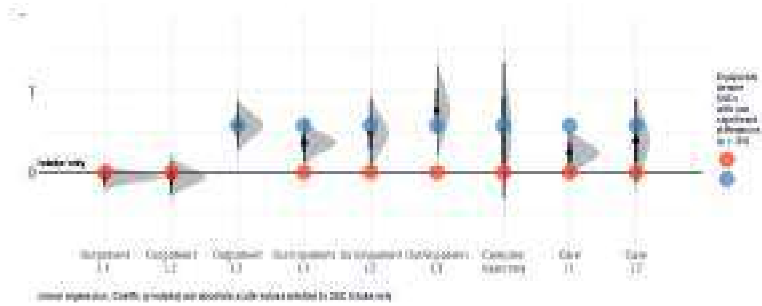
S5.1 Physical complaints
[0-40]
n = 3278

R^2
0.029



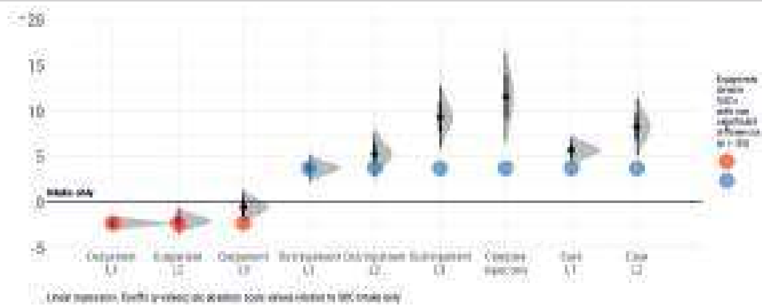
S6.1 Personality
[0-8]
n = 3246

R^2
0.014



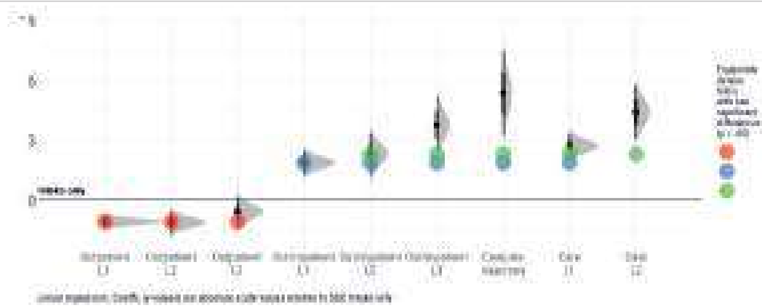
S7.1 Limitations - Total
[0-76]
n = 3251

R^2
0.079



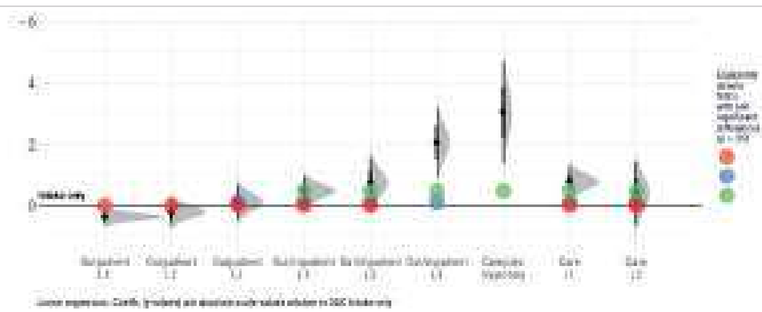
S7.2 Limitations - Basic
[0-32]
n = 3249

R^2
0.094



S7.3 Limitations - Relational
[0-20]
n = 3256

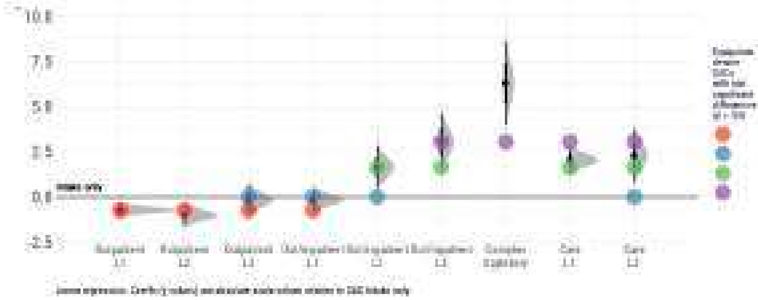
R^2
0.018



Supplementary Figure 3b. Prematurely ended episodes. Cramér's V and R^2 coefficients of determination for the dependent variables PPS, Sex, Age and MATE-scores and the independent variable Service Use Cluster

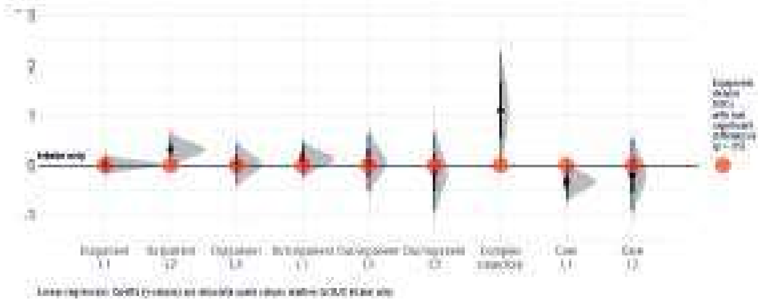
S7.4 Care & support
[0-32]
n = 3250

R^2
0.042



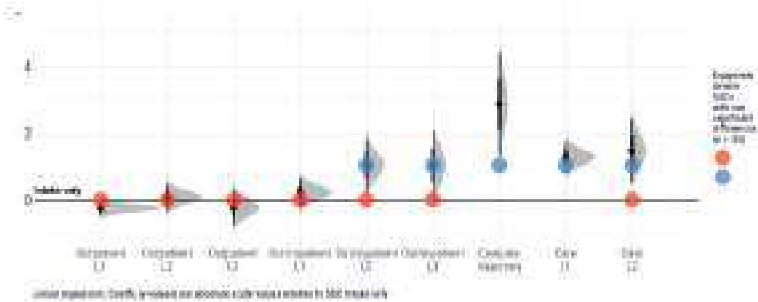
S8.1 Positive external influence
[0-12]
n = 3208

R^2
0.004



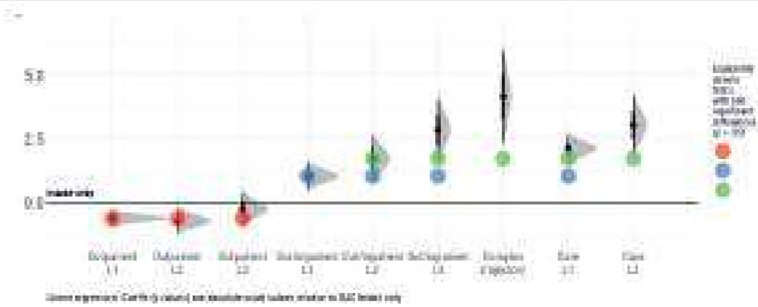
S8.2 Negative external influence
[0-20]
n = 3209

R^2
0.022



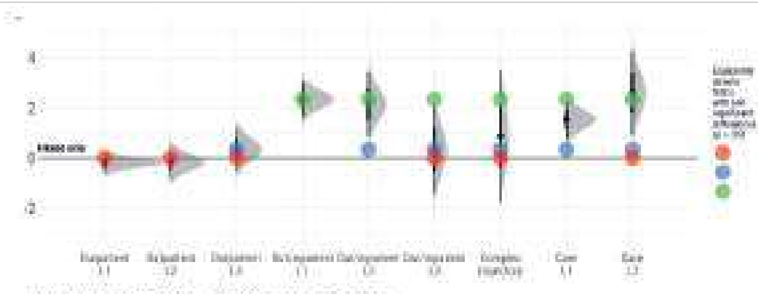
S8.3 Need for care
[0-20]
n = 3258

R^2
0.065



SQ1.1 Craving
[0-20]
n = 3248

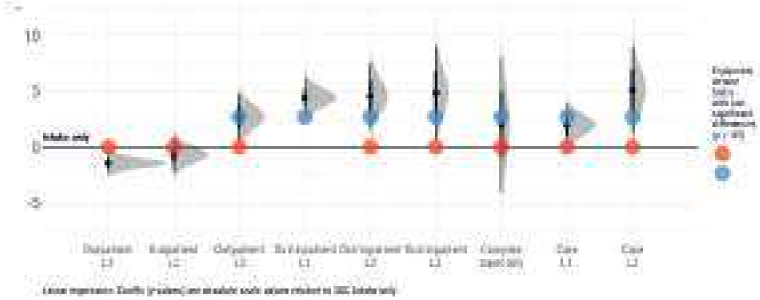
R^2
0.024



Supplementary Figure 3b. Prematurely ended episodes. Cramér's V and R^2 coefficients of determination for the dependent variables PPS, Sex, Age and MATE-scores and the independent variable Service Use Cluster

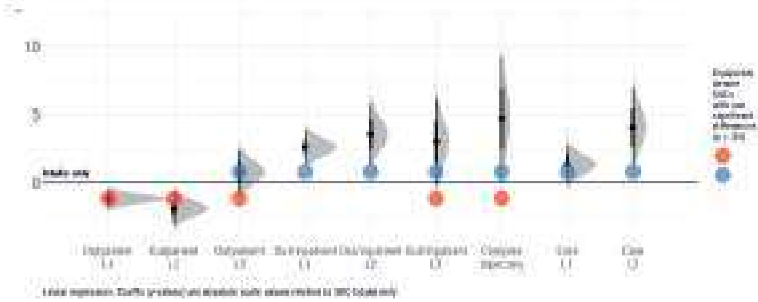
SQ2.1 Depression
[0-42]
n = 3241

R^2
0.025



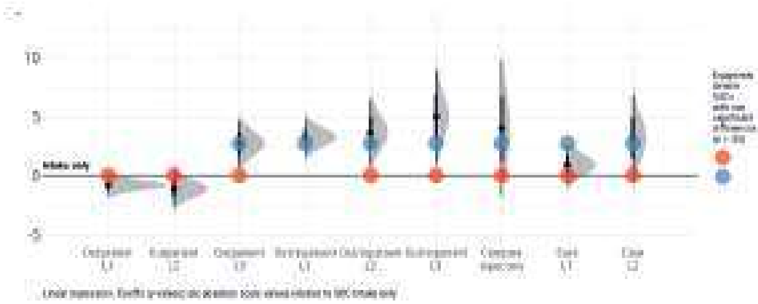
SQ2.2 Anxiety
[0-42]
n = 3241

R^2
0.024



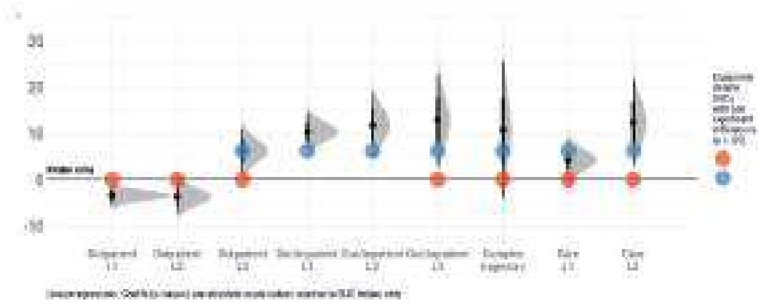
SQ2.3 Stress
[0-42]
n = 3240

R^2
0.017

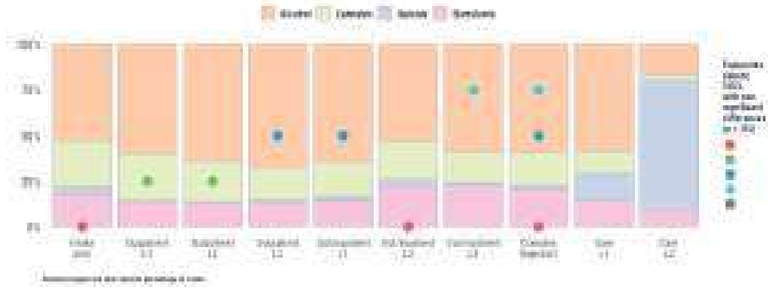
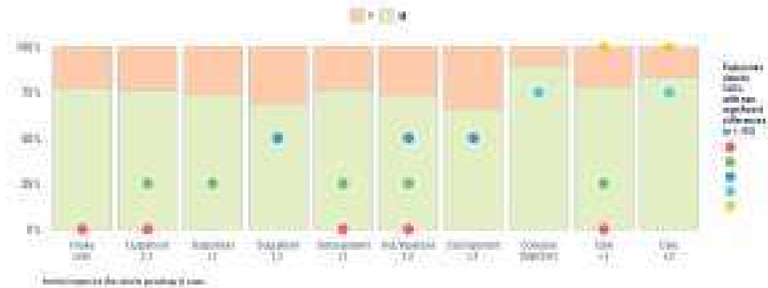
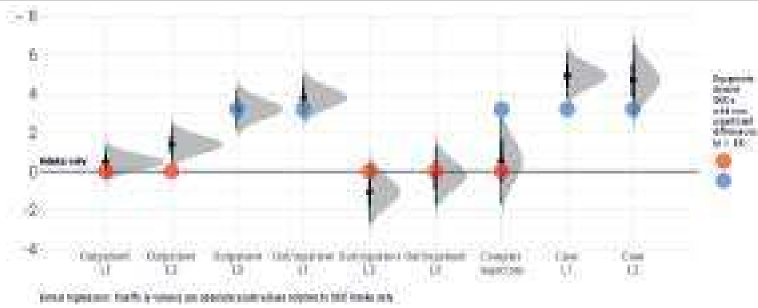
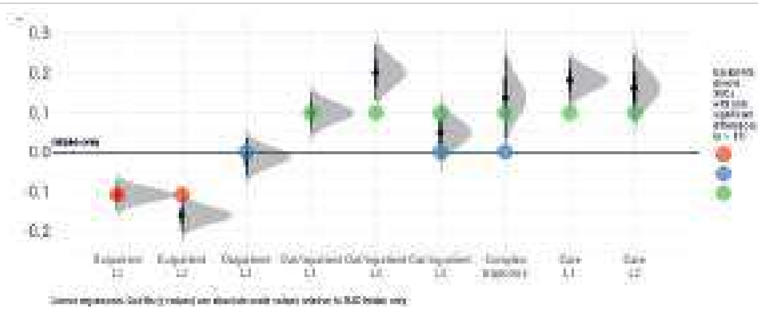
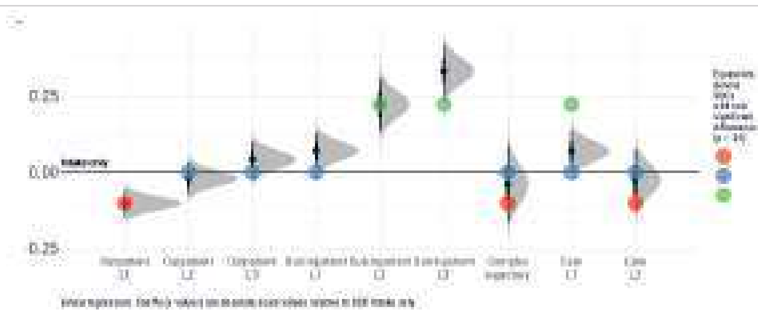


SQ2.4 Depression
Anxiety Stress - Total
[0-126]
n = 3240

R^2
0.026



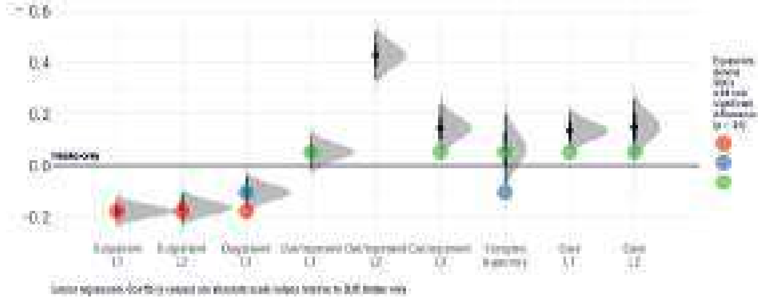
Supplementary Figure 3c. All episodes. Cramér's V and R^2 coefficients of determination for the dependent variables PPS, Sex, Age and MATE-scores and the independent variable Service Use Cluster

Dependent variable	Coefficient	Service Use Cluster (percent stacked bars / or coefficients). Equipoints (colored circles) denote nonsignificant difference between SUCs
PPS n = 9717	Cramér's V 0.329	
Sex n = 9841	Cramér's V 0.087	
Age n = 9717	R^2 0.016	
S2.1 Characteristics of physical comorbidity [0-4] n = 9642	R^2 0.030	
S2.2 In psychiatric or psychological treatment [0-2] n = 9648	R^2 0.016	

Supplementary Figure 3c. All episodes. Cramér's V and R^2 coefficients of determination for the dependent variables PPS, Sex, Age and MATE-scores and the independent variable Service Use Cluster

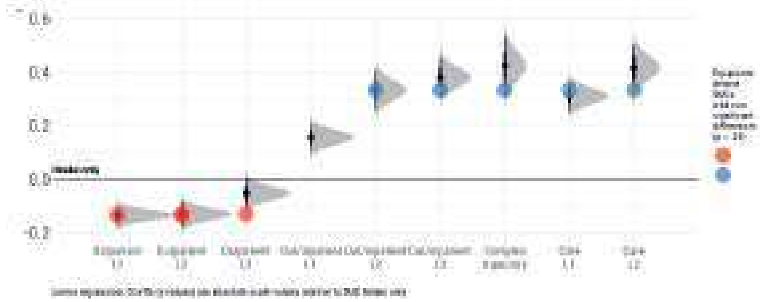
S2.3 Characteristics of psychiatric comorbidity
[0-5]
n = 9640

R^2
0.030



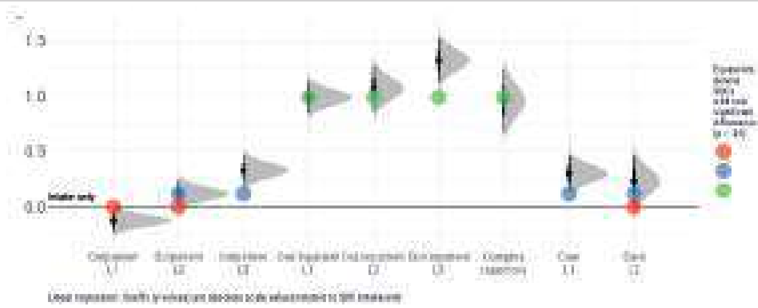
S3.1 History of treatment for addiction disorder - SQRT(n)
[0-6]
n = 9686

R^2
0.068



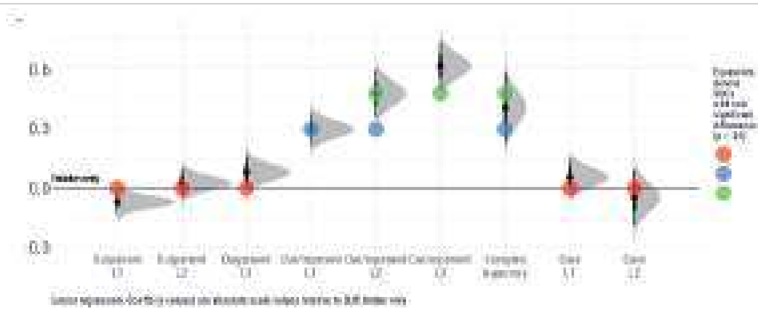
S4.1 Dependence
[0-7]
n = 9688

R^2
0.054



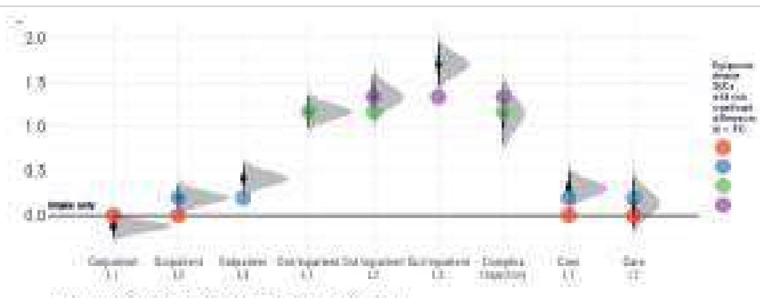
S4.2 Abuse
[0-4]
n = 9687

R^2
0.026

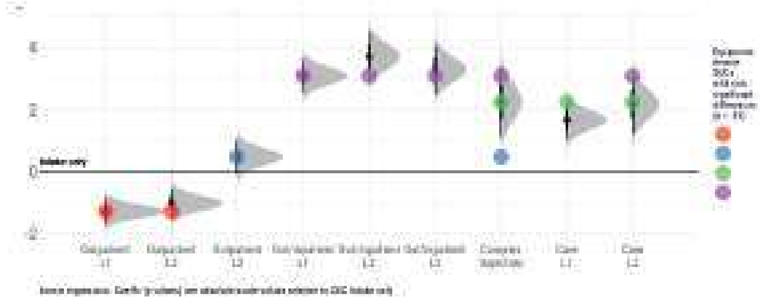
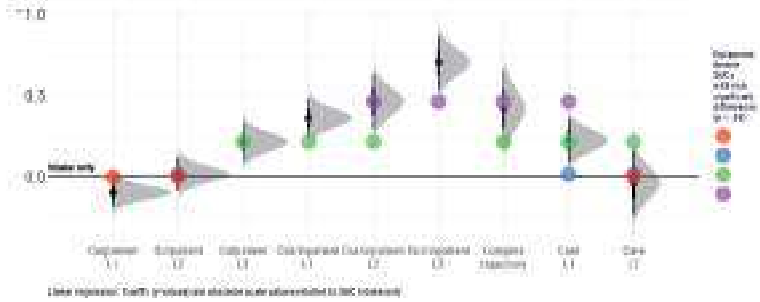
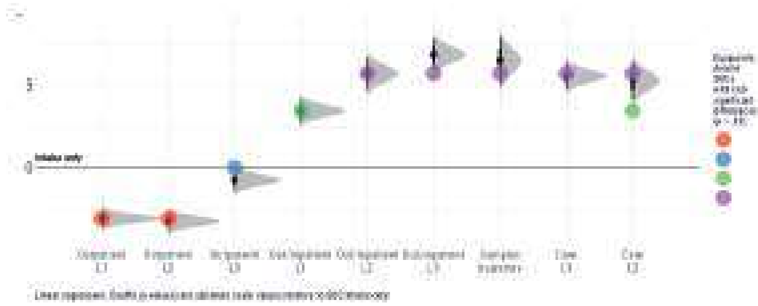
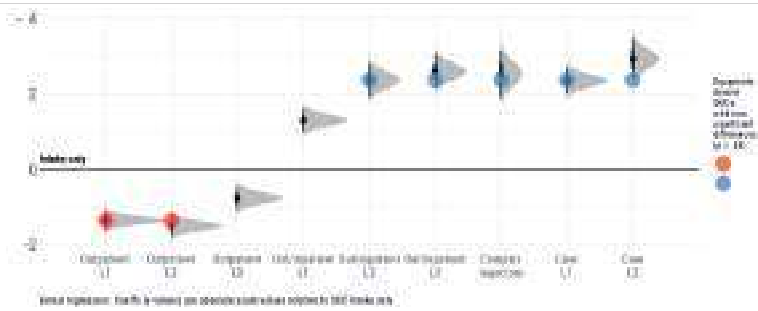
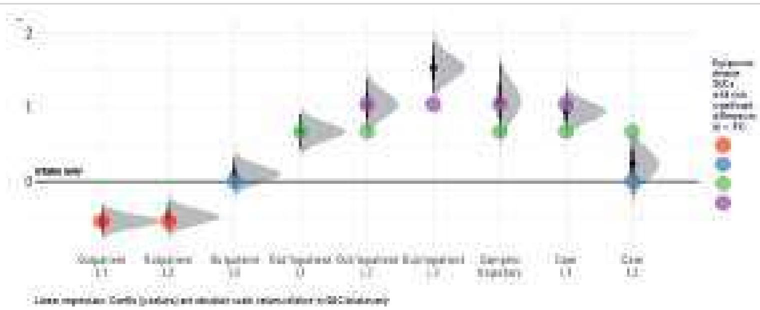


S4.3 Severity dependence/abuse
[0-9]
n = 9687

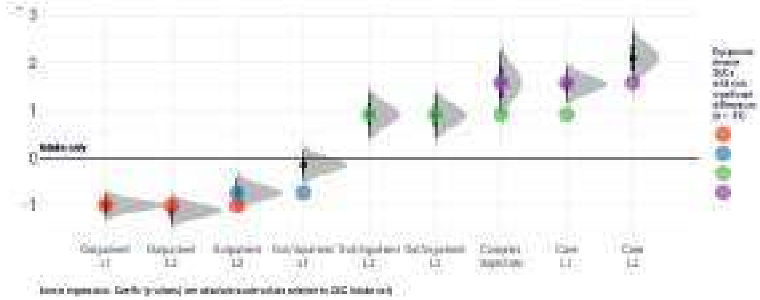
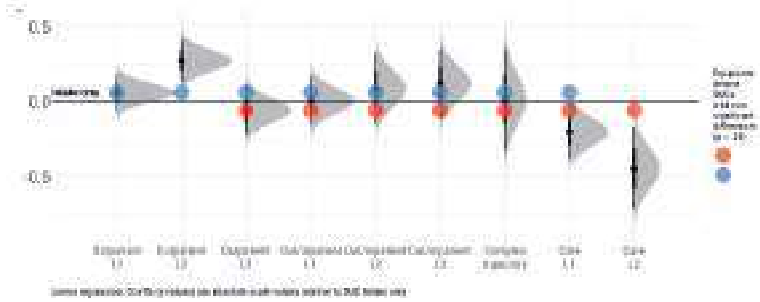
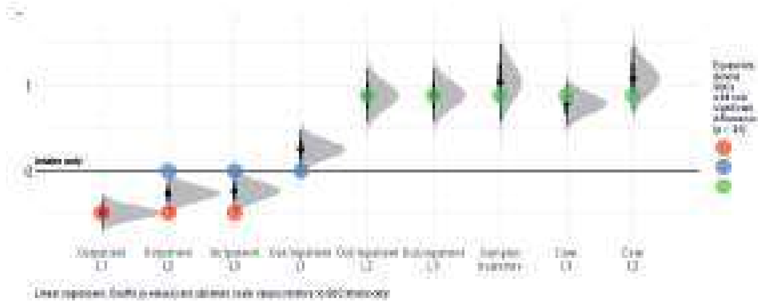
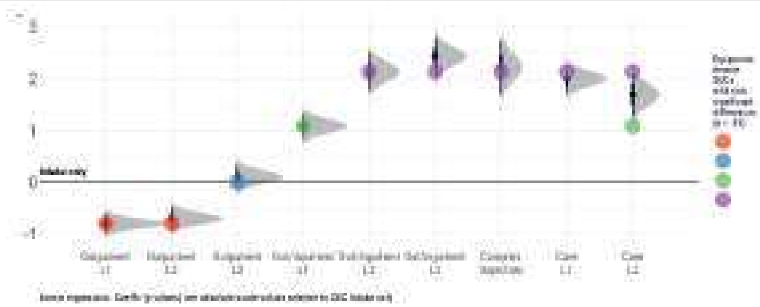
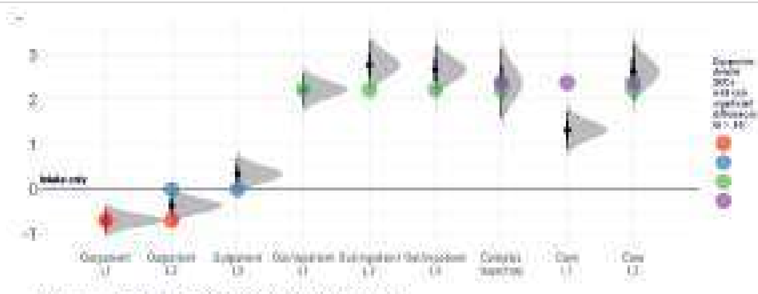
R^2
0.053



Supplementary Figure 3c. All episodes. Cramér's V and R^2 coefficients of determination for the dependent variables PPS, Sex, Age and MATE-scores and the independent variable Service Use Cluster

S5.1 Physical complaints [0-40] n = 9701	R^2 0.050	
S6.1 Personality [0-8] n = 9585	R^2 0.019	
S7.1 Limitations - Total [0-76] n = 9639	R^2 0.131	
S7.2 Limitations - Basic [0-32] n = 9638	R^2 0.125	
S7.3 Limitations - Relational [0-20] n = 9653	R^2 0.038	

Supplementary Figure 3c. All episodes. Cramér's V and R^2 coefficients of determination for the dependent variables PPS, Sex, Age and MATE-scores and the independent variable Service Use Cluster

S7.4 Care & support [0-32] n = 9639	R^2 0.045	
S8.1 Positive external influence [0-12] n = 9521	R^2 0.005	
S8.2 Negative external influence [0-20] n = 9523	R^2 0.030	
S8.3 Need for care [0-20] n = 9656	R^2 0.099	
SQ1.1 Craving [0-20] n = 9627	R^2 0.058	

Supplementary Table 1a Ongoing or completed episodes. Patient demographics and MATE-scores by Service Use Cluster

Characteristic	Overall, N = 6,502[1]	Intake only, N = 661[1]	Outpatient L1, N = 1,488[1]	Outpatient L2, N = 1,229[1]	Outpatient L3, N = 872[1]	Out/inpatient L1, N = 707[1]	Out/inpatient L2, N = 304[1]	Out/inpatient L3, N = 351[1]	Complex trajectory, N = 147[1]	Care L1, N = 521[1]	Care L2, N = 222[1]
PPS - Primary Problem Substance											
Alcohol	4,031 (63%)	370 (56%)	979 (67%)	801 (66%)	590 (69%)	470 (67%)	163 (54%)	209 (60%)	85 (59%)	326 (63%)	38 (17%)
Opioids	323 (5.0%)	43 (6.6%)	10 (0.7%)	6 (0.5%)	9 (1.0%)	14 (2.0%)	12 (4.0%)	4 (1.2%)	4 (2.8%)	63 (12%)	158 (71%)
Stimulants	877 (14%)	84 (13%)	170 (12%)	157 (13%)	112 (13%)	90 (13%)	64 (21%)	76 (22%)	30 (21%)	73 (14%)	21 (9.5%)
Cannabis	1,202 (19%)	158 (24%)	312 (21%)	250 (21%)	149 (17%)	129 (18%)	62 (21%)	58 (17%)	25 (17%)	55 (11%)	4 (1.8%)
Sex											
F	1,686 (26%)	160 (24%)	385 (26%)	324 (26%)	270 (31%)	171 (24%)	78 (26%)	122 (35%)	17 (12%)	121 (23%)	38 (17%)
M	4,816 (74%)	501 (76%)	1,103 (74%)	905 (74%)	602 (69%)	536 (76%)	226 (74%)	229 (65%)	130 (88%)	400 (77%)	184 (83%)
Age	41.13 (13.9)	41.17 (15.6)	40.87 (15.5)	40.26 (14.3)	41.76 (12.9)	42.73 (13.3)	37.65 (13.4)	38.32 (10.0)	39.36 (12.3)	44.25 (12.3)	43.04 (9.4)
S2.1 Characteristics of physical comorbidity [0-4]	0.36 (0.7)	0.39 (0.7)	0.26 (0.5)	0.21 (0.5)	0.35 (0.6)	0.47 (0.7)	0.59 (0.8)	0.42 (0.7)	0.51 (0.7)	0.57 (0.8)	0.50 (0.7)
S2.2 In psychiatric or psychological treatment [0-2]	0.70 (0.8)	0.69 (0.8)	0.58 (0.7)	0.67 (0.8)	0.72 (0.8)	0.78 (0.8)	0.89 (0.8)	1.00 (0.8)	0.63 (0.7)	0.76 (0.8)	0.64 (0.7)
S2.3 Characteristics of psychiatric comorbidity [0-5]	0.42 (0.8)	0.49 (1.0)	0.27 (0.6)	0.29 (0.7)	0.34 (0.7)	0.50 (0.9)	0.89 (1.2)	0.61 (1.1)	0.53 (0.8)	0.59 (1.0)	0.59 (1.0)
S3.1 History of treatment for addiction disorder - SQRT(n) [0-6]	0.48 (0.7)	0.49 (0.7)	0.30 (0.5)	0.30 (0.6)	0.39 (0.6)	0.60 (0.8)	0.74 (0.9)	0.79 (0.8)	0.85 (0.9)	0.77 (0.8)	0.87 (0.9)
S4.1 Dependence [0-7]	4.66 (1.8)	4.17 (2.1)	4.13 (1.8)	4.49 (1.7)	4.71 (1.6)	5.36 (1.6)	5.51 (1.5)	5.76 (1.4)	5.41 (1.7)	4.72 (1.9)	4.68 (2.1)
S4.2 Abuse [0-4]	2.03 (1.1)	1.87 (1.2)	1.82 (1.1)	1.97 (1.1)	2.03 (1.0)	2.23 (1.0)	2.44 (1.0)	2.57 (1.0)	2.37 (1.1)	2.03 (1.2)	1.86 (1.3)
S4.3 Severity dependence/abuse [0-9]	5.90 (2.2)	5.28 (2.6)	5.27 (2.2)	5.74 (2.1)	5.96 (2.0)	6.71 (1.9)	6.96 (1.9)	7.31 (1.8)	6.79 (2.1)	5.92 (2.4)	5.71 (2.7)
S5.1 Physical complaints [0-40]	10.80 (7.4)	9.96 (7.7)	8.83 (6.7)	9.42 (6.5)	10.74 (6.7)	13.42 (7.2)	14.26 (8.1)	13.84 (7.3)	12.61 (8.0)	12.14 (7.8)	12.18 (8.1)
S6.1 Personality [0-8]	3.49 (1.5)	3.32 (1.5)	3.24 (1.5)	3.41 (1.5)	3.54 (1.4)	3.73 (1.5)	3.83 (1.5)	4.08 (1.5)	3.79 (1.5)	3.59 (1.6)	3.27 (1.6)
S7.1 Limitations - Total [0-76]	13.71 (9.5)	13.25 (9.6)	9.89 (7.5)	10.17 (7.0)	12.88 (7.5)	16.98 (9.1)	19.41 (10.2)	20.28 (10.4)	19.68 (10.1)	19.09 (10.6)	18.42 (12.3)
S7.2 Limitations - Basic [0-32]	4.05 (4.3)	4.11 (4.2)	2.54 (3.1)	2.54 (2.9)	3.33 (3.3)	5.25 (4.4)	6.50 (5.2)	6.62 (4.8)	6.40 (5.0)	6.35 (5.2)	6.82 (6.0)
S7.3 Limitations - Relational [0-20]	3.67 (3.1)	3.46 (3.2)	2.91 (2.7)	3.09 (2.7)	3.72 (2.8)	4.34 (3.1)	4.72 (3.4)	5.12 (3.6)	4.54 (3.4)	4.61 (3.5)	3.83 (3.6)
S7.4 Care & support [0-32]	3.18 (4.2)	3.67 (4.5)	2.33 (3.9)	2.35 (3.8)	2.66 (3.7)	3.35 (4.0)	4.26 (4.5)	4.19 (4.6)	4.64 (4.4)	4.89 (4.7)	5.56 (5.0)
S8.1 Positive external influence [0-12]	3.59 (2.1)	3.57 (2.1)	3.64 (2.0)	3.81 (2.1)	3.47 (2.0)	3.52 (1.9)	3.63 (2.2)	3.68 (2.1)	3.46 (2.3)	3.38 (2.2)	3.05 (2.2)
S8.2 Negative external influence [0-20]	3.03 (2.8)	2.90 (2.8)	2.36 (2.4)	2.76 (2.7)	2.86 (2.5)	3.34 (2.9)	3.95 (3.0)	3.98 (3.0)	3.98 (3.4)	3.72 (3.1)	4.12 (3.5)
S8.3 Need for care [0-20]	4.00 (3.4)	3.62 (3.5)	2.75 (2.6)	3.03 (2.8)	3.89 (2.8)	4.83 (3.4)	5.95 (3.9)	6.15 (3.7)	5.80 (3.9)	5.69 (4.0)	5.23 (4.6)
SQ1.1 Craving [0-20]	7.68 (4.9)	6.88 (5.2)	6.08 (4.3)	6.83 (4.1)	7.57 (4.2)	9.41 (5.3)	10.13 (5.2)	10.11 (5.0)	9.76 (5.4)	8.47 (5.3)	9.86 (5.6)
SQ2.1 Depression [0-42]	13.04 (11.2)	11.66 (11.4)	9.59 (9.6)	10.90 (10.3)	13.72 (10.7)	16.58 (11.3)	18.02 (11.3)	20.37 (12.2)	17.38 (11.9)	14.85 (11.8)	12.85 (11.7)
SQ2.2 Anxiety [0-42]	8.74 (8.5)	7.84 (8.4)	6.66 (7.5)	7.13 (7.6)	8.76 (7.8)	11.39 (8.9)	12.79 (9.4)	13.35 (9.4)	11.09 (8.9)	9.81 (8.9)	9.04 (8.5)
SQ2.3 Stress [0-42]	14.62 (10.5)	13.14 (10.6)	11.86 (9.7)	13.07 (9.9)	15.77 (10.0)	17.59 (10.3)	19.15 (10.7)	20.51 (10.3)	17.56 (11.0)	15.63 (10.9)	12.21 (10.2)
SQ2.4 Depression Anxiety Stress - Total [0-126]	36.41 (26.8)	32.64 (27.2)	28.12 (23.7)	31.09 (24.5)	38.25 (24.5)	45.56 (26.3)	49.96 (27.3)	54.23 (28.4)	45.96 (28.6)	40.30 (27.9)	34.11 (27.4)

[1] n (%); Mean (SD)

Supplementary Table 1b Prematurely ended episodes. Patient demographics and MATE-scores by Service Use Cluster

Characteristic	Overall, N = 3,339[1]	Intake only, N = 1,395[1]	Outpatient L1, N = 1,087[1]	Outpatient L2, N = 240[1]	Outpatient L3, N = 123[1]	Out/inpatient L1, N = 195[1]	Out/inpatient L2, N = 56[1]	Out/inpatient L3, N = 30[1]	Complex trajectory, N = 13[1]	Care L1, N = 166[1]	Care L2, N = 34[1]
PPS - Primary Problem Substance											
Alcohol	1,678 (51%)	708 (51%)	546 (51%)	128 (54%)	69 (57%)	104 (54%)	25 (45%)	14 (47%)	6 (60%)	73 (45%)	5 (15%)
Opioids	121 (3.7%)	42 (3.0%)	5 (0.5%)	0 (0%)	2 (1.7%)	5 (2.6%)	2 (3.6%)	0 (0%)	0 (0%)	40 (25%)	25 (74%)
Stimulants	620 (19%)	282 (20%)	182 (17%)	40 (17%)	21 (18%)	40 (21%)	15 (27%)	11 (37%)	1 (10%)	26 (16%)	2 (5.9%)
Cannabis	865 (26%)	347 (25%)	331 (31%)	69 (29%)	28 (23%)	42 (22%)	14 (25%)	5 (17%)	3 (30%)	24 (15%)	2 (5.9%)
Sex											
F	712 (21%)	306 (22%)	221 (20%)	55 (23%)	34 (28%)	41 (21%)	16 (29%)	7 (23%)	0 (0%)	28 (17%)	4 (12%)
M	2,627 (79%)	1,089 (78%)	866 (80%)	185 (77%)	89 (72%)	154 (79%)	40 (71%)	23 (77%)	13 (100%)	138 (83%)	30 (88%)
Age	36.81 (13.1)	36.84 (12.9)	35.75 (13.5)	36.25 (12.4)	39.14 (13.8)	39.54 (13.3)	34.59 (12.0)	34.70 (10.9)	32.00 (14.4)	39.70 (12.7)	42.24 (8.5)
S2.1 Characteristics of physical comorbidity [0-4]	0.33 (0.6)	0.35 (0.6)	0.26 (0.5)	0.16 (0.4)	0.39 (0.7)	0.46 (0.7)	0.43 (0.7)	0.37 (0.6)	0.38 (0.7)	0.48 (0.7)	0.74 (0.8)
S2.2 In psychiatric or psychological treatment [0-2]	0.65 (0.8)	0.68 (0.8)	0.58 (0.7)	0.61 (0.8)	0.76 (0.8)	0.65 (0.8)	0.98 (0.8)	1.13 (0.8)	0.77 (0.6)	0.72 (0.8)	0.74 (0.8)
S2.3 Characteristics of psychiatric comorbidity [0-5]	0.42 (0.8)	0.45 (0.9)	0.31 (0.7)	0.34 (0.7)	0.46 (0.8)	0.56 (0.9)	0.89 (1.2)	0.57 (0.9)	0.46 (0.7)	0.62 (1.1)	0.74 (1.1)
S3.1 History of treatment for addiction disorder - SQRT(n) [0-6]	0.40 (0.7)	0.41 (0.7)	0.30 (0.6)	0.30 (0.6)	0.35 (0.6)	0.54 (0.7)	0.91 (0.8)	1.09 (1.0)	0.97 (0.9)	0.67 (0.8)	0.74 (0.7)
S4.1 Dependence [0-7]	4.66 (1.8)	4.54 (1.9)	4.53 (1.7)	4.76 (1.6)	5.03 (1.5)	5.56 (1.5)	5.32 (1.8)	5.47 (1.6)	5.00 (2.0)	4.72 (1.9)	4.42 (2.4)
S4.2 Abuse [0-4]	2.09 (1.1)	2.03 (1.1)	2.02 (1.1)	2.17 (1.1)	2.22 (0.9)	2.43 (1.0)	2.52 (1.1)	2.90 (1.0)	2.54 (1.0)	2.04 (1.2)	2.36 (1.5)
S4.3 Severity dependence/abuse [0-9]	5.93 (2.2)	5.76 (2.3)	5.78 (2.1)	6.13 (2.0)	6.41 (1.8)	7.01 (1.8)	6.82 (2.1)	7.30 (1.8)	6.38 (2.4)	5.86 (2.4)	5.94 (3.0)
S5.1 Physical complaints [0-40]	10.45 (7.3)	10.57 (7.3)	9.43 (7.0)	8.96 (6.5)	11.59 (7.7)	13.55 (7.3)	13.05 (7.1)	11.47 (7.0)	12.62 (7.5)	11.67 (7.6)	14.85 (8.5)
S6.1 Personality [0-8]	3.46 (1.5)	3.41 (1.5)	3.35 (1.5)	3.35 (1.6)	3.98 (1.4)	3.77 (1.5)	3.89 (1.8)	4.17 (1.8)	3.92 (1.3)	3.65 (1.5)	3.79 (1.5)
S7.1 Limitations - Total [0-76]	13.77 (9.4)	13.88 (9.5)	11.59 (7.9)	11.83 (8.4)	13.36 (7.3)	17.63 (9.4)	19.18 (10.2)	23.28 (11.9)	25.46 (12.2)	19.61 (11.4)	22.18 (11.2)
S7.2 Limitations - Basic [0-32]	4.09 (4.1)	4.15 (4.1)	3.08 (3.2)	3.05 (3.4)	3.58 (3.2)	6.05 (4.6)	6.48 (4.3)	7.93 (5.6)	9.54 (5.2)	6.88 (5.4)	8.59 (5.8)
S7.3 Limitations - Relational [0-20]	3.71 (3.1)	3.73 (3.2)	3.36 (2.7)	3.52 (3.0)	3.84 (2.8)	4.20 (3.2)	4.46 (3.7)	5.79 (3.7)	6.77 (4.3)	4.50 (3.8)	4.12 (3.7)
S7.4 Care & support [0-32]	3.27 (4.3)	3.40 (4.4)	2.67 (3.8)	2.39 (3.6)	3.24 (3.6)	3.23 (4.4)	5.04 (5.3)	6.45 (6.9)	9.69 (4.7)	5.44 (5.0)	5.68 (4.4)
S8.1 Positive external influence [0-12]	3.54 (2.1)	3.52 (2.1)	3.53 (2.0)	3.83 (2.2)	3.54 (2.0)	3.64 (2.2)	3.57 (2.2)	3.38 (1.9)	4.62 (3.1)	3.19 (2.2)	3.32 (2.3)
S8.2 Negative external influence [0-20]	3.26 (2.9)	3.21 (2.9)	2.97 (2.6)	3.29 (2.9)	2.98 (2.8)	3.43 (2.7)	4.25 (3.2)	4.24 (3.1)	6.08 (4.5)	4.48 (3.7)	4.68 (3.3)
S8.3 Need for care [0-20]	3.84 (3.4)	3.83 (3.4)	3.23 (2.9)	3.13 (3.0)	3.60 (2.8)	4.88 (3.4)	5.57 (3.9)	6.69 (4.0)	8.00 (4.8)	5.97 (4.4)	6.88 (4.5)
SQ1.1 Craving [0-20]	7.66 (4.8)	7.45 (5.0)	7.24 (4.4)	7.26 (4.3)	7.78 (4.3)	9.77 (5.1)	9.59 (5.2)	7.79 (4.8)	8.31 (6.8)	8.97 (5.6)	10.03 (6.1)
SQ2.1 Depression [0-42]	12.72 (11.3)	12.60 (11.5)	11.17 (10.5)	11.93 (10.1)	15.30 (10.9)	17.03 (12.2)	17.14 (12.0)	17.43 (11.9)	14.62 (12.9)	14.58 (11.6)	17.70 (12.4)
SQ2.2 Anxiety [0-42]	8.80 (8.5)	8.92 (8.7)	7.76 (7.9)	7.04 (6.8)	9.71 (8.2)	11.52 (9.1)	12.46 (8.9)	11.93 (10.2)	13.62 (10.1)	10.25 (9.7)	12.97 (10.2)
SQ2.3 Stress [0-42]	15.07 (10.6)	14.94 (10.6)	14.11 (10.5)	13.79 (9.3)	17.66 (9.6)	18.19 (10.6)	18.57 (11.3)	19.93 (9.2)	18.92 (9.5)	15.82 (10.7)	18.12 (12.1)
SQ2.4 Depression Anxiety Stress - Total [0-126]	36.57 (26.8)	36.43 (27.5)	33.04 (25.5)	32.76 (22.1)	42.67 (24.1)	46.74 (27.9)	48.18 (28.5)	49.29 (27.1)	47.15 (29.1)	40.65 (27.8)	48.79 (31.8)

[1] n (%); Mean (SD)

Supplementary Table 1c All episodes. Patient demographics and MATE-scores by Service Use Cluster

Characteristic	Overall, N = 9,841[1]	Intake only, N = 2,056[1]	Outpatient L1, N = 2,575[1]	Outpatient L2, N = 1,469[1]	Outpatient L3, N = 995[1]	Out/inpatient L1, N = 902[1]	Out/inpatient L2, N = 360[1]	Out/inpatient L3, N = 381[1]	Complex trajectory, N = 160[1]	Care L1, N = 687[1]	Care L2, N = 256[1]
PPS - Primary Problem Substance											
Alcohol	5,709 (59%)	1,078 (53%)	1,525 (60%)	929 (64%)	659 (67%)	574 (64%)	188 (53%)	223 (59%)	91 (59%)	399 (59%)	43 (17%)
Opioids	444 (4.6%)	85 (4.2%)	15 (0.6%)	6 (0.4%)	11 (1.1%)	19 (2.1%)	14 (3.9%)	4 (1.1%)	4 (2.6%)	103 (15%)	183 (72%)
Stimulants	1,497 (15%)	366 (18%)	352 (14%)	197 (14%)	133 (14%)	130 (15%)	79 (22%)	87 (23%)	31 (20%)	99 (15%)	23 (9.0%)
Cannabis	2,067 (21%)	505 (25%)	643 (25%)	319 (22%)	177 (18%)	171 (19%)	76 (21%)	63 (17%)	28 (18%)	79 (12%)	6 (2.4%)
Sex											
F	2,398 (24%)	466 (23%)	606 (24%)	379 (26%)	304 (31%)	212 (24%)	94 (26%)	129 (34%)	17 (11%)	149 (22%)	42 (16%)
M	7,443 (76%)	1,590 (77%)	1,969 (76%)	1,090 (74%)	691 (69%)	690 (76%)	266 (74%)	252 (66%)	143 (89%)	538 (78%)	214 (84%)
Age	39.66 (13.8)	38.24 (14.0)	38.71 (14.9)	39.60 (14.1)	41.44 (13.0)	42.04 (13.4)	37.17 (13.2)	38.03 (10.1)	38.76 (12.6)	43.15 (12.6)	42.93 (9.3)
S2.1 Characteristics of physical comorbidity [0-4]	0.35 (0.6)	0.37 (0.7)	0.26 (0.5)	0.21 (0.5)	0.35 (0.6)	0.47 (0.7)	0.57 (0.8)	0.41 (0.7)	0.50 (0.7)	0.55 (0.8)	0.53 (0.7)
S2.2 In psychiatric or psychological treatment [0-2]	0.69 (0.8)	0.68 (0.8)	0.58 (0.7)	0.66 (0.8)	0.72 (0.8)	0.75 (0.8)	0.90 (0.8)	1.01 (0.8)	0.64 (0.7)	0.75 (0.8)	0.66 (0.7)
S2.3 Characteristics of psychiatric comorbidity [0-5]	0.42 (0.8)	0.46 (0.9)	0.29 (0.7)	0.30 (0.7)	0.36 (0.8)	0.52 (0.9)	0.89 (1.2)	0.61 (1.0)	0.53 (0.8)	0.60 (1.0)	0.61 (1.0)
S3.1 History of treatment for addiction disorder - SQRT(n) [0-6]	0.46 (0.7)	0.43 (0.7)	0.30 (0.5)	0.30 (0.6)	0.38 (0.6)	0.59 (0.8)	0.77 (0.9)	0.82 (0.8)	0.86 (0.9)	0.75 (0.8)	0.85 (0.9)
S4.1 Dependence [0-7]	4.66 (1.8)	4.42 (2.0)	4.30 (1.8)	4.54 (1.7)	4.75 (1.6)	5.41 (1.6)	5.48 (1.6)	5.74 (1.4)	5.38 (1.7)	4.72 (1.9)	4.65 (2.2)
S4.2 Abuse [0-4]	2.05 (1.1)	1.98 (1.1)	1.91 (1.1)	2.00 (1.1)	2.06 (1.0)	2.27 (1.0)	2.45 (1.1)	2.59 (1.0)	2.38 (1.1)	2.03 (1.2)	1.93 (1.3)
S4.3 Severity dependence/abuse [0-9]	5.91 (2.2)	5.61 (2.4)	5.48 (2.2)	5.80 (2.1)	6.02 (2.0)	6.77 (1.9)	6.94 (2.0)	7.31 (1.8)	6.76 (2.1)	5.91 (2.4)	5.74 (2.7)
S5.1 Physical complaints [0-40]	10.68 (7.3)	10.37 (7.5)	9.08 (6.8)	9.34 (6.5)	10.84 (6.9)	13.45 (7.3)	14.07 (8.0)	13.66 (7.3)	12.61 (8.0)	12.03 (7.7)	12.54 (8.2)
S6.1 Personality [0-8]	3.48 (1.5)	3.38 (1.5)	3.28 (1.5)	3.40 (1.5)	3.59 (1.4)	3.74 (1.5)	3.84 (1.6)	4.09 (1.5)	3.80 (1.5)	3.60 (1.5)	3.34 (1.6)
S7.1 Limitations - Total [0-76]	13.73 (9.4)	13.68 (9.5)	10.61 (7.7)	10.44 (7.3)	12.94 (7.4)	17.12 (9.2)	19.37 (10.1)	20.51 (10.5)	20.15 (10.3)	19.21 (10.8)	18.93 (12.2)
S7.2 Limitations - Basic [0-32]	4.06 (4.2)	4.13 (4.1)	2.77 (3.1)	2.62 (3.0)	3.36 (3.2)	5.42 (4.4)	6.50 (5.1)	6.72 (4.9)	6.65 (5.1)	6.48 (5.2)	7.06 (6.0)
S7.3 Limitations - Relational [0-20]	3.68 (3.1)	3.64 (3.2)	3.10 (2.7)	3.16 (2.8)	3.74 (2.8)	4.31 (3.2)	4.68 (3.5)	5.17 (3.6)	4.72 (3.5)	4.58 (3.6)	3.87 (3.6)
S7.4 Care & support [0-32]	3.21 (4.3)	3.48 (4.4)	2.47 (3.8)	2.36 (3.8)	2.74 (3.7)	3.32 (4.1)	4.38 (4.6)	4.37 (4.9)	5.06 (4.6)	5.02 (4.8)	5.58 (4.9)
S8.1 Positive external influence [0-12]	3.57 (2.1)	3.53 (2.1)	3.60 (2.0)	3.81 (2.1)	3.48 (2.0)	3.54 (2.0)	3.62 (2.2)	3.66 (2.0)	3.55 (2.4)	3.33 (2.2)	3.09 (2.2)
S8.2 Negative external influence [0-20]	3.11 (2.8)	3.11 (2.9)	2.62 (2.5)	2.84 (2.7)	2.87 (2.5)	3.36 (2.9)	3.99 (3.0)	4.00 (3.0)	4.15 (3.5)	3.90 (3.2)	4.19 (3.5)
S8.3 Need for care [0-20]	3.94 (3.4)	3.76 (3.4)	2.95 (2.7)	3.05 (2.8)	3.86 (2.8)	4.84 (3.4)	5.89 (3.9)	6.19 (3.8)	5.98 (4.0)	5.76 (4.1)	5.45 (4.6)
SQ1.1 Craving [0-20]	7.67 (4.9)	7.26 (5.1)	6.57 (4.4)	6.90 (4.1)	7.60 (4.2)	9.49 (5.3)	10.04 (5.2)	9.93 (5.0)	9.64 (5.5)	8.59 (5.3)	9.88 (5.7)
SQ2.1 Depression [0-42]	12.93 (11.2)	12.30 (11.5)	10.25 (10.0)	11.07 (10.3)	13.91 (10.7)	16.67 (11.5)	17.88 (11.4)	20.15 (12.2)	17.15 (12.0)	14.79 (11.8)	13.49 (11.8)
SQ2.2 Anxiety [0-42]	8.76 (8.5)	8.57 (8.6)	7.12 (7.7)	7.11 (7.5)	8.88 (7.9)	11.42 (8.9)	12.74 (9.3)	13.24 (9.4)	11.30 (9.0)	9.92 (9.1)	9.56 (8.8)
SQ2.3 Stress [0-42]	14.77 (10.5)	14.36 (10.7)	12.80 (10.1)	13.19 (9.8)	16.01 (9.9)	17.72 (10.4)	19.06 (10.7)	20.47 (10.3)	17.67 (10.9)	15.68 (10.8)	12.99 (10.7)
SQ2.4 Depression Anxiety Stress - Total [0-126]	36.46 (26.8)	35.21 (27.5)	30.19 (24.6)	31.37 (24.1)	38.80 (24.5)	45.81 (26.6)	49.68 (27.5)	53.87 (28.3)	46.06 (28.5)	40.38 (27.9)	36.04 (28.4)

[1] n (%); Mean (SD)

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