Mental distress and ADHD symptoms among individuals in Opioid Maintenance Treatment

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Oslo, January 2018

Kristine

PREFACE

My interest in patients with co-occurring substance use disorders (SUD) and mental health problems is rooted in my work as a clinical psychologist in an outpatient SUD clinic at Oslo University Hospital for the past nine years. During these years I have found myself in the middle of an exciting development with an increasing interest for psychological knowledge and a sharpened focus on evidence-based treatment. I was, surprisingly enough, surprised to find many similarities between the patients I met in SUD treatment and those from the general psychiatric care unit where I previously worked. There are still misconceptions floating between the hospital divisions of psychiatry and SUD treatment and hopefully more research on SUD related issues in particular will contribute to overcome this in time. The patient's struggles are not so different and we should all be focused on building expertise on both SUD and mental health issues – and to generously share this knowledge.

Many of my patients have been in opioid maintenance treatment, many have not; common to all are prolonged and severe polysubstance use and comorbid social, somatic- and mental health problems. Sometimes the treatment goals have turned out different from what I honestly wished for. It has been important to practice how to sort out my own agenda to be able to help the patient to sort out his; making progress can be many things. I have learned to open the door to the therapeutic room (on many levels), and to appreciate interdisciplinary collaboration as crucial to help individuals with severe and multifaceted difficulties.

Mental health problems in SUD patients are still under-focused in clinical practice. While it is easy to find plenty of reasons not to perform diagnostic assessments with our patients, I hope the work presented in this thesis will contribute the very least as a reminder of how important it is to maintain this focus and to build clinical expertise on both diagnosing and treating mental health problems in individuals with SUD.

Our patients have had hard lives and many of them still do while in our care. The emotional pressure on clinical staff is considerable and the importance of reflective practice cannot be stressed enough. Not only does this refer to the clinical practice directly, but just as

important how we are skilled to reflect upon our personal reactions, attitudes and beliefs as therapists. If we don't the chances of expressing emotional reactions inexpediently are enhanced. If we dare, these reflections will become the most precious tool.

Finally, I cite the words from *Who will comfort Toffle* by the Finnish poet Tove Jansson, who on cloudier days remind me of why working with attachment is essential.

”Han gikk og gikk, men ikke noe hendte, skjønt det var fullt av folk på alle hold.
Og knøttet møtte ingen som han kjente, for knøttet var et meget ensomt lite troll,
og altfor sky og blyg til å si: Hei! Kan jeg få snakke litt med deg?
Og fire filifjonker kjørte hvinende forbi
og åtte ekvipasjer kom med grønne homser i
og mymlen bandt en pyntekrans med lyng av tyttebær
Og knøttet gjemte seg så godt at ingen så ham der.
Men hvem skal trøste knøttet ved å si ham simpelthen;
at hvis du bare flyr din vei så får du ingen venn”

SUMMARY

Background: A substance use disorder is a severe and chronic condition with considerable impact on the individual and their social environment. Patients in opioid maintenance treatment (OMT) are frequently considered a particularly marginalized subgroup of substance users and often suffer from a range of multimorbidities that require additional clinical attention. While OMT is now accepted to be the gold standard treatment for opioid dependence and a large body of research has led to the formation of best practices, commonly occurring mental health problems such as depression, anxiety and ADHD are insufficiently understood and addressed within this treatment.

Study aims: The overarching aim of this thesis was to gain more knowledge about mental distress and ADHD in patients in OMT. The specific aims were to investigate factors related to the prevalence and development of self-reported mental distress during the first year of OMT; to investigate the prevalence and impact of ADHD symptoms in OMT patients and to explore whether treatment with central stimulants is a viable option for patients in OMT with ADHD.

Materials and methods: This thesis was based on two different samples from different settings. The first sample (papers I-III) was a prospective national cohort study with participants from 21 treatment facilities throughout Norway, the NorComt study (papers I-III). Between 2012 and 2015, 548 participants entering either outpatient Opioid Maintenance Treatment (OMT) or other inpatient treatment were interviewed (T0-baseline). This thesis focuses on the subset who entered OMT (n=278). After one year (T1-follow-up) 63% were re-interviewed (n=179). The interview guide covered a variety of life domains including demographics, substance use, psychosocial measures, self-control and criminal activity. The second sample (paper IV) consisted of 42 OMT patients who applied for pharmacological ADHD treatment in a clinical, naturalistic study conducted at Oslo University Hospital from 2007 through 2010 (paper IV). The relationships between independent and dependent variables were examined using regression analysis generating relative risk ratios (RRR) for multinomial regression analysis (paper I) and odds ratios (OR) for binary logistic regression analysis (paper II). Linear regression (β) was used in paper III. In paper IV we used pairwise t-tests.

Results: Fifty-four percent entered OMT with mental distress scores above cut-off. Higher mental distress was associated with low self-control (aRRR 0.88; 0.84-0.92), but also with more frequent use of alcohol (aRRR 3.41; 1.11-10.42) and benzodiazepines (prescribed: aRRR 2.87; 95% CI 1.05-7.80; illicit: aRRR 2.79; 1.05-7.41), use of a higher number of substances (aRRR 1.41; 1.14-1.73) and higher Severity of dependence scores (aRRR 1.15; 1.03-1.29). Finally high mental distress was associated with having been subjected to violence (aRRR 4.21; 1.73-10.24) and mental health care throughout life (aRRR 5.55; 2.26-13.66). Thirty-three percent of the OMT patients reported ADHD symptoms above clinical cut-off score at one-year follow-up. These patients reported more mental distress (aOR 1.61; 95% CI 1.03–2.50) and more use of stimulants (aOR 2.55; 1.13–5.76) at baseline. At follow-up, 57% reported mental distress scores above cut-off, indicating no change in mental distress during the first year of treatment. We found change in mental distress to be associated with use of benzodiazepines at baseline and change in Severity of dependence (β 0.32; 0.051-0.592 and β 0.05; 0.02-0.088 respectively). In addition, patients with increased ADHD symptoms had worsened mental distress on a group level. In our clinical trial, the patients who remained in pharmacological ADHD treatment throughout the observation period reported symptom relief and no increase in substance use, but their ADHD symptoms and psychosocial problems remained substantial.

Conclusions: We found a high prevalence of self-reported mental distress and ADHD symptoms among this sample of OMT patients. Mental distress was equally high after one year in treatment and was related to substance dependence severity. Patients with high ADHD symptom score had even more mental distress and a poorer development of mental distress, compared to those with low ADHD symptom scores. Our clinical trial showed some promise regarding pharmacological treatment of ADHD in OMT. Our findings should encourage focus on mental health and systematic screening to appropriately identify, diagnose and treat all conditions simultaneously.

SAMMENDRAG (NORWEGIAN)

Bakgrunn: Rusmiddelavhengighet er en alvorlig og kronisk tilstand med en rekke negative konsekvenser for individet og omgivelsene. Pasienter i legemiddelassistert rehabilitering (LAR) blir ofte betraktet som en særlig marginalisert gruppe rusmiddelavhengige med komorbide lidelser som krever et bredt klinisk fokus. Selv om LAR har blitt den foretrukne behandlingen for opioidavhengighet og omfattende forskning har bidratt å forme dagens praksis, er det likevel for lite fokus på komorbide psykiske helseplager som depresjon, angst og ADHD.

Forskningsspørsmål: Den overordnede hensikten med denne studien var å få mer kunnskap om forekomst av psykiske helseplager og ADHD symptomer blant pasienter i LAR, samt hvilke faktorer og kjennetegn som kan knyttes til dette. De spesifikke forskningsspørsmålene var å estimere forekomst av selvrapporterte symptomer på angst og depresjon ved behandlingsstart og ett år senere og å utforske faktorer forbundet med forekomst og endring (artikkel I og III); å undersøke forekomst av ADHD symptomer hos LAR pasienter og betydningen av disse (artikkel II og III); å utforske hvorvidt behandling med sentralstimulerende legemidler kan være nyttig for pasienter med ADHD i LAR (artikkel IV).

Metode: Denne studien ble basert på to ulike utvalg fra to ulike settinger. Det første utvalget var en prospektiv nasjonal kohort med 548 deltagere fra 21 rusbehandlingssteder i Norge; NorComt-studien (artikler I-III). Mellom 2012 og 2015 ble deltagerne intervjuet ved oppstart i enten poliklinisk LAR-behandling eller annen døgnbehandling (T0-baseline). Denne avhandlingen fokuserer på gruppen med de 278 pasientene som begynte i LAR. Ett år senere ble 63 % intervjuet igjen (n=179) (T1-oppfølgning). Intervjuguiden var omfattende og dekket mange ulike temaer som demografi, rusbruk, psykososiale mål, selvkontroll og deltagelse i kriminalitet. Det andre utvalget (artikkel IV) bestod av 42 LAR-pasienter som søkte om behandling med sentralstimulerende legemidler behandling for ADHD i et forsøksprosjekt ved Oslo Universitetssykehus i årene 2007-2010. Dette var en klinisk, naturalistisk studie som skulle evaluere denne behandlingen. Vi undersøkte forholdet mellom uavhengige og avhengige variabler med regresjonsanalyse (artikler I-III). Justerte relativ risk ratioer (RRR) og 95 % konfidensintervaller ble beregnet ved hjelp av multinomial regresjonsanalyse (artikkel I) og justerte odds ratioer (OR) ved hjelp av logistisk regresjonsanalyse (artikkel II). I artikkel III brukte vi lineær regresjonsanalyse (β). I artikkel IV brukte vi paret t-test.

Resultater: Ved behandlingsstart i LAR rapporterte 54 % om angst- og depressive plager over klinisk cut-off. Høy grad av angst- og depressive symptomer hadde sammenheng med redusert selvkontroll (aRRR 0.88; 0.84-0.92), hyppig bruk av alkohol (aRRR 3.41; 1.11-10.42) og benzodiazepiner (forskrevet: aRRR 2.87; 95% CI 1.05-7.80; illegal: aRRR 2.79; 1.05-7.41), høyere antall rusmidler (aRRR 1.41; 1.14-1.73) og høyere skåre på et avhengighetsmål (SDS) (aRRR 1.15; 1.03-1.29). Høy grad av angst- og depressive plager var også forbundet med å ha vært utsatt for vold (aRRR 4.21; 1.73-10.24) og å ha mottatt psykisk helsehjelp i løpet av livet (aRRR 5.55; 2.26-13.66). Trettitre prosent av LAR-pasientene rapporterte om ADHD symptomer over klinisk cut-off på oppfølgningsintervjuet og her fant vi en sammenheng med høy grad av angst- og depressive symptomer (aOR 1.61; 95 % CI 1.03–2.50) og mer bruk av stimulanter (aOR 2.55; 1.13–5.76) ved behandlingsstart. På oppfølgningsintervjuet rapporterte 57 % om høy grad av angst- og depressive symptomer, noe som indikerer at det på gruppenivå ikke var noen endring i løpet av det første året i LAR. Vi fant at endring i angst- og depressive symptomer var forbundet med bruk av benzodiazepiner ved behandlingsstart og endring i psykologisk avhengighet (SDS) (henholdsvis β 0.32; 0.051-0.592 og β 0.05; 0.02-0.088). De med ADHD symptomskårer over klinisk cut-off rapporterte om en økning i angst- og depresjonsplager på oppfølgningstidspunktet. I den kliniske studien (artikkel IV) rapporterte pasientene som forble i behandling gjennom observasjonstiden om symptomlette, men deres ADHD-symptomer og psykososiale problemer var likevel betydelige.

Konklusjoner: I denne studien fant vi høy forekomst av selvrapporterte symptomer på angst og depresjon og ADHD blant pasienter i LAR. Nivået av angst- og depressive symptomer forble høyt etter ett år i LAR, og var relatert til opplevd avhengighet (SDS). Pasienter med ADHD symptomer over klinisk cut-off rapporterte mer symptomer på angst og depresjon på begge måletidspunkter og en forverring i løpet av det første året i LAR. Vår kliniske studie gir grunn til forsiktig optimisme når det gjelder medikamentell behandling av ADHD hos pasienter i LAR. Disse funnene bør oppmuntre satsning på systematisk screening av psykiske plager i LAR for å få mulighet til å identifisere, diagnostisere og behandle alle tilstandene samtidig.

LIST OF PAPERS

I. Abel KF, Skjærvø I, Ravndal E, Clausen, T, Bramness JG. (2018). Mental distress is related to self-control in patients entering substance use treatment. Substance Use and Misuse.

II. Abel KF, Ravndal E, Clausen T, Bramness JG. (2017). ADHD symptoms are common in patients in Opioid Maintenance Treatment. European Addiction Research.

III. Abel KF, Stavseth MR, Clausen, T, Ravndal E, Bramness JG. (2018). Self-reported mental distress remains high after one year in opioid maintenance treatment. Submitted.

IV. Abel KF, Martinsen E, Bramness JG. (2014). Stimulant Medication for ADHD in Opioid Maintenance Treatment. Journal of Dual Diagnosis.

LIST OF ABBREVIATIONS

ADHD: Attention Deficit Hyperactivity Disorder

ASRS: Adult ADHD Self-Report Scale

BSCS: The Brief Self-Control Scale

CI: Confidence Interval

DSM-IV: Diagnostic and Statistical Manual of Mental Disorders, 4th edition.

DSM-5: Diagnostic and Statistical Manual of Mental Disorders, 5th edition.

GSI: General Symptom Index describes the mean total sum score of the HSCL. GSI is also referred to as mental distress/ mental distress scores in this thesis.

HSCL-25: Hopkin's Symptom Checklist-25 measures symptoms of mental distress (anxiety, depression and somatization) (25 items version).

ICD-10: International Classification of Mental and Behavioral Disorders, 10th version.

NorComt: The Norwegian Cohort of Patients in Opioid Maintenance Treatment and Other Substance Treatment

OMT: Opioid Maintenance Treatment

OR: Odds Ratio

RRR: Relative Risk Ratio

SDS: Severity of Dependence Scale

SUD: Substance Use Disorder

1. INTRODUCTION

This thesis covers the topics of mental distress and ADHD symptoms in two samples of Norwegian patients in Opioid Maintenance Treatment (OMT). Patients in OMT rarely suffer with only opioid dependence, lending to a complex clinical picture. To convey a fuller appreciation of the individuals affected, this introduction will briefly cover common features of substance use disorders (SUD), central historical and cultural aspects of SUD and OMT, common substance use patterns and characteristics of mental distress and ADHD in OMT.

The core of a substance use disorder could be summarized as loss of control; willful behavior is being replaced by continuation of use, despite the adverse consequences for the user and their environment (1). Humans have used substances with sedative, euphoric or hallucinogenic effects for religious, medical and recreational purposes at all times and the issue of loss of control was already being discussed in the 17th century (2). While alcohol has occupied a unique position in Norway through centuries, the prevalence of drugs has been minimal in comparison. Not until the 1960's did society begin to focus on drugs as a social and medical problem (3). The common feature of is their ability to alter perception, thoughts and mood, but the environmental and genetic trajectories are complex and far from fully understood. (4). Health risks are commonly assumed to be associated with quantity and frequency of use. The ability to control substance use varies widely however, meaning that some will experience severe problems while others with a similar pattern of use may not (5). Alcohol and opiates are often used in illustrations of dependence; one legal and the other not, both induce the need to increase doses (tolerance), produce adverse physical symptoms when use is discontinued (withdrawal) and can create adverse psychosocial effects (6). In comparison to other substances, and alcohol in particular, opioid dependence affects a small number of individuals, but may cause the most potential harm and adverse health consequences among all substances (7).

1.1 FAILING MORAL OR A REAL DISEASE?

The way a society interprets behaviours as normal or abnormal has implications for how the individuals who practice these behaviours are met, including the ways treatment is organized. It is not always clear why some conditions are defined as diseases and some are not. Is dependence caused by the substance itself, the individual's vulnerability, genetics,

psychological or social factors (8)? Society has indeed struggled to acknowledge the pathology underlying problematic substance use and this has had implications for how the individuals affected have been treated (9). Traditionally, normative thinking about dependence has been divided between moral-, social- and medical models (10). Moral theories imply that individuals make a conscious choice to abuse substances and they should thus be held accountable for their problems. Social theories highlight the influence of disruptive social factors such as unemployment and poverty to explain development and maintenance of substance use. The medical (or disease) model on the other hand, sees substance dependence as a neurobiological disease characterized by compulsive and relapsing substance use over which the individual has limited control (10). Over the past decades a biopsychosocial framework has become influential as an alternative to the dominant medical model (11). This framework attributes occurrence and maintenance of disease (such as dependence) to the interaction of biological, psychological and social factors (11).

The two first versions of the Diagnostic and Statistical Manual of Mental Disorders (DSM) (12, 13) listed dependence with societally disapproved disorders stemming from personality disorder, along with antisocial reaction, dissocial reaction and sexual deviation (8). With the launch of DSM-III in 1980 came a radical paradigm shift that revolutionized the field of psychiatry and the previously dominating psychodynamic tradition was left to the benefit of research (14). The harsh moral judgements on addictive behaviors were replaced with a medical model emphasizing dependence as a disease of the brain (8). With the recent advantages in the understanding of its underlying biological mechanisms, dependence is today widely accepted as a medical condition with complex sociological and individual determinants. The World Health Organization state that “substance dependence per se should be regarded as a health problem and not a legal one” (15).

Despite being established as a formal diagnosis in the new paradigm, the underlying concept of dependence as a brain disease continues to be questioned (5), perhaps reflecting its complexity (2) and the deeply ingrained values about personal responsibility that frame substance use as a voluntary and hedonistic act (5). Substance use disorders are more closely linked to questions of shame and guilt than many other diseases, and these attitudes are continuously expressed in the public domain (16). The stigma attached to SUD may

create additional shame, guilt and fear and in has in turn been associated with increased substance use and relapse (17). Subgroups such as injecting opioid users, pregnant women and mothers who abuse substances appear to be judged even more harshly (17, 18). Within certain SUD treatment traditions such as the 12 step fellowships, it is a stigma attached to the use of opioid substitution medications (19) and reports of persons experiencing pressure to discontinue the medication (20). In Norway, certain treatment collectives refuse to welcome patients included in Opioid Maintenance Treatment (OMT) as they are not perceived abstinent while using OMT medication. The complexity of stigma can further be illustrated by the Norwegian official attitude that actions related to illegal substances are prosecuted, even when committed by someone who is classified as dependent by the nomenclatures. This practice is endorsed despite that individual- or general preventive effects are yet to be documented (21).

1.2 Prevalence and impact of substance use

Substance Use Disorders continues to represent a severe global health challenge, both for licit and illicit substances. Globally SUD account for an estimated 37 million disability-adjusted life years (22). Up to 15% of adults develop a substance use disorder sometime in their life (23). Cannabis is the most frequently used illicit substance worldwide, but opioids remain the substance that causes the most potential harm and adverse health consequences. Although affecting a relatively small number of the general population, the impact of illicit opioid use can be devastating for the user, their network and community. Overdose deaths contribute to up to half of all substance related deaths, with opioids involved in most cases (4). Both natural (opium and morphine) and synthetic opioids (e.g. methadone) can be misused and cause deaths and health problems. Stimulants (e.g. amphetamines) cause fewer deaths than opioids, but excessive use can still lead to severe problems. While the prevalence for cannabis use (life time) in the Norwegian adult population in 2013 was 23%, the rate for the second most used illicit substance cocaine was 4%. For heroin the rate was less than 1% (24).

Only a fraction of people who use substances ultimately become addicted, in the same way that not everyone is equally at risk for the development of other chronic diseases (5). A range of genetic, environmental and social factors (largely unknown) contribute to the

individual's susceptibility to initial and continued substance use and undergo the brain changes that characterizes SUD (5). Epidemiologic research has shown that SUD commonly follows a chronic course, often developing in adolescence and lasting for decades (25, 26). The process towards recovery is typically marked by cycles of recovery, relapse and repeated treatment (25).

1.3 Patterns of substance use among patients in OMT

1.3.1 Opioid use

The term opioids refer to naturally derived opiates from the opium poppy (morphine and codeine commonly used in medical treatment of pain), semi-synthetic derivates (heroin and buprenorphine) and fully synthetic opioids (methadone and fentanyl) (7). Opioids have multiple actions such as altering of body temperature, sedation, depressed respiration, and dysphoria or euphoria (27).

While all substance use entails an enhanced health risk, inappropriate use of opioids is considered especially harmful (28). Heroin overdose is identified as the main reason for premature death among people who inject, and concurrent use of other substances such as benzodiazepines and alcohol further increases the risk (7). Also, people who inject have high rates of somatic and psychological comorbidities further contributing to the high mortality risk in this group, for instance due to sharing of needles and syringes (28-30). Despite the upscaling of OMT programmes, overdose mortality remains a significant health concern. The average overdose mortality in Europe is estimated to be 18 per million people while Scandinavian countries experience more than 40 deaths per million (31). Thus, overdose mortality is indeed a significant public health concern in Scandinavia, Norway being no exception, with almost a threefold rate of overdose deaths compared to other European countries (31). There are between 6 200 and 10 300 high risk opioid users in Norway, with the majority injecting heroin (24).

In Europe and North America the growing problems of highly potent synthetic opioids such as fentanyl, also among marginalized user populations, causes considerable worry (31). Additionally, the increased use of newer psychoactive substances, such as the injecting of cathinone among opioid users, has been associated with increased somatic and mental health problems (31).

The opioid withdrawal syndrome occurs after discontinuation of opioid intake and includes symptoms of irritability, anxiety, muscular and abdominal pain, vomiting, chills, sweating, sneezing and insomnia. While uncommon, death is a possible outcome of opioid withdrawal, underlining the severity of this condition and the need for appropriate medical management (32).

1.3.2 Stimulant use

Amphetamine and methamphetamine are two closely related synthetic substances that act as stimulants of the central nervous system (33). After cannabis, amphetamines (including methamphetamine) are the second most commonly used class of illegal substance (4). Amphetamines are commonly ingested, snorted or injected and crystalline methamphetamine can be smoked (33). Amphetamines produce euphoria and mood elevation in combination with increased energy, increased alertness and concentration. Intensive amphetamine use often occurs in "binges" followed by a "crash", the latter with commonly experienced symptoms such as depression, fatigue and sleeping difficulties. Psychosis, depression, suicidal behavior, anxiety and violent behavior have been associated with amphetamine use (34). The annual Norwegian Status report for OMT concludes that stimulant use among patients in OMT is considerably lower than use of other substances such as cannabis or benzodiazepines. In 2016, 15% of the Norwegian OMT patients reported use of amphetamine derivates and cocaine in the past four weeks, however data was not collected for frequency (35).

1.3.3 Benzodiazepine use

Benzodiazepines are among the most frequently prescribed psychotropic substances in western societies and considered a safe and efficient short term treatment of anxiety, insomnia, epilepsy and muscle spasms (36). However, there is a potential for abuse and dependence even when used appropriately (37). Dependence may eventually develop, including tolerance, withdrawal symptoms and craving. Long term users may experience only the adverse effects such as sleeping difficulties and anxiety problems, thus the benzodiazepines cause an increase in the problems they were meant to cure (36). Benzodiazepine use has been found to be widespread among heroin users, both in and outside of treatment (38), with prevalence rates of 46-71% for patients in OMT (27). Prescription of benzodiazepines to patients in the Norwegian OMT programme is quite

common; one study reported that 40% had been prescribed benzodiazepines during the past year (39). Benzodiazepine use by patients in OMT is associated with poorer psychosocial adjustment, higher levels of polysubstance use, more risk-taking behaviors and poorer retention in treatment, in addition to substance related deaths (40). In one study, one third of heroin users reported injecting benzodiazepines and these were more likely to report anxiety- and depressive disorders compared to those who swallowed the benzodiazepines (38). Benzodiazepines have been identified in 40-80% of heroin- and methadone related deaths and in 80% of buprenorphine-related deaths (27). However, one study did not report any differences of survival in treatment for those with or without severe comorbid benzodiazepine dependence (40). A review of studies examining individuals with co-occurring opioid and benzodiazepine use found that use of benzodiazepines was primarily recreational, e.g. used to enhance the effects of the opioids and dampen withdrawal more than self-medication of mental problems (27). Furthermore, a significant relationship has been reported between inadequate doses of OMT medication as experienced by the patient and positive urine-testing for benzodiazepines (41).

1.3.4 Cannabis use

After nicotine and alcohol, cannabis is the most commonly used substance in Europe (and worldwide) among all age groups (31). A recent study highlighted a 50% increase in the number of individuals entering specialized SUD treatment for cannabis related problems in the EU between 2003 and 2014 (42). Regular and long-term cannabis use is associated with increased risk of health problems including dependence (43). Rates of cannabis dependence are higher among individuals with any life time psychiatric disorder, mood disorder, anxiety disorder, conduct disorder, personality disorder or ADHD (44). While cannabis use is not correlated with increased mortality, cannabis dependence may lead to cognitive impairment, mental problems, cardiovascular disease and other severe somatic conditions (45). Withdrawal symptoms are both psychological (e.g. irritability, anxiety, depression, restlessness) and somatic (e.g. pain, shivering, sweating) (46).

Studies have reported a high prevalence of cannabis use among individuals enrolled in OMT, ranging from 39%-66% (47). Continuation of cannabis use in OMT can be problematic, partly because these individuals continue to be exposed to risks associated with cannabis use and

they can experience interaction of cannabis metabolites and OMT agents (47). It is however not established whether cannabis has adverse impact on treatment outcomes (48, 49).

1.3.5 Alcohol use

Four percent of the global burden of disease is attributable to alcohol use, determined by both doses and drinking pattern (50). In the Norwegian population the prevalence is 8% for alcohol use disorders and 5% for alcohol dependence (51). In addition to a range of somatic harms associated with alcohol abuse or dependence (50), epidemiological research has reported a clearly increased risk of developing additional substance use disorders (52, 53) and mental problems, in particular affective disorders (54) .

An estimated 20% to 50% of patients in OMT are thought to have alcohol related problems (55). Excessive alcohol consumption among OMT patients has been associated a number of adverse factors such as reduced quality of life (56), higher mortality rates and higher rates of mood disorders, anxiety disorders, additional SUDs and personality disorders (57). Furthermore, a large scale Australian cohort study reported liver disease to be the most common contributing or underlying cause of death in an ageing OMT population. They found the major sources of liver mortality to be chronic hepatitis C infection, chronic liver disease and concurrent heavy alcohol use (58).

1.3.6 Polysubstance use

Among substance users, polysubstance consumption is common (31). Broadly, polysubstance use is defined as the use of two or more licit or illicit psychoactive substances within a specific time frame (59). An analysis of European polysubstance use from 2002-2013, found that 63% of primary opioid users were polysubstance users, while the proportion was 61% of cocaine users, 50% of cannabis users and 63% of stimulant users (59). Common reasons for polysubstance use were to potentiate the effect of one substance, to counterbalance it or manage symptoms of withdrawal. The most frequently used secondary substances for opioid users were cannabis, cocaine and hypnotics/sedatives. For all substance users, the most common combinations were:

- Opioids, cannabis plus cocaine
- Cocaine, cannabis plus alcohol (either cocaine or cannabis as primary substance)
- Stimulants, alcohol plus cannabis

- Other groups less frequent, but still relevant for treatment (e.g. benzodiazepines plus opioids) (59)

Polysubstance use is of great concern because it elevates health risks due to additive or multiplicative toxicity of the substances (59). In general, SUD treatment seekers with polysubstance use tend to have even greater depressive and suicidal symptomatology at treatment admission than single substance users (60). They have also been found to have greater social anxiety symptomatology than alcohol-only users (61). A ten year prospective study reported a dose-response relationship where mental distress increased in both magnitude and over time with the number of substances used (62).

Polysubstance use is a well-documented problem in OMT (7, 31, 63-65). A recent 17-year register analysis examined short- and long term changes in substance use in OMT patients (66). They found that alcohol use increased during the observation period while there was a decline in use of heroin and cocaine. Decline in use was associated with improved social functioning (66). Continued illicit substance use has been reported as a significant risk for premature termination of OMT, with those testing positive for multiple substances being at a quadrupled risk compared to those testing positive for one substance (67).

Continued use of (multiple) substances in OMT is commonly understood as self-medication of withdrawal distress, self-medication of dysphoric emotional states, pleasure seeking, impulsive response to offerings and a manifestation of co-occurring substance dependencies (67).

1.4 Diagnostics and treatment of SUD

There are two widely used classification systems for diagnoses; the Diagnostic and Statistical Manual for Mental Disorders (DSM-5), published by the American Psychiatric Association (68), and the International Classification of Diseases (ICD-10), published by the World Health Organization (69). According to both classification systems any substance, medication and toxin is considered a substance. Substance dependence is defined as the behavioral, cognitive and physiological consequences of repeated substance use. This includes a strong desire to take the substance, trouble controlling the use despite harmful consequences, physiological withdrawal symptoms, increased tolerance, and increased indifference

towards other (previously) joyous activities (68). In the DSM- IV the distinction between abuse and dependence was based on the former preceding the latter. The ICD-10 made a similar distinction between harmful use and dependence (69). A change took place when DSM-V was published in 2013. This manual no longer differentiates between abuse and dependence, but has a dimensional approach to problematic use of substances. Further, SUD refers to recurrent use of alcohol or other substances that cause significantly clinical and functional impairment. Depending on level of severity, SUD is classified as mild, moderate or severe (68).

Considerable human and economic resources are invested in the treatment of SUD annually. Norway has a well-developed welfare system, which provides treatment and low-threshold services for free. Nearly 32,000 individuals received SUD treatment from the specialist health services in 2015. In addition up to half of the 148,000 who receive other psychiatric services are estimated to have a SUD (70). Individuals with problems related to substance use will initially get help from the municipal services and their general practitioner, but if interventions at this level prove insufficient they can apply for interdisciplinary specialist substance use treatment. The specialist health facilities consist of outpatient treatment services (including opioid maintenance treatment), specialized teams for hard- to -reach groups and different types of inpatient (residential) treatment (71).

Individuals who present with problems related to substance use *and* mental health will be offered treatment in either the SUD treatment facilities (including OMT) or in the mental health care services depending on the severity of the mental illness and the SUD. Severe mental illness such as psychosis (substance related or not) should initially be referred to the mental health care services (71). The systems are however not waterproof and some fall between the cracks. The mental health services have traditionally had their primary focus on mental health issues, and not towards pursuing identification of substance use in their patients. The opposite could be claimed for patients entering SUD treatment, where mental health issues are far from sufficiently addressed nor treated. As a consequence an individual with comorbid disorders could enter SUD treatment facilities several times over a number of years with little attention given to his mental health issues. These challenges exist in spite of

the official attitude which recommends integrated treatment over sequential treatment, e.g. a combination of medical and psychosocial interventions (71) .

1.4.1 Opioid maintenance treatment

Opioid dependence treatment strategies are dominated by abstinence-oriented treatment, maintenance-oriented treatment and a combination of the two (72). In Scandinavia, abstinence-oriented treatment programmes such as therapeutic communities and detoxification programmes continue to be on offer for individuals in need of treatment (73). Maintenance-oriented treatments are however the most widespread treatment for opioid dependence worldwide (7, 74) and opioid maintenance treatment (OMT) is the common designation for the pharmacotherapy for opioid dependence. Different to detoxification treatments, the purpose of OMT is not to achieve a "substance-free" state, but to avoid illicit substance use and to enable the individual to live without the disturbances associated with such use and increase the possibilities for rehabilitation (75).

An estimated 630 000 patients in the EU received OMT in 2015, approximately half of the target population (31). OMT aims to minimize the harms related to opioid use and optimize the individual's psychosocial functioning such as reducing illicit substance use and crime, and increase participation in community life. Compared to no treatment or medication free treatment, OMT have been shown to reduce use of illegal opioids and injection behaviour and to increase retention in treatment (74, 76). Further, studies have documented substantial reduction in crime (77) somatic illness (29) and mortality (28). However, combinations of medications and behavioural therapies generally appear to be more effective than either approach used on its own (72). OMT is considered a life-long treatment and the risk of relapse into opioid use, with a high mortality rate, is well documented for those who leave the programme planned or prematurely (78-81). Opioid dependence is a complex condition and long-term observations have confirmed that full recovery from opioid dependence is not easily attained. For example 72% of the original subjects in the Substance Abuse Treatment Outcome Studies (DATOS) were not classified as recovered after five years in OMT (82).

1.4.1.1 Medications in OMT

The most common medications in OMT include methadone, buprenorphine and buprenorphine-naloxone combinations. The dominant OMT medication worldwide is methadone, but buprenorphine variations are increasingly used (75).

Methadone is a long-acting, synthetic opioid medication with a half-life of about 24-36 hours. It was first synthesized as an analgesic to treat pain prior to World War II in Germany. Long-term treatment with methadone began as a research project in 1964 after researchers had discovered that heroin dependent patients who had reached the stabilization level of methadone could be maintained with one daily dose without further increase. The patients showed clear improvement on several parameters such as cravings, substance use, social functioning and employment (83, 84).

The therapeutic effects of methadone have been well documented, particularly in terms of increased retention in treatment and reduced heroin use (76, 85). Although methadone is regarded as having few long term problems, dose dependent cardiac effects have been reported (86). Further, it is regarded as a less safe medication compared to the alternatives because the slow methadone metabolization may cause accumulation and because other substances may have synergic effects on sedation and respiratory depression (75).

Buprenorphine is a synthetic opioid and partial agonist with a ceiling effect on respiratory depression. It is presumed to be less likely to produce intoxication, but may be less effective for those in need of high dosage OMT (75). Buprenorphine is commonly abused in several countries and may also be hazardous in combination with other psychoactive substances, in particular benzodiazepines and/or alcohol (87). To address this problem, a safer substance combining buprenorphine and naloxone has been developed (87, 88). Evidence supporting the efficacy of buprenorphine has come from a range of controlled trials, with the most frequently reported outcomes being retention in treatment, reduction in substance use and criminal activity (75).

1.4.2 Opioid Maintenance Treatment in Norway

In Norway OMT has been available since 1998 and included nearly 7500 individuals by the end of 2015 (89). According to the Norwegian National Treatment Guideline for OMT, buprenorphine (preferably the naloxone combination) is recommended as first line

medication because it is considered the safest option (88). In 2016 38% of OMT patients were treated with methadone, 39% with buprenorphine and 20% with buprenorphine/naloxone combinations. Contrary to official recommendations, prescriptions of benzodiazepines to Norwegian OMT patients has increased slowly during the past years to reach the 2016 level of 28% (35).

In its earlier days the OMT programme in Norway aimed for total abstinence from all substance use and discharged patients who did not adhere. This has changed dramatically, mainly due to the large body of research that has evolved and advised against this practice (87). Even though continued use of substances is discouraged and an important topic in treatment, it is no longer considered a sufficient reason to terminate OMT and retention in treatment is now considered a treatment goal in its own right (87, 88). In the 2016 status report, 71% of the Norwegian OMT patients reported abstinence as their treatment goal (35). There are no longer any inclusion criteria (e.g. age limit) besides an opioid dependence diagnosis to enter OMT in Norway.

As OMT has been a treatment option for the last 20 years in Norway, the patient group is ageing due to improved living conditions (90). The mean age is now 43 years (35). The share of older (>45 years) patients in OMT will continue to increase in the years to come. As somatic health problems, poor cognitive functioning and social isolation have been found to be more prevalent in the older OMT population, this may pose particular challenges to the treatment services (90).

The Norwegian OMT label *LAR* translates to “medically assisted rehabilitation”; suggesting that OMT consists of more than the medication. There is a continuous debate concerning whether the psychosocial interventions offered are sufficient (91). In Norway many inhabitants live in small communities with limited access to the resources of the bigger cities, and differences in health services on offer are inevitable. In Oslo, it may seem like a challenge to get to your appointment at the hospital in a different area, but if you live on an island in the north the trip might take the whole day – or the appointment is not on offer at all. It is a long lasting gap between the mental problems reported annually by Norwegian OMT patients and the amount of psychiatric care they actually receive (35, 89, 92).

1.5 Mental health problems in OMT

It is well established from epidemiologic and clinical research that SUD and mental health problems frequently co-occur (93-97) and this includes patients in OMT (30, 79). Although it can be difficult to diagnose comorbid conditions and methods between studies differ, an estimated 80% of SUD patients would have an additional psychiatric diagnosis if personality disorders were included (98). One recent review investigated changes in mental health during OMT (99). They found that mental health in general improved, but that this improvement may not continue beyond 12 months (99). This tendency is in line with findings from a recent longitudinal, observational study in Norway who reported that symptoms of depression and anxiety had returned to baseline level at 10 year follow-up, after a period of reduction (30).

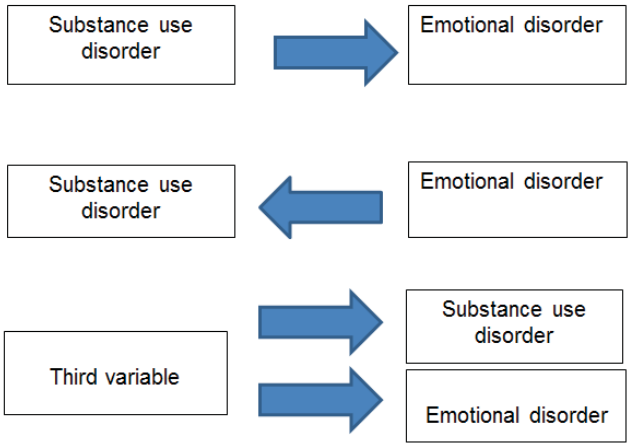
1.5.1 Depression and anxiety

In addition to personality disorders, the prevalence of depression and anxiety is high among individuals with SUD (100-102), with the highest levels found among treatment seeking polysubstance users (62, 102, 103). In the Norwegian status report for 2016, 20% of OMT patients self-reported current depressive symptoms and 28% severe anxiety symptoms (35). These estimates are comparable to findings from larger clinical trials assessing current major depressive disorder- or symptoms (104, 105) and anxiety disorders (98) among patients in OMT.

Aetiology of co-occurring SUD and anxiety/depression

Different models offer explanations of the high prevalence of co-occurring SUDs and mental disorders (106, 107). As detailed in figure 1, three primary pathways have been suggested from the culmination of studies to date (108).

Figure 1. Primary pathways for the comorbidity between SUD and mental disorders (labelled emotional disorders in the model) (108).



The first two panels in the figure assume the same form of causation between the SUD and the mental disorder. These are based on the presumption that one primary disorder precedes the secondary disorder in time and that primary disorders in different ways may cause the co-occurrence of the secondary disorder. The first panel is consistent with a substance induced mental disorder. Causation could occur directly, e.g. through pharmacological effects of a substance producing aversive, stress-like subjective states such as anxiety and depression (109). Causation could however also occur indirectly, e.g. a marital divorce due to a SUD could induce the onset of a depressive episode (110). Alternatively, it is the presence of a mental disorder that causes the SUD, e.g. when a person uses a substance to cope with anxiety and/or depressive symptoms. This last pathway is in line with the influential self-medication hypothesis (111). The third panel in the model illustrates that a common etiological variable underlies the comorbidity. In this case there is no direct causal relation between the disorders. The third variable could be common genetic factors that predispose to both types of disorders such as personality (112) or it could consist of environmental risk factors (106, 107).

Once present in an individual, both the SUD and the mental disorder can be maintained and promoted by interaction in a “vicious circle”. For example an individual may use alcohol to cope with depressive symptoms, while the physiological and psychological effects of the

alcohol use might accentuate depressed feelings in the long run, thus stimulating to more self-medication (109, 113).

Clinical impact of co-occurring SUD and depression/anxiety

In general, co-occurring mental health problems in individuals with SUD have been associated with more severe substance use, higher rate of relapse and attrition from treatment, lower quality of life as well as poorer psychosocial functioning and increased risk of suicide (114-116). Although substance induced depression and anxiety might improve notably after sustained abstinence, primary symptoms will persist beyond detoxification (117). Symptoms of anxiety and depression, regardless of etiology, can decrease the individual´s ability to engage in treatment and to sustain abstinence. This should encourage the identification of such comorbidities at an early stage (117). Further, a number of studies have shown that patients with concurrent mental health problems and SUD have increased suicide risk (118), elevated risk of being a victim of crime (119) and poorer prognosis (114, 120, 121). Prospective studies have reported depression and anxiety to have negative predictive effects on treatment outcome for heroin users (122).

1.5.2 Attention Deficit Hyperactivity Disorder

Adults with Attention Deficit Hyperactivity Disorder (ADHD) are clearly overrepresented among treatment seeking SUD patients (123, 124). Relatively few studies of ADHD in OMT exist and they report prevalence rates of ADHD or ADHD symptoms in the range of 8%-31% (125-127). Individuals with opioid dependence and high ADHD symptom scores tend to report more severe dependence and more comorbid psychopathology, compared to those with low ADHD symptom scores (125-129).

ADHD is the diagnostic term for a neurobiological, heritable disorder characterized by persistent problems of inattention, hyperactivity and impulsivity (68). An overview over the core symptoms is presented in Figure 2.

Figure 2. Core symptoms of ADHD (130).

Attention problems	Quickly distracted, quickly bored Difficulty finishing things Switching from one activity to another Having no overview of main issues and side issues Poor ability to plan, organize and choose Inability to read for more than a short time, able to concentrate only if topic is very interesting Difficulty listening, taking in information Getting lost in details or being excessively accurate Postponing things endlessly Difficulty filling in forms, understanding instructions, remembering things Doubting Forgetfulness Often losing things Chaotic Temporary overconcentration or hyper focus
Hyperactivity	Difficulty sitting still Always busy Constantly having to go and pick something up A feeling of inner restlessness Fidgeting Inability to relax peacefully Excessive talking
Impulsivity	Blurting things out Interrupting others Impatience Acting without thinking (spending too much, gambling, stealing, impulsive binges, etc.) Impulsively starting or leaving relationships and jobs

Although long considered a disorder of childhood, studies in the last decades have demonstrated that ADHD persists into adulthood in at least 50% of childhood cases (131, 132). Adults with ADHD can be easily distracted, have poor planning skills, poor organizational abilities and suffer from mood fluctuations. Many are restless, impulsive and thrill seeking. All in all this causes problems with functioning at school, work and in

relationships (130). There are indications that symptoms such as hyperactivity can change appearance or even wear off as people grow older (130, 131). However, for many individuals the negative impact of ADHD persists into late adulthood (133-135).

1.5.2.1 Aetiology of co-occurring SUD and ADHD

The aetiology of ADHD is largely unknown, but is likely to result from the contribution of multiple genetic and environmental factors (136, 137). It is suggested that the increased association of ADHD and SUD is the product of a developmental interaction with ADHD symptoms (e.g. impulsivity) and the consequences of ADHD (e.g. poor academic performance), creating an increased opportunity for the development of a SUD (138). Young adults with ADHD are at increased risk of several adverse outcomes through the transition from adolescence into adulthood, such as leaving school prematurely and to engage in criminal activity (139). Also, having ADHD increases the risk of early onset of substance abuse (140).

1.5.2.2 Treatment of ADHD in OMT

The central stimulant formulation methylphenidate is the first choice for pharmacological treatment of ADHD for adults, with documented efficacy from a number of studies (141). However, there are several concerns about the safety and utility for individuals with any SUD, including those who receive OMT medication. Research results are mixed but suggest less efficacy for individuals with SUD (138, 142), including those in OMT (143-145). National guidelines regulate treatment with central stimulants for patients in OMT in a number of countries due to concern of combining these medications with strong opioids, thus restricting access to central stimulant treatment (88, 144, 145). Until 2016, it was prohibited to prescribe central stimulants to patients in OMT in Norway (without special permission) because both medications are registered as narcotics. This practice was changed with the new national guidelines for the assessment and treatment of ADHD (146). According to these guidelines treatment with central stimulants for patients with ADHD in OMT is now possible, though it should be administered by the specialist health services and under strict surveillance due to the abuse potential and risks of diversion of the medications (146). Recent studies have shown positive outcomes of cognitive behavioural therapy (CBT) in adults with ADHD but without SUD (147), though this has not been sufficiently studied in patients with both conditions (148). However, the shared genetic profile of SUD and ADHD

and their functional consequences suggest that integrated treatment of SUD and ADHD with CBT may improve treatment outcomes (149).

In summary, previous research on patients with SUD has documented high rates of mental health problems such as anxiety and depression. Recent studies have also reported a high prevalence of ADHD in these patients, though methodological challenges are present and results difficult to interpret. For patients in OMT, research is more limited and inconclusive, particularly when it comes to ADHD. While mental health problems are likely to present a substantial challenge in OMT, these comorbidities remain insufficiently addressed in clinical practice. Investigation of characteristics and correlates may broaden our understanding of these comorbidities.

2. AIMS

The overarching aim of the thesis was to gain more knowledge about prevalence and characteristics associated with mental distress and ADHD among men and women entering opioid maintenance treatment in Norway.

The specific aims were:

1. To investigate factors related to the prevalence and development of self-reported mental distress during the first year of OMT (papers I and III)

2. To investigate the prevalence and impact of self-reported ADHD symptoms in OMT patients (papers II and III)

3. To explore whether treatment with central stimulants is a viable option for patients in OMT with ADHD (Paper IV)

3. MATERIAL AND METHODS

This study was based on two different samples from two settings: one prospective, observational study (papers I, II and III); and one clinical, naturalistic study at Oslo University Hospital (paper IV).

3.1 MATERIAL

3.1.1 STUDY DESIGN FOR PAPERS I, II AND III

Paper I-III comprised data from the NorComt (Norwegian Cohort of Patients in Opioid Maintenance Treatment and Other Substance Treatment) study. Paper I used data from the whole sample, while papers II and III used data from a subset with OMT patients only.

The NorComt study was established in 2012 and funded by the Norwegian Centre for Addiction Research (SERAF). It was organized as a project group, consisting of two project leaders and from 2013/14 three PhD students. The study aimed to increase knowledge of factors impacting treatment adherence and outcomes, for a diverse patient population, and was developed from an earlier cost-effectiveness study with similarly sized national sample (30, 150). Extensive information has been collected in the study, included on treatment interruptions and treatment goals, exposure to criminality, physical and mental health issues, pets, nutrition and quality of life. NorComt involved 21 treatment facilities across Norway; 14 were OMT outpatient centers and seven were inpatient treatment centers. The patients who entered the inpatient treatment facilities did with very few exceptions not receive OMT (96.2% of inpatients did not receive OMT at baseline data collection). Data collection began in late 2012 and concluded in 2015. Baseline data collection point (T0) was at inclusion to treatment and data collection at follow-up (T1) was approximately one year later.

Project leaders designed the study in collaboration with clinicians and user organisations. They recruited the collaborating treatment centres and implemented the study. Invitations to join the study were distributed to all OMT facilities in the country (15 at the time), of which one rejected to participate. The other group of SUD inpatient treatment facilities was selected based on geographical availability (mainly near bigger towns and cities in the southern part of the country). Another selection criterion was that they accommodated few

or none OMT patients. There were no financial gains or expenses related to participation, but the facilities committed themselves to consider all new patients for eligibility and conduct the interviews accordingly. Clinicians were expected to log reasons for non-participation and keep the research group updated.

The 14 participating OMT facilities were outpatient centres. They covered all four administrative health regions of Norway, from the OMT facilities in heavy populated cities (such as Oslo and Bergen) to widespread and scarcely populated areas (such as OMT region North which was responsible for all OMT in Northern Norway).

Inpatient treatment in Norway is usually provided for 3-12 months, with aftercare available for 1-3 years after completion. The participating in-patients facilities were located in the southern part of Norway. Problematic use of illicit substances was main reason for referral. The in-patient facilities had no other specific intake criteria, however two did not accept OMT medication, one accepted only women, two had a lower age limit of 23 years and two had an upper age limit of respectively 28 and 35 years. They mostly based themselves on methods from therapeutic community models. The centres included were Veksthuset Rogaland, Veksthuset Molde, Samtun Sauherrad, Arken, Sollia, Renåvangen and Phoenix House Haga.

To prepare for the data collection, the project leaders had established a formal agreement with the management at each treatment facility who in return appointed 1-2 clinicians as key contacts. The research group trained facility staff through a series of in-person trainings and training guides and created a website (www.norcomt.no) where instructions, interview guides, information about the project and all contact information to participating facilities could be found, in addition to status updates from the study. The website additionally contained a section where guidance to frequently asked questions (e.g. “Should I register OMT medication under Substance use and medication profile?”) was maintained by the research group.

Data collection at baseline (T0)

The only inclusion criterion at T0 was admittance into a SUD treatment facility within the past twelve weeks, regardless of primary substance type(s). The median time from

treatment-start to interview was 18 days (OMT: 19 days, other SUD in-patient treatment: 17 days).

Trained treatment staff provided information about the study to new patients, obtained informed, written consent and conducted the structured interviews. The participants were informed that non-participation or later withdrawal would have no consequences for treatment. The questionnaire at T0 (Appendix 1) collected information from a wide variety of life domains; sociodemographic information, current and previous substance use, somatic and psychological health, exposure to criminality, social networks and health related behaviors such as exercise and nutrition. The interviews took an average of 90 minutes to complete, longer for some patients who e.g. struggled with anxiety. We aimed at interviews to be completed within six weeks after treatment initiation; however interviews completed within 12 weeks were accepted. The average time between treatment initiation and interview was three weeks. At the end of the interview, participants could consent to being contacted by the research group after one year for a follow-up interview. Those who consented provided their contact information (telephone/e-mail/postal address). Most participants also provided contact-information of one or more family-members, and a contact at social services or similar. The interview forms were either scanned into a database with a manual check of the software interpretation of the forms, or manually punched into the database. The data-files were cleaned and checked and the original interview forms were consulted for responses that were flagged as incoherent.

Data collection at follow-up (T1)

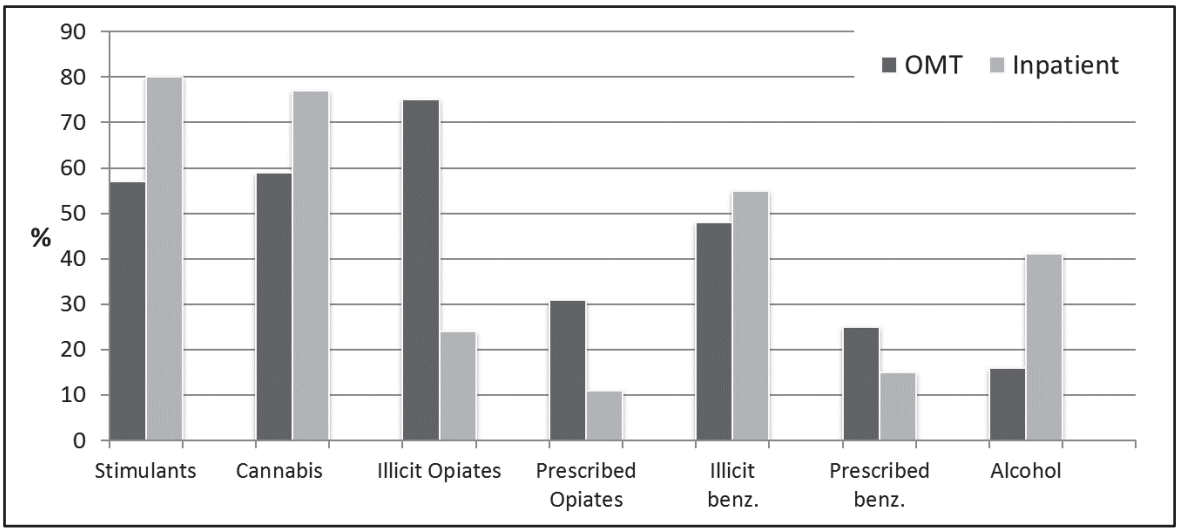
The second data collection point (T1) started one year after completion of the T0 interview, in 2013. The T1 interviews concluded in 2015. Staff from the NorComt research group; the three doctoral students and two trained interviewers conducted these interviews. Making contact with participants was sometimes easy, but mostly very time consuming. Interviewers therefor began this process 11 months after the T0 interview with a limit of six months to schedule the second interview. The T1 interview was conducted 11-18 months after T0 (median 14.5 months). The T1 questionnaire (Appendix 2) was similar to the one at T0 (Appendix 1) with a few additions such as the Adult ADHD Self-Report Scale (ASRS), questions pertaining evaluation of treatment and self-assessed changes post treatment.

The participants chose the location of the interview and were met there by the interviewer, frequently in their homes or in a café. We refunded travel expenses and gave all participants a gift voucher of NOK 300 (30 Euros) to compensate for their time. If a participant missed an interview, we tried to reschedule and were flexible in terms of time and location. Nineteen interviews were conducted by telephone. In these instances, participants were asked to have pen and paper at hand, and instructed to draw the Likert style response options for scales where the visual presentation of the response options may influence the participant's choices.

3.1.2 STUDY SAMPLE

Of 1415 patients entering treatment during the data collection, 670 were not considered for eligibility, mainly due to logistical difficulties at the facilities (Figure 4). Of the 745 patients who were considered eligible 548 (74%) enrolled, while 129 declined, 45 did not meet for interview appointments and 23 were not interviewed for other reasons. The mean age at treatment inclusion was 34 years. Two hundred and eighty three participants were outpatient OMT patients and 265 were provided inpatient treatment. Ninety-six percent of the participants admitted to the inpatient facilities were non-OMT. As shown in Figure 3, there were some differences in substance use pattern between the OMT and inpatient groups, although both groups reported use of a number of different substances.

Figure 3. Types of substances used at baseline (T0) for participants entering OMT and inpatient treatment (n=548).

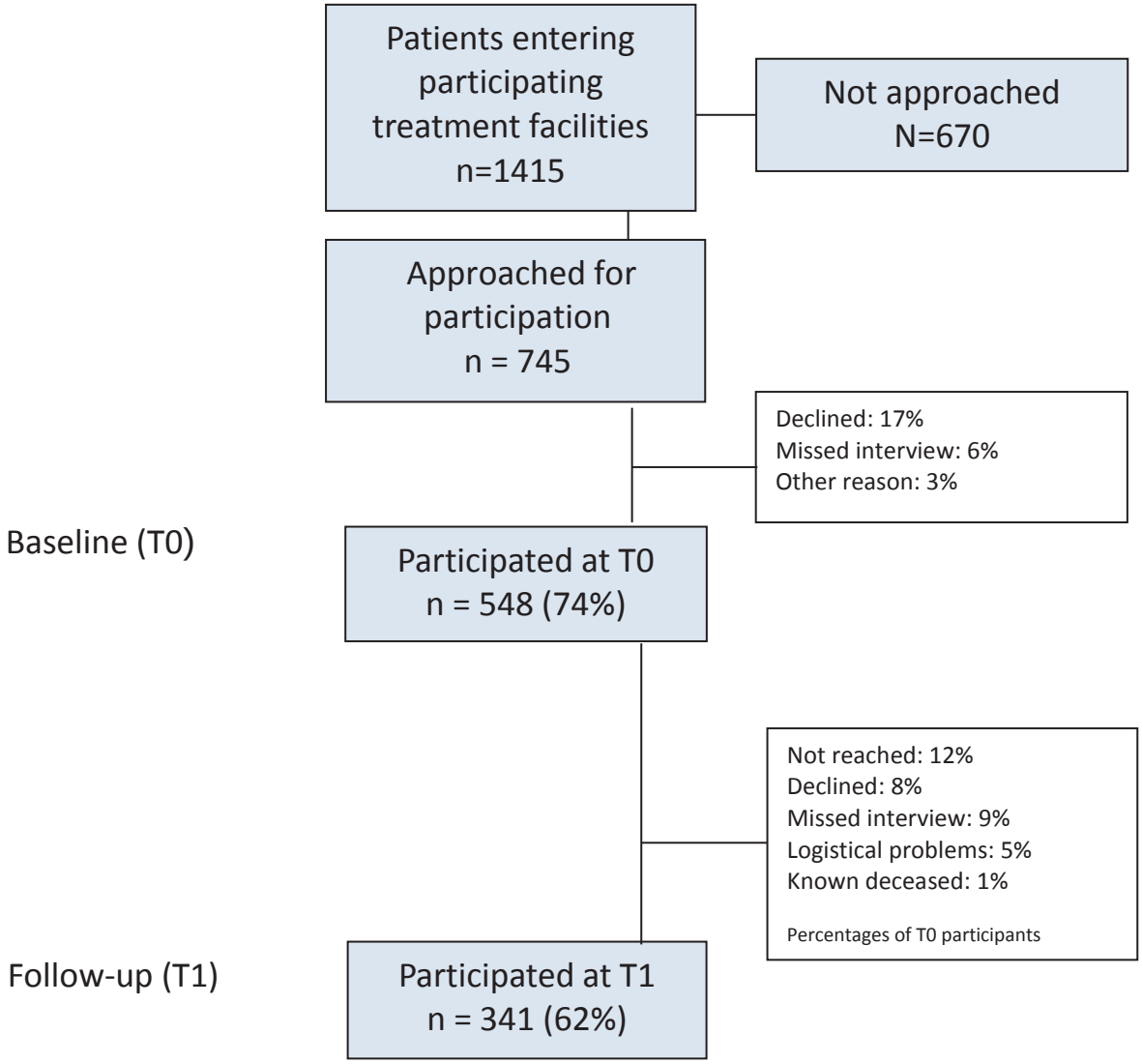


Three hundred and forty one (62%) contributed data at T1. We conducted t-tests and chi-square tests to compare the baseline responses of the participants that were included at T1 with those who were lost to follow-up. We did not detect differences in gender, substance use or treatment characteristics between participants who were interviewed and those who were lost to follow-up. Neither did we find differences in self-reported mental distress or self-control scores. In addition, we logged general life situation evaluations for 84 of the 207 who were lost to follow-up. Evaluations were based on information given by participants themselves or the given contacts. These were positive for 48% and negative for 52%.

Table 1. The study samples in Papers I-III (2012-2015)

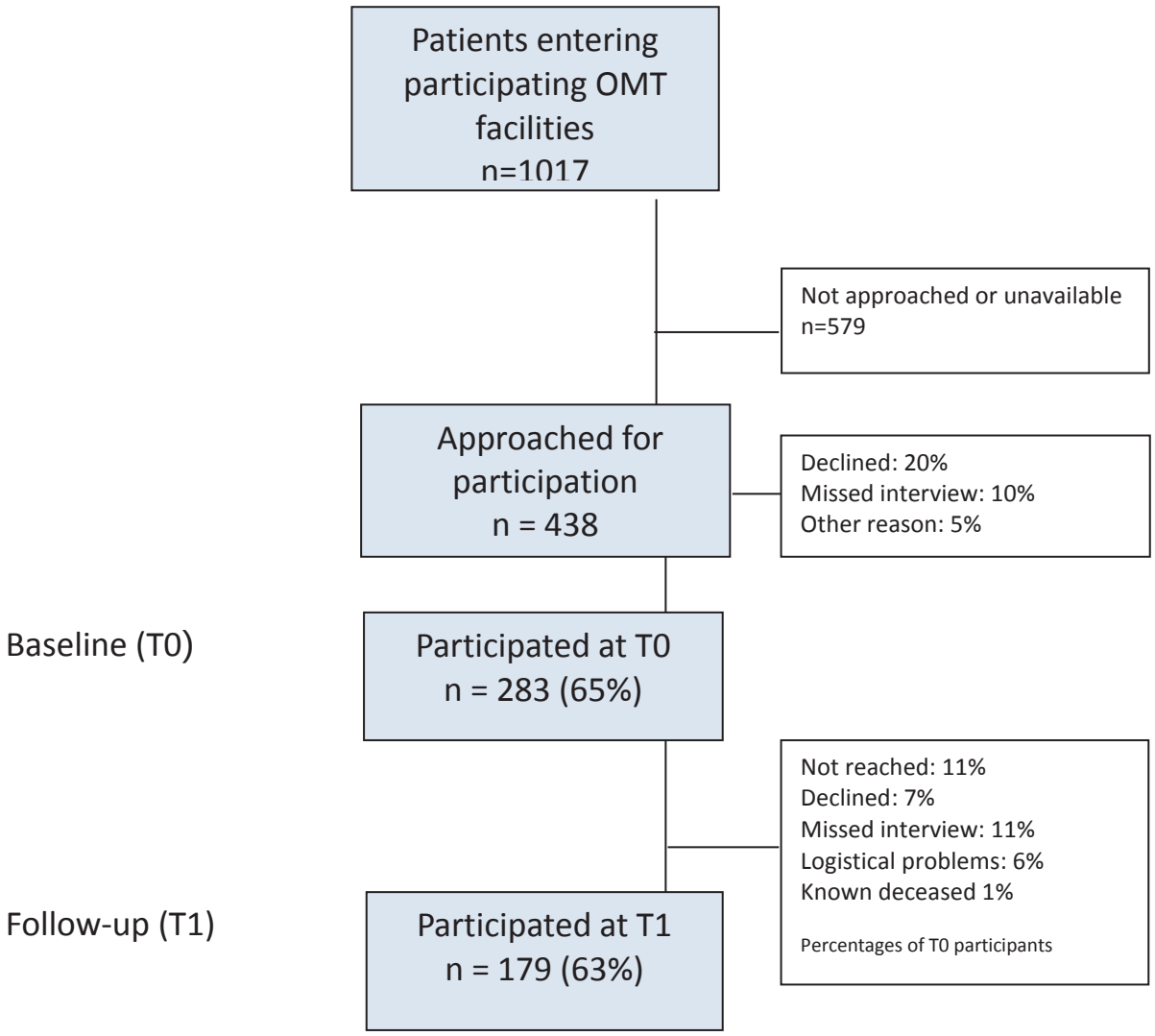
	Paper I	**Paper II**	**Paper III**
N	**548**	**175**	**179**
Mean age (SD)	**33.7 (9.9)**	**35.3 (8.7)**	**36.5 (8.7)**
Men, n (%)	**393 (72.0)**	**128 (73.1)**	**130 (72.6)**
Observation period	**T0**	**T0, T1**	**T0 - T1**

Figure 4. NorComt participant flow chart showing reasons for participation and non-participation in the study at T0 and T1 (paper I).



Paper I reported on the entire study population (n=548), stratified by treatment type at T0 (OMT or inpatient treatment).

Figure 5. NorComt participant flow chart for a subset of study participants entering OMT, showing reasons for participation and non-participation at T0 and T1 (papers II and III).



3.1.3 Study design for paper IV

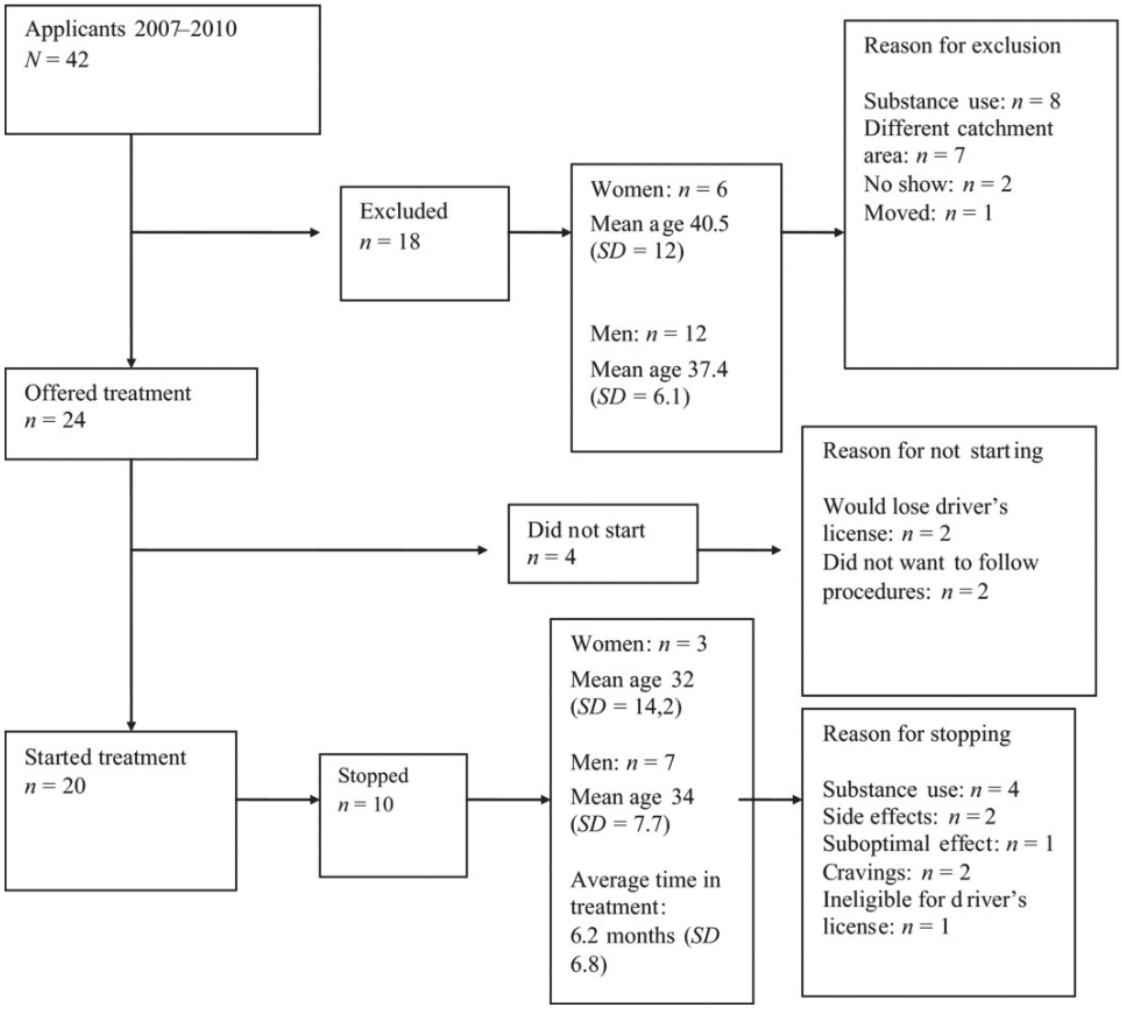
The fourth paper comprised data from a naturalistic study on pharmacological ADHD treatment for OMT patients, collected from a trial project in the outpatient SUD department at Oslo University Hospital from 2007 through 2010.

As mentioned in the Introduction section of this thesis, Norwegian Health Authorities until 2016 prohibited the prescribing of central stimulants to individuals in OMT. However, following increasing demand from patients, clinicians and patient organizations, from the early 2000's the government had licensed a number of trial project groups in SUD treatment units to initiate this treatment. Our project in Oslo University Hospital was one of these projects. The project group comprised of a psychiatrist, a specialized nurse and me as project leader and specialized psychologist. The project group received and considered applications, initiated and evaluated pharmacological treatment. We followed the patients very closely and additionally offered counseling to the patient's main therapists and community health services.

3.1.4 Study sample

Patients were recruited from departments in Oslo University Hospital, from general practitioners, other outpatient clinics and community health center and from treatment centers outside the hospital. Patients stabilized in OMT and with a confirmed adult ADHD diagnosis and no more than occasional substance use, stable housing and satisfactory health status were considered for eligibility. Patients with severe mental disorders, such as ongoing psychosis, and somatic or neurological conditions requiring treatment were not included. Out of 42 patients considered for eligibility, 18 were not included mainly due to extensive substance use and belonging to a different catchment area than Oslo. Of the 24 who were eligible, 20 started the combined treatment, and 10 stayed in the program. The mean age was 34.2 years. 15 (75%) were men.

Figure 6. Distribution of patients in Opioid maintenance treatment who applied for central stimulant medication, 2007–2010 (n = 42).



3.2 METHODS

3.2.1 MEASUREMENTS PAPERS I-III

For papers I-III we used data obtained from the interview protocol developed for the NorComt study (Appendices I and II). This included sociodemographic information and measures of substance- and medication use, self-control, mental health, ADHD symptoms, criminal activity and social network. All variables were included at both T0 and T1, with the exception of ASRS to measure ADHD symptoms, which was added at T1.

The sociodemographic information was based on the National Patient Registry questionnaire (151), a standard intake form used in Substance Treatment Units in Norwegian hospitals (Appendices I and II). Similar questions are found in the EuropASI, a validated version of the Dependence Severity Index adapted for European use (152).

The defined time-periods participants were asked to base their response upon varied between the measures. At T0, for measures that asked about the past 4 weeks or 6 months before treatment, the interviewers were instructed to exclude stays in "controlled environments" such as prison or hospital immediately prior to the index-treatment. If a patient had spent two weeks in a detoxification unit before starting the index treatment, he would be asked about the time-period prior to this detoxification.

Use of specific substances. Participants were categorized as users of a substance if they listed it among their four most frequently used in the past six months. These questions were adopted from Norwegian Patient Registry (151). Combined substances that were pharmacologically related were organized into the following categories: opioids (heroin, illegally obtained buprenorphine, methadone and other opioids) and stimulants (amphetamines, cocaine, other stimulants, crack cocaine). The other categories were prescribed opioids, prescribed benzodiazepines, illicit benzodiazepines, cannabis and alcohol. Participants were also asked whether they smoked tobacco. Participants could be included in up to four different substance categories, which allowed statistical adjustment for polysubstance use.

Number of substances was reported for the last six months and *Intravenous substance use in the last 6 months* (yes/no) at T0 and T1 was based on the intake-method for the four most used substances in the last 6 months.

Severity of Dependence Scale. As a measure of level of dependence, the Severity of Dependence Scale (SDS), a validated five-item scale, was used (153). The scale ranges from 0 to 15 (low to high), and is devised to measure dependence of specific substances, primarily for research purposes. Because our focus was not on one specific substance, we rephrased the items to reflect general dependence (e.g. "Did you think your use of substances was out of control?" instead of e.g. "Did you think your use of amphetamines was out of control?"). Responses were given on a 4-point Likert scale. We used the SDS as a continuous measure.

Hopkin's Symptom Checklist. To collect information about mental distress, we used Hopkin's Symptom Checklist, 25 item version (HSCL-25) (154). HSCL-25 is a self-administered symptom inventory investigating symptoms of depression, anxiety and somatization (155). Respondents indicate whether they have experienced different problems during the past week on a 5-point Likert scale ranging from 0 ("not at all") to 4 ("extremely"). The term Global Symptom Index (GSI) was used to describe the mean total sum score. We used 1.0 (mean score) as clinical cut-off point in accordance with previous studies (30, 62).

Brief Self-Control Scale. Self-control was assessed with the Brief Self-Control Scale (BSCS), a validated 13-item scale (156). The scale ranges from 13 to 65 (low to high self-control), and consists of statements (e.g. "I refuse things that are bad for me"). Responses were given on a 5-point Likert scale ranging from 1 ("not at all") to 5 ("very much"), assessing a tendency toward impulsivity ("I do certain things that are bad for me, if they are fun") and self-discipline ("I am able to work effectively toward long-term goals") as components of self-control. A higher score indicated greater self-control. We used the BSCS as a continuous measure.

Adult ADHD Self-Report Scale. Collection of ADHD symptoms was added at follow-up interviews and used in papers II and III. We used the 6-item version of the Adult ADHD Self-Report Scale (ASRS), an instrument developed in collaboration with the World Health Organization (157). We calculated ASRS scores with a clinical cut-off score of 14 (scores added) (threshold for likely ADHD).

Criminality. We used one variable to collect information about exposure to violence ("Have you been exposed to any violence for the past six months?") and offending ("Have you

committed any crime in the past six months?"), excluding possession and use of illicit substances.

Mental health care. Participants were asked how many months of mental health care (as in-patients or out-patients) they had previously received in their life-time. The variable was dichotomized to allow comparison of participants who had previously received a minimum of 3 months of treatment with those who had received less or no treatment.

Social network. We dichotomized one variable from the Europ-ASI to collect information about social network (*With whom do you spend most of your free time?)* into spending most time with abstinent or substance using network (including both friends and family).

3.2.2 Measurements paper IV

In the fourth paper, data was collected as part of a clinical trial. Before entering treatment thorough information concerning physical and mental health was collected and evaluated to decide whether the patient should be offered inclusion in the project. If this information was inconclusive, we requested more information such as a neuropsychological examination and/or meetings with other health professionals with knowledge of the patient and/or with family members. Patients who were considered eligible were initially monitored for any medical issues and after starting with the medication for any adverse reactions with blood samples and other physical examinations. They also provided regular urine samples for information regarding substance abuse.

We collected information about ADHD symptoms using the ASRS (18-item version) (158) at the following time points: before escalation of ADHD medication, after patients were stabilized on the central stimulant medication (roughly at 6-8 weeks), again at 12 weeks, 24 weeks and 2 years. The 18-version scores range from 0-72 and a score of 24 or greater indicates high likelihood of ADHD. In this trial we used the ASRS mainly to monitor symptom change after escalation of ADHD medication.

3.2.3 Missing data

The NorComt study had low levels of missing data, probably due to the interviews being conducted face to face and the resources invested in training the interviewers. For the SDS, the individual mean was imputed when only one item was missing, while those with more

than one missing were excluded from the analysis. For the HSCL-25, interviews with up to five missing items were imputed using imputation of the individual mean, while those with more than five missing items were excluded from the analysis in accordance with other studies (159). For the BSCS, the individual mean was imputed for interviews with up to two missing items, while those with more than two missing items were excluded from the analysis. For interviews with one missing item on the ASRS the individual mean was imputed, while interviews with more than one missing item were excluded from the analysis (160).

Collection of data was quite demanding in the clinical trial (paper IV), even though it was a small study. Patients frequently forgot appointments despite reminders, resulting in missing data. Data were analysed using two strategies; using data only from those who had responded at each time point (per protocol) and imputing the last observation and carrying it forward ("Intention to treat").

3.2.4 Statistical analysis

Independent variables were selected based on previous research, clinical relevance and on the bivariate analyses. The IBM Statistical package for Social Sciences (SPSS) versions 20, 22 and 24 were used for all statistical analysis. Count data was presented as numbers (%) and continuous data as median or means (standard deviations). For comparison of two groups we used Student's t-test groups for continuous variables and Pearson's Chi-Square test or Fischer's exact test for categorical variables. For the comparison of three groups, One-Way ANOVA was applied for continuous variables and Pearson's Chi-Square test for categorical variables. The level for statistical significance was 5%. The relationships between independent and dependent variables were examined using regression analysis generating relative risk ratios (RRR) for multinomial regression analysis (paper I) and odds ratios (OR) for binary logistic regression analysis (paper II). Linear regression generating Beta (β) was used in paper III. In paper IV pairwise t-tests were conducted to determine whether follow-up ASRS scores differed significantly from baseline.

In paper III GSI change was used as the outcome variable. The change was calculated as GSI score measured at baseline minus the GSI score measured at follow-up. The same was done to calculate SDS change. A positive change score thus indicated improvement, while a

negative score indicated getting worse. The correlation between change in GSI and SDS was examined using Pearson's Correlation.

3.2.5 Ethical approvals

Papers I-III: The NorComt study was approved by the Regional Ethics Committee for Medical Research (ref: 2012/1131/REK). Participation in the study was voluntary and it was made clear that declining participation would not affect the treatment provided.

Paper IV: This was a clinical trial that was reviewed by the Regional Ethics Committee for Medical Research (REK) and deemed to be exempt from further review. The study was conducted in accordance with the Declaration of Helsinki. Participation in the study was voluntary and it was made clear that declining participation would not affect the original treatment provided (OMT).

4. RESULTS

The results of the four papers that correspond with the three aims of the study are summarized in the following section.

4.1 AIM 1: TO INVESTIGATE FACTORS RELATED TO PREVALENCE AND DEVELOPMENT OF SELF-REPORTED MENTAL DISTRESS IN INDIVIDUALS ENTERING OMT (PAPERS I AND III)

As part of the NorComt study, 283 participants were interviewed when entering outpatient OMT (71.4 % men). Level of mental distress was high at baseline with 149 (54.0 %) scoring above clinical cut-off point on the Global Symptom Index (GSI) of the HSCL-25.

In order not to "hide" effects on mental distress due to clustering around the cut-off and also to pick up on more dynamic effects, the sample was divided into three strategic same-size groups based on the participants' GSI scores. Those with high GSI had more frequent use of benzodiazepines (p=0.013) and alcohol (p=0.050), used a higher number of substances (p<0.001) and had higher Severity of dependence scores (p<0.001). Further, lower self-control, having been subjected to violence and having received mental health care throughout life (all p<0.001) were associated with reporting high GSI. Regression analysis confirmed that use of illicit benzodiazepines (aRRR 2.79; 1.05-7.41), prescribed benzodiazepines (aRRR) 2.87; 95% CI 1.05-7.80), alcohol (aRRR 3.41; 1.11-10.42) and a higher number of substances (aRRR 1.41; 1.14-1.73) increased the likelihood of reporting high GSI, while use of stimulants was associated with low GSI (aRRR 0.23; 0.09-0.56). Further, higher severity of dependence (aRRR 1.15; 1.03-1.29) increased the risk of reporting medium GSI, while higher self-control scores decreased the likelihood of reporting high GSI (aRRR 0.88; 0.84-0.92).

After one year in treatment, 100 (57.1 %) participants scored above clinical cut-off on HSCL-25 (mean GSI=1.30, SD=0.87 at follow-up versus mean GSI=1.25, SD=0.86 at baseline), indicating no change on a group level. When categorized, eighty-seven patients (50.3%) had no change in GSI between baseline and follow-up, 47 (27.2%) had worsening in GSI, while 39 (22.5%) had an improvement in GSI. Thirty-nine participants (22.3%) reported being abstinent from substances at follow up. The abstainers had significantly lower mental distress compared to those who continued to use substances (p=0.005). In the final multivariate model, illicit benzodiazepines at baseline and change in Severity of dependence

remained significant (p=0.020 and p=0.002, respectively). Change in GSI scores was associated with change in severity of dependence; those with negative GSI change also had a negative SDS change.

4.2 Aim 2: To investigate the prevalence and impact of ADHD symptoms in OMT patients (papers II and III)

Overall 57 (33%) of the participants reported ADHD symptoms above clinical cut-off (14 points sum score) at follow-up interview with no gender differences. Patients who scored above clinical cut-off were younger (p<0.001) and they more frequently reported use of stimulants (p<0.001), illicit benzodiazepines (p=0.042) and cannabis (p=0.038). The number of different substances used was higher for the participants who scored above clinical ASRS cut-off (p<0.001) and the same was true for SDS (p=0.019). Participants with an ASRS score above clinical cut-off had higher mental distress, measured with HSCL-25, compared to those who scored below cut-off (p=0.009). Using an alternative cut-off point of 4 (weighted scores), the number of patients who scored above cut-off point increased to 68 (39%). The same variables remained significant compared to the original cut-off point of 14. We also performed the analysis with ASRS as a continuous measure using linear regression, confirming previous results (paper II).

All variables significantly related to the outcome variable ASRS above vs. below clinical cut-off score in the unadjusted analysis were included in the multivariate analysis, in addition to gender. Use of stimulants (OR 2.55; 95% CI 1.13-5.76) and a higher GSI score (OR 1.61; 95% CI 1.03-2.50) at intake to treatment were associated with scores above clinical cut-off point on the ASRS among the OMT-patients (paper II).

Mental distress scores were higher for patients with ASRS scores above cut-off at one year follow-up, compared to those who scored below cut-off (paper III). The effect of ASRS on change in mental distress was only significant in the univariate analysis. When adjusting for change in SDS, the effect was statistically insignificant, indicating an association between ASRS and change in SDS. Further analysis showed that mental distress in fact increased for those with ASRS scores above cut-off during the first year of treatment (p<0.05), different from those who scored below cut-off. When investigating SDS scores at baseline and follow-up with ASRS scores at follow-up, we found that those who scored above clinical cut-off on

the ASRS reported significantly higher SDS scores at baseline and follow-up compared to those who scored below. SDS scores decreased significantly between baseline and follow-up ($p<0.05$) for both patients with ASRS scores above and below cut-off (paper III). Fewer participants with scores above ASRS cut-off reported abstinence at follow-up (10.5% versus 24.8% of those scoring below cut-off) (data not shown in the papers).

4.3 Aim 3: To explore whether treatment with central stimulants is a viable option for patients in OMT with ADHD (Paper IV)

Among 42 patients initially offered the combined treatment, 24 were actually eligible, 20 started the combined treatment, and 10 stayed in the program. We were not able to identify a single major cause of treatment dropout. Patients reported significantly fewer symptoms of ADHD at the 6- to 8-week point. At baseline, mean ASRS score was 51.8 (SD=13.1). This was reduced significantly by the next point of measurement 6 to 8 weeks later. When analysed using an intention to treat model (last observation carried forward), the mean ASRS score was reduced to 42.7 (SD = 13.2), a mean reduction of 9.1 points ($p <0 .01$). When analysed per protocol (only those with data at all time points), the score was reduced to 39.2 (SD = 13.7), a mean reduction of 13.5 points ($p < 0.001$). In both analyses, the scores at follow-up still remained above the threshold for likely ADHD (24 or greater), suggesting persistent functional impairment. Neither severe complications nor increase in substance abuse were observed during treatment with central stimulants. The patients who completed did not report craving or increased substance use.

5. Discussion

5.1 Methodological considerations

Both systematic and random errors can distort the accuracy of research results (161). A bias refers to systematic errors that may occur at all stages in a research project e.g. in data collection or analysis (161). Random errors on the other hand, are due to chance and would typically not skew the data in a certain direction (162). While the effects of random errors are reduced with the size of the study, are systematic errors not affected by this (161). In this section I will discuss theoretical and practical issues that may affect the internal and external validity of the results presented in the thesis, in addition to ethical aspects.

5.1.2 Study designs

The NorComt study was a naturalistic and observational study with no interaction with participants beyond the interviews. Neither did the study influence treatment nor in other ways manipulate the circumstances. Observations were made exclusively at two time points (T0 and T1). Papers I and II had a cross-sectional design. Paper I used only T0 data. Paper II used one variable from T1 (ADHD symptoms measured with the ASRS) as the dependent variable and all independent variables from T0. With data from one time point only, this study design was suitable for estimating prevalence and associations between variables without inferring causation. Paper III used a longitudinal design, allowing for more interpretations of the associations.

Paper IV was a clinical trial where we followed a small group of patients over time with multiple interaction points and investigated their development with both clinical observations and a screening tool. Due to the design and sample size, we analysed the data on a descriptive level.

While traditionally considered second to randomized research designs, observational studies can have important advantages such as providing data closer to reality than experimental settings. The nature of experiments (such as the complexity of the design and the resources demanded) will often lead to limitations in the number of participants that can enrol and the length of the study – these limitations do not apply equally to observational studies.

Obviously, there are important challenges for the non-experimental designs such as the lack of a control group for intervention comparison and lack of randomization.

5.1.3 Internal validity

Internal validity refers to the study's ability to measure what it set out to do. The main concerns for internal validity are bias (161). In the following section, internal validity is discussed with regard to selection bias, information bias and confounding.

5.1.4 Selection bias

Selection bias is a type of systematic error that arises from the selection of participants in a study, particularly when the participants are not chosen randomly (161). Thus, selection bias refers to procedures for selection of participants and factors that influence study participation. If there is no randomization in the selection process, there is a risk that the study population differs from the target population and therefore is not representative. This could pose a threat to the internal validity (161).

Papers I-III

For the NorComt study, it is relevant to consider how the facilities were selected because it is possible that these facilities had characteristics that differed from the ones who declined, e.g. interest in research or the topics of the NorComt study. However, only one OMT center and one inpatient facility declined the invitation to participate in the study. The risk of selection bias was probably not severe at this level.

The selection of participants within the treatment facilities could be of more concern to internal validity. While entering a participating treatment facility was the only inclusion criteria for NorComt, the patients had already fulfilled two important criteria to get admitted into the facilities; their treatment application had been accepted by the health authorities implying both severe SUD and that they were likely to benefit from the treatment (163). According to the NorComt protocol, all patients who entered the facilities should be considered for eligibility by treatment staff. However, 670 (47%) of the 1415 patients who entered treatment at T0 were not asked about study participation, mainly because of logistical problems (lack of capacity to screen in time) (Figure 4). For OMT the share of unapproached patients was higher than for the inpatients; 579 (57%) out of 1017 new OMT

patients were not approached for participation. It is understandable that it was more difficult to conduct research interviews with outpatients (OMT) than inpatients and that this is a likely explanation for the difference in numbers of patients not approached or unavailable. Logistical challenges (46%), unknown reasons (38%) and mental health problems (7%) accounted for the most frequently reported reasons why OMT patients were not approached or unavailable for participation (Figure 5).

Selection bias could also arise from self-selection (161). We do not know whether the patients who agreed to participate differ from those who declined, from those who did not meet for the interview or those whose reasons are unknown. We also need to consider selection bias for the participants who completed the follow-up interview compared to those who did not. Our follow-up rate was 62% for the whole sample (63% for OMT) and even though this may be acceptable for this patient group, we could be looking at potential follow-up bias. We did however not detect differences between those who participated at T0 and those who participated at T1 in baseline variables relevant to the data used for papers I-III. Still, there is the possibility that other unmeasured events after T0 could have affected the participation at T1. We made an effort to collect information about the patients declining the T1 interview and were left with the impression that this group was heterogeneous. We obtained contact with 84 of the 207 individuals lost to follow-up or their contacts and asked them about their general life situation today. Of the 84 we talked to, 48% reported positive outcomes such as “I am working full time and I do not want to prioritize a second interview”. Fifty-two percent reported negative outcomes. It could pose a threat to internal validity if those lost to follow-up were in poorer situations than most of those followed up who reported improved conditions, e.g. less substance use. However, we must underline that these are not systematically collected data of high quality. Additionally, we lack information about 120 individuals whom we did not get in touch with for T1 and acknowledge the possibility that they could have reported more negative outcomes. However, our analysis of baseline characteristics reduces concern for a major selection bias.

<u>Paper IV:</u>

This study could be described as an open labelled non-controlled study. The aim of the study was to examine whether patients with ADHD in OMT would benefit from pharmacological treatment. As resources were lacking, we only considered for eligibility patients from the catchment area of Oslo University Hospital. We did not advertise the treatment, and the applicants would have heard of it by chance from their primary physician or other health- or social workers. Further we only considered those with no or occasional substance use. Excessive substance use was main reason for not being included (n=8) and for interruption of the treatment (n=4). This way of sampling is likely to be biased, both from self-selection and from the choices made by the investigators.

5.1.5 Investigator-derived information bias

Papers I-III

Information bias refers to systematic errors in data collection and may occur as a result of the interview setting, the self-report methods or the validity of measures (161).The NorComt study used self-report data from structured interviews. The social setting of an interview can be vulnerable to information bias, for instance the interviewer could elicit inaccurate information from the participant, not necessarily being conscious about doing so (164).

In the NorComt project the interview guide had been piloted before it was implemented. At T0, only clinicians who had received training were approved to conduct interviews. We checked every interview that was returned to us for missing information and oddities. For instance we soon realized that many of our interviewers had trouble understanding how to complete the substance use profile and were confused by the instructions (such as: should medications be included or not?). When we contacted the clinician who had signed the interview, he or she would redo the questions with the participant. We posted additional instructions on the website and sent an e-mail to all facilities to clarify this section of the interview. Overall we believe that our efforts with quality assurance and thorough training have reduced the risk of systematic information bias.

Paper IV

We based the inclusion in the study on an ADHD diagnosis made by other clinicians in a range of clinical settings. However, we did spend a lot of time reviewing the assessments

and in a number of cases we required further documentation. Still, we were not in full control of the standard of these assessments and we cannot exclude the possibility that some of them would have concluded differently if retested.

5.1.6 Validity of instruments

Measurement involves operationalization of theoretical constructs into defined variables such as self-control, mental distress and severity of dependence. Key indicators of the quality of a measuring instrument are their validity and reliability to reduce errors in the measurement process (165). Reliability refers to a measure's stability (test-retest) and internal consistency, the latter concerns how well items meant to measure the same concept, correlate. The degree to which the chosen measures accurately reflect the concepts is crucial for the validity of the research (165). In the following section I will discuss the instruments that were used in this study.

Substance use (papers I-III)

Participants were considered users of a substance if it was among their four most used in the last six months. This was taken from the National Patient Registry Form which is a routine questionnaire for patients entering SUD treatment in Norway (151). A downside is possibly the combined registration of substances and medications; in theory prescribed medications could take up places that otherwise would have been used to report substances used (almost or just) as frequently as the medications. However, we obtained detailed data on substance use and assume that the most important substances were identified for each participant. This way of operationalization also allowed us to control for polysubstance use which added valuable information to the analysis.

Hopkin's Symptom Checklist-25 (papers I-III)

The HSCL-25 is considered a reliable and valid measure of anxiety, somatization and depression (166) and has been widely used, including in SUD samples (30, 62). HSCL-25 has been criticized for not separating satisfactory between anxiety and depression (167), however these conditions frequently co-occur (168). In accordance with others (30, 62), we chose to report the total General Symptom Index (GSI) to describe the individual's self-reported mental distress. We used the 5-point Likert scale, also in accordance with other

studies on SUD samples (30, 169) which further enabled us to compare our results with a 10-year Norwegian follow-up study that used the same scale (30). A possible disadvantage with the 5-point scale is that the 4-point scale is more commonly used internationally. It has been argued that an odd number of response alternatives tend to result in neutral answers, while an even number would force the participant to take sides (170).

The Brief Self-Control Scale (paper I)

The Brief Self-Control Scale (156) is widely used in psychological research on self-control (171). In this study it was used in paper I to explore possible associations with mental distress. There is substantial support for the BSCS being useful in predicting a variety of behavioral outcomes in adolescents, students, apprentices, adults and substance using jail inmates (171, 172). The development of this 13-item scale (a shortened version of the original) was guided by the conception of trait self-control as "the self's capacity to override or change one's inner responses, as well as to interrupt undesired behavioral tendencies and to refrain from acting on them" (156, 171). However, the concept of self-control is operationalized different in different research studies, bringing about possible validity challenges (173, 174). One review to address this matter concluded that convergent validity was both sufficient and much stronger among self-control questionnaire measures compared to task measures of self-control, but to administer both types would be the optimal measurement strategy (175). Others have examined the psychometric properties of the BSCS specifically (171, 174, 176) and found that it reflects impulse control and self-discipline/restraint (174) with good content validity (176). One study also found that the shorter version is more accurate in the measuring of the constructs compared to the original version (174). Another recommendation to enhance validity is to use the total score of the BSCS as a broader unitary construct (171). We adhered to these recommendations in our use of the BSCS.

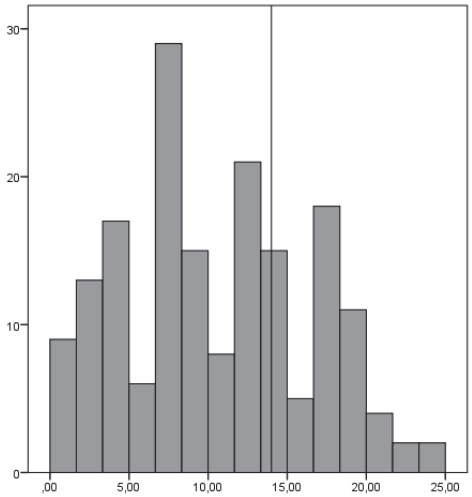
Adult ADHD Self-Report Scale (paper II-IV)

We used the ASRS 6-item screener in papers II and III, and the original version with 18 items in paper IV. The latter include questions about the frequency of all 18 DSM-IV Criterion A symptoms of adult ADHD (177, 178), but have largely been replaced by the ASRS screener. Both versions of the ASRS have shown good sensitivity and specificity in non-SUD adult

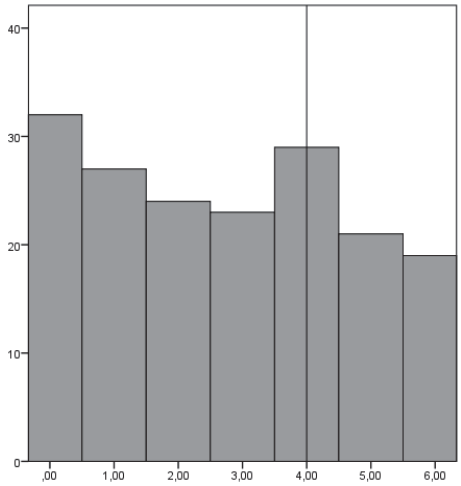
samples (177, 178). Besides the psychometric properties being as good as the original version, an important advantage with the 6- item version is how quick it is. However obvious this point may seem it is important for impatient individuals, also in terms of response accuracy. If the 6-item version of the ASRS had been validated previously, we would have used it for the data collection in paper IV.

The validity of the ASRS has been found to be reduced, though acceptable, in SUD samples including individuals with opioid dependence (179). Different cut-off scores have been used to optimize validity in different samples, even though research in this field remains limited and particularly among OMT patients. We used a continuous scoring method (scores summed) with 14 as the clinical cut-off point, suggested by developers of the ASRS as this improved both sensitivity and specificity (177). The large International ADHD in Substance Use Disorders Prevalence study (IASP) used an ASRS cut-off of 4 in their SUD sample, including subgroups of different preferred substances (179). This is a method where a score of 3 or more on items 1-3 gives one points and a score of 2 or more on items 4-6 gives one point. A sum score of 4 is considered a positive ADHD screen result. This cut-off point was also used by Young et al. (126) and Lugoboni et al. (125) in their studies of opioid dependent patients. Because choice of cut-off point is important as it may alter results, we performed an additional analysis with ASRS as a continuous measure in paper II, which did not change the results significantly. We further performed yet another analysis with the cut-off score of 4, which increased the prevalence of those scoring above ASRS cut-off from 33% to 39%, suggesting the cut-off point we used is more conservative. This point is also illustrated in Figure 7, where there seems to be a congestion of individuals just below the cut-off point of 14 in a), while this does not seem to be the case when using the cut-off point of 4 in b).

Figure 7. Distribution of ASRS scores with a cut-off of 14 (a) and 4 (b) in our sample of individuals in OMT (n=175).



a)



b)

To address concerns of substance influence, we analyzed current substance use at T1 in individuals screening above or below ASRS cut-off. At T1, those who scored below ASRS cut-off more frequently reported abstinence compared to those who scored above cut-off (61% vs. 39%). Further, the group who scored above cut-off reported significantly more frequent use of stimulants, benzodiazepines and cannabis than those who scored below cut-off. An ongoing discussion addresses the validity of measuring ADHD symptoms in individuals with SUD and in particular in those who have not reached stable abstinence (180). Substance use and abstinence can in different ways mimic symptoms of ADHD, e.g. being restless or poorly concentrated is hardly uncommon when under the influence of substances, thus making assessment of symptoms challenging. Because of this it is recommended that diagnostic assessment of ADHD should follow a period of abstinence to avoid false-positive ADHD diagnosis (180). Other studies have however found the ASRS to be a relative stable measure of ADHD among substance users (181). Further, the findings from a recent study suggests that evaluating ADHD in substance using individuals can be justifiable as symptom- and diagnostic stability remained high over time (182).

The ASRS could be a sensitive and useful screening tool in individuals with SUD (179, 183), though one should be aware that not only individuals who meet the full diagnostic criteria for ADHD will score above clinical cut-off score. However, the most important aim of a screening instrument is to detect ADHD in the maximum number of affected individuals and to miss the disorder in a minimum number. As such sensitivity is arguably a more important factor to consider than specificity in evaluating clinical utility (184). One could also argue that ASRS results are clinically relevant regardless of an ADHD diagnosis, as the difficulties reported are true for the person who reported them and should be addressed in clinical practice accordingly. The purpose of a screening instrument is to provide guidance regarding who should receive a diagnostic interview (185). It cannot be stressed enough that a screener is not a diagnostic tool. A screener is a list of symptoms that allows for a brief inquiry, thus raising consideration for more thorough assessment. While such screeners are time efficient and easily can be administered to all patients, reduced specificity can lead to over diagnosing and consequently inappropriate treatment (186). In the current study we do not discuss diagnosis based on results from screening tools.

Self-control and ADHD symptoms

The relationship between perceived self-control (as measured by the BSCS) and perceived ADHD symptoms (as measured by the ASRS) was investigated using Pearson product-moment correlation coefficient. Preliminary analysis was performed to ensure no violation of the assumptions of normality and linearity. There was a strong negative correlation between the two variables ($r=-0.56$, $p<0.001$) with high levels of ADHD symptoms associated with low levels of self-control. This has also been found in previous studies (160). On these grounds, we chose to leave out the BSCS measure from papers II and III.

Severity of Dependence Scale (papers I-III)

In three papers we used a revised version of the Severity of Dependence Scale (SDS). In its original form the SDS was devised to provide a short and easily administered scale to measure degree of psychological dependence experienced by users of different kinds of substances. The SDS consists of five items specifically concerned with the individual's feelings of impaired control and preoccupation over their own substance use (187). However,

evaluating the severity of only one substance may produce a misleading picture of dependence severity in a sample that uses multiple substances (188). Because we wanted it to provide information about the general severity of dependence, we changed the scale to reflect this. The SDS has in its original version shown good validity (187) and we believe it to provide useful information and supplement the other measures of substance use.

5.1.7 Participant-derived information bias

All papers in this study were based on self-report. A common source of error in self-reports is when a participant answers a question incorrectly based on memory. However, memory errors are only defined as bias if e.g. certain subgroups of patients are more likely to remember something inaccurately than others (161). Memory errors can have various reasons, e.g. cognitive impairment. Neuropsychological tests have shown that many adults with ADHD have impaired short term and long term memory that affect their ability to remember both childhood and adulthood symptoms (189). Memory errors are also relevant for individuals with SUD because current or past substance use can cause permanent or temporary cognitive impairment that also may affect memory (190).

Papers I-III

The NorComt interviews lasted between one and two hours. The interviewers would end the session or offer breaks if it became apparent that participants, for one reason or another, were not following the questions. Some participants found the length burdensome even with breaks and a few did not complete all of the items for this reason. Another aspect that took us by surprise was the lack of reading skills and proper glasses among quite a few of our participants. Early in the data collection we started to ask gently about this when starting the interview. This may seem trivial, but could be important when participants are expected to fill out self-report scales. Although we did not count systematically, many expressed reliefs about not having to answer questionnaires on their own and were happy to get assistance.

Memory errors may have impact on questions about lengthy time-periods or periods with intoxication. An alternative to only asking about frequencies of substance use for the past 6 months in NorComt, could have been to add an additional question about use in the past 24 hours or past three days which may have enhanced actual recall (165). A final aspect worth

consideration are the participant's views of "normality" and what a person is expected to endure which could be different from the views of the society in general. This may in turn influence the way he or she rate problems, such as the self-report of mental distress.

Paper IV

It was common that the participants in the clinical trial expressed difficulties with reporting their ADHD- symptoms when presented with the ASRS. Fortunately, we got additional information from others; either spouse, parents or health professionals where the patient resided. The importance of others in such demanding clinical work is an important lesson learned from this study. Using objective measures when evaluating this kind of treatment, such as the Conner's Continuous Performance Test (191), could also have contributed to reduce possible memory errors. The patients gave urine samples which provided information about substance use; this gave an additional indication of progression in terms of ADHD symptoms.

Social desirability bias (papers I-IV)

Social desirability bias occurs when participants with or without intent, to present themselves in the best possible light underreport unfavorable topics (192). In the NorComt study (papers I-III) OMT clinicians conducted the interviews at T0. One the one hand, knowing they were going to establish a therapeutic relationship with the interviewer could have facilitated the discussion and sharing of difficult experiences for the participants. On the other hand, it could cause the participants holding back information they feared staff member would disapprove of perhaps would licit negative sanctions. At T1 only the research group conducted interviews and the participant chose the location; these factors may have generated more trust and less motivation to withhold information towards a neutral part. Underreporting may be due to other factors than social desirability. For instance is underreporting ADHD symptoms not uncommon, but could reflect being accustomed to one's ADHD related characteristics ("this is just who I am") and having adapted behavior accordingly (193). This could also be the other way around, e.g. that one would exaggerate ADHD symptoms to increase the possibility of being included in the clinical trial. It is difficult to assess the effects of social desirability on our results; nonetheless we

have no reason to believe potential errors to be systematic in our sample. Additionally, substance using populations generally give reliable information in research settings (194).

5.1.8 Confounding

Confounding refers to a type of bias where a variable (typically unobserved) is associated with both the outcome variable and the independent variable. Confounding is an important issue in observational designs and may lead to an incorrect estimate of the association between the independent and the dependent variable (161).

Papers I-III

In general, the effect of confounding may be reduced through multivariate analyses (195), which were applied in papers I-II. In the previous section we discussed cognitive impairment as a source of potential memory error as this variable was not measured in the study. Being a frequently occurring challenge for individuals with severe SUD (190), cognitive impairment could represent a possible confounder of the relationship between self-control and mental distress. In paper I we investigated this relationship and we found that impaired self-control was associated with high levels of mental distress. Lower self-control and impaired cognitive functioning share characteristics such as poor planning capacities and impulsivity. Further, cognitive deficits can be present in individuals with higher degrees of mental distress, for example depression (196). If cognitive impairment was present at baseline, the observed association between self-control and mental distress may partly be a result of cognitive impairment and if so, we have overestimated the importance of self-control. Thus, information about cognitive functioning could have provided us with a more nuanced picture. However, these data would have been hard to obtain within the frames of this study as a cognitive assessment is time consuming to conduct and interpret.

In paper II and III we investigate associations between mental distress and ADHD symptoms. As previously discussed, cognitive impairment is frequently observed in adults with ADHD (189). Cognitive impairment could also represent a potential confounder in the relationship between mental distress and ADHD symptoms, as cognitive impairment could both mimic and exacerbate ADHD symptoms (e.g. poor planning skills, being poorly concentrated, memory problems) (189). Also other frequently occurring psychiatric conditions common

among SUD patients, such as conduct disorder (197) and post-traumatic stress disorder (PTSD) (198), could mimic ADHD symptoms. The possible presence of these conditions could pose challenges to the interpretation of symptoms measured by ASRS and thus confound the relationship between mental distress and ADHD.

As we cannot rule out all confounding factors in an observational design, their potential influence is uncertain. We did however have a data set which allowed us to adjust for a wide variety of factors and we do not believe that confounders had important influence on our results.

Paper IV

In paper IV we describe experiences from a clinical trial. The trial has a range of possible confounders. Despite that we followed the patients closely, this was outpatient treatment. We cannot rule out that factors beyond of our control confounded the relationship between the central stimulant medication and the ASRS scores, e.g. cognitive impairment, underreported use of substances or symptoms of anxiety; as discussed in the previous section these are all known to frequently occur in SUD patients.

5.1.9 External validity

External validity refers to whether the results of a study on a selected group can be generalized to the target population as a whole. The external validity of a study rests upon its internal validity (161).

Papers I-III

While selection bias could pose a threat to the internal and external validity of the study, we do not consider it severe. NorComt enrolled a high number of geographically widespread patients without any exclusion criteria to ensure representability.

Concerning the subset of OMT patients, we included all but one OMT facility in Norway at the time, which should strengthen external validity. Further, when we compare the OMT sample in the NorComt study with patients in the 2015 National OMT Status Report (89) and the 10 year prospective Norwegian study (30), sample characteristics such as high burden of mental distress, low level of education and employment and norm of polysubstance use appear to be comparable. This is also true when we compare the findings of others (30, 199)

with the NorComt sample as a whole, which was a part of the analysis in paper I. Altogether this strengthens the likelihood that the OMT sample is generalizable to the larger OMT population in Norway. Whether our sample and outcomes are applicable internationally is more complicated as the organization of health care delivery systems differs between countries. This also applies for the organization and treatment philosophies of OMT. Some countries adhere to the high-threshold rehabilitation model, such as the original American and Norwegian OMT (200). Others, such as the Netherlands, Germany and Portugal have traditionally been founded on a harm reduction perspective (201). As discussed in the introduction part of this thesis, the Norwegian programme has in the past years developed in this direction.

However, comparable characteristics to the NorComt sample as a whole as well as for the subset of OMT patients, such as low level of employment and norm of polysubstance use, have been reported elsewhere both nationally (30, 202) and internationally (4, 25, 100, 203). Further, the level of mental distress symptoms we reported is comparable to national (62, 204) and international studies (104). Concerning symptoms of ADHD, our results are in line with the large European IASP study (123); though different from the Norwegian results of the IASP (123), which will be further reviewed in the results discussion.

Paper IV

The sample size in paper IV was very small, and therefore random extremes may have had impact on the results. Generalizing the finding to other groups, even another group of patients in OMT with ADHD, may be problematic. Also, the patients were recruited in the catchment area of Oslo University Hospital. It is possible that the largest city in the country accumulates individuals with more severe problems, and that our patients also may differ from those enrolled in OMT in more rural parts of the country.

5.2 Ethical considerations

The participants in the NorComt study may be regarded as ”particularly vulnerable” according to the Ethical Principles for Medical Research Involving Human Subjects in the Declaration of Helsinki (205). Vulnerable in this sense refers to that the participants are likely to have insufficient power, intelligence, education and resources to protect their own

interests (206). This could imply difficulties in giving free and informed consent of being participants in research and thus need special protection in order not to be exploited. The guidelines of The Council for International Organizations of Medical Sciences (CIOMS) mention individuals with SUD as an example of groups who have previously been excluded from research based on vulnerability criteria, primarily by their presumed non-compliance. This illustrates an important dilemma between protection on the one hand and unjustly depriving competent adults making their own decisions with the result of being left out of research, on the other (206).

5.2.3 Are individuals with SUD vulnerable?

The individuals we recruited to the NorComt study were as heterogeneous as the rest of us. They differed with regards to aspects such as age, duration and type of SUD, family situation, health situation and living conditions. Others have discussed the risk of "stereotyping"; problems with undifferentiated labelling of someone being vulnerable based solely on the persons associations with a group that is considered vulnerable (207). A proposition has been made to distinguish between this static vulnerability and dynamic vulnerability where the latter is context dependent. Of course, one person could be vulnerable in both senses, but it could also be that she only fulfils criteria for the first and not the latter. It is perhaps more fruitful to look at what aspects the presumed vulnerability is related to such as reduced ability to understand (due to for example reduced cognitive capacity or low level of education) or reduction of degree of voluntariness in participation. Vulnerability could also be associated with low socioeconomic status. The important notion here is that individuals with SUD could fit into all of these boxes, but not necessarily in any of them. Instead of excluding vulnerable people from research, one should make great efforts in many steps of the development of a project. This could imply involving patient advocacy organizations in planning of the study design to insure the information about the study was adjusted to the needs of their members (207).

5.2.4 Ethical considerations for papers I-III

This study was observational and did not affect treatment. The privacy of the participants was protected according to legal requirements, through appropriate security measures in handling personal information (e.g. to isolate factors that could identify participants). We collected written consent and trusted the facilities that it was as well informed in reality as

the intention was. Participants were informed at T0 and T1 that they could withdraw from the study at any time without consequences. At T1, we explicitly acknowledged the efforts of the participant and shared thoughts about the project with those who were interested. At T1, we gave the participants a voucher of NOK 300 (EUR 30) and travel expenses were covered. At T0 they received nothing. We are aware of the debate concerning potential problems with offering money for research participation (e.g. reduced degree of voluntary consent) (208). However, substance users rarely have monetary gain as their only motivation for participation (209). This is in line with our experiences at T1; in general participants consented before the gift voucher was mentioned.

5.3.2.1 Adverse consequences

The main ethical concern was related to possible negative effects of sensitive questions. It was emphasized that participants could choose not to respond to items or to withdraw from the study at any time. At T1 we conducted most interviews in the participant's homes or in public places (such as a café or library). Firstly, public places were not an ideal location for a research interview about sensitive topics. Secondly, questions could elicit more information than we asked for. E.g. questions like "Have you had suicidal thoughts in the past four weeks?" could disclose reflections about other challenging topics, sometimes causing us to worry about the participant's situation. It was a balance act not to reject the participant´s wish to share his thoughts and at the same time to be clear about the limitations of a research interview. On a few occasions our concern led us to convey contact information to health professionals or encourage the participant to seek help. We continuously reflected upon our role and situations like these in the project group, to insure we had made sufficient effort to help the participants.

5.3.3 Ethical considerations for paper IV

This paper describes a clinical trial where we spent a lot of time informing patients (and helpers) about the project. All participants were already OMT patients and thereby protected by official patient rights. We believe the ethical aspects of this project to be well taken care of. As an example of an ethical dilemma, we were anxious to terminate the treatment with central stimulants for one older woman who had used amphetamines for thirty years. Initially she benefited from the combination treatment, but various conditions

contributed to multiple relapses. When we discussed this conclusion with her, she (surprisingly) agreed and she said that the experience she had with symptom relief with central stimulants nonetheless had induced hope for recovery at a later stage.

5.3 Discussion of results

The main results of this study were presented in chapter 4 and will now be discussed more in depth and in relation to existing knowledge.

5.3.1 Aim 1

To investigate factors related to prevalence and development of self-reported mental distress in individuals entering OMT (papers I and III).

Our main finding in paper I was that 54% of the OMT patients reported above clinical cut-off point on HSCL-25, indicating a high level of mental distress. High mental distress was associated with lower self-control, but also with substance use pattern and -severity and being a victim of violence. Our main finding from paper III was that OMT patients continued to report high mental distress after one year in treatment with 57% scoring above clinical cut-off, indicating no change on a group level. Those who had negative change in mental distress also had negative change in severity of dependence scores and frequent use of benzodiazepines at baseline.

Prevalence of mental distress at baseline: The prevalence of mental distress we found at baseline (paper I) is comparable to what others have found in OMT samples (98, 104, 105). A Norwegian 10-year prospective study also found a high level of mental distress at baseline among OMT patients measured with GSI, although with a lower mean score compared to our study (GSI=1.03 vs. GSI=1.27) (30). As intake criteria for OMT have changed in a more liberal direction the last decade, patient characteristics may have changed. One explanation of the discrepancy could be that the 10-year study included the first group of patients admitted to the Norwegian OMT program. These early OMT patients had waited for a long time to enter OMT and were a selected group comprising of those worst off. Initially, this context could suggest a higher level of mental distress in these early patients, in contrast to our findings. However, the lower mental distress scores reported in the 10-year study could also be viewed as treatment optimism that overshadowed the true nature of the problems (30).

Development of mental distress. Our sample had no change in mental distress scores at follow-up on a group level (paper III). This contrasts the findings of a systematic review of changes in mental health during OMT concluding that mental health improved early in

treatment (99). The majority of these studies did, however, observe the participants for less than 12 months. The one study with longer follow-up suggested the greatest positive change occurred early in treatment and may not have lasted beyond 12 months (210). Also the Norwegian 10-year prospective study found a small improvement in GSI scores after one year in OMT, but after the 10 years symptoms of mental distress had returned to the baseline level (30). It may be at some point in time, the benefits of OMT start to wane and patients get disillusioned when confronted with demands and obstacles (99). OMT patients enter treatment with severe SUD and a range of practical problems and this could explain why their mental health needs do not get the proper attention. This is unfortunate as depression and anxiety may have negative effects on treatment outcome (122).

Substance use: We found an association between higher mental distress and different substance use patterns at baseline (paper I and paper III). The relationship between substance use and mental health problems, with depression and anxiety among the most common, has been observed in a number of previous studies on SUD samples (100-102) included among OMT patients (210). In our sample frequent use of benzodiazepines at baseline was associated with higher mental distress at baseline (paper I) and with worsening of mental distress at follow-up (paper III). Frequent use of alcohol was associated with reporting higher mental distress at baseline. Alcohol use is closely related to depression and anxiety in the general population in clinical samples (211), indicating that even licit substance use should be addressed in OMT. The same is true for benzodiazepines, often prescribed for anxiety and insomnia, conditions closely associated with depression (212), even if not a treatment of depression as such (213). In our study patients with higher mental distress at baseline reported more polysubstance use and severity of dependence was associated with both high mental distress when entering treatment (paper I) and with poorer development of mental distress at follow-up (paper III). A vicious circle has been described to illustrate the maintenance and promotion of SUD and mental problems. For example an individual may use benzodiazepines to cope with anxiety symptoms; however the physiological and psychological effects of the substance use might accentuate the anxiety in the longer run, thus stimulating to more self-medication (109, 113).

Self-control: In paper I we found an association between low self-control scores and high mental distress. The finding remained significant, even after adjusting for several sociodemographic- and substance related variables. While self-control has been operationalized in different ways, a common understanding views self-control as the capacity to exhibit willpower, illustrated in the iconic delay-gratification experiment where little children were given the choice between getting one marshmallow they could eat immediately or two if they waited for up to 20 minutes (214). Self-control has been implicated as an important part of explaining psychological problems and substance use and dependence (156, 215). Lower self-control in childhood increases the risk for substance use at a later age (216) and higher self-control may act as a buffer towards other risk factors for substance abuse, such as negative life events (217). Substance use may also in itself reduce self-control by disrupting underlying brain circuits responsible for self-control (215). In the light of this knowledge we would expect levels of self-control to be reduced among our participants; however we still find a clear association between mental distress and low self-control.

Exposure to violence: Previous exposure to violence was also associated with reporting mental distress at baseline (paper I). Mental distress has previously been associated with victimization among substance users and criminal offenders (218, 219). Longitudinal studies have reported a bidirectional explanation of this relationship, where victimization could lead to increased mental distress and additionally that mental distress could increase vulnerability and increase the risk of future victimization (219).

5.3.2 Aim 2

To investigate the prevalence and impact of ADHD symptoms in OMT patients (papers II and III).

The main finding from paper II was that 33% of the OMT patients scored above the clinical cut-off point for ADHD, measured with the ASRS at follow-up. Scoring above ASRS cut-off was associated with younger age and frequent use of stimulants and cannabis before treatment entry. High ASRS scores were also associated with more mental distress at both baseline (paper II) and follow-up (paper III). Furthermore, patients with ASRS scores above

cut-off had a worsening in mental distress during the first year of treatment (paper III). Fewer patients with scores above ASRS cut-off reported abstinence at follow-up (10.5% versus 24.8% of those scoring below cut-off).

Prevalence of ADHD symptoms: The share of ASRS symptoms in our OMT sample was originally a little lower than the results of the large European IASP study where 41% of participants with mixed SUDs scored above clinical cut-off point. Nonetheless, when we used the same cut-off score as the IASP (4 with weighted scores), our prevalence increased to 39%, similar to the IASP (123) (paper II). Thus, the use of different cut-offs could explain this difference in prevalence. Due to the low number of studies and the wide range in the results of comparable studies, it is barely possible to suggest a prevalence of ADHD symptoms in OMT patients. One Italian study reported a prevalence of 19% ADHD symptoms (125), while a study from Taiwan found that 8 % of patients in OMT screened positive for ADHD (127). These are both in contrast to an Australian study that reported 31% positive screens for users of heroin (126), which is more in line with our results.

In addition to differences in methodological choices, the wide prevalence range of ADHD symptoms has been explained with cultural differences (123, 127). For example, the high prevalence of both ADHD symptoms and diagnosis in the Nordic countries in the IASP study was partly explained by a high public awareness of ADHD that facilitated practices such as referral, assessment and treatment (123). The IASP study also introduced selection bias as a possible explanation for the very high prevalence rate that was reported for Norway. However, they considered this unlikely after all as the participating facilities had indicated they were representative for the national situation (123). The differences in ADHD screening rates between countries in the IASP were substantial, with results varying between 29% (Switzerland) and 66% (Norway) (123). Interestingly, the Norwegian IASP contribution reported almost a double prevalence rate compared to our findings. As addressed in the methods section of this thesis, this difference in prevalence could partly be due to the use of different cut-offs. Also, our ASRS prevalence rate was calculated for OMT patients only (n=175) while the Norwegian IASP reported on a mixed SUD sample (n=385). To investigate this, we performed an additional analysis including the whole NorComt sample (n=337), which should be comparable in both size and SUD characteristics (not published in the

papers). With the cut-off of 14 (summed scores), the prevalence of screening results above cut-off for the sample as a whole increased to 36%; with a cut-off of 4 (weighted scores) it further increased to 41%.The results with the cut-off of 4 are the same as for our OMT sample and for the general results of the IASP. We have to acknowledge that we cannot offer an explanation for the persistent difference in screening results between the two Norwegian studies.

Gender: There was no gender difference related to ASRS scores in this study (paper II). This is in line with previous epidemiological studies of ADHD in adults where the gender distribution has been shown to be equal (220) or with only a slight predominance of men (221). The adult gender distribution differs from epidemiological findings among children where boys are in majority, a distribution that increases dramatically in clinical samples, and it has been suggested that ADHD may be underdiagnosed in girls (135, 222). A higher prevalence of the inattentive subtype with more subtle symptoms, often being discounted in favor of other comorbid conditions, could explain why fewer girls are referred for ADHD assessment (135). Maybe a more gender-specific threshold on rating scales could overcome this (223) along with increased awareness among health care professionals that ADHD is an equally important medical issue in girls and women (222).

Age: We found patients with increased ASRS score to be younger than the patients who reported below cut-off score (paper II). This is in accordance with previous research, included the results of the Norwegian IASP study and the Italian investigation of ADHD symptoms in OMT (125, 224). Higher prevalence in younger age groups, could be interpreted as age-related improvement of certain ADHD symptoms (125). However, another explanation could be that patients with an increased rate of ADHD symptoms have a more severe course of the SUD with an earlier age of onset and therefor start in treatment earlier (225).

Substance use pattern: As expected from previous research on ADHD in SUD samples (124, 225, 226), scoring above clinical cut-off on the ASRS was associated with more frequent use of stimulants (paper II) and benzodiazepines (paper III) at baseline and higher severity of dependence scores (paper III). Frequent use of benzodiazepines (paper II) could be

attributed to the higher prevalence of co-existing mental disorders, but also to the specific influence benzodiazepines may have on ADHD symptoms (129). Their use could be interpreted as self-medication to manage sleeping problems (36, 227) or as sedative after using stimulants (228). Other studies have also reported more use of amphetamines among other substances, in individuals with SUD and increased rate of ADHD symptoms (126) and among those with an ADHD diagnosis (123, 225) compared to those with SUD and no ADHD. Stimulants are often believed to represent a kind of self-medication for ADHD symptoms (126, 229), however this is disputed (128, 129). These inconsistencies are also expressed in opinions regarding whether individuals with ADHD prefer different kinds of substances compared to those without ADHD, such as stimulants (230), alcohol and cannabis (231) or not (232, 233). As targeted in the introduction of this thesis, it is common for individuals in OMT to be poly-substance users (7) and this could be a reflection of the failure to identify particular substance use patterns among illicit substance users with ADHD (124, 229).

Higher mental distress: Mental distress at baseline was higher among patients who scored above ASRS cut-off at follow-up, compared to those who scored below cut-off (paper II). These findings are in line with reports from other studies, showing that adults with both ADHD and SUD have higher rates of comorbid psychiatric disorders, especially depressive and anxiety disorders, compared to adults with only SUD, only ADHD or neither (232, 234, 235). To what extent these conditions develop as a result of, or independently of the ADHD is disputed (135). Adults with ADHD often have multiple struggles in their everyday life; they can be easily distracted, restless, have poor planning skills, reduced organizational abilities or/and suffer from mood fluctuations. All in all this may cause problems with functioning at school, work and in relationships (130). Symptoms of depression and anxiety are sometimes best understood in terms of the context, such as despair due to own failures or panic as a result of chaos. However, these interpretations are not always sufficient and independent diagnosis need to be considered when the symptoms persists and lead to increased impairment in functioning (130). The high comorbidity between ADHD, SUD and mental distress has important clinical implications as they individually present and increased risk of developing other comorbidities as well as a poorer treatment prognosis.

Negative development of mental distress: A main result from paper III was that ASRS scores above cut-off was associated with worsening of mental distress during the first year of OMT.

This means that patients with already high mental distress scores at baseline actually experienced more symptoms of mental distress after one year in treatment. It has been suggested that the increased association of ADHD and SUD is a consequence of the developmental interaction with ADHD symptoms (e.g. impulsivity) and the consequences of the ADHD itself (e.g. poor academic performance), creating an increased opportunity for the development and maintenance of a SUD (138). Higher severity of dependence could be attributed to the higher mental distress in patients with increased ADHD symptoms, but also to the specific influence substances might have on ADHD symptoms (132), such as self-medication to manage sleeping problems (45, 228). These processes may be enhanced if the ADHD symptoms are overlooked in the treatment services.

Continued substance use (67) and cognitive impairment (190) have been reported to be independently associated with treatment drop-out among OMT and SUD patients respectively. Despite having more treatment exposure, individuals with ADHD and SUD have also been reported to have poorer SUD treatment outcomes than individuals without ADHD. Thus, untreated ADHD may impair the ability to benefit from SUD treatment (138). The negative development of mental distress in our study is of great concern in the light of this knowledge. It inevitably leads to question the content of their treatment – the rehabilitation aspect of the OMT programme. To further illuminate this aim, we explored how the patients in our study had responded to items in the questionnaire pertaining to whether they had ever been assessed for ADHD (not necessarily completed), had received an ADHD diagnosis or ADHD medication (not published in the papers). According to self-report, out of 57 patients with scores above ASRS cut-off, 35 (61%) had been assessed for ADHD and 25 (44%) had received a diagnosis. Only two patients (4%) had received ADHD medication (data not shown in the papers).

Even though one should be cautious with diagnosing ADHD in patients who abuse substances or have not been abstinent for some time (146, 180), this is not always possible (138). In these cases, a pragmatic, careful and thorough approach including collateral information may be recommended to identify a likely ADHD diagnosis and plan treatment accordingly (138). In this respect it is also relevant that the ASRS has shown stability over time when used in a mixed SUD sample by the IASP study (179). This was supported by a

smaller study (n=75) using the 18-item version of ASRS reporting that scores obtained at intake to treatment were strongly predictive of scores after six months (181).

5.3.3 Aim 3

To explore whether treatment with central stimulants is a viable option for patients in OMT with ADHD (Paper IV).

The main finding was that use of central stimulants showed some promise with regard to safety and utility. For those who stayed in the program we detected neither diversion nor abuse of the central stimulants. The patients in the project did not report craving or increased substance use. Furthermore, completers reported reduction in ADHD symptoms, even though the symptom burden remained high.

Safety of central stimulant medication prescribed to OMT patients: Frequently addressed safety issues in the literature include the abuse potential of central stimulants and the risk of diversion (selling or giving the medication to someone it was not described for) (236). In our study we detected neither diversion nor abuse of the prescribed medications in accordance with other trials, including another naturalistic OMT study (143, 144, 237, 238). Nonetheless, we monitored our patients closely and perhaps these experiences would have been different if the treatment had been conducted in a less structured setting or as standard treatment over time.

We did not detect craving or increase in substance use that could be attributed to the central stimulant medication among the patients who remained in the project. These findings are in line with others (144, 239). While results are mixed, a systematic review reported a risk of adverse cardiac effects associated with the use of central stimulant medications in adults, particularly when used over time in high doses (240). As pharmaceutical stimulants can produce effects similar to the illicit stimulants, there is also the risk of abuse – and of diversion. However, this risk may be reduced with the use of extended-release formulations (236).

Utility of central stimulant medication: The patients in our study reported a significant reduction of ADHD symptoms at the 6- to 8-week measure point, but the scores remained fairly high throughout the study period, suggesting permanent functional impairment.

Among a majority of the treatment completers, urine samples confirmed decreased substance use and reaching abstinence after one year.

According to a Norwegian registry study, 2.8% of patients in OMT received ADHD medication in 2010 (241). This number is high compared to the general population, but low compared to the estimated prevalence of ADHD in the OMT population (241). The rationale for using ADHD medication in SUD patients is to improve ADHD symptoms and positively influence SUD outcomes; e.g. effective treatment would help patients to remain abstinent by improving their cognitive functioning and reduce impulsivity (242). However, research findings are mixed with regard to such effects of central stimulant treatment in SUD samples (239, 243, 244). A small naturalistic study from Sweden among OMT patients also reported improvement of certain ADHD related problems and decrease in substance use (144). However, these results contrast the findings of the only RCT among OMT patients (143). They found no difference in reduction of ADHD symptoms between those receiving placebo and central stimulants. This lack of effect of active treatment was partly attributed to ongoing substance use and high psychiatric comorbidity (143). To explain the relatively poor treatment effect, it has been suggested that opioid dependent patients may especially difficult to treat, either due to their multiple problems or to the specific characteristics of opioid dependence (98, 116, 242). However, very few studies have been conducted and it is currently difficult to draw any conclusions. While lack of control can produce bias, one advantage of the two small naturalistic studies is their prolonged time frame compared to the RCT. One cannot rule out that the results of Levin et al. (143) would have improved if they had continued for e.g. one year; again this is a challenge for the RCT design.

Studies on ADHD conducted in mixed SUD samples also report conflicting results. As a tendency, case studies have reported better effects on both ADHD and SUD outcomes than RCT's (242). While our study was not a case study, one could argue that its open design has more in common with case studies than RCT's and that this in part could explain our positive outcomes. One recent review of 13 RCT's however found only a small to moderate reduction in ADHD symptoms, while no positive effect on abstinence or treatment retention was recorded (244). Another reason for these relatively poor results could be the dosage of the central stimulants. It has been suggested that substantially higher doses may be required to

produce treatment effects in SUD patients because many have developed a tolerance to stimulants after long-term use (239, 242, 245). Further, a longer titration period than what is common could prove necessary for these patients (239, 245, 246). One Swedish registry study obtained information about methylphenidate doses for 14314 adults, included 4870 individuals with SUD. They found that the latter group was prescribed 40% higher methylphenidate doses than the adults with ADHD and no SUD (245). Two RCT's reported improvement of ADHD symptoms and SUD outcomes using higher stimulant doses than previous studies (239, 246). This is in contrast to our study where we adhered strictly to the official recommendations concerning doses and followed a more traditional upscaling of the medication. Ten patients in our sample requested to change their medication to dextroamphetamine, believing this would further improve their functioning. We cannot rule out that the effect of the methylphenidate would improve with higher dosages. While we only allowed two patients to switch medication, it is interesting that in a recent randomized trial with cocaine users, Levin et al. (246) found active treatment to significantly reduce ADHD symptoms and improve SUD outcomes, with better abstinence in the highest dosage group.

Also, ongoing or recently stopped substance use can influence treatment of ADHD, both by neurobiological influences and by reduced therapeutic compliance under the influence of substances (242). We did not demand total abstinence but accepted limited use from the patients at treatment start, different to the official recommendations (146). However, one review did not find differences in treatment efficacy between studies where abstinence was an inclusion criterion compared to those for which it was not (244). In our study periodic substance use was a challenge, in particular the use of benzodiazepines, but in our experience it did not increase during the combined treatment. The frequently occurring problem of persistent substance use during stimulant treatment was also reported in a recent review including 15 RCT's and suggested as an important explanation of the relatively disappointing results (242).

Another possible explanation of low medication efficacy would be an incorrect ADHD diagnosis (242). The patients in our study were characterized by long-term substance dependence, severe psychosocial problems, psychiatric comorbidities and impaired daily life

functioning. These observations are in line with the complex clinical picture of patients with ADHD in OMT (116, 129) and with other SUD (129, 235, 247) described by others. Previously discussed as a possible confounder to the study, overlapping symptoms with comorbid psychiatric disorders can produce a confusing clinical picture (129). We did not diagnose the patients ourselves but checked the diagnostic reports closely. While all reports included standardized diagnostic instruments, the risk of an incorrect diagnosis is still present. For example is the frequent presence of conduct disorder, bipolar disorder and post-traumatic stress disorder well documented among those with ADHD (135, 197, 248) and pose a true challenge to diagnostic work as differential diagnoses also can be present as comorbidities. Psychiatric comorbidity can also influence medication effects negatively through neurobiological processes or more indirectly e.g. diminished therapeutic compliance (242).

6. SUMMARY AND CLINICAL IMPLICATIONS

This thesis supports and elaborates on previous findings showing that mental distress is high among substance users entering both opioid maintenance treatment and other inpatient treatment (paper I). Factors associated with high mental distress in our study were use of benzodiazepines and alcohol, general substance use severity, low perceived self-control, and exposure to violence (paper I). For OMT patients, mental distress remained high during the first year of treatment. Also change in mental distress was associated with change in severity of dependence and use of benzodiazepines at baseline (paper III). On a less investigated topic, we found a high prevalence of ADHD symptoms among patients in OMT. Increased ADHD symptoms were associated with more mental distress and use of stimulants (paper II). Also, this patient group had a poorer development of mental distress compared to the OMT group as a whole (paper III). Our open clinical trial showed that treatment with central stimulants may be a viable treatment option for OMT patients with ADHD, but diagnostics and treatment poses challenges to the health services (paper IV).

On a general level these findings underlines the need for systematic screening of mental health related topics in all SUD treatment. Screening provides information that needs to be evaluated and processed by the clinicians *and* the patient together in the planning of treatment – if the results are put in a drawer only, all kinds of screening would be ethically questionable. Screening typically helps clinicians to determine if further assessment is warranted. Treatment interventions should be based on results of screening or more comprehensive assessments and this will demand broad clinical competence from clinicians working in the field of SUD, also on topics regarding mental health. This is an interesting issue in SUD treatment where, in a Norwegian context, clinicians who are not medical doctors or psychologists are expected to work with a variety of challenges presented by their patients. As discussed briefly in the introduction of this thesis, individuals admitted to any SUD treatment in Norway are likely to present with a wide range of severe social, psychological and somatic needs and to prioritize and work systematically with this can be challenging – even though if treatment is anchored interdisciplinary.

The poor development in mental distress described in paper III among patients with ADHD symptoms above clinical cut-off, should specifically encourage systematic screening of ADHD. Because substance use as well as withdrawal symptoms may mimic symptoms of mental disorders, continual assessment of mental illness symptoms is essential to ensure accurate diagnosis. This indeed applies to ADHD. However, while a diagnosis may be practical and enable e.g. pharmacological treatment, subclinical threshold symptoms of ADHD should not be ignored. These symptoms may pose challenges for the patients even though they do not result in a diagnosis, and clinicians should be encouraged to work specifically with e.g. attention problems and customize treatment accordingly such as reduce the lengths of meetings or remind the patient of appointments. As addressed in the discussion of aim 3, there are dilemmas concerning the pharmacological ADHD treatment in patients with SUD as research is inconclusive when it comes to whether the medication is effective or not. There are also safety issues such as the risk of exacerbating SUD or diversion of the ADHD medication. Together such concerns may create an atmosphere of uncertainty and potential conflicts among health professionals demanding high professional standards to handle. Perhaps an open-minded, knowledge based attitude is recommendable, implicating that treatment options are thoroughly discussed and decided for each patient.

Knowledge of factors that influence mental distress could help to guide and improve treatment. In paper I we highlighted that self-control may be important to consider in this context. We suggested that patients with reduced self-control could benefit from specific self-control training tasks. Another clinical implication is related to alcohol use. When individuals are admitted to treatment with severe illegal substance use, the use of alcohol can easily be overlooked and perhaps not even considered a substance among neither patients nor clinicians. This may illustrate the importance of validated screening tools to avoid the more random examination of e.g. substance use that easily can be influenced by culture or personal beliefs. We also found that having been exposed to violence was associated with mental distress. This could serve as a reminder that symptoms of mental distress are often symptoms of disabling underlying pathologies such as psychological traumas that need to be understood and treated along with the SUD, to enable targeting any of these conditions. In paper III we found that mental distress remained high after one year in OMT, and that this development was worse for those with high severity of dependence

and use of benzodiazepines at baseline interview. This should encourage continuous examination of all substance use in OMT, and just as importantly to explore the function of this use.

7. FUTURE RESEARCH

The high prevalence of mental distress among OMT patients is well established and more consideration should be given to how mental distress changes over time and factors associated with change. This project currently has two observation points available; however NorComt has been granted access to link data to national health registries in the future which will provide extensive information in a longitudinal perspective, including on correlates of mental health. To gain more insight into factors that influence mental health in OMT, future projects could consider more frequent measuring than once a year to explore whether mental distress is affected by periods of abstinence, changes in frequency of use and doses used in addition to the specific substances, but also psychosocial measures such as quality of life and cognitive functioning.

Further exploration of ADHD among OMT patients is another future research topic. We found a high prevalence of ADHD symptoms in the OMT patients and these patients had a poorer development in mental distress. However, there is still uncertainty about prevalence of ADHD and efficacy of pharmacological treatment in OMT patients. Future studies could investigate ADHD assessment and treatment strategies (included pharmacological treatment) with a tighter follow-up and a more structured evaluation regime than we have described in our clinical trial, preferably in inpatient settings. This would provide better conditions for valid diagnosis and treatment evaluation. An RCT framework could be considered for assessing new components of treatment, where some patients receive specific interventions such as Cognitive Behavioural Therapy, while others receive treatment as usual.

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APPENDICES

APPENDIX 1

Senter for rus- og avhengighetsforskning

Tiltaksnr	Løpenr

Norsk oppfølgingsstudie av opioid-avhengige i behandling (NorComt)

Intervjuskjema

Behandlingsoppstart

Samarbeid mellom SERAF, regionale LAR-sentre og rusbehandlingsinstitusjoner

SERAF 2012

Kontaktpersoner:
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Liste over tiltaksnummer

01 = LAR Vestfold
02 = LAR Vest-Agder
03 = Helse Bergen
04 = LAR Nord
05 = SPA, Oslo
06 = LAR Telemark
07 = LAR Buskerud
09A = LAR Hamar (Innlandet)
09B = LAR Gjøvik (Innlandet)
09C = LAR Lillehammer (Innlandet)
10 = Veksthuset Rogaland
11 = Samtun Sauherrad
12 = Arken
13 = Sollia
14 = Tyrili 1 (Høvringen)
15 = Tyrili 2 (Frankmotunet)
16 = Tyrili 3 (Tyrilihaugen)
17 = Tyrili 4 (Tyrilitunet)
18 = Tyrili 5 (Kampen)
19 = Tyrili 6 (Tyrili Sør)
20 = Veksthuset Molde
21 = LAR Midt
22 = LAR Akershus
23 = LAR Aust-Agder
24 = Renåvangen
25 = LAR Fredrikstad (Østfold)
26 = LAR Moss (Østfold)
27 = LAR Sarpsborg (Østfold)
28 = LAR Askim (Østfold)
29 = LAR Halden (Østfold)

Bare for LAR-tiltak

LAR-medisiner i dag

	Dose mg/dag
Subutex / buprenorfin	…….....
Subuxone	…….....
Metadon	…….....
Annet	…….....

Utleveringsordning LAR-medisin

LAR-senter	☐
Apotek	☐
Fastlege	☐
Hjemmesykepleier	☐
Annet: ……..	☐

Henteordning for LAR-medisin

	Antall dager per uke
Observert inntak	…….....
Ta med hjem-dosering	…….....

Kontrolltiltak mht rusmiddelinntak

	Antall ganger per uke
Urinprøvekontroller	…….....
Spyttprøvekontroller	…….....
Sporadiske spytt/urinprøvekontroller	☐ Nei ☐ Ja

Fødselsnummer

Kjønn

1 = Mann
2 = Kvinne

Dato for start kartlegging (NPR)

dag måned år

Dato for første behandlingsdag
(for LAR-pasienter første dag med LAR medisin)

dag måned år

Behov for tolk

1 = Ja
2 = Nei

Fødeland og etnisk bakgrunn

1 = Norge
2 = Norden utenom Norge
3 = Vest-Euroopa utenom Norden
4 = Øst-Europa
5 = Asia (inkl. Tyrkia)
6 = Afrika
7= Sør- og Mellom-Amerika (ink.l Mexico)
8 = Nord-Amerika
9 = Oceania
99 = Ukjent

Fødeland Mors fødeland Fars fødeland

Sivilstatus

0 = Ikke oppgitt
1 = Aldri gift
2 = Gift
3 = Enke / enkemann
4 = Separert
5 = Skilt
6 = Registrert partner
7 = Separert partner
8 = Skilt partner
9 = Gjenlevende partner

Høyeste fullførte utdanning

1 = Ikke avsluttet grunnskole
2 = Grunnskole
3 = Videregående skole/gymnas/yrkesskoleutdanninger
4 = Faglig yrkesutdanning
5 = Treårig høyskole/universitet
6 = Mer enn treårig høyskole/universitet
9 = Ukjent

Yrkesstatus

1 = Utenfor arbeidsmarkedet og ikke under utdanning
2 = Heltidsjobb
3 = Deltidsjobb
4 = Under utdanning
5 = Deltidsjobb og under utdanning
9 = Ukjent

Viktigste inntekt siste 4 uker

1 = Lønnet arbeid
2 = Forsørget
3 = Arbeidsledighetstrygd
4 = Syke-/rehabiliteringspenger
5 = Atføringspenger
6 = Uførepensjon
7 = Alderspensjon
8 = Sosial stønad
9 = Annet
10 = Ukjent
11 = Studielån/stipend
12 = Stønad til enslig forsørger

Bor sammen med (NPR)
(flere valg mulig)

1 = Bor alene
2 = Bor i parforhold
3 = Bor sammen med venner
4 = Bor sammen med foreldre
5 = Bor sammen med barn under 18 år
6 = Bor sammen med barn over 18 år
7 = Bor sammen med andre
9 = Ukjent

Boligforhold siste 4 uker (NPR)

1 = Ingen bolig
2 = Hospits/hybelhus/hotell
3 = Institusjon
4 = Egen privat bolig
5 = Privat bolig eid av annen
6 = Annet

Hatt en stabil bosituasjon siste 4 uker

1 = Ja
2 = Nei
9 = Ukjent

Barn (NPR)

Antall egne barn uansett alder og bosituasjon (NPR) ☐

Alder og bosituasjon for barn under 18 år (NPR)

	0-6 år	7-12 år	13-17 år
Hjemmeboende barn (egne), angi antall	☐	☐	☐
Hjemmeboende barn (andres), angi antall	☐	☐	☐

Tiltak for barn under 18 år (ikke NPR)

	1 = Ikke behov	2 = Bør iverksettes	3 = Er iverksatt	9 = Ukjent
Hjemmeboende barn (egne), angi antall	☐	☐	☐	☐
Hjemmeboende barn (andres), angi antall	☐	☐	☐	☐

Graviditet (NPR)

☐
1 = Ja
2 = Nei
9 = Ukjent

☐☐ **Antall uker gravid**
(Eks.: 1 uke = 01; 2 uker = 02; 10 uker = 10)

Vedvarende somatiske sykdommer eller skader (NPR)

☐
1 = Ja
2 = Nei
9 = Ukjent

Testet for blodsmittevirus?

☐	☐	☐
Hepatitt B	**Hepatitt C**	**HIV**

1 = Ja
2 = Nei
9 = Ukjent

Egen kunnskap om blodsmittevirus

☐	☐	☐
Hepatitt B	**Hepatitt C**	**HIV**

1 = Ja
2 = Nei
9 = Ukjent om pasienten vet

Psykiske vansker/lidelser (NPR)

Siste 4 uker	**Tidligere i livet**	(begge kolonnene må besvares for hvert spørsmål) 1 = Ja 2 = Nei 9 = Ukjent
☐	☐	Hatt alvorlige depresjoner
☐	☐	Hatt alvorlig angst
☐	☐	Hatt vrangforestillinger/hallusinasjoner
☐	☐	Blitt forskrevet medisiner for et eller annet psykisk/følelsesmessig problem
☐	☐	Hatt alvorlige tanker om å ta livet av seg

Forsøk på selvmord

☐
1 = Nei
2 = Ja, ved overdose
3 = Ja, på annen måte
4 = Både ved overdose og på annen måte
9 = Ukjent

Mottatt profesjonell hjelp for psykiske vansker/lidelser

☐
1 = Ja
2 = Nei
9 = Ukjent

Type tidligere behandling rus

☐
1 = Kun avrusning (institusjon eller poliklinisk)
2 = Poliklinisk vedlikeholdsrehabilitering (LAR)
3 = Annen poliklinisk behandling, inkludert dagtilbud
4 = Døgnbehandling ut over avrusning
5 = Poliklinisk-(LAR eller annen) og døgnbehandling (inkludert avrusning)
6 = Behandling utenfor rusinstitusjon/rustiltak
8 = Ikke tidligere behandlet
9 = Ukjent

Tid siden siste behandling rus

☐☐☐ **Angi antall måneder siden siste behandling**
(Eks.: 1 mnd = 001; 12 mndr = 012; 12 år = 144)

000 = Vært i behandling, men ukjent når sist

Antall rusmidler brukt siste 6 måneder

☐☐ **Angi antall rusmidler**
(Eks.: 1 rusmiddel = 01; 2 rusmidler = 02; 10 rusmidler = 10)

00 = Ingen
99 = Ukjent

Rusmiddel-/medikamentprofil siste 6 måneder (før kontrollert miljø)

	Type rusmiddel/medikament(NPR) (Bruk koden nedenfor)	**Inntaksmåte (NPR)** (Bruk koden nedenfor)	**Hvor ofte brukt siste 4 uker (NPR)** (Bruk koden nedenfor)	**Alder brukt første gang (NPR)**	**Hvor lenge problemfylt bruk** (Antall år)
Mest brukte rusmiddel/ medikament	☐	☐	☐	☐☐	☐☐
2. mest brukte	☐	☐	☐	☐☐	☐☐
3. mest brukte	☐	☐	☐	☐☐	☐☐
4. meste brukte	☐	☐	☐	☐☐	☐☐

0 = Ingen
1 = Alkohol
2 = Cannabis
3 = Heroin/Opium
4 = Metadon, buprenorfin, andre opiater/opioder forskrevet i LAR-program
5 = Metadon, buprenorfin, andre opiater/opioder forskrevet utenfor LAR-program
6 = Metadon, buprenorfin, andre opiater/opioder ervervet uten at forskrevet av lege
7 = Benzodiazepiner forskrevet av lege
8 = Benzodiazepiner ikke forskrevet av lege
9 = Andre vanedannende medikamenter
10 = Amfetamin
11 = Kokain
12 = Crack
13 = Andre sentralstimulerende midler
14 = LSD og likn.
15 = Ecstasy
16 = Løsemidler
17 = Rødsprit o.l
18 = Annet
99 = Ukjent

1 = Drikker/spiser
2 = Injiserer
3 = Røyker
4 = Sniffer
8 = Annet
9 = Ukjent

1 = Ikke brukt
2 = Sjeldnere enn 1 gang i uken
3 = Omtrent ukentlig
4 = 2-4 dager i uken
5 = 5-6 dager i uken
6 = Daglig
9 = Ukjent

99 = Ukjent

00 = Ikke
01 = Et år eller mindre
99 = Ukjent

Brukt sprøyter før?

☐

1 = Ja
2 = Nei
9 = Ukjent

Alder første sprøytebruk

☐☐

Angi alder i år

00 = Aldri brukt sprøyter
99 = Ukjent

Sprøytebruk siste 4 uker (NPR)

☐

1 = Ikke brukt sprøyte
2 = Sjeldnere enn 1 gang i uken
3 = Omtrent ukentlig
4 = 2-4 dager i uken
5 = Daglig eller nesten daglig
9 = Ukjent

Antall ganger overdose hele livet

Antall for hvert av stoffområdene

☐☐ Alkohol

☐☐ Narkotika

☐☐ Medikament

☐☐ Kombinasjon

00 = Ingen ganger
99 = Ukjent

Behandlingserfaring

Hvor mange måneder til sammen har du vært i døgnbehandling uten LAR i ditt liv?
(Eks.: 1 mnd = 001; 12 mndr = 012; 12 år = 144)

Hvor mange måneder til sammen har du vært i døgnbehandling med LAR i ditt liv?
(Eks.: 1 mnd = 001; 12 mndr = 012; 12 år = 144)

Hvor mange måneder til sammen har du vært i poliklinisk behandling uten LAR i ditt liv?
(Eks.: 1 mnd = 001; 12 mndr = 012; 12 år = 144)

Hvor mange måneder til sammen har du vært i poliklinisk behandling med LAR i ditt liv?
(Eks.: 1 mnd = 001; 12 mndr = 012; 12 år = 144)

Hva er ditt behandlingsmål med dette behandlingsopplegget?

1 = Rehabilitering med rusfrihet
2 = Stabilisering med bedre rusmestring

Ønske for varighet av behandling?
(Eks.: 1 mnd = 001; 12 mndr = 012; 12 år = 144, Livslang = 999)

Kontrollert miljø

I løpet av de siste 30 dagene før denne behandlingen,
har du vært innlagt i det vi kan kalle et «kontrollert miljø»?

1 = Nei
2 = Fengsel
3 = Behandlingsinstitusjon for rusmiddelmisbrukere
4 = Somatisk sykehus
5 = Psykiatrisk sykehus/klinikk
6 = Bare avrusning/avgiftning
7 = Annet kontrollert miljø, spesifiser: ……

Var dette miljøet/behandling med LAR?

☐ Nei
☐ Ja

Sosialt nettverk siste 6 måneder (før kontrollert miljø)

Hvem er du mest sammen på fritiden vanligvis?
(Lengeværende kjæresteforhold defineres som familie/minst 1 år)

1 = Familie uten nåværende problemer med alkohol/stoff/medikamenter
2 = Familie med nåværende problemer med alkohol/stoff/medikamenter
3 = Venner uten nåværende problemer med alkohol/stoff/medikamenter
4 = Venner med nåværende problemer med alkohol/stoff/medikamenter
5 = Er mest alene

Utsatthet for kriminalitet siste 6 måneder (før kontrollert miljø)

	Siste 6 mnd		
	Nei	Ja	Ant ganger
Har du blitt frastjålet personlige ting som penger, mobiltelefon eller andre ting?	☐	☐	
Har du blitt utsatt for vold som førte til synlige merker eller skader på kroppen?	☐	☐	
Har du blitt utsatt for vold som ikke førte til synlige merker eller skader på kroppen?	☐	☐	
Har du noen gang blitt utsatt for seksuelt motivert vold, overgrep eller voldtekt, eller forsøk på dette?	☐	☐	

Egen kriminalitet siste 6 måneder (før kontrollert miljø)

	Siste 6 mnd		
	Nei	Ja	Ant ganger
Har du vært involvert i kriminelle handlinger? (unnntatt egen bruk og besittelse)	☐	☐	
Hvis Ja: Herunder vinningskriminalitet?	☐	☐	
Hvis Ja: Narkotikaforbrytelser? (unnntatt egen bruk og besittelse)	☐	☐	
Hvis Ja: Voldskriminalitet?	☐	☐	
Hvis Ja: Trafikk kriminalitet?	☐	☐	
Hvis Ja: Annen kriminalitet?	☐	☐	

LAR-medisiner og kriminalitet hele livet

	Nei	Ja	Ikke aktuelt	Ønsker ikke å svare
Har du noen gang omsatt/delt ditt eget LAR medikament?	☐	☐	☐	☐
Har du noen gang kjøpt illegalt LAR-medikament?	☐	☐	☐	☐

Soning hele livet

	Nei	Ja	Ant ganger	Dersom soning, ant måneder totalt
Har du sonet dom i fengsel?	☐	☐		

SCL – 25. Hvor mye har du vært plaget av: (den siste uka)

(samme spørsmål i SCL-90)

Sett en ring rundt det svaret som passer deg best.	0 Ikke i det hele tatt	1 Litt	2 Moderat	3 Ganske mye	4 Veldig mye
1. Hodepine	0	1	2	3	4
2. Skjelving	0	1	2	3	4
3. Matthet eller svimmelhet	0	1	2	3	4
4. Nervøsitet, indre uro	0	1	2	3	4
5. Plutselig frykt uten grunn	0	1	2	3	4
6. Stadig redd eller engstelig	0	1	2	3	4
7. Hjertebank, hjerteslag som løper avgårde	0	1	2	3	4
8. Følelse av å være anspent, oppjaget	0	1	2	3	4
9. Anfall av angst eller panikk	0	1	2	3	4
10. Så rastløs at det er vanskelig å sitte stille	0	1	2	3	4
11. Mangel på energi, alt går langsommere enn vanlig	0	1	2	3	4
12. Lett for å klandre seg selv	0	1	2	3	4
13. Lett for å gråte	0	1	2	3	4
14. Tanker om å ta ditt liv	0	1	2	3	4
15. Dårlig matlyst	0	1	2	3	4
16. Søvnproblemer	0	1	2	3	4
17. Følelse av håpløshet med tanke på fremtiden	0	1	2	3	4
18. Nedtrykt, tungsindig	0	1	2	3	4
19. Følelse av ensomhet	0	1	2	3	4
20. Tap av seksuell lyst og interesse	0	1	2	3	4
21. Følelse av å være lurt i en felle eller fanget	0	1	2	3	4
22. Mye bekymret eller urolig	0	1	2	3	4
23. Uten interesse for noe	0	1	2	3	4
24. Følelse av at alt er et slit	0	1	2	3	4
25. Følelse av å være unyttig	0	1	2	3	4

Somatisk helse. Hvor mye har du vært plaget av: (siste 6 måneder) (før kontrollert miljø)

Sett en ring rundt det svaret som passer deg best.	0 Ikke i det hele tatt	1 Litt	2 Moderat	3 Ganske mye	4 Veldig mye	Kronisk lidelse? (minst 3 mnd i løpet av siste halvår før inntak)	
						Ja	Nei
Fordøyelsesplager	0	1	2	3	4	☐	☐
Diare	0	1	2	3	4	☐	☐
Forstoppelse	0	1	2	3	4	☐	☐
Luftveisplager	0	1	2	3	4	☐	☐
Eksem	0	1	2	3	4	☐	☐
Hudinfeksjoner	0	1	2	3	4	☐	☐
Leddsmerter	0	1	2	3	4	☐	☐
Hodepine	0	1	2	3	4	☐	☐
Brystsmerter	0	1	2	3	4	☐	☐
Svimmelhet	0	1	2	3	4	☐	☐
Nedsatt hukommelse	0	1	2	3	4	☐	☐
Synsforstyrrelser	0	1	2	3	4	☐	☐
Urinveisplager	0	1	2	3	4	☐	☐
Kjønnsykdommer	0	1	2	3	4	☐	☐
Blodpropp	0	1	2	3	4	☐	☐
Tann/tannkjøttsplager	0	1	2	3	4	☐	☐

Har du noen av de nevnte sykdommer per i dag?

	Ja	Nei	Ukjent/ vet ikke	Hvis Ja, har du i løpet av de siste 6 mnd fått behandling for din(e) sykdom(mer)?	
				Ja	Nei
Diabetes	☐	☐	☐	☐	☐
Høyt blodtrykk	☐	☐	☐	☐	☐
Hjertesykdom	☐	☐	☐	☐	☐
KOLS	☐	☐	☐	☐	☐
Astma	☐	☐	☐	☐	☐
Hepatitt B	☐	☐	☐	☐	☐
Hepatitt C	☐	☐	☐	☐	☐
Leverchirrose	☐	☐	☐	☐	☐
HIV	☐	☐	☐	☐	☐
Kreft	☐	☐	☐	☐	☐
Annet ……..	☐	☐	☐	☐	☐

Livskvalitet før oppstart i behandling (før kontrollert miljø)

Sett en ring rundt det svaret som passer deg best.

	Ikke aktuelt	0 Meget dårlig	1 Dårlig	2 Verken god/t eller dårlig	3 God/t	4 Meget god/t
Hvordan synes du selv din fysiske helse var før behandling?		0	1	2	3	4
Hvordan synes du selv din psykiske helse var før behandling?		0	1	2	3	4
Hvordan var ditt forhold til deg selv før behandling?		0	1	2	3	4
Hvordan var ditt forhold til dine venner før behandling?		0	1	2	3	4
Hvordan var ditt forhold til din partner før behandling?	☐	0	1	2	3	4
Hvordan var din evne til å være glad i andre mennesker før behandling?		0	1	2	3	4
Hvordan fungerte du seksuelt før behandling?		0	1	2	3	4
Hvordan fungerte du sosialt før behandling?		0	1	2	3	4
Hvordan var din arbeidsevne før behandling?		0	1	2	3	4
Hvordan synes du kvaliteten på livet ditt var før behandling?		0	1	2	3	4
Hvordan var kontakten med din familie før behandling?		0	1	2	3	4
Hvordan var kontakten med egne barn før behandling?	☐	0	1	2	3	4

Mål på psykologisk avhengighet siste 4 uker

Som du opplevde det mht til rusmidler siste måned før du begynte i behandling (avrusning er behandling).	0 Aldri	1 Noen ganger	2 Ofte	3 Alltid
Tenkte du at ditt forbruk av rusmidler var ute av kontroll?	0	1	2	3
Gjorde tanken på å ikke ta rusmidler at du følte deg engstelig eller bekymret?	0	1	2	3
Har ditt forbruk av rusmidler bekymret deg?	0	1	2	3
Skulle du ønske du kunne klare å slutte?	0	1	2	3
	Ikke i det hele tatt	Litt vanskelig	Vanskelig	Umulig
Hvor vanskelig synes du det var å stoppe? (gjelder ikke LAR-medisiner)	0	1	2	3

Selvkontroll

Nedenfor skal du vurdere påstandene etter hvor godt de passer for deg.	0 Passer ikke det hele tatt	1 Litt	2 Moderat	3 Ganske mye	4 Passer svært godt
Jeg er flink til å motstå fristelser	0	1	2	3	4
Jeg synes det er vanskelig å endre dårlige vaner	0	1	2	3	4
Jeg er lat	0	1	2	3	4
Jeg sier upassende ting	0	1	2	3	4
Jeg gjør enkelte ting som er morsomt, selv om det ikke er bra for meg	0	1	2	3	4
Jeg motstår ting som er dårlig for meg	0	1	2	3	4
Jeg skulle ønske jeg hadde mer selvdisiplin	0	1	2	3	4
Folk vil si jeg har jerndisiplin	0	1	2	3	4
Ønsket om å ha det gøy forhindrer meg noen ganger i å få jobben gjort	0	1	2	3	4
Jeg har konsentrasjonsvansker	0	1	2	3	4
Jeg klarer å jobbe effektivt mot langsiktige mål	0	1	2	3	4
Enkelte ganger klarer jeg ikke å stoppe meg selv i å gjøre noe jeg vet er galt	0	1	2	3	4
Jeg handler ofte uten å ha vurdert alle alternativene	0	1	2	3	4

Generelle matvaner siste 4 uker før inntak til behandling (før kontrollert miljø)

Hvor mange måltider spiste du per dag? ☐

Hvor mange varme måltider spiste du vanligvis per dag? ☐

Hvor mange mellommåltider (snack) spiste du per dag? ☐

Hvor mange brødmåltider spiste du vanligvis per dag? ☐

Med hvem spiste du vanligvis dine måltider? ☐

1 = Alene
2 = Med famile
3 = Med venner
4 = Med andre

Generelle matvaner siste 4 uker før inntak til behandling (før kontrollert miljø)

Sett en ring rundt det svaret som passer deg best.	0 Aldri	1 Sjelden	2 Av og til	3 Ofte
Hvor ofte spiste du tilberedt mat som ble servert på for eksempel suppestasjoner/institusjon/værested?	0	1	2	3
Hvor ofte spiste du «fast food» (hamburgere, pizza, pølser etc) som et hovedmåltid?	0	1	2	3
Hvor ofte spiste du halvfabrikatmat (frossenpizza, supper etc) som du varmet selv?	0	1	2	3
Hvor ofte lagde du/familiemedlem varme hjemmelagde måltider som du spiste?	0	1	2	3
Hvor ofte mottok du «matposer» fra for eksempel Frelsesarmeen?	0	1	2	3
Benyttet du deg av kosttilskudd	0	1	2	3

Tobakksvaner siste 6 måneder før behandling (før kontrollert miljø)

Røyket du tobakk?

☐ 1 = Ja
2 = Nei

Hvis ja, hvor mange sigaretter daglig? ☐

Brukte du snus?

☐ 1 = Ja
2 = Nei

Hvis ja, antall dager per boks? ☐

Dopingmidler siste 6 måneder før behandling (før kontrollert miljø)

Brukte du dopingmidler?

☐ 1 = Ja
2 = Nei

Hvis ja, hvor mange ganger per uke? ☐

Hvis ja, hvilken type dopingmidler?

☐ Anabole steroider ☐ Andre: .....

Hvis ja, brukte du sprøyter?

☐ 1 = Ja
2 = Nei

Fysisk trening siste 6 måneder før behandling (før kontrollert miljø)

Drev du med fysisk trening, enten organisert eller i privat regi?

☐ 1 = Ja
2 = Nei

Hvis ja, hva slags trening? .....

Hvis ja, hvor mange dager per uke? ☐

Høyde og vekt

Selvrapportert vekt i kilo ☐☐☐

Selvrapportert høyde i cm ☐☐☐

Hvordan vurderer du din egen vekt i dag?

☐ For lav ☐ Passe ☐ For høy

Deltagelse i denne studien innebærer at vi vil forsøke å få høre hvordan det har gått med deg igjen etter noe tid (1-5 år). For at vi skal kunne komme i kontakt med deg ved oppfølgingstidspunktene, må vi ha oppdatert kontaktinformasjon.

Vi ber også om at du i tillegg til egen informasjon oppgir minst 2 andre kontaktpersoner som vet hvor du stort sett befinner deg. Vi har erfaring fra at mange skifter adresse, og telefonnummer i oppfølgingstiden. Vi trenger derfor informasjon fra tilleggskontaktene for å kunne nå deg.

Kontaktinformasjon for pasienten:

Navn:

Adresse:

Telefonnr 1:

Telefonnr 2:

Telefonnr 3:

E-mail:

Din kontakt i kommunen:

Kontaktperson 1

Relasjon/rolle: familie, behandler, venn, annet ……

Navn:

Adresse:

Telefonnr 1: Telefonnr 2:

E-mail:

Kontaktperson 2

Relasjon/rolle: familie, behandler, venn, annet ……

Navn:

Adresse:

Telefonnr 1: Telefonnr 2:

E-mail:

Appendix 2

Senter for rus- og avhengighetsforskning

Tiltaksnr	Løpenr

Norsk oppfølgingsstudie av opioid-avhengige i behandling (NorComt)

1. oppfølgningsintervju
for døgn- og LAR klienter

Inklusjonskriterier: 12 måneder etter første intervju.
(ikke «veteraner»)

Intervjuskjema

Samarbeid mellom SERAF, regionale LAR-sentre og rusbehandlingsinstitusjoner

SERAF 2014

Kontaktpersoner:
Edle Ravndal: edle.ravndal@medisin.uio.no
Thomas Clausen: thomas.clausen@medisin.uio.no

Liste over tiltaksnummer

01 = LAR Vestfold
02 = LAR Vest-Agder
03 = Helse Bergen
04 = LAR Nord
05 = SPA, Oslo
06 = LAR Telemark
07 = LAR Buskerud
09A = LAR Hamar (Innlandet)
09B = LAR Gjøvik (Innlandet)
09C = LAR Lillehammer (Innlandet)
10 = Veksthuset Rogaland
11 = Samtun Sauherrad
12 = Arken
13 = Sollia
14 = Tyrili 1 (Høvringen)
15 = Tyrili 2 (Frankmotunet)
16 = Tyrili 3 (Tyrilihaugen)
17 = Tyrili 4 (Tyrilitunet)
18 = Tyrili 5 (Kampen)
19 = Tyrili 6 (Tyrili Sør)
20 = Veksthuset Molde
21 = LAR Midt
22 = LAR Akershus
23 = LAR Aust-Agder
24 = Renåvangen
25 = LAR Fredrikstad (Østfold)
26 = LAR Moss (Østfold)
27 = LAR Sarpsborg (Østfold)
28 = LAR Askim (Østfold)
29 = LAR Halden (Østfold)

Hvis i LAR

LAR-medisiner i dag

	Dose mg/dag
Subutex / buprenorfin	…….....
Subuxone	…….....
Metadon	…….....
Annet	…….....

Utleveringsordning LAR-medisin

LAR-senter	☐
Apotek	☐
Fastlege	☐
Hjemmesykepleier	☐
Annet: …….	☐

Henteordning for LAR-medisin

	Antall dager per uke
Observert inntak	…….....
Ta med hjem-dosering	…….....

Kontrolltiltak mht rusmiddelinntak

	Antall ganger per uke
Urinprøvekontroller	…….....
Spyttprøvekontroller	…….....
Sporadiske spytt/urinprøvekontroller	☐ Nei ☐ Ja

Fødselsnummer

☐☐☐☐☐☐ ☐☐☐☐☐

Kjønn

☐

1 = Mann
2 = Kvinne

Dato for start kartlegging (NPR)

☐☐ ☐☐ ☐☐☐☐

dag måned år

Behov for tolk

☐

1 = Ja
2 = Nei

Sivilstatus, per i dag

☐

0 = Ikke oppgitt
1 = Aldri gift
2 = Gift
3 = Enke / enkemann
4 = Separert
5 = Skilt
6 = Registrert partner (samboer)
7 = Separert partner
8 = Skilt partner
9 = Gjenlevende partner

Høyeste fullførte utdanning, per i dag

☐

1 = Ikke avsluttet grunnskole
2 = Grunnskole
3 = Videregående skole/gymnas/yrkesskoleutdanninger
4 = Faglig yrkesutdanning
5 = Treårig høyskole/universitet
6 = Mer enn treårig høyskole/universitet
9 = Ukjent

Yrkesstatus, per i dag

☐

1 = Utenfor arbeidsmarkedet og ikke under utdanning
2 = Heltidsjobb
3 = Deltidsjobb
4 = Under utdanning
5 = Deltidsjobb og under utdanning
9 = Ukjent

Viktigste inntekt siste 4 uker

☐

1 = Lønnet arbeid
2 = Forsørget
3 = Arbeidsledighetstrygd
4 = Syke-/rehabiliteringspenger
5 = Atføringspenger
6 = Uførepensjon
7 = Alderspensjon
8 = Sosial stønad
9 = Annet
10 = Ukjent
11 = Studielån/stipend
12 = Stønad til enslig forsørger

Bor sammen med (NPR), per i dag (flere valg mulig)

☐ 1 = Bor alene
☐ 2 = Bor i parforhold
☐ 3 = Bor sammen med venner
☐ 4 = Bor sammen med foreldre
☐ 5 = Bor sammen med barn under 18 år
☐ 6 = Bor sammen med barn over 18 år
☐ 7 = Bor sammen med andre
☐ 9 = Ukjent

Boligforhold siste 4 uker (NPR)

☐

1 = Ingen bolig
2 = Hospits/hybelhus/hotell
3 = Institusjon
4 = Egen privat bolig
5 = Privat bolig eid av annen
6 = Annet

Hatt en stabil bosituasjon siste 4 uker

☐

1 = Ja
2 = Nei
9 = Ukjent

Barn (NPR), per i dag

Antall egne barn uansett alder og bosituasjon (NPR) ☐

Alder og bosituasjon for barn under 18 år (NPR)

	0-6 år	7-12 år	13-17 år
Hjemmeboende barn (egne), angi antall	☐	☐	☐
Hjemmeboende barn (andres), angi antall	☐	☐	☐

Tiltak for barn under 18 år (ikke NPR)

	Ikke behov	Bør iverksettes	Er iverksatt	Ukjent
Hjemmeboende barn (egne), angi antall	☐	☐	☐	☐
Hjemmeboende barn (andres), angi antall	☐	☐	☐	☐

Graviditet (NPR), per i dag

☐

1 = Ja
2 = Nei
9 = Ukjent

☐☐ **Antall uker gravid**
(Eks.: 1 uke = 01; 2 uker = 02; 10 uker = 10)

Testet for blodsmittevirus siste år?

☐	☐	☐
Hepatitt B	**Hepatitt C**	**HIV**

1 = Ja
2 = Nei
9 = Ukjent

Psykiske vansker/lidelser (NPR) siste 4 uker

Siste 4 uker

(begge kolonnene må besvares for hvert spørsmål)
1 = Ja 2 = Nei 9 = Ukjent

☐	Hatt alvorlige depresjoner
☐	Hatt alvorlig angst
☐	Hatt vrangforestillinger/hallusinasjoner
☐	Blitt forskrevet medisiner for et eller annet psykisk/følelsesmessig problem
☐	Hatt alvorlige tanker om å ta livet av seg

Forsøk på selvmord siste år

☐

1 = Nei
2 = Ja, ved overdose
3 = Ja, på annen måte
4 = Både ved overdose og på annen måte
9 = Ukjent

Mottatt profesjonell hjelp for psykiske vansker/lidelser siste år

☐

1 = Ja
2 = Nei
9 = Ukjent

Antall rusmidler brukt siste 6 måneder

☐☐ **Angi antall rusmidler**
(Eks.: 1 rusmiddel = 01; 2 rusmidler = 02; 10 rusmidler = 10)

00 = Ingen
99 = Ukjent

Rusmiddel-/medikamentprofil siste 6 måneder

	Type rusmiddel/medikament(NPR) (Bruk koden nedenfor)	**Inntaksmåte (NPR)** (Bruk koden nedenfor)	**Hvor ofte brukt siste 4 uker (NPR)** (Bruk koden nedenfor)	**Alder brukt første gang (NPR)**	**Hvor lenge problemfylt bruk** (Antall år)
Mest brukte rusmiddel/ medikament					
2. mest brukte					
3. mest brukte					
4. meste brukte					

0 = Ingen
1 = Alkohol
2 = Cannabis
3 = Heroin/Opium
4 = Metadon, buprenorfin, andre opiater/opioder forskrevet i LAR-program
5 = Metadon, buprenorfin, andre opiater/opioder forskrevet utenfor LAR-program
6 = Metadon, buprenorfin, andre opiater/opioder ervervet uten at forskrevet av lege
7 = Benzodiazepiner forskrevet av lege
8 = Benzodiazepiner ikke forskrevet av lege
9 = Andre vanedannende medikamenter
10 = Amfetamin
11 = Kokain
12 = Crack
13 = Andre sentralstimulerende midler
14 = LSD og likn.
15 = Ecstasy
16 = Løsemidler
17 = Rødsprit o.l
18 = Annet
99 = Ukjent

1 = Drikker/spiser
2 = Injiserer
3 = Røyker
4 = Sniffer
8 = Annet
9 = Ukjent

1 = Ikke brukt
2 = Sjeldnere enn 1 gang i uken
3 = Omtrent ukentlig
4 = 2-4 dager i uken
5 = 5-6 dager i uken
6 = Daglig
9 = Ukjent

99 = Ukjent

00 = Ikke
01 = Et år eller mindre
99 = Ukjent

Brukt sprøyter siste år?

1 = Ja
2 = Nei
9 = Ukjent

Sprøytebruk siste 4 uker (NPR)

1 = Ikke brukt sprøyte
2 = Sjeldnere enn 1 gang i uken
3 = Omtrent ukentlig
4 = 2-4 dager i uken
5 = Daglig eller nesten daglig
9 = Ukjent

Antall ganger overdose siste år

Antall for hvert av stoffområdene

Alkohol
Narkotika
Medikament
Kombinasjon

00 = Ingen ganger
99 = Ukjent

Kontrollert miljø

I løpet av de siste 30 dagene har du vært innlagt i det vi kan kalle et «kontrollert miljø»? ☐

1 = Nei
2 = Fengsel
3 = Behandlingsinstitusjon for rusmiddelmisbrukere
4 = Somatisk sykehus
5 = Psykiatrisk sykehus/klinikk
6 = Bare avrusning/avgiftning
7 = Annet kontrollert miljø, spesifiser: ……

Var dette miljøet/behandling med LAR?

☐ Nei
☐ Ja

Kjæledyr

Har du eget kjæledyr?

☐ Nei ☐ Hund ☐ Katt ☐ Fugl ☐ Hest ☐ Annet, spesifiser: ……..

Dersom ja, hva er de viktigste grunnene til at du har eget kjæledyr?

☐ Min beste venn
☐ Føler trygghet
☐ Liker dyr
☐ Enklere relasjon med dyr enn mennesker
☐ Har alltid hatt dyr
☐ Ingen spesiell grunn
☐ Vet ikke
☐ Annet, spesifiser: ……..

Sosialt nettverk siste 6 måneder

Hvem er du mest sammen på fritiden vanligvis? ☐
(Lengeværende kjæresteforhold defineres som familie/minst 1 år)

1 = Familie uten nåværende problemer med alkohol/stoff/medikamenter
2 = Familie med nåværende problemer med alkohol/stoff/medikamenter
3 = Venner uten nåværende problemer med alkohol/stoff/medikamenter
4 = Venner med nåværende problemer med alkohol/stoff/medikamenter
5 = Er mest alene

Hvor mange av dem du er mest sammen med er jevnlig involvert i kriminalitet (unntatt egen bruk og besittelse)

☐ Ingen ☐ De færreste ☐ Omtrent halvparten ☐ De fleste ☐ Alle ☐ Vet ikke / vil ikke svare

Utsatthet for kriminalitet siste år

	Siste år		
	Nei	Ja	Ant ganger
Har du blitt frastjålet personlige ting som penger, mobiltelefon eller andre ting?	☐	☐	
Har du blitt utsatt for fysisk vold som førte til synlige merker eller skader på kroppen?	☐	☐	
Har du blitt utsatt for fysisk vold som ikke førte til synlige merker eller skader på kroppen?	☐	☐	
Har du blitt utsatt for trusler?	☐	☐	
	Siste året		
Har du noen gang **det siste året** blitt utsatt for seksuelt motivert vold, overgrep eller voldtekt, eller forsøk på dette?	☐	☐	

Hvem utførte kriminaliteten mot deg ved siste hendelse?

☐ Ukjent person ☐ Bekjent/venn ☐ Person som brukte makt i sitt arbeid

☐ Familie/partner ☐ Andre ☐ Vil ikke svare

Egen kriminalitet det siste året

	Siste år		
	Nei	Ja	Ant ganger
Har du vært involvert i kriminelle handlinger? (unntatt egen bruk og besittelse)	☐	☐	
Hvis Ja: Herunder vinningskriminalitet? (alle typer tyveri, bedrageri, innbrudd, heleri)	☐	☐	
Hvis Ja: Narkotikaforbrytelser? (unntatt egen bruk og besittelse, gjelder narkotika og doping, solgt, smuglet, tilvirket, annet)	☐	☐	
Hvis Ja: Voldskriminalitet? (Med vilje påført andre fysisk smerte/skade)	☐	☐	
Hvis Ja: Trafikk kriminalitet? (Kjørt ruspåvirket, uten førerkort, for fort, annet)	☐	☐	
Hvis Ja: Annen kriminalitet?	☐	☐	

LAR-medisiner og kriminalitet det siste året

	Nei	Ja	Ikke aktuelt	Ønsker ikke å svare
Har du siste år omsatt/byttet ditt eget LAR-medikament?	☐	☐	☐	☐
Har du siste år gitt bort/delt ditt eget LAR-medikament?	☐	☐	☐	☐
Har du siste år blitt frastjålet ditt eget LAR-medikament?	☐	☐	☐	☐
Har du siste år kjøpt illegalt LAR-medikament?	☐	☐	☐	☐

Soning det siste året

	Nei	Ja	Ant ganger	Dersom soning, ant måneder totalt
Har du sonet dom i fengsel siste år?	☐	☐		

SCL – 25. Hvor mye har du vært plaget av: (den siste uka)

(samme spørsmål i SCL-90)

Sett en ring rundt det svaret som passer deg best.	0 Ikke i det hele tatt	1 Litt	2 Moderat	3 Ganske mye	4 Veldig mye
1. Hodepine	0	1	2	3	4
2. Skjelving	0	1	2	3	4
3. Matthet eller svimmelhet	0	1	2	3	4
4. Nervøsitet, indre uro	0	1	2	3	4
5. Plutselig frykt uten grunn	0	1	2	3	4
6. Stadig redd eller engstelig	0	1	2	3	4
7. Hjertebank, hjerteslag som løper avgårde	0	1	2	3	4
8. Følelse av å være anspent, oppjaget	0	1	2	3	4
9. Anfall av angst eller panikk	0	1	2	3	4
10. Så rastløs at det er vanskelig å sitte stille	0	1	2	3	4
11. Mangel på energi, alt går langsommere enn vanlig	0	1	2	3	4
12. Lett for å klandre seg selv	0	1	2	3	4
13. Lett for å gråte	0	1	2	3	4
14. Tanker om å ta ditt liv	0	1	2	3	4
15. Dårlig matlyst	0	1	2	3	4
16. Søvnproblemer	0	1	2	3	4
17. Følelse av håpløshet med tanke på fremtiden	0	1	2	3	4
18. Nedtrykt, tungsindig	0	1	2	3	4
19. Følelse av ensomhet	0	1	2	3	4
20. Tap av seksuell lyst og interesse	0	1	2	3	4
21. Følelse av å være lurt i en felle eller fanget	0	1	2	3	4
22. Mye bekymret eller urolig	0	1	2	3	4
23. Uten interesse for noe	0	1	2	3	4
24. Følelse av at alt er et slit	0	1	2	3	4
25. Følelse av å være unyttig	0	1	2	3	4

Somatisk helse. Hvor mye har du vært plaget av: (siste 6 måneder)

Sett en ring rundt det svaret som passer deg best.	0 Ikke i det hele tatt	1 Litt	2 Moderat	3 Ganske mye	4 Veldig mye	Kronisk lidelse? (minst 3 mnd i løpet av siste halvår)	
						Ja	Nei
Fordøyelsesplager	0	1	2	3	4	☐	☐
Diare	0	1	2	3	4	☐	☐
Forstoppelse	0	1	2	3	4	☐	☐
Luftveisplager	0	1	2	3	4	☐	☐
Eksem	0	1	2	3	4	☐	☐
Hudinfeksjoner	0	1	2	3	4	☐	☐
Leddsmerter	0	1	2	3	4	☐	☐
Hodepine	0	1	2	3	4	☐	☐
Brystsmerter	0	1	2	3	4	☐	☐
Svimmelhet	0	1	2	3	4	☐	☐
Nedsatt hukommelse	0	1	2	3	4	☐	☐
Synsforstyrrelser	0	1	2	3	4	☐	☐
Urinveisplager	0	1	2	3	4	☐	☐
Kjønnsykdommer	0	1	2	3	4	☐	☐
Blodpropp	0	1	2	3	4	☐	☐
Tann/tannkjøttsplager	0	1	2	3	4	☐	☐

Har du noen av de nevnte sykdommer per i dag?

	Ja	Nei	Ukjent/ vet ikke	Hvis Ja, har du i løpet av de siste 6 mnd fått behandling for din(e) sykdom(mer)?	
				Ja	Nei
Diabetes	☐	☐	☐	☐	☐
Høyt blodtrykk	☐	☐	☐	☐	☐
Hjertesykdom	☐	☐	☐	☐	☐
KOLS	☐	☐	☐	☐	☐
Astma	☐	☐	☐	☐	☐
Hepatitt B	☐	☐	☐	☐	☐
Hepatitt C	☐	☐	☐	☐	☐
Leverchirrose	☐	☐	☐	☐	☐
HIV	☐	☐	☐	☐	☐
Kreft	☐	☐	☐	☐	☐
Annet ……..	☐	☐	☐	☐	☐

Nåværende livskvalitet

Sett en ring rundt det svaret som passer deg best.

	Ikke aktuelt	0 Meget dårlig	1 Dårlig	2 Verken god/t eller dårlig	3 God/t	4 Meget god/t
Hvordan synes du selv din fysiske helse er?		0	1	2	3	4
Hvordan synes du selv din psykiske helse er?		0	1	2	3	4
Hvordan er ditt forhold til deg selv?		0	1	2	3	4
Hvordan er ditt forhold til dine venner?		0	1	2	3	4
Hvordan er ditt forhold til din partner?	☐	0	1	2	3	4
Hvordan er din evne til å være glad i andre mennesker?		0	1	2	3	4
Hvordan fungerer du seksuelt?		0	1	2	3	4
Hvordan fungerer du sosialt?		0	1	2	3	4
Hvordan er din arbeidsevne?		0	1	2	3	4
Hvordan synes du kvaliteten på livet ditt er?		0	1	2	3	4
Hvordan er kontakten med din familie?		0	1	2	3	4
Hvordan er kontakten med egne barn?	☐	0	1	2	3	4

Mål på psykologisk avhengighet siste 4 uker

Som du opplever det mht til rusmidler siste måned.	0 Aldri	1 Noen ganger	2 Ofte	3 Alltid
Tenker du at ditt forbruk av rusmidler er ute av kontroll?	0	1	2	3
Gjør tanken på å ikke ta rusmidler at du føler deg engstelig eller bekymret?	0	1	2	3
Bekymrer ditt forbruk av rusmidler deg?	0	1	2	3
Skulle du ønske du kunne klare å slutte?	0	1	2	3

	Ikke i det hele tatt	Litt vanskelig	Vanskelig	Umulig
Hvor vanskelig synes du det er å stoppe? (gjelder ikke LAR-medisiner)	0	1	2	3

Selvkontroll

Nedenfor skal du vurdere påstandene etter hvor godt de passer for deg.	0 Passer ikke det hele tatt	1 Litt	2 Moderat	3 Ganske mye	4 Passer svært godt
Jeg er flink til å motstå fristelser	0	1	2	3	4
Jeg synes det er vanskelig å endre dårlige vaner	0	1	2	3	4
Jeg er lat	0	1	2	3	4
Jeg sier upassende ting	0	1	2	3	4
Jeg gjør enkelte ting som er morsomt, selv om det ikke er bra for meg	0	1	2	3	4
Jeg motstår ting som er dårlig for meg	0	1	2	3	4
Jeg skulle ønske jeg hadde mer selvdisiplin	0	1	2	3	4
Folk vil si jeg har jerndisiplin	0	1	2	3	4
Ønsket om å ha det gøy forhindrer meg noen ganger i å få jobben gjort	0	1	2	3	4
Jeg har konsentrasjonsvansker	0	1	2	3	4
Jeg klarer å jobbe effektivt mot langsiktige mål	0	1	2	3	4
Enkelte ganger klarer jeg ikke å stoppe meg selv i å gjøre noe jeg vet er galt	0	1	2	3	4
Jeg handler ofte uten å ha vurdert alle alternativene	0	1	2	3	4

Generelle matvaner siste 4 uker

Hvor mange måltider spiser du per dag? ☐

Hvor mange varme måltider spiser du vanligvis per dag? ☐

Hvor mange mellommåltider (snack) spiser du per dag? ☐

Hvor mange brødmåltider spiser du vanligvis per dag? ☐

Med hvem spiser du vanligvis dine måltider? ☐

1 = Alene
2 = Med familie
3 = Med venner
4 = Med andre

Generelle matvaner siste 4 uker

Sett en ring rundt det svaret som passer deg best.	0 Aldri	1 Sjelden	2 Av og til	3 Ofte
Hvor ofte spiser du tilberedt mat som blir servert på for eksempel suppestasjoner/institusjon/værested?	0	1	2	3
Hvor ofte spiser du «fast food» (hamburgere, pizza, pølser etc) som et hovedmåltid?	0	1	2	3
Hvor ofte spiser du halvfabrikatmat (frossenpizza, supper etc) som du varmet selv?	0	1	2	3
Hvor ofte lager du/familiemedlem varme hjemmelagde måltider som du spiser?	0	1	2	3
Hvor ofte mottar du «matposer» fra for eksempel Frelsesarmeen?	0	1	2	3
Benytter du deg av kosttilskudd?	0	1	2	3

Tobakksvaner siste 6 måneder

Røyker du tobakk?

☐ 1 = Ja
2 = Nei

Hvis ja, hvor mange sigaretter daglig? ☐

Bruker du snus?

☐ 1 = Ja
2 = Nei

Hvis ja, antall dager per boks? ☐

Dopingmidler siste 6 måneder

Bruker du dopingmidler?

☐ 1 = Ja
2 = Nei

Hvis ja, hvor mange ganger per uke? ☐

Hvis ja, hvilken type dopingmidler?

☐ Anabole steroider ☐ Andre: …….

Hvis ja, bruker du sprøyter?

☐ 1 = Ja
2 = Nei

Fysisk trening siste 6 måneder

Driver du med fysisk trening, enten organisert eller i privat regi?

☐ 1 = Ja
2 = Nei

Hvis ja, hva slags trening? ……

Hvis ja, hvor mange dager per uke? ☐

Høyde og vekt

Selvrapportert vekt i kilo ☐☐☐

Selvrapportert høyde i cm ☐☐☐

Hvordan vurderer du din egen vekt i dag?

☐ For lav ☐ Passe ☐ For høy

ADHD – selvrapporteringsskjema for voksne-V1.1 (ASRS-V1.1)					
Kryss av for den ruten som best beskriver hvordan du har følt og oppført deg de siste 6 månedene.	0 Aldri	1 Sjelden	2 I blant	3 Ofte	4 Svært Ofte
Hvor ofte har du problemer med å avslutte en oppgave etter at de interessante delene er unnagjort?	0	1	2	3	4
Hvor ofte er det vanskelig for deg å få orden på ting når du skal utføre en oppgave som krever organisering?	0	1	2	3	4
Hvor ofte har du problemer med å huske avtaler eller forpliktelser?	0	1	2	3	4
Når du har en oppgave som krever at du tenker nøye igjennom det du skal gjøre, hvor ofte unngår eller utsetter du å begynne på den?	0	1	2	3	4
Hvor ofte sitter du og fikler med noe når du må sitte lenge i ro?	0	1	2	3	4
Hvor ofte føler du deg overdrevet aktiv og tvunget til å gjøre noe, som om du var drevet av en indre motor?	0	1	2	3	4

Spørsmål om ADHD		
	Nei	Ja
Har du noen gang lurt på om du har ADHD?	☐	☐
Har du noen gang vært utredet for ADHD?	☐	☐
Har du etter en utredning fått en ADHD diagnose?	☐	☐
Er du medisinert for ADHD?	☐	☐

Rusbehandling siste år
(Eks.: 1 mnd = 01; 12 mndr = 12)

	Antall måneder	Fullført etter planen
Hvor mange måneder til sammen har du vært i døgnbehandling uten LAR siste år?	☐☐	☐
Hvor mange måneder til sammen har du vært i døgnbehandling med LAR siste år?	☐☐	☐
Hvor mange måneder til sammen har du vært i poliklinisk behandling uten LAR siste år?	☐☐	☐
Hvor mange måneder til sammen har du vært i poliklinisk behandling med LAR siste år?	☐☐	☐

Behandling psykisk/somatisk helse siste år
(Eks.: 1 mnd = 01; 12 mndr = 12)

	Antall måneder	Fullført etter planen
Hvor mange måneder til sammen har du vært i poliklinisk behandling psykisk helse siste år?	☐☐	☐
Hvor mange måneder til sammen har du vært i døgnbehandling psykisk helse siste år?	☐☐	☐
Hvor mange måneder til sammen har du vært i poliklinisk behandling for somatikk (spesifikk lidelse) siste år?	☐☐	☐
Hvor mange måneder til sammen har du vært i døgnbehandling for somatikk (sykehus e.l.) siste år?	☐☐	☐

Behandlingsavbrudd siste år (indexbehandling)

Hvor mange avbrudd fra LAR har du hatt siste år? (Med avbrudd menes minst 30 dagers opphold fra LAR-medisiner)	☐☐ ☐ Ikke aktuelt
Hvor mange avbrudd fra døgnbehandling har du hatt siste år? (Med avbrudd menes utskrevet fra institusjon)	☐☐ ☐ Ikke aktuelt

Årsaker til avbrudd **siste** avbruddsepisode

LAR		Døgnbehandling	
☐ Ufrivillig utskrevet	☐ Frivillig behandlingsavbrudd	☐ Ufrivillig utskrevet	☐ Frivillig behandlingsavbrudd

Årsak til siste behandlingsavbrudd (flere valg mulig)	
☐ Rusmisbruk	☐ Ønske om nedtrapping og avslutning av LAR-medisin (planlagt)
☐ Manglende behandlingsnytte	☐ Bivirkninger av LAR-medisin
☐ Trusler og/eller vold mot pasient/ansatt	☐ Misnøye med regler og rammer under behandlingen
☐ Ønske om annen behandling	☐ Annet
☐ Misnøye med medikament (LAR eller annet)	

Behandling/oppfølging i dag

Er du i behandling i dag?

☐ Nei

☐ Poliklinisk med LAR

☐ Poliklinisk uten LAR

☐ Døgn med LAR

☐ Døgn uten LAR

Hva er ditt behandlingsmål med dette behandlingsopplegget? ☐

1 = Rehabilitering med rusfrihet
2 = Stabilisering med bedre rusmestring

Ønske for varighet av behandling? ☐☐☐
(Eks.: 1 mnd = 001; 12 mndr = 012; 12 år = 144, Livslang = 999)

☐ Vet ikke

Oppfølging fra hjelpeapparatet siste 6 mnd (flere valg er mulig)	
☐ Individuell plan	☐ Ansvarsgruppemøter
☐ Bistand mht bolig	☐ Bistand kurs; skole, utdanning
☐ Bistand mht jobb	☐ Bistand sosiale aktiviteter
☐ Oppfølging somatisk helse	☐ Oppfølging psykisk helse
☐ Oppfølging ernæring	☐ Oppfølging fysisk aktivitet/trening
☐ Oppfølging LAR-medisiner	☐ Forskrevet benzodiazepin
☐ Oppfølging økonomi	☐ Oppfølging hos fastlege

I forhold til tiden **før** du begynte i behandling, hvordan vurderer du **nå**

	Bedre	Som før	Dårligere	Uaktuelt	
Boligforhold	☐	☐	☐	☐	
Sosiale relasjoner til venner/familie	☐	☐	☐	☐	
Deltagelse i rusfrie nettverk	☐	☐	☐	☐	
Psykiske helse	☐	☐	☐	☐	
Kroppslige helse	☐	☐	☐	☐	
Ernæringsstatus	☐	☐	☐	☐	
Samlet vurdering av livssituasjon/kvalitet	☐	☐	☐	☐	
	Ikke lenger	Mindre	Som før	Større/ mer	Uaktuelt
Samlet rusmiddelforbruk	☐	☐	☐	☐	☐
Bruk av alkohol	☐	☐	☐	☐	☐
Bruk av benzodiazepiner	☐	☐	☐	☐	☐
Bruk av opioider (inkl heroin) (ikke LAR-medisin)	☐	☐	☐	☐	☐
Bruk av cannabis	☐	☐	☐	☐	☐
Bruk av andre illegale rusmiddel	☐	☐	☐	☐	☐
Deltagelse i kriminell aktivitet	☐	☐	☐	☐	☐
Utsatthet for kriminalitet	☐	☐	☐	☐	☐
Grad av oppfølging fra hjelpeapparatet/helsevesen	☐	☐	☐	☐	☐
Behov for ytterligere behandling for rusproblem	☐	☐	☐	☐	☐
	Godt	Både og	Dårlig		
Hvordan har behandlingen fungert i forhold til dine forventninger?	☐	☐	☐		
Samlet sett hvor fornøyd er du med behandlingen?	☐	☐	☐		

1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 Intervju måned

BEHANDLING

RUSBRUK

BOFORHOLD

AKTIVITET/ARBEID

Viktige livshendelser (+/-)

Var det noe du savnet i behandlingen?

……
……

……
……

Det er en mulighet for at vi igjen ønsker å komme i kontakt med deg for oppfølgingsintervju i løpet av de neste 5 årene. For at vi skal kunne komme i kontakt med deg ved oppfølgingstidspunktene, må vi ha oppdatert kontaktinformasjon.

Vi ber også om at du i tillegg til egen informasjon oppgir minst 2 andre kontaktpersoner som vet hvor du stort sett befinner deg. Vi har erfart at mange skifter adresse, og telefonnummer i oppfølgingstiden. Vi trenger derfor informasjon fra tilleggskontaktene for å kunne nå deg.

Kontaktinformasjon for pasienten:

Navn:

Adresse:

Telefonnr 1:

Telefonnr 2:

Telefonnr 3:

E-mail:

Din kontakt i kommunen:

Kontaktperson 1

Relasjon/rolle: familie, behandler, venn, annet ……

Navn:

Adresse:

Telefonnr 1: Telefonnr 2:

E-mail:

Kontaktperson 2

Relasjon/rolle: familie, behandler, venn, annet ……

Navn:

Adresse:

Telefonnr 1: Telefonnr 2:

E-mail:

Errata

Forkortelser for type rettelser:

Cor – korrektur

Celtf – endring av sidelayout eller tekstformat

Side	Linje	Fotnote	Originaltekst	Type rettelse	Korrigert tekst
8	23		Diagnostic and Statistical Manual for Mental Disorders (DSM-V)	Cor	Diagnostic and Statistical Manual for Mental Disorders (DSM-5)
23	11		Of the 746 patients who were considered eligible 548 (74%) enrolled, while 129 declined, 45 did not meet for interview appointments and 23 were not interviewed for other reasons.	Cor	Of the 745 patients who were considered eligible 548 (74%) enrolled, while 129 declined, 45 did not meet for interview appointments and 23 were not interviewed for other reasons.
25	Fig 4		Approached for participation n = 438	Cor	Approached for participation n = 745
63	18		Also, ongoing or recently stopped substance use can influence treatment of ADHD, both by neurobiological influences and by and reduced therapeutic compliance under the influence of substances (242).	Cor	Also, ongoing or recently stopped substance use can influence treatment of ADHD, both by neurobiological influences and by reduced therapeutic compliance under the influence of substances (242).