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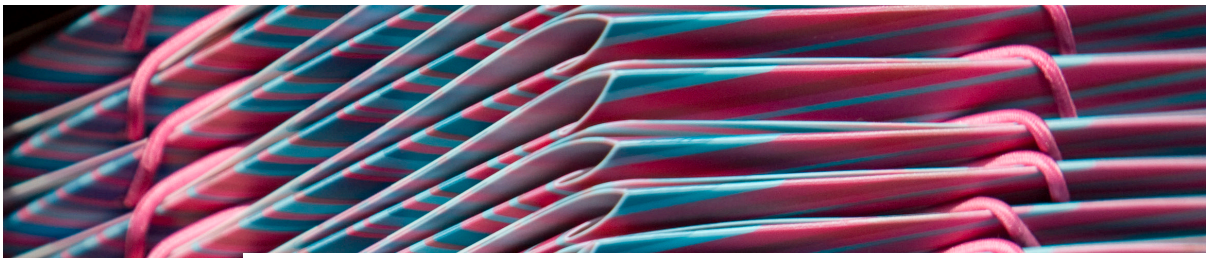

Problematic substance use and co-occurring psychiatric problems in young clinical patients and in criminal justice clients

Studies of mortality, measurements and intervention

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Martin Olsson

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Title and subtitle

Problematic substance use and co-occurring psychiatric problems in young clinical patients and in criminal justice clients. Studies of mortality, measurements and intervention.

Abstract

Background: Substance use disorders commonly involve psychiatric co-morbidity in adolescents and young adults, who are at risk of further negative development including criminality. This thesis aims to study intervention for psychiatric symptoms and new techniques for drug detection among adolescents and young adults, and risk factors for psychiatric hospitalization and self-inflicted death among criminal justice clients.

Methods: Adolescents and young adults (N=73) recruited at a treatment facility in Malmö, Sweden, participated in a randomized controlled trial during three months, using an automated telephone technique (Interactive Voice Response, IVR), measuring stress and mental health symtoms twice weekly. The intervention group received personlized feed-back on their ratings (improved or not) as an add-on intervention to treatment as ususal (paper III). Effects on these measurements were analyzed with mixed model analysis. In addition, hair samples were obtained to investigate the prevalence of non-medical prescription opioid use (n= 59, paper IV). Psychiatric (MINI) and socio-demographic (Ung-DOK) data were collected. Comparisons were made between patients positive and negative for prescription opioids with reference to socio-demographic and psychiatric background variables.

Clients in the criminal justice system interviewed with the Addiction Severity Index (ASI) were followed after release in national Swedish patient registers with respect to psychiatric hospitalization (N=4,081, paper I) and self-inficted death; suicide, accidental intoxication, so called overdose, or death of undetermined intent, using Cox regression analyses including background variables from the ASI interviews (N=6,744, paper II).

Results: IVR with personal feed-back, compared to the control condition, significantly improved stress and anxiety symptoms, but not depression or substance use. All but one patients used cannabis. In hair analysis, tramadol was the most prevalent opioid drug, used by almost one third of the sample. This group did not differ from the others regarding psychiatric or socio-demographic problems. Polysubstance use was common.

Ten percent of the population of released prisoners were hospitalized for psychiatric in-patient treatment. Significant predictors were previous psychiatric hospitalization, previous suicide attempt, depression, anxiety and use of sedatives. Use of amphetamines negatively predicted hospitalization. Death of undetermined intent was more closely associated with substance-related risk factors, and had more in common with accidental intoxications, whereas psychiatric risk factors predicted suicide.

Conclusions: Intervention with IVR shows promising results and merits further development. It is of importance to screen for different kinds of drugs among adolescents. The results point to the importance of paying attention to both psychiatric and substance use problems before and after release form prison, in order to prevent future psychiatric hozpitalization and unnatural deaths.

Key words: Substance use, psychiatric co-morbidity, Addiction Severity Index, criminal justice population, adolescent, young adult, RCT, Interactive Voice Response, Non-Medical Prescription Opioid Use, hair analysis

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II. Olsson M O, Brådvik L, Öjehagen A, Håkansson A (2016). **Risk factors for unnatural death: Fatal accidental intoxication, undetermined intent and suicide: Register follow-up in a criminal justice population with substance use problems.** Drug and Alcohol Dependence. 2016;162:176-81. Reprinted by permission of Elsevier Ireland Ltd.

III. Andersson C, Öjehagen A, Olsson M O, Brådvik L, Håkansson A (2016). **Interactive Voice Response with feedback intervention in outpatient treatment of substance use problems in adolescents and young adults: A randomized controlled trial.** International Journal of Behavioral Medicine. 2016; DOI 10.1007/s12529-016-9625-0. Published with open access at Springerlink.com.

IV. Olsson M O, Öjehagen A, Brådvik L, Kronstrand R, Håkansson A (2017). **High rates of tramadol use among treatment-seeking adolescents in Malmö, Sweden. A pilot study of hair analysis of non-medical prescription opioid use.** Submitted.

Introduction

The Global Burden of Disease study from 2013 (GBD 2013) has suggested that the disease burden attributed to substance use has increased world-wide among adolescents and young adults. Extensive reviews based on GBD data [1] systematic reviews on risks for various negative outcomes [2] and reviews on intervention and treatment [3] have pointed to the vital importance of addressing this problem internationally.

Early onset of substance use is a risk factor for development of delinquency and criminal behavior [4, 5] Psychiatric problems often precede the onset of substance use [6] in adolescents and young adults. Therefore, there is a need to develop interventions targeted at both psychiatric problems and substance use problems. In this thesis, two different populations of substance users were investigated: a clinical sample of adolescents and young adults seeking treatment for problematic substance use, and a sample of adults in the criminal justice system. In the population of young, treatment-seeking patients, psychiatric co-morbidity and intervention as a possible new treatment of psychiatric symptoms were investigated, as well as new substance use patterns in this group. In the criminal justice population, prospective risk factors were investigated for psychiatric hospitalization and predictors for self-inflicted death.

Background

History

Substance use has a long history in mankind. Alcohol and other mind-altering drugs have been known for 8,000-10,000 years [7]. Still, alcohol is the most common addictive substance among adolescents [8]. Use of cannabis has been known in recorded history for almost 5,000 years [9], and the use of opium has been known for almost 3,000 years [10]. With the development of refined narcotics in the end of the 19th century, such as morphine, heroin and amphetamine, and the invention of the injection syringe during the same period, drug addiction became a widespread problem internationally during the 20th century [11]. In the late 1960's, cannabis smoking spread massively to the adolescent and young adult population, especially in the "hippie" movement [9].

Before the 1960's, illicit drug use among adolescents in the US was seen as an extremely deviant behavior, whereas from the 1970's, authors [12] pointed out it had developed to epidemic proportions. From the 1970's, national surveys in the US, such as Monitoring the Future [13] and the National Survey on Drug Use and Health [14], have provided epidemiological data on trends in substance use in the adolescent population.

The concept of "dual diagnosis" – a co-occurrence of substance use problems and mental health problems – was developed in the 1970's through observations in clinical samples of institutionalized, or treatment-seeking patients, where the prevalence of co-morbidity between substance use and mental health problems was high [15-22]. The definition of psychiatric co-morbidity has varied, according to the diagnostic criteria, interviews and protocols used [23].

Substance use and psychiatric co-morbidity in studies of the general population

In the 1970's, the necessity to further investigate the mental health of the US population was formulated by the 1978 report of the President's Commission of Mental Health, which led to the development of nationwide epidemiological surveys in the general US population, the third generation of mental disorder epidemiological studies: the *Epidemiological Catchment Area (ECA)* project in the 1980's [24, 25], the *National Comorbidity Survey (NCS)* in the 1990's [26, 27], followed in the 2000's by the *National Epidemiologic Survey on Alcohol and Related Conditions, NESARC* [28-33]

The Epidemiological Catchment Area (ECA) study, based on a sample of five local areas (more than 200,000 respondents), covering both an institutionalized population and the general population, could show a lifetime prevalence of "any alcohol, drug or mental disorder", measured by DSM-III, in almost one third (32.7%) of the population. More than one fifth (22.5%) had a mental disorder except alcohol and drug use disorder. In the institutionalized population, mental hospitals and prisons displayed the highest lifetime rates (82.2% and 82.0%, respectively) of any alcohol, drug or mental disorder [25].

The National Comorbidity Survey (NCS) was conducted as a household survey in the general population in the US, to determine the prevalence and correlates of DSM-III-R mental and substance disorders. Results from the NCS study showed higher prevalence rates for mental disorders and substance use disorders: more than half of the sample with a mental disorder had a lifetime substance use disorder, and half of the sample with a substance use disorder were likely to develop a mental disorder [26]. Data from the NCS – representative for the whole US population – could be used for understanding the temporal relationship between onset of a mental disorder and the development of a substance use disorder. In the majority of the cases, a mental disorder occurred before the onset of a substance use disorder. In follow-up surveys (NCS-2, NCS – Adolescent supplement) researchers could identify certain mental disorders as specific risk factors for substance use [34, 6].

However, the diagnostic instruments in the surveys, DSM-III (ECA) or DSM-III-R (NCS), were not considered specific enough for differentiating between substance-induced states and independent states of psychiatric co-morbidity. Therefore, the first wave of *NESARC*, the National Epidemiological Survey on Alcohol and Related Conditions, so far the most updated national survey in the US, was issued by the National Institute on Alcohol Abuse and Alcoholism from 2001-2002. The survey comprises more than 43,000 respondents, civilian, and non-institutionalized US citizens, together with oversampled groups of the population with heavy

substance use patterns. NESARC, with a second survey in 2004-2005 (wave 2), has been the basis for a solid body of epidemiological research in psychiatric co-morbidity [35, 36]. Merikangas and McClair have compared the results from both NCS and NESARC in a review [37].

In Europe, a national prospective study, the Netherlands Mental Health Survey and Incidence Study (NEMESIS), followed a representative sample of the population (18-64 years) in Holland with repeated measurements between 1996 and 1999 [38]. Data from NEMESIS and NEMESIS-2, conducted 2007-2012, have given important information on first incidence of substance use and psychiatric disorders [39, 40] and specifically on associations between substance use and obsessive-compulsive disorder [41] in the general population.

In Munich, Germany, a longitudinal study, the EDSP (Early Developmental Stages of Psychopathology), began in 1975, following a cohort of adolescents and young adults (14-24 age), on four occasions. As in the NESARC surveys, DSM-IV diagnostic interviews (CIDI) were used. Data from this prospective study have provided important information on the onset of psychiatric symptoms, relations between psychiatric symptoms and substance use, and risk factors for substance use, especially cannabis use [42-56].

Substance use and co-occurring psychiatric problems in adolescents and young adults

Data from SAMHSA [57] and the extended NCS-Adolescent Supplement survey study [58-61], as well as reviews on community samples [62-64] and treatment-seeking samples [65-67], have shown a considerable co-morbidity for substance use and psychiatric symptoms among adolescents. Mental and substance use disorders are the leading causes of disability among adolescents and young adults world-wide [68]. Robinson and Riggs [69] have summed up the current research findings, suggesting implementation of evidence-based treatment models.

Follow-up studies in longitudinal cohorts, such as the EDSP in Munich and the Dunedin cohort in New Zealand [70-74] have elucidated the link between substance use and psychiatric problems. Conway and co-workers [6] showed, in an analysis of the National Comorbidity Survey – Adolescent Supplement, that prior mental disorders (anxiety disorders and behavioral disorders) represent risk factors for transition to substance use and drug- or alcohol-related problems. This finding is consistent with previous studies [75, 76] on co-morbidity in adolescent populations, where it has been established, that both *externalizing* behaviors, such as conduct disorder (CD) or oppositional defiant disorder (ODD), most common among boys,

and *internalizing* disorders, as depression and anxiety, more common among girls, have a strong association with developing substance use problems in early adolescence [77, 78].

Cannabis

An extensive prevalence study based on epidemiological data from the Global Burden of Disease 2010 study showed an estimate of more than 13 million cannabis-dependent people globally, where the prevalence peaked in young adulthood, between 20 and 24 years [79].

Most epidemiological studies concerning the association between substance use and mental health problems have focused on effects of cannabis smoking. The Victoria Adolescent Health Cohort Study, an Australian cohort study on the effects of cannabis use in adolescence could show increased risks of developing mental health problems in early adulthood [80, 81]. Findings from the EDSP have shown that early symptoms of anxiety and depression precede the development of cannabis use [46]. Findings from the Dunedin cohort suggest that the association between mental health and cannabis use works in both directions [73].

The association between cannabis use and development of psychotic symptoms, specifically schizophrenia, was first established by Andreasson et al [82] using a cohort from the Swedish national register of conscripts followed for in-patient care in hospital records. The association between cannabis and psychosis has been verified since then from different studies and reviews [83-89], and the effects of cannabis on the course of schizophrenia, notably the effect of early exposure to cannabis, have been suggested by Arsenault et al [84] and Konigs et al [90]. Arendt and co-workers [91] could show that 44% of those treated for cannabis-induced psychosis between 1994 and 1999 in Denmark had developed schizophrenia-spectrum disorders at follow-up five years later.

Non-medical prescription opioid use

Non-medical prescription opioid use (NMPOU) has reached epidemic proportions in the US over the last two decades [92] and prescription opioid use is also increasing in the UK [93] and in the rest of Europe [94]. The problem of adolescent prescription opioid use in the US has been investigated by Zosel et al [95]. Sung et al [96] reported a difference between adolescents using prescription opioids, compared to the adult population, where young opioid users had more risk factors in common with other abusers of illicit drugs. Swendsen et al [97], using data from

the NCS-Adolescent Supplement, could show a substantial psychiatric co-morbidity among adolescents with NMPOU.

Wu and co-workers [98], using data from NESARC from the adult population, saw a difference between subtypes of NMPOU users, where NMPOU users with other prescription drug use were more likely to have psychiatric disorders, in particular women, who were affected by depression and anxiety disorders. The same authors [99] saw that heroin users differed from prescription opioid users; the combined heroin and prescription opioid group had more severe substance use problems than the opioid-only group, who had more problems with concurrent sedative and tranquilizer use disorders, as well as problems with mood, anxiety, personality problems and pathological gambling.

Katz and co-workers investigated NESARC data in the adult population on incident NMPOU, and found that co-morbid disorders, taking into account both mental and physical health, predicted later NMPOU, abuse and dependence [100].

An association between depression and opioid abuse in adolescents was shown by Edlund and co-workers [101]. Having a major depressive episode constituted an important risk factor for NMPOU. Depression also preceded the NMPOU.

Tramadol, a “weak opioid” with both opioid and serotonergic/noradrenergic effects, has been suggested to have an anti-depressant effect in preclinical [102, 103]. It has also been suggested, that tramadol could have an anti-depressant effect in humans [104, 105]. Tramadol has effects different from opioids, such as provoking epileptic seizures [106]. In a large study of university students in Egypt, tramadol use was associated with co-occurring psychiatric problems [107], particularly mood disorders, as half of the sample with tramadol use endorsed criteria for mood disorders, compared to one fourth in the control group. While tramadol use has not been very common in the US, compared to other prescription opioids [92, 95], it appears as if tramadol use is more common in Europe [108] and in the Middle East [109-111], in China [112, 113], and in Africa among adolescents and young adults, often in socially disadvantaged groups [114]. In a study of alleged misuse of buprenorphine and methadone among adolescents and young adults on a national level in Sweden, Richert and Johnsson [115] found that tramadol use was dominant, and had increased among adolescents and young adults in the Malmö area in the south of Sweden.

New techniques for intervention and drug detection

IT-based intervention studies in adolescent and young adult populations

Over the last two decades, follow-up and monitoring in real time has been possible through the rapid development of IT-based solutions, such as electronic diaries, internet panels, cellphone-based technologies and smartphone applications. Instead of assessing the patient at the clinic or in hospital, the new technologies allow for a more naturalistic following of the clinical course in patients, in comparison with older, paper-and-pencil-based techniques of assessment.

First presented by Stone and Schiffman [116], the concept of *Ecological Momentary Assessment, EMA*, has developed into a powerful research tool, involving repeated measurements in real time in the natural environment of patients. The techniques used have been successfully tested in psychology research [117] and addiction research [118]. An extensive review of the literature on EMA-based techniques in assessing craving and substance use is presented by Serre and co-workers [119].

With the rapid development of technology-based solutions, techniques for intervention in treatment have been developed [120], in supplement to substance use treatment, with promising results [121, 122]. Recent European research on EMA has used smartphone applications to assess mental health problems in adolescents [123] and to intervene in treatment settings for adolescents with substance use and co-morbid severe psychiatric disorders [124].

Intervention with Interactive Voice Response (IVR)

Interactive Voice Response (IVR) is a well-established method, in clinical use since the 1980's [125]. The technology has advantages, in terms of integrity, in comparison with text messaging and smartphone applications [126, 127], and has been used for follow-up of substance use, primarily alcohol use [128-130]. Despite the possibility to use the technology to give automated feedback interventions, few studies have reported intervention results [131-134]. The use of IVR for follow-up and intervention purposes, both for substance use and psychiatric symptoms, has been successful in different settings [135-137]. An extensive review of automated telephone assessments in different settings, both in general medicine and psychiatry, has been published recently [138].

Hair analysis

Given the development of non-medical prescription drug use, as well as the use of "party drugs" in populations of substance users, it is of great importance to develop techniques of drug detection that can analyze more substances than could be covered by the routine urine testing used today. As polysubstance use today is common, also among adolescents and adolescents, routine drug screening could miss out drugs of abuse not included in routine panels. Also, there is a need to minimize the risk for manipulation of tests.

Hair analysis for drug detection has been developed over the last two decades, and has gained recognition for its ability to monitor drug intake over time, both retrospectively [139, 140] as well as to determine causes of death in post-mortem examinations [141]. The possibility to monitor a longer time period of drug intake, and the ability to detect far more drugs and illegal substances, is an advantage for this technique in comparison to conventional drug tests, such as blood and urine.

Hair analysis has been used clinically in Sweden for follow up of re-granting of drivers' licenses [142] and for screening analyses of drugs [143]. It has been clinically used to follow buprenorphine intake during opiate withdrawal [144], as well as to follow patients during opioid maintenance treatment, OMT [145-147]. Hair analysis also has been used to investigate alcohol and drug intake in general population surveys [148]. To the best of my knowledge, hair analysis has not been used specifically for monitoring substance use in adolescents and young adults.

Substance use disorders and psychiatric co-morbidity in prison populations

Regarding substance abuse and dependence among prison inmates, Fazel et al [149] conducted a systematic review of the literature, comprising more than 7,000 prisoners, and found that the prevalence of both alcohol and substance abuse were many orders of magnitude higher than in the general population, especially for female prisoners. Four years earlier, Fazel and Danesh [150] conducted a literature review of 62 surveys on the mental health of prisoners worldwide, concluding that prisoners were several times more likely to have psychosis and depression, and ten times more likely to have a personality disorder, than the general population. Ten years later, Fazel and Seewald [151] conducted a new review and meta-regression analysis to determine the prevalence of psychiatric disorders among incarcerated individuals world-wide. It was estimated that almost four percent of incarcerated individuals over the world had a psychosis, and for depression, one tenth of male prisoners and fifteen percent of female prisoners were estimated to have the

diagnosis. In a review of the literature, Fazel and Baillargeon [152] could show that mental disorders and infectious diseases were more common among incarcerated individuals than in the general population.

To investigate the adolescent population, Fazel et al [153] conducted a review of the literature on adolescents in juvenile detention and correction facilities, and found that the prevalence of psychiatric problems was considerably higher than among age-equivalent individuals in the general population [64]. Prevalence of depression among detained girls was particularly high, in comparison to what is reported among adult women. Also, the prevalence of conduct disorder was considerably higher: among girls, 10 to 20 times higher, and among boys, five to ten times higher. Fazel et al [154] compared adolescent and young adult criminal offenders with adult offenders through examining forensic psychiatric examinations, and found that young offenders had higher rates of depression and childhood and developmental disorders but lower rates of psychosis, bipolar disorder and substance use disorders. A comparison between young offenders and general psychiatric inpatients showed that depression and attention-deficit or disruptive disorders were more common among young offenders, whereas alcohol and drug use disorders were less common.

Colins et al [155] investigated the prevalence of psychiatric disorders among detained and incarcerated male adolescents, and found that the mean prevalence of any psychiatric disorder was 69.9%, where the most common diagnoses were conduct disorder (46.4%) and substance use disorder (45.1%). Internalizing disorders, such as depression and anxiety, were more prevalent than in the general population.

A large Swedish register study [156] could show that 1% of the population was responsible for a majority of all violent crimes, with a significant association with substance abuse and personality disorders. Moberg et al [157] showed, using the Swedish conscript cohort, that after mental retardation, substance-related disorders were the most important predictors for later convictions for violent crime, followed by personality disorders and early behavioral problems.

Simpson et al [158] reviewed the literature on serious mental illness in prisons, and suggested improvement of psychiatric treatment facilities in prison, as well as post-release interventions. Durbeej et al [159, 160] studied post-release treatment in a cohort of offenders with mental health problems and problematic substance use, and found that participation in treatment post-release significantly reduced criminal recidivism.

ADHD and psychiatric co-morbidity

Youths and adults with ADHD are overrepresented in the criminal justice system [161]. A meta-analysis of co-morbidity with ADHD was made by Young et al, indicating that all psychiatric co-morbidity was increased among adults with ADHD in prison, and that mood disorders were more common among young inmates [162].

Knecht et al [163] reviewed the literature on ADHD, substance use and criminality among young offenders. The relationship between ADHD and delinquency has been reviewed by von Polier et al [164], pointing to the strong association between ADHD and conduct disorder (CD) and oppositional defiant disorder (ODD). Moffit et al defined, from the Dunedin study, two trajectories or subtypes: "early starters" with antisocial behavior and aggression from a young age, often before their teens, and "late starters" where the antisocial behavior had started in adolescence. The former group displayed, not surprisingly, a more severe picture; they were more frequently engaged in violence, spent more time in jail and in psychiatric wards, and experienced more mental and physical health problems [165]. Rasmussen and co-workers [166] showed that early treatment of ADHD with central stimulants offered some protection to the development of alcohol and substance abuse, as well as criminality, an observation consistent with earlier findings among ADHD samples [167-171].

Personality disorders

It is therefore not surprising, that a large proportion of offenders have ADHD and antisocial personality disorder. Konstenius et al [172] could show a strong co-morbidity with antisocial personality and ADHD in female prisoners. Wetterborg et al [173] found that there was a significant overlap between personality disorders and psychiatric symptoms for male offenders on probation with a diagnosed borderline personality disorder (BPD); antisocial personality disorder (91%), major depressive disorder (82%), substance dependence (73%), ADHD (70%) and alcohol dependence (64%). BPD was diagnosed in one fifth of the sample. The role of impulsivity in both BPD and SUD was discussed in a literature review by Bornovalova et al [174].

The association between antisocial personality disorder, crime and substance use disorder

Data from NESARC could show a strong association between drug use disorders and antisocial behavioral syndromes [31]. The relation between antisocial personality disorder and drug use has been investigated by Alterman and Cacciola [175]. Antisocial personality disorder has been identified as a predictor for poor

outcome in treatment settings [176, 177]. Fridell et al [178, 179] could show that antisocial personality disorder was a strong predictor of criminal activity among substance users.

Suicide, death of undetermined intent, and fatal accidental intoxication

Harris and Barraclough [180, 181] presented – in two extensive meta-analyses – that standard mortality rates (SMR), both for mortality in general, and suicide, were higher among patients with alcohol and drug use disorders. For male alcoholics, the risk of suicide was 5.5 times higher, while for female alcoholics, it was 18 times higher. Suicide was 10 times more common among opioid users, and death by fatal accidental intoxication (not classified as suicide) was 13 times more common in this group. Wilcox and co-workers [182] confirmed these findings in a review article on cohort studies and could show a further increased risk of completed suicide for opioid users, and an increased risk of suicide for intravenous injection users. Darke and co-workers have extensively studied opioid-related deaths, both accidental intoxication – "overdose" – and suicide, among substance users in Australia [183-192]. The risk of completing suicide is 14 times higher [182] for illicit opioid users. Darke et al [190] could show, in toxicological analyses, that intentional fatal overdose among heroin addicts was a separate entity, different from accidental intoxication, characterized by higher morphine concentrations, and presence of antidepressants in toxicological analyses.

The relation between accidental intoxication – overdose – and suicide attempts has been explored to a large extent in the literature [193, 194, 187, 189, 192, 195]. Risk factors for suicide attempts were suicidal ideation and polydrug use at baseline [189, 192]. The number of addictive substances also contributed to the risk of unnatural death by undetermined death, but not suicide [195]. While many studies have confirmed the relation between suicide and unintentional intoxication among substance users, they are distinct phenomena, with different risk factors [193, 194, 184, 187, 189, 195, 196]. Patients with a history of both events, therefore, represent a specifically vulnerable sub-sample.

Post-release mortality in prison populations

Mortality after release from prison has been extensively documented in Europe, in Australia and in the US [197-204]. Drug overdose (accidental poisoning), often occurring within weeks after release, is by far the most common cause of death [205-208, 199, 203], especially during the two weeks following release from prison [209].

Suicide, overdose and events of undetermined intent

Suicide rates after release from prison, especially during the first year after release, were also substantially elevated compared to the general population [198], especially for women. An important factor, associated with suicide after release, was hospitalization for mental illness during imprisonment [200].

Bohnert and co-workers [210] analyzed the massive increase of unintentional intoxication deaths in the US and found that unintentional deaths were more prevalent among males. In a literature review [211], Bohnert et al found an overlap between suicide and unintentional overdose among substance users, calling for a better understanding of the differences between the two events. In a study of a large sample of Veterans Administration (VA) patients [212], an association with overdose was seen with both psychiatric and substance use disorders, and in an analysis of the same VA sample [213], events of undetermined intent had a stronger association with substance use disorders than intentional overdoses. However, Bohnert concluded that some events ruled undetermined may have been misclassified suicides.

Self-inflicted death of undetermined intent – often labelled "undetermined suicide" – is a category which poses great problems of classification, especially when it comes to establishing a cause of death by intoxication. Since the introduction of this category in the ICD-8, in 1968, authors have pointed to risks of misclassification of this category. Due to a variability in classification by coroners and medical examiners, authors have argued that many events of undetermined intent are "hidden suicides" – thus leading to an under-reporting of suicide [214-217]. Because of this, Linsley et al [218] argued that "open verdicts" should be included in suicide research, after excluding cases where "suicide was unlikely".

In a large Swedish register study, Björkenstam and co-workers [219] analyzed the background variables for more than 40,000 deaths classified as suicide (n=31,883) or undetermined intent (n=9,196) from the Swedish Causes of Death Register. In contrast to previous findings, events of undetermined intent differed from suicides in nearly all the studied background factors, socio-demographic as well as psychiatric. While suicide was more common among persons with a higher level of education and for women hospitalized for self-inflicted harm, events of undetermined intent were more common among persons hospitalized for substance abuse and for men born outside Sweden. In conclusion, the authors argue that some of the deaths classified as deaths with undetermined intent may in fact have been accidents. The findings of Björkenstam et al, in a large population sample, therefore challenged the previous findings of "under-reported suicides" leading to the integrating of all events of undetermined intent into the category of suicide.

Aims

General aims of the thesis

The aim of present thesis was to study concurrent psychiatric problems in two different populations: one population of prisoners with substance use problems, focusing on psychiatric disease and self-inflicted mortality after release from prison, and one clinical population of young, treatment-seeking adolescents and young adults with substance use problem, at risk of developing a negative life course, with a focus on intervention and drug detection, using new technologies.

Study-specific aims

Paper I

The aim was to study psychiatric hospitalization in ex-prisoners with substance use problems, through linking data to a national register on inpatient treatment, with a focus on non-substance psychiatric diagnoses, to analyze predictors for psychiatric hospitalization.

Paper II

The aim was to identify risk factors, differences and similarities for the different categories of self-inflicted death in a population of criminal justice clients, using the national Causes of Death register for suicide, deaths of undetermined intent and accidental intoxication.

Paper III

This paper reports a randomized controlled trial (RCT) of Interactive Voice Response (IVR) in a clinical sample of adolescents and young adults. The aim of the study was to assess whether a brief automated intervention as add-on to treatment could influence stress and mental health symptoms, and secondarily substance use during treatment.

Paper IV

The aim was to determine the prevalence of tramadol misuse and other non-medical prescription opioid use (NMPOU), and whether patients, positive for opioid drugs, displayed different characteristics regarding socio-demographic and psychiatric background factors.

Methods and material

Papers I and II are based on register data from ASI (Addiction Severity Index) interviews carried out between 2001-2006 in the Swedish criminal justice system, linked to large Swedish registers, the Swedish National Patient Register (paper I) and the Swedish National Causes of Death Register (paper II).

Paper III investigated, in a randomized controlled design, the effect of an intervention by the IVR-automated telephone system on psychiatric symptoms and drug use as an add-on to the usual treatment. Paper IV, based on the same material as paper III, investigated hair analysis for drug detection, especially non-medical prescription opioid use with special reference to tramadol use. Papers III and IV are based on clinical data from the Swedish assessment instrument Ung-DOK, and psychiatric interviews using MINI and DSM-IV interviews.

Tabel 1
Sample, design and measurements

	Paper I	**Paper II**	**Paper III**	**Paper IV**
Sample	Criminal justice clients released from prison (N=4,081)	Criminal justice clients released from prison, or on probation or parole (N=6,744)	Treatment-seeking adolescents and young adults (N=73)	Treatment-seeking adolescents and young adults (N=59)
Study design	Register follow-up study	Register follow-up study	Randomized Controlled Trial of IVR feed-back intervention	Pilot observational study
Outcome	Non-substance psychiatric diagnoses at hospitalization	Causes of death in national mortality register	Intervention effect on depression, anxiety, stress, global substance use	Hair analysis for drug detection of past 1-1.5-month substance use
Assessment	ASI interview	ASI interview	MINI interview, DSM-IV symptom criteria count (ADHD), Ung-DOK data	MINI interview, DSM-IV symptom criteria count (ADHD), Ung-DOK data, hair analysis
Statistical analysis	Cox regression analysis	Cox regression analysis	Mixed model analysis	Chi-square statistics

Study design, setting and participants

Studies in the Criminal Justice System

The ASI Project in the Swedish Prison and Probation Service

Papers I and II are based on a database of ASI interviews carried out in the Swedish Prison and Probation Service between 2001 and 2006. From 2001, the Swedish Prison and Probation Service initiated a project using ASI for clients reporting illicit substance use [220]. During five years, a total of 7,085 clients with reported substance use problems were interviewed, either in prison, on probation or on remand.

In the sample studied [221-225], among clients interviewed both in prison and on probation, 62% reported a primary drug problem, five percent reported a combined problem of drugs and alcohol, and 13% reported a primary alcohol problem. A clear majority of clients assessed with ASI were prisoners, compared to clients on probation, on remand or institution treatment, thus representing an oversampling of prisoners, compared to criminal justice clients on probation. Acquisitive crime and drug crime are over-represented in the material. Clients sentenced for violent crime had, to a lesser degree, substance use problems and are under-represented in the present material.

The sample was predominantly male. Twelve percent of the sample studied were women, which is an overrepresentation of women in comparison with the population in the criminal justice system.

Developed in the US as a research instrument [226, 227], a European version of ASI was developed in the 1990's, EuropASI [228, 229], and a Swedish standard version was established in 2003 [230]. For the ASI interview used in this project, an extended version of ASI, ASI-X, was developed [231], including variables for homelessness, sexually transmittable and infectious diseases, and victimization of emotional, physical or sexual abuse. This version, used in the interviews, was based on EuropASI [229].

In analyzing the variables from the ASI interviews, assessment of composite scores, or the interviewer's rating or estimation of the client's need for help, were not used. Composite scores have been subject to criticism for inconsistency [232, 233]. Therefore, independent variables from the ASI interviews were analyzed as separate items.

Paper I.

This study was conducted as a data-linkage study, linking data from ASI interviews to the Swedish National Patient Register (NPR) for non-substance psychiatric diagnoses. From the original sample of 7,081 clients, clients interviewed in prison (n=5,177) were followed post-release, until hospitalization, or until censorship on the 31st of December, 2008.

From 5,177 clients interviewed in prison, 847 clients were excluded, since they had not reported any dominant problem with substance use. Clients still in prison, or excluded for other reasons amounted to 189, thus leaving 4,081 clients for post-release follow-up.

Paper II.

This study was conducted as a register follow-up study, examining risk factors for self-inflicted death, combining ASI variables with diagnoses from the Swedish National Causes of Death Register. From the original sample of 7,085 clients, clients assessed in prison (72%), on probation (17%) or on remand (5%) were included. From this sample, 341 clients were excluded, either for not reporting any substance use, or having been assessed with the adolescent version of ASI, ADAD (Friedman and Utada, 1989). In the final analysis, 6,744 clients were followed, until death or until censorship, the on the 31st of December, 2008.

Studies in a clinical population of treatment-seeking adolescents and young adults with substance use problems

3M – The Maria Malmö Mobile Study

Between the 1st of October, 2012, and the 31st of December, 2013, a randomized controlled study of intervention by Interactive Voice Response was carried out in an outpatient facility for treatment-seeking adolescents and young adults, the Maria Malmö Clinic in Malmö, Sweden (ClinicalTrials.gov registration number NCT01706380). The intervention study was performed as an add-on to the regular treatment programs offered by the clinic. Upon inclusion in the study, and after completing the three-month period using IVR, twice a week, patients were asked to leave a hair specimen for drug detection with hair analysis.

Paper III.

During the period the study was performed (1st of October, 2012 – 31st of December, 2013), 367 patients were referred to the clinic for treatment. Of these, 30% were women. Patients were offered to participate in the study by a counselor upon their first or second visit to the clinic. Patients with severe psychiatric disorders, severe intellectual disability or difficulties to understand the Swedish language were not

offered to participate. Patients were also excluded if they could not register a private cell-phone number. Eighty patients (21%) did not show up for their initial appointment, and 52 (36%) chose to discontinue their treatment after one visit, and were not informed about the study. Of the remaining 235 patients, potentially eligible for the study, 158 did not participate for various reasons; either they actively declined participation, or were not approached with an offer to participate in the study.

Of the remaining 77 patients, two never turned up for treatment, and two did not turn up for study assessment. The remaining 73 patients were randomized to either a control group with treatment as usual (TAU) and IVR follow-up (36 patients), or an intervention group with TAU and IVR with a personalized feedback intervention (37 patients). The primary aim of the RCT study was to see, whether the intervention affected the retention in treatment, which could not be confirmed. The analysis on effects on stress and mental health symptoms was the secondary aim of the study.

Comparisons between those who entered the study and those referred to the clinic, without participating in the study, did not identify significant differences in baseline data regarding gender or the type of facility referring the patient. Neither did we find any significant differences between those enrolled in the study and those applying for treatment the following year, 2014, regarding gender, criminal convictions or primary drug of abuse.

Paper IV.

Out of 73 patients entering the IVR study, 14 patients could not present a hair sample, one declined participation, and 12 had too short hair to obtain a hair specimen. One left his specimen too late. The remaining 59 patients could leave at least one hair specimen upon inclusion in the study.

Comparing those who did leave a hair specimen with the whole group (59/73), a majority of those who did not leave a hair specimen reported tramadol as a problem drug ($p=0.019$). All of those not leaving a hair sample were male ($p=0.002$).

Measurements

Papers I and II

Variables from the ASI interviews

Predictors or risk factors for psychiatric co-morbidity, measured as hospitalization for in-patient treatment, or self-inflicted death, were sampled from the ASI questionnaires. Demographic data, data on self-reported psychiatric symptoms, drug use and criminality data (paper II) were used as independent variables in the analysis.

In paper I, the following variables were used:
Demographic characteristics: male sex, born in the Nordic countries, homelessness. *Lifetime history of psychiatric problems*: previous psychiatric hospitalization, suicide attempt, depression, anxiety, cognitive problems (troubles understanding, concentrating, or remembering), difficulties controlling violent behavior, hallucinations.

Lifetime history of substance abuse (> 1 year): alcohol binge drinking, heroin, other opiates, sedatives, cocaine, amphetamine, cannabis, injection drug use.
In paper II, the variables *overdose*, and *criminality variables* (violent crime, property crime and drug crime) were added in the analysis.

The Swedish National Patient Register (NPR)

The Swedish National Patient Register (Slutenvårdsregistret) is held by the National Board of Health and Welfare [234]. The register covers both primary and secondary ICD-10 diagnoses for all in-patient treatment episodes in Sweden, with an attrition rate of less than 1%, thus making it a reliable and well established instrument for epidemiological research. Specifically, we investigated the psychiatric diagnoses according to ICD-10 (F00-F90). The outcome variable in our analysis was dichotomized to *hospitalized (for a psychiatric diagnosis) versus not hospitalized for any psychiatric disorder (including SUD).*

The Swedish Causes of Death Register

The Swedish Causes of Death Register (Dödsorsaksregistret) is held by the National Board of Health and Welfare. This register, in its present form, has collected data on causes of death since 1961. Until 2011, all deaths were registered for Swedish citizens, even if the person was deceased abroad. From 2012, all causes of death recorded in Sweden are reported, even if the deceased person is a foreign citizen,

According to Swedish legislation, all causes of death considered ”unnatural”, as well as deaths of ”known substance abusers” deceased outside hospital, must, after application from the police authorities, undergo forensic medical examination [235]. It is therefore plausible, that the causes of unnatural deaths in the categories we have studied, have been certified after forensic examination.

Outcome variables in paper III were: fatal accidental intoxication (”overdose”), X40-X49; fatal intoxication/injury of undetermined intent, Y10-Y34; and suicide, X60-X84. Deaths recorded in the respective group were compared to the group alive, or deceased from another cause than the studied categories.

Papers III and IV

The Ung-DOK assessment instrument

The DOC instrument (referred to in Swedish as DOK) – DOC stands for ”documentation and evaluation regarding treatment of alcohol and drug abusers” – is an instrument for assessment and evaluation developed in Sweden as a collaboration between the National Board of Institutional Care and the School of Education at Växjö University [236]. Constructed on the basis of ASI, with the addition of items such as treatment history and family upbringing, the DOC instrument is completed both on admission and upon discharge from the institution. The instrument is used not only in compulsory institutional settings, but also in residential treatment centers and open treatment facilities in Sweden [236].

Data from DOC covers demographic data, family history, data on self-reported psychiatric problems, drug history and present drug use patterns. Drug use is defined as either ”main drug” or ”problem drug”, the latter being the subjective drug problem to address in treatment. In the present study, an adaptation of DOC to adolescents and young adults (”Ung-DOK”) has been used.

Data from the DOC instrument used in papers II and IV were: male gender, age, tobacco use (paper III) and male gender, age above 18 years, born in Sweden, any

parent born outside Sweden, sentenced for crime, victim of crime, and psychiatric problems in family during childhood (paper IV).

Diagnostic interviews: M.I.N.I. and symptom criteria for ADHD according to DSM-IV

All patients included in the RCT study were interviewed using the M.I.N.I structured diagnostic interview [237]. Because of the small size of the sample, criteria for different DSM-IV axis I diagnoses were pooled together to diagnostic groups, whereas anti-social personality disorder was studied separately. ADHD screening was made using symptom assessment above cut-of level, using the DSM-IV manual [238]. We had no access to childhood anamnestic data, nor to data on assessment of function in daily life.

In paper III, the following diagnostic groups were used as baseline data: any MINI diagnosis, MINI substance use disorder, MINI alcohol use disorder, MINI other substance use disorder, MINI non-substance use disorder, current depression, agoraphobia, generalized anxiety disorder, and antisocial personality disorder.

In paper IV, the following diagnostic groups were used: MINI all alcohol disorders, MINI all drug use disorders, MINI affective disorders, MINI anxiety disorders, MINI psychotic disorders, MINI antisocial personality disorder, and ADHD symptoms above cut-off.

Interactive Voice Response

In paper III, Interactive Voice Response system was used for monitoring the participants two times a week for 12 weeks. This was done regardless of whether the participants continued treatment at the clinic or had discontinued their treatment. The IVR monitoring consisted of 19 items, and one additional item for reporting drug use. The first 15 items dealt with seven items of the Arnetz and Hasson stress questionnaire, AHSS [239], and eight items of anxiety and depression with the Symptoms Checklist 8D, SCL-8D [240]. Participants could score between 0 (bad) and 9 (good), meaning that increased scores indicated an amelioration of symptoms. Alcohol and drug use were reported dichotomously, either “yes” (1) or “no” (0) using four variables, summarized into two sub scores, one alcohol sub score and one drug sub score, and one summarized substance score (ranging from 0 to 4). The last question specified, through a recorded message, what drug the patient had used.

Hair Analysis

In paper IV, hair samples were analyzed according to previously validated and published procedures [241, 242]. The following drugs were possible to detect and to identify in the analysis:

Table 2.
Drugs, possible to detect in hair analysis

Opioids	Benzodiazepines and benzodiazepine-like medications	Stimulants	Sedatives
Morphine	Diazepam	Amphetamine	Alimemazine
Codeine	7-amino-clonazepam	Methamphetamine	Hydroxizine
Acetylmorphine	7-amino-nitrazepam	Cocaine	Prometazine
Buprenorphine	7-amino-flunitrazepam	Bensoylecgonine	Propiomazine
Methadone	Alprazolam	MDMA	
Oxycodone	Zopiclone		
Tramadol	Zolpidem		
Ethylmorphine	Zaleplon		
Ketobemidone			
Fentanyl			
Propoxyphene			

In addition, 130 synthetic cannabinoids were possible to identify in the analysis according to this procedure. Tetra-hydro-cannabinol (THC), the active, psychotropic compound in cannabis, could for technical reasons not be analyzed.

Statistical analyses

In papers I and II, predictors and risk factors for psychiatric in-patient hospitalization, and self-inflicted death, respectively, were calculated as increased risk over time, using the Cox regression model. Independent base line variables with a significant association with the outcome variable in bivariate analysis were introduced in a Cox regression model, yielding hazard ratios (HR), calculated with 95% confidence intervals.

As the time variable in the Cox regression model, we chose, in paper I, days from release from prison to the first episode of in-patient hospitalization, or until data were censored on the 31st of December, 2010. For paper II, the time variable was defined as the time from interview (for clients on probation or on remand) or time from release from prison until death (suicide, injury/intoxication of undetermined intent or fatal accidental intoxication) or until data were censored on the 31st of December, 2008.

In paper III, a repeated measurement design was used, using a Mixed Models approach, and outcomes were the changes in score reported by the patients over a three-month period. The variables analyzed were scores for AHSS, SCL-8 total scores, sub-scores for anxiety and depression, respectively, as well as a global score of alcohol and drug use. The outcome variables were analyzed using a mixed models approach for repeated measures.

In paper IV, bivariate analysis was used for testing associations between baseline factors and positive results in hair analysis for opioids. The Pearson chi-squared test was used for differences between groups regarding categorical data, and Fisher's exact test was used for small group sizes.

Statistical calculations were performed using SPSS software, versions 20, 21 and 22.

Results

Paper I

A first analysis of all patients hospitalized for any psychiatric diagnosis (including substance use diagnoses) was made, where 34% of all patients in the sample were hospitalized. Patients were followed for an average of 4.3 years. Several substance-related variables predicted hospitalization, including use of heroin, sedatives and polysubstance use. In a second analysis, where we excluded all substance-related diagnoses, or personality disorder diagnoses, ten percent of the sample were hospitalized. In this analysis, patients were followed for an average of 5.1 years. The following baseline predictors were significant: previous psychiatric hospitalization (HR 1.83), previous suicide attempt (HR 1.91), depression (HR 1.33), anxiety (HR 1.37), sedative use (1.46). Amphetamine use was negatively associated with hospitalization (HR 0.71).

Paper II

Patients were followed for an average of 3.8 years. In Cox regression analysis, each manner of self-inflicted death was analyzed in separate groups, comparing each cause of death (suicide, undetermined intent or accidental intoxication) with those still alive, or deceased from another cause.

Death from fatal accidental intoxication was associated with male gender (HR 4.09), use of heroin (HR 2.86) and use of cannabis (HR 1.94). Death from injury/intoxication of undetermined intent was associated with use of heroin (HR 3.48), binge drinking of alcohol (HR 2.46) and previous psychiatric hospitalization (HR 2.41), while it was negatively associated with depression (HR 0.33). Death from suicide was associated with previous suicide attempts (HR 2.78) and use of sedatives (HR 2.17).

Paper III

Differences in change scores were analyzed using a mixed-model approach between the intervention and control group. Compared to the control group, the intervention group demonstrated significantly greater improvement in the AHSS stress scale (p=0.019), the total SCL-8D score (p=0.037) and the SCL-8D anxiety sub-score (p=0.017) and on a summarized feedback score (p=0.026), but not on the depression subscale. No differences were seen in the substance use scores between intervention and control group.

Table 3
By intervention group (n=73); Mixed model analysis of repeated measures (Andersson et al., 2016)

	Estimate	df	t	*p* value	95% CI
Feedback score	9.40	65.15	2.28	0.026*	1.16, 17.65
AHSS	4.49	64.84	2.41	0.019*	0.77, 8.21
SCL-8D	5.20	64.94	2.13	0.037*	0.32, 10.08
Anxiety	3.23	63.91	2.44	0.017*	0.59, 5.87
Depression	1.98	65.21	1.60	0.114	-0.49, 4.45
Substance score	-0.08	57.24	-0.08	0.452	-0.28, 0.13
Alcohol use	-0.02	50.77	-0.24	0.809	-0.15, 0.12
Drug use	-0.07	56.18	-0.94	0.351	-0.23, 0.08

Paper IV

In hair analysis, 19/59 (32%) hair samples were positive for non-medical prescription use opioids, and of these, 18/59 (31%) were positive for tramadol. Nineteen percent were positive for cocaine, 8% for synthetic cannabinoids ("spice"), 7% for amphetamine, and 5% for MDMA (ecstasy). Patients positive for opioids were significantly more likely to be positive for any non-opioid drug, in comparison with the patients negative for opioids, 37% vs 13% (p=0.04, Fisher's exact test).

In self-report of problem drug, 98% reported cannabis, 34% tramadol, and 24% reported cocaine, ecstasy and "spice", respectively.

Out of 59 patients, 38 (64%) met criteria for at least one MINI diagnosis. Fifty-one percent met criteria for any affective disorder, 47% for any anxiety disorder, and 20% for any psychotic disorder. Fifty-three percent had ADHD symptoms above cut-off level.

Eighty percent met criteria for any drug use diagnosis according to MINI, and 25% for any alcohol use disorder.

In bivariate analysis, no significant differences were seen between those positive for opioids (tramadol in all cases but one) and those negative, with reference to socio-demographics, criminality, and psychiatric baseline variables. While we could not see any statistically significant difference between the groups positive for NMPOU (tramadol) *in hair analysis* and those negative, with reference to socio-demographic background factors and psychiatric diagnoses, we could find significant associations, despite the small sample, when we made a sensitivity analysis including all who had *reported problem use* of opioids - where all except one reported use of tramadol**.** Those who reported opioids (tramadol) as their problem drug were more likely to have an immigrant background (p=0.015), and they were less likely to have problems with alcohol (p=0.044) or a psychosis diagnosis (p=0.005)

General discussion

Methodological considerations

Papers I and II

Two studies were based on a large material of clients in the criminal justice system, interviewed with ASI, where patients were followed in two large national registers. In the first study, data from the ASI interview were linked to the National Patient Register for psychiatric diagnoses upon hospitalization. In the second study, data from interviews of clients, not only performed in a prison setting, were followed in the National Causes of Death Register.

The statistical method used was survival analysis, using the proportional hazards Cox regression model, since we wanted to analyze the predictors, or risk factors for hospitalization or self-inflicted death over time, from the interview, or from release from prison. Using the Cox regression model, in comparison with logistic regression, has the advantage of integrating the time variable in the analysis.

In the first article, we chose in-patient hospitalization for a psychiatric diagnosis as a marker for psychiatric co-morbidity. Hospitalization for in-patient treatment requires a certain level of severity of symptoms, which makes it plausible that the patient at the time for hospitalization displayed symptoms that demanded full-time, inpatient treatment for a defined psychiatric diagnosis. We also chose to exclude all events, which were related to substance use diagnoses, in order to narrow the outcomes to exclusively psychiatric in-patient episodes.

To the best of our knowledge, this follow-up of psychiatric hospitalization of clients in the prison and probation system in Sweden is the first to address inmates with substance problems, using a longitudinal design. In the literature, follow-up of criminally convicted patients are restricted to inmates with a defined psychiatric diagnosis [243, 244], whereas our sample concerns clients that are not recruited because of a clinical psychiatric diagnosis. Also, studies of hospitalization have often focused on re-hospitalization of patients with a defined diagnosis, mostly patients with psychosis or schizophrenia [245].Therefore, the studies add to the knowledge of substance use and co-morbid psychiatric problems in the prison

population [246-248], since they use large population registers for follow-up. The National Patient Register, where psychiatric diagnoses were followed, and the National Causes of Death Register, are reliable epidemiological databases with a coverage of almost 100% of the Swedish population.

Baseline variables from the ASI interviews were based on self-reported data, which is a limitation, both considering recall bias, and that the psychiatric problems reported are defined by symptoms as they are described in the ASI manual, not as diagnoses, defined by a diagnostic interview. However, the psychiatric problems reported should have lasted for a significant time, and they should not include symptoms experienced under the influence, or during withdrawal, from alcohol and drugs. Data from ASI interviews on psychiatric symptoms have been used for follow-up of psychiatric outcomes, with a strong predictive value [249-253].

Papers III and IV

The RCT design was chosen to assess the effect of intervention on both stress, measured by the AHSS, and psychiatric symptoms, measured by SCL-8D, and secondarily the global changes of alcohol and drug use. Using a randomized controlled design, the golden standard for clinical trials, we could study the effect of intervention by the IVR technique, since all participants, also the control condition, were followed by IVR. The main target was the effect of feed-back on stress and psychiatric symptoms.

For reasons of accessibility, brief symptom scales were used, and the psychiatric items were limited to symptoms of anxiety and depression. Alcohol and drug use were measured dichotomously, “yes” or “no”, since it was not possible to collect detailed changes in alcohol and drug intake. This is an obvious limitation; likewise, we could not use recorded data on which drugs the patient used, because of a low response rate for the question where the patients could specify drug intake. Another limitation is, that we did not give personalized feed-back on substance use problems.

All patients included in the study were interviewed using the MINI diagnostic interview, a diagnostic structured interview designed to focus on the existence of current psychiatric disorders [254]. In comparison to diagnostic interviews such as CIDI or SCID, the interview does not assess the severity of symptoms [255, 254]. In our study, the use of MINI was motivated by the need to use a less time-consuming instrument, for use in this population of adolescents. MINI has been used in a multicenter study of treatment-seeking adolescents with substance use comprising 47 treatment units in 10 countries [256], as a screening instrument. Since diagnostic interviews took place shortly after inclusion in the study, it cannot be excluded, that some symptoms reported in the interview could be caused by effects of withdrawal, or influence of drugs. Therefore, considered as a screening

instrument, with the limitations mentioned above, data from MINI interviews must be considered as preliminary.

In article IV, where baseline data were used in the group comparisons, all psychiatric, non-substance diagnoses were pooled together to diagnosis groups to adjust for the small sample size (affective disorders, anxiety disorders, psychotic disorders). Substance diagnoses were divided into alcohol use disorders and substance use disorders. The only MINI diagnosis for personality disorder was the antisocial personality disorder. ADHD symptoms were included, since there is a well-known co-morbidity in clinical samples [169, 170, 257] with substance use problems. As ADHD is not included in MINI, this was measured as symptoms above a cut-off level according to DSM-IV. Since we did not have access to childhood anamnestic information from parents or teachers, nor did we have information on the level of functioning in different areas, we cannot say that we have diagnosed ADHD, rather, we have noted existing ADHD symptoms.

Socio-demographic variables were restricted to demographic data, criminality and family background items according to the "Ung-DOK" assessment instrument. The criminality item (sentenced, or victim of crime) was used, since there is an overrepresentation of criminally convicted among treatment-seeking adolescents at follow-up [258-261], as well as a strong association between ADHD and criminality [163, 262]. The item on a family history of psychiatric problems was chosen to explore the possible connection to psychiatric co-morbidity problems [263, 264].

Hair analysis was used in article IV in order to achieve a more precise method for drug detection, compared to standard analyses, such as urine tests, used in clinical practice. Hair testing has the advantage of a longer detection time: since the drugs analyzed are incorporated in the hair, it is possible to sample data on drug intake over time, thus making it possible to see patterns of drug intake up to three months in retrospect. Hair analysis has been used in many treatment settings [265] and has recently been used in a study of patients transferred from syringe exchange program to OMT [266] to investigate patters of poly-substance use as well as compliance to treatment. This is an advantage in comparison with drug detection in urine, blood or oral fluid [267-270], where the detection time is shorter. Although the method has, to our knowledge, not been compared to more recent developments in the drug detection area, such as drug detection in exhaled breath, developed by Beck and co-workers [271-273], we can presume that the detection time still is longer for hair testing. A limitation for hair testing is, of course, the length of hair required; in our sample, among those who did not leave a hair specimen, in all cases but one, it was because of too short hair.

Main findings

Earlier psychiatric problems predict future hospitalization in prisoners

Ten percent of clients in the criminal justice system, who developed psychiatric symptoms to the degree that in-patient psychiatric hospitalization was needed, represent a minority of the prison population with substance use. In comparison with a study of psychiatric hospitalization in a population of urban homeless people in Sweden [274], where the elevated risk for hospitalization – compared to the general population - was associated with substance use-related diagnoses, we could affirm that one tenth of our population displayed non-substance-related psychiatric symptoms requiring in-patient hospitalization. This does not necessarily mean that the remaining 90% have no psychiatric problems; rather, they could present problems, such as personality disorders or neuropsychiatric disorders which do not necessarily lead to in-patient hospitalization.

A history of previous psychiatric hospitalization, previous suicide attempts, depression, anxiety symptoms according to ASI, and the use of sedatives, predicted hospitalization. The first findings on previous hospitalization and previous suicide attempts are not surprising, since these experiences are strong indicators of a psychiatric co-morbidity. Interestingly, self-reported symptoms of anxiety and depression also had a strong predictive value. This suggests that well-established screening procedures for psychiatric problems are of great value in this population of identified substance users, with the possibility to treat problems already in prison and after release, to possibly avoid future psychiatric in-patient episodes.

While the strongest predictors for all hospitalizations, including substance-related events (occurring in 34% of the sample), were to be found both in substance-related and psychiatric factors in the Cox regression model, in the analysis of non-substance-related hospitalizations, the psychiatric baseline factors predicted future in-patient hospitalization. The only substance-related predictors for non-substance-related hospitalizations were the use of sedatives, with a positive association, and amphetamine use, where we saw a negative association.

In this population of incarcerated substance users, it appears as if use of sedatives could be perceived as a proxy variable for psychiatric problems, even if this question item in the ASI interview does not distinguish between prescribed medication and "self-medication". General population studies have also pointed to a high co-

morbidity with psychiatric problems among substance users with sedatives/tranquilizer use [275]. In earlier studies, non-medical use of sedatives has been associated with depression, anxiety and panic disorders [276, 277]. Reported use of sedatives might therefore – in this population – be a possible marker for psychiatric problems and merits attention from health professionals working in the prison setting.

The finding that amphetamine use negatively predicted future psychiatric hospitalization is in contrast to the well-established fact that amphetamine use causes psychotic effects, which are often treated acutely in hospital. In the first analysis of all hospitalizations, we saw that amphetamine, cocaine and cannabis were negatively associated with this outcome. This is in contrast to the assumption that amphetamine users were hospitalized for substance-related psychotic episodes. Use of amphetamines was negatively associated with this outcome, in comparison with the use of other drugs in this material. This finding might reflect the fact that amphetamine users are less likely to seek treatment for reasons that could be explained by factors related to provision of treatment for amphetamine users. In comparison to treatment options for heroin users, there are no established treatments for amphetamine detoxification (since the syndrome of amphetamine withdrawal, with an increased need to sleep and increased appetite, does not necessarily need in-patient treatment) or for stimulant dependence as such [278, 279].

Self-inflicted death of undetermined intent has more in common with fatal accidental intoxication

In the following article, based on the same sample, our intention was to study different risk factors for self-inflicted death with a special reference to the category of "undetermined intent". Here, we saw a discrepancy between suicide and events of undetermined intent. While suicide was associated with previous suicide attempts, use of sedatives and depression were not associated with this outcome, which is surprising, since depression is a well-known risk factor for suicide in the general population [280, 281]. Previous suicide attempt is a well-established risk factor for suicide, also in the general population, which indicates that this risk factor has a strong predictive value, also in this population. For fatal, accidental intoxication, risk factors were heroin use, male gender, and, somewhat surprisingly, with cannabis use. Even if cannabis use cannot cause a fatal intoxication, it could be interpreted as a proxy variable for more advanced patterns of polysubstance use, a well-known risk factor for accidental overdoses [282].

When analyzing the events of undetermined intent, we found that risk factors diverged from those for suicide, which is an important finding, since these events are often included in the suicide category, labeled "undetermined suicides" [283] in

the general population. In our population, risk factors for this event were heroin use, binge drinking of alcohol, and previous psychiatric hospitalization. Surprisingly, depression had a negative association. Heroin use even had a stronger association to death of undetermined intent than to overdose, and binge drinking of alcohol had a stronger association than previous psychiatric hospitalization, indicating that substance use variables may have had a stronger association to this outcome than psychiatric variables. This is also supported by the fact that depression had a negative association with this event. It is possible, that a history of depression, in this group of patients, could act as a protective factor against impulsive actions, such as intoxication, whereas a trait of impulsivity, also expressed in a binge drinking pattern of alcohol use, is a risk factor for these events. As has been shown by Brådvik and co-workers [284], persons deceased by self-inflicted death of undetermined intent had higher levels of alcohol in the blood upon forensic examination. Although we have been studying risk factors at baseline, and not proximal risk factors prior to death, such as intoxications, our data suggest that events of undetermined intent appear to have more in common with fatal accidental intoxications in this group of criminal justice clients. Our data, as in the previous study, also underline the importance of assessing the psychiatric co-morbidity, both the psychiatric history, and a history of suicide attempts among criminal justice clients with substance use.

Having studied risk factors for psychiatric co-morbidity in a population of substance users in prison, a stigmatized group, not only because of the criminality which has led to prison sentences, but also for a high degree of socio-demographic problems, we chose to investigate the possibility to intervene in a group of adolescents and young adults, to treat psychiatric problems co-occurring with substance use. Treating both substance use problems and psychiatric symptoms, which is strongly recommended, there might be a possibility of avoiding a development of a negative life course in a population which is already characterized by both socio-demographic and psychiatric problems.

A vulnerable clinical population with a high degree of substance use problems and concurrent psychiatric problems

In analyzing the data from the MINI and DSM-IV interview in the clinical sample of adolescents and young adults who participated in the Maria Malmö Mobile ("3M") Study, it is striking that almost two thirds of the sample endorsed criteria for any MINI diagnosis (other than a substance diagnosis). This is consistent with the previous literature, both internationally, where 60% of youth in the general population had a co-morbid psychiatric diagnosis [63, 66], and in Sweden, in a clinical population, where more than 80% had concurrent psychiatric symptoms

[264]. Therefore, our findings are probably generalizable to other samples of treatment-seeking adolescents and young adults. We also found that one third of the sample reported having been convicted for a crime, and more than half of the sample had been victims of crime. In comparison with long-term follow-up of a similar clinical population in Stockholm, Sweden [259, 261], we have investigated criminality at baseline, not as an outcome, as has been done in the studies from Hodgins and co-workers in Stockholm. However, this item, together with other socio-demographic items pointing to a problematic background history, confirms the picture of a highly disadvantaged and vulnerable clinical population, consistent with the findings in earlier literature. In comparison with earlier studies [264, 258, 259], the percentage of criminally convicted in our material is approximately the same, 25-30% of the sample.

Interactive Voice Response follow-up with intervention has a positive effect on stress and anxiety

During three months of IVR following as add-on to treatment, patients in the feedback intervention group were receiving messages from the IVR system to contact with a counselor if they reported more symptoms of stress, anxiety and depression, than at the previous assessment. This apparently simple intervention implied a significant amelioration of symptoms during a three-month assessment period on the stress scale and on the subscale for anxiety. Depression symptoms, measured by the SCL-8D subscale, were not altered. Nor did we see any effect on alcohol and substance use. The findings of effects on stress and anxiety are consistent with earlier studies of a CBT-based intervention in a group of substance users with co-morbid psychiatric problems [285], where stress and anxiety symptoms were reduced, but not symptoms of depression. A possible explanation is that depressive symptoms, by their nature, are more long-lasting and therefore difficult to influence through feedback interventions [286]. A recent RCT study of on-line intervention treatment of co-morbid depression and problematic alcohol use, but not drug use, in Australian adolescents [287], could show improvements both on depressive symptoms and a decrease of alcohol intake in the short term, and these improvements were maintained at 6-month follow-up. In comparison, in the present study, we did not have a specific intervention towards drug and alcohol use.

In an earlier study of an IVR feedback intervention [135] used in a sample of paroled offenders, feedback on substance use was given as a part of the intervention, and the study subjects could assess their substance use pattern on a 10-digit scale. It is possible, that the use of more precise tools of assessment could have captured changes in alcohol and drug use patterns, and that a specific intervention to drug and alcohol use would have been beneficial for the result.

In a review of RCTs of psychotherapeutic applications of mobile-based technologies, used in both adolescent and adult populations [288], an effect was found on alcohol problems and smoking cessation, as well as an effect on depression, bipolar disorders and anxiety, by the use of mobile apps, which indicates, consistent with our results, that smartphone- or cellphone-based technologies have an effect as add-ons to conventional treatment. The effect of IVR as a tool of intervention, as add-on to regular treatment for young substance users with psychiatric symptoms, is promising.

New patterns of substance use in an adolescent and young adult population – the example of tramadol

The fact that tramadol use was so predominant in our study sample is interesting. The combination of tramadol with other drugs (poly-substance use was more common in the opioid positive group), including with cannabis, suggests an advanced polysubstance use pattern. The relatively high prevalence of cocaine also suggests that this group of young substance users has a different pattern of drug consumption, more related to the "club drug" scene, where cocaine use is prevalent [289]. The use of tramadol thus seems to differ from use of other opioids, as has been shown by Winstock [108], pointing out that tramadol users appear to be more risk-taking, more interested in the "club scene". Our sample had experimented with synthetic cannabinoids, MDMA, and cocaine, but relatively seldom used benzodiazepines, or amphetamines, drugs that are more common among older, more marginalized Swedish substance users.

It is also important to note, that the only opioid detected except for tramadol was one specimen positive for methadone (together with tramadol), and one specimen exclusively positive for codeine. Other prescription opioids, such as buprenorphine, fentanyl, or oxycodone, common among prescription opioid users, both in Sweden and in the rest of Europe [94], could not be detected, nor did we find classical morphine-based drugs such as morphine or heroin.

The strong prevalence of cannabis in our sample, where all included patients except one reported a problematic cannabis use, is consistent with international literature [81]. This is a factor influencing the psychiatric co-morbidity, calling for attention to address both the substance use and the psychiatric symptoms of anxiety and depression which are so common in our sample, in order to prevent the development of a possibly negative life course that could lead to an aggravation of psychiatric symptoms and to social and criminal problems.

Because of a small sample size, we could not draw significant conclusions on the difference between opioid-positive and negative patients regarding socio-economic and psychiatric variables; a large proportion of the sample displayed a strong

psychiatric co-morbidity which adds to the problematic substance use, where we found that almost all patients used cannabis as a problem drug. The combination of tramadol and cannabis is therefore a new, interesting finding, which warrants attention in future research.

Clinical implications

Our findings in the prison population suggest that an increased vigilance and attention to the possibility of psychiatric symptomatology among inmates is necessary for prison staff in the criminal justice system. Through assessment with validated instruments, such as the ASI, it is possible for prison staff to detect psychiatric symptoms. These could be treated already in prison, in order to avoid the development of more severe symptoms, possibly leading to in-patient hospitalization or even self-inflicted death.

Therefore, our findings warrant attention from treatment providers both in the criminal justice system and in general psychiatric settings in order to increase the availability for psychiatric assessment of incarcerated individuals in the future. It is also important to develop routines for transfer from prison to evidence-based psychiatric treatment post-release, in order to facilitate follow-up on an adequate level.

Specialized treatment programs for facilitating the transfer to treatment of drug addiction have been initiated in the Swedish criminal system, where patients with opioid use have had the possibility to start opioid maintenance treatment (OMT) already in prison. Internationally, OMT in prison has been an established practice with promising results [290], and this treatment has been implemented at specialized prison units in Sweden [291]. Likewise, providing treatment for ADHD has been successful [292] in Swedish prison settings, however, the issue of medication for ADHD symptoms in prison is still controversial, although there is a growing consensus for the need to treat different behavioral problems arising from this condition in prison settings [293, 294]. As for treatment of psychiatric problems, generally, in prison, the need for development of research on the co-morbidity of substance use and psychiatric problems in prison was formulated already more than twenty years ago [295], and recent reviews have pointed to the need to develop psychiatric care in prison settings [296].

There is also a need to further develop evidence-based treatments for substance use disorders in the prison, not only for established practices, such as OMT, but also for alcohol, cannabis and stimulant use. Therefore, further research is needed to develop treatment modalities addressing the specific needs for prisoners, such as ADHD treatment, taking into account the psychiatric co-morbidity in this population.

It is also of great importance for prison staff to assess the risk for suicide or overdose. A history of suicide attempts or previous overdoses should lead to a further psychiatric assessment of suicidality, and possibly, evidence-based

treatment programs, both for the underlying psychiatric disease and the substance use problem. Treatment of substance use in prison [297] is a protective factor to avoid post-release death.

Prescription of sedatives in the prison population might both mask psychiatric symptoms and add to the risk of intoxication after release from prison, and must therefore be used with caution. Not only benzodiazepines, well known for their intoxicating effects, but also other sedatives must be considered potentially harmful in the long-term perspective [298].

It is therefore important for treatment providers, both in the health care system and the criminal justice system, to develop a "prison psychiatry" that is able to treat the psychiatric problems and concurrent substance use that exists among clients.

In an RCT design of intervention with feedback for psychiatric problems in an adolescent and young adult population, Interactive Voice Response had an effect on stress and anxiety over the time followed, as an add-on to regular treatment. This is a promising result that calls for further development of the IVR technology itself. More precise questions to assess the alcohol and drug intake could help reinforcing effects of treatment. Moreover, smartphone-based technologies, directed towards substance use, could be developed. Thus far, smartphone-based applications in the substance use field have been used for smoking cessation and alcohol problems, so there is a need to develop technical solutions suitable for substance use and psychiatric problems in the adolescent population. This could be exemplified by the study protocol presented by Benarous and co-workers [124] in France, addressing both cannabis use and psychiatric disorders.

The finding of the high prevalence of tramadol in the same population of adolescents and young adults has clinical implications that encompass many aspects: pharmacological epidemiology, substance use patterns and motivations for use. Concerning the prescription of tramadol, it is important to inform prescribing physicians about the non-medical prescription use of this substance, since one important source for the abuse of tramadol may be prescribed medications. It is also important for police and customs authorities to increase the vigilance for potential illegal importation and growing internet importation of the substance. It is also important to follow intoxications and causes of death associated with tramadol, since tramadol, after dextropropoxyphene, was the most common opioid associated with suicide, over the period 2002-2013 [299].

It is also important to follow new patterns of substance use in the adolescent population. As we have seen in this population of young substance users, a different pattern of substance use, with MDMA, "spice" and cocaine, has developed, and which is different from traditional drug use patterns, such as amphetamines and traditional opioids.

Directions for future research

Further research is needed to develop treatment programs for substance use and co-morbid psychiatric conditions in prison settings. There is a need to study treatment programs in prison for other substances than opioids, such as alcohol, cannabis and stimulants. Also, the transition from the criminal justice system to psychiatric services and for substance use disorders could be further developed.

In the adolescent and young adult population, there is a need to further explore factors that are related to adverse outcomes, such as criminality and antisocial behaviors, through longitudinal studies.

Regarding the specific use of tramadol, it is important to further explore motivation for use, patterns of use and a possible association to psychiatric co-morbidity.

It is also important to develop treatment programs for tramadol users, both for detoxification and tapering, as well as for abstinence treatment.

As IVR appears promising as add-on treatment, further research and development of this kind of intervention is suggested.

General conclusions

Clients in the Swedish criminal justice system, identified as problematic substance users, displayed a psychiatric co-morbidity when followed in national patient registers. Ten percent of the population investigated were hospitalized for a psychiatric diagnosis after release from prison, after excluding substance-related in-patient episodes. Psychiatric baseline factors predicted future psychiatric hospitalization. Our findings confirm the necessity to screen for psychiatric problems already in the prison setting, also for clients without a known psychiatric diagnosis.

In the same population of clients in the Swedish criminal justice system, factors associated with suicide, self-inflicted death and fatal accidental intoxication (overdose) were analyzed. Suicide was associated with psychiatric background factors and overdose was associated with factors related to substance use. Deaths of undetermined intent had different risk factors in comparison with suicide, with a stronger association to substance-related factors, suggesting that deaths of undetermined intent in this population have more in common with overdose deaths, thus also having consequences for statistics on causes of death.

The findings highlight the need to screen for both a history of overdose and a history of suicide attempts in the prison population, even if the clients have no known psychiatric history.

In a clinical sample of treatment-seeking adolescents and young adults at a treatment center for young substance users, Interactive Voice Response with feedback intervention had positive effect on symptoms of stress and anxiety, tested in a randomized controlled design, in a population with a high prevalence of co-morbid psychiatric diagnoses. IVR with feedback is therefore promising as an add-on instrument, possibly reinforcing effects of ordinary treatment.

In a pilot study, investigating the prevalence of non-medical prescription opioid use with hair analysis in the same population of adolescents and young adults, tramadol was the most prevalent opioid, used by almost one third of the sample. Problematic cannabis use was reported by all but one in the sample. In hair analysis, tramadol users were more likely to use other drugs, such as cocaine, MDMA and synthetic cannabinoids. No significant differences were detected in group comparison between tramadol users and non-users in hair analysis, with respect to socio-

economic and psychiatric baseline variables. The use of cannabis and tramadol is possibly a new substance use pattern in this population,

In investigating the co-occurrence of psychiatric symptoms in two populations of substance users, we have, through different methods, found a significant co-morbidity, which merits attention for both treatment providers and staff, working directly with clients and patients. Recognition of the need to screen for, and possibly to treat psychiatric symptoms at an early stage in treatment settings is important, both to avoid the development of a negative life course for young people, and to avoid hospitalization, overdose and suicide among released clients in the criminal justice system.

Ethical considerations

Papers I and II are based on a large database of ASI interviews where all data was anonymous to the research group. The study was approved by the Regional Ethics Committee in Lund (file number 2011/447 [paper I] and 2009/328 [paper II]).

Papers III and IV are based on a study conducted at a treatment center for adolescents and young adults. All patients received information about the study before participation. Informed consent was obtained from patients older than 18 years, and from parents or guardians for minors. All data from DOK assessment documents and psychiatric interviews, as well as data from the IVR monitoring were anonymous for the research group. Hair samples was obtained for the study, and the risk of adverse reactions, damage or pain for the patient was considered to be low for this type of body sample.

The study was approved by the Regional Ethics Committee in Lund (file number 2012-217) and is registered at ClinicalTrials.gov (NCT01706380).

Populärvetenskaplig sammanfattning

Denna avhandling handlar om missbruk och psykisk ohälsa hos ungdomar som söker vård för missbruksproblem och hos intagna inom kriminalvården som har angett att de har problem med missbruk. Avhandlingen består av två delar, en som undersöker förekomst av psykisk sjukdom hos klienter i kriminalvård som har intervjuats med bedömningsinstrumentet ASI (Addiction Severity Index) i svenska fängelser mellan 2001 och 2006 och en del som undersöker behandlingsmöjligheter och missbruksmönster hos ungdomar som söker behandling för missbruksproblem.

Artikel 1

Den första artikeln undersöker psykisk ohälsa hos klienter inom kriminalvård som lämnat fängelse. Den studie som ligger till grund för artikeln är en registerstudie, där vi har följt upp patienter som deltagit i intervjuundersökningen efter frigivning genom att använda det svenska slutenvårdsregistret för att se, om de har vårdats inneliggande för någon psykiatrisk diagnos.

Vid en första analysgenomgång kunde vi se, att mer än en tredjedel hade vårdats för psykisk ohälsa, men en stor del av dessa slutenvårdstillfällen var kopplade till missbruksrelaterade diagnoser. När vi renodlade vår analys så, att vi tog bort samtliga diagnoser som var kopplade till missbruk fann vi att en tiondel av klienterna i kriminalvård hade vårdats i psykiatrisk slutenvård. De faktorer som hade ett samband med senare slutenvårdsinläggning var psykiatriska problemvariabler i ASI-intervjun. Tidigare psykiatrisk slutenvårdserfarenhet, tidigare självmordsförsök samt tidigare depression och ångest var tydligt kopplat till senare slutenvård, liksom användning av lugnande läkemedel, något som tyder på att användning av lugnande läkemedel kan vara en markör för psykisk ohälsa i denna grupp. Den enda missbruksvariabel som hade betydelse för senare slutenvård var amfetaminanvändning, där vi såg ett negativt samband – det vill säga, amfetaminanvändare var i mindre utsträckning vårdade i psykiatrisk slutenvård.

Studiens resultat visar på betydelsen av att aktivt undersöka och fråga efter psykiatriska symtom hos fängelseinterner med en missbruksproblematik, då dessa kan behandlas redan under tiden i fängelse. Det är också viktigt att klienter som behandlas inom kriminalvården i samband med frigivning får kontakt med den

psykiatriska vården, så att försämring, med intagning i slutenvård som följd, kan undvikas eller minskas.

Artikel 2

Den andra artikeln i avhandlingen följer klienter i kriminalvården efter frigivning från fängelse eller intervju i frivården, i det svenska dödsorsaksregistret, där vi har undersökt vilka riskfaktorer som finns för självförvållad död: självmord, självförvållad död av oklar avsikt eller oavsiktlig, dödlig förgiftning, vanligen kallad ”överdos”.

Riskfaktorer för självmord var tydligt kopplade till psykiatriska problemvariabler, som tidigare självmordsförsök och användning av lugnande medel, medan överdos hade ett samband med manligt kön, heroinanvändning och cannabisanvändning. Eftersom cannabisanvändning i sig inte kan ge överdos, tolkades fyndet som en markör för blandmissbruk, något som har ett starkt samband med död i överdos.

Riskfaktorer för självförvållad död av oklar avsikt var kopplade till missbruksvariabler som heroinanvändning och berusningsdrickande av alkohol. Även tidigare inläggning i psykiatrisk slutenvård var en riskfaktor. Ett paradoxalt fynd var, att en historia av depression hade en negativ koppling till denna dödsorsak. Sannolikt har dödsfall i denna kategori mer att göra med missbruk än med depressivitet i denna grupp patienter – depression är annars en känd riskfaktor för självmord i den allmänna befolkningen.

Våra fynd talar för att det är viktigt att kartlägga och fråga efter självmords-benägenhet och tidigare självmordsförsök hos kriminalvårdens klienter, och att det också är viktigt att fråga efter tidigare överdoser, för att kunna genomföra behandlingsinsatser i förebyggande syfte.

Artikel 3

Avhandlingens tredje artikel rapporterar en behandlingsstudie, en randomiserad kontrollerad prövning av intervention med hjälp av automatiserad telefoni, IVR (Interactive Voice Response) i en grupp behandlingssökande ungdomar med missbruksproblem på ungdomsmottagningen Maria Malmö i Malmö. IVR är ett uppföljningsinstrument via mobiltelefon som har använts sedan 1990-talet för uppföljning av olika symptom inom vården. På senare år har det gjorts studier där systemet även ger återkoppling, feedback, till patienterna.

Sjuttiotre ungdomar rekryterades till studien och fördelades slumpmässigt till antingen behandling eller kontrollgrupp. Alla fick uppföljning med IVR och

rapporterade in hur de mådde via mobiltelefonen, där frågeformulär om stress, psykiskt mående och missbruk hade lagts in, under tre månaders tid, två gånger i veckan. Behandlingsgruppen fick återkoppling, avseende stress och psykiskt mående sedan senaste registrering: sämre, bättre eller ingen förändring. Om de rapporterade att de mådde sämre, fick de råd om att ta kontakt med behandlare, eller någon de hade förtroende för, på mottagningen.

Studien visade att de som hade fått återkoppling mådde bättre avseende stress och ångestsymtom medan vi inte såg någon skillnad mellan grupperna med avseende på depression. Vi kunde heller inte konstatera någon förändring vad gäller ett globalt mått på missbruk.

Eftersom den ungdomsgrupp vi har undersökt har rapporterat en hög psykiatrisk samsjuklighet, där mer än hälften hade rapporterat ångest och depression är vår slutsats att feedback med IVR kan ha en effekt som tillägg till behandling i denna grupp av patienter.

Artikel 4

I samma grupp patienter undersöktes förekomsten av icke-medicinsk användning av opioidläkemedel (NMPOU: non-medical prescription opioid use), genom hårprovsteknik. Hårprover har använts inom rättsmedicinen och används inom beroendeforskning för att kunna se ett intag av droger under en längre tid, eftersom droger (och andra substanser) inlagras i hår. I denna studie kunde vi se intag av droger upp till en och en halv månad tillbaka. Femtionio patienter av de 73, som gick in i studien, kunde lämna hårprover för analys.

Hårprovsanalyserna visade att nästan en tredjedel hade missbrukat opioid-läkemedlet tramadol, ett läkemedel som har blivit allt mer vanligt i ungdomsgruppen under senare år. Förutom ett prov, positivt för metadon och ett prov positivt för kodein, såg vi inga andra opioider (morfinpreparat, som morfin, heroin, buprenorfin eller oxykodon) i proverna. Samtliga utom en i den undersökta gruppen hade rapporterat ett problematiskt intag av cannabis. De som uppvisade positiva hårprover för tramadol var också positiva för andra missbruksdroger, i större utsträckning än de som var negativa för detta läkemedel.

Sextiofyra procent av gruppen hade någon psykiatrisk diagnos, förutom missbruksdiagnoser, enligt den diagnostiska intervjun MINI. Mer än en tredjedel av de undersökta rapporterade att de hade dömts för brottslighet, och en lika stor andel rapporterade att föräldrarna hade haft psykiatriska problem under uppväxten.

En jämförelse mellan opioid-positiva och opioid-negativa visade ingen statistiskt säkerställd skillnad med avseende på psykiatriska eller sociala bakgrundsfaktorer.

Pilotstudien visar, att tramadolmissbruk är vanligt och utgör ett nytt missbruksmönster i ungdomspopulationen, ofta tillsammans med cannabis. Studien bekräftar den bild som har beskrivits i tidigare internationella och svenska studier: att ungdomar som söker vård för missbruksproblem har en hög psykiatrisk samsjuklighet.

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