Recent substance intake and drug influence among patients admitted to acute psychiatric wards

A cross-sectional study of toxicological findings, physician assessment and patient self-report in two Norwegian hospitals

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To Maria

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Acknowledgements

Ever since my medical studies I have had a special interest for the field of psychiatry. My interest for psychoactive substance use and addiction medicine started during my first year as a physician: As a civilian worker in 2003, I worked as a therapist for patients with a problematic use of alcohol and/or medicinal drugs at A-senteret, Kirkens Bymisjon in Oslo. I am thankful to the staff there for showing me the art of meeting these patients with hope, knowledge and respect.

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Summary

Background: Patients presenting for emergency psychiatric evaluation have a high prevalence of combined medical and psychiatric illness and psychoactive substance use. This comorbidity causes differential diagnostic challenges and deserves careful attention. Detection of recent substance intake, which may be required for appropriate diagnosis and intervention, can be based upon clinical assessment, patients' self-report or toxicological analyses. There is, however, no consensus on how this assessment should be performed, and the utility of laboratory analyses has not been widely evaluated. Also, estimates of psychoactive substance use among acutely admitted psychiatric patients vary among studies, and few have used comprehensive laboratory methods.

Objectives: The first main objective was to identify the rates of psychoactive substance use and drug influence among patients admitted to acute psychiatric wards, by using chromatography-based analyses of blood and urine. The second objective was to investigate associations between substance use and various clinical variables, and the third was to compare physician assessment and on-site urine testing with the results of comprehensive toxicological analyses.

Methods: A cross-sectional and laboratory-based pilot study was conducted in 2003 in Oslo, Norway. The study sample comprised 100 acute psychiatric admissions (86% of all consecutive admissions in the project period). Blood and urine samples were collected as soon as possible after admission and extensively analyzed for alcohol, medicinal and illegal drugs, and drug influence at the time of admission was estimated on the basis of blood drug concentrations. The main study was conducted in 2006/2007, in two psychiatric departments situated in Oslo and Arendal, Norway. The study sample comprised 309 consecutive admissions in Oslo (88% of all) and 47 (42%) in Arendal. Blood and urine samples were collected and analyzed for alcohol, medicinal and illegal drugs, and a routine on-site urine screening test was performed in 92 of the cases. At admission, the physician on call performed an overall judgment of recent drug intake and of current drug influence. Psychotic symptoms were assessed with the positive subscale of the Positive and Negative Syndrome Scale. Patient self-report questionnaires included the Alcohol and Drug Use Disorder Identification Tests. Both patients and physicians were asked if they thought that the admission was related to substance use, and patients were also asked if they needed

professional help for substance use. Sociodemographic variables, clinical characteristics and medication history were obtained through the review of medical records.

Results: In the pilot study, psychoactive substances were detected in 63% of the 100 admissions, medicinal drugs in 47%, alcohol in 8% and illegal drugs in 36%. On the basis of blood drug concentrations, drug influence was estimated in 26% of the patients. In the main study, similar rates were found: Substances were detected in 63% of the 298 admissions, medicinal drugs in 46%, alcohol in 12% and illegal drugs in 28%. A total of 20 different substances were identified, with up to 10 in a single patient. Nonprescribed use of medicinal drugs was found for 36% of patients. Patients using alcohol had a high suicidal risk score at admission and the shortest length of stay (median one day). Use of illegal drugs was associated with psychotic symptoms and readmission. Self-report questionnaires indicated harmful use of alcohol for half of the patients and of other substances for one-third. A need for professional help for substance use was reported by one-third of patients. When comparing clinical and laboratory data, our findings indicated clinical under-detection of recent substance intake. On-site urine testing identified substance use that was not recognized by the physician's initial assessment, although specificity for cannabis and benzodiazepines was low. Finally, patients were judged by the physician as being under the influence of drugs and/or alcohol in 28% of the cases. The clinical assessment of drug influence showed a moderate positive relationship with the blood drug concentration scores, and also to symptoms of hyperactivity/agitation and to the detection of alcohol, cannabis and amphetamines.

Conclusion: Our findings demonstrate the major impact of both recent and long-term substance use. Given the high rates of substance use and the important clinical associations, drug screening seems warranted in acute psychiatric settings. Chromatographic urine analyses should be considered for routine screening, and clinical staff using on-site urine screening tests should be aware of their inaccuracy. Also, interventions designed for substance-using patients should be developed and integrated.

List of papers

This thesis is based on the following publications, which are referred to by their roman numerals:

I. Mordal J, Bramness JG, Holm B, Morland J: Drugs of abuse among acute psychiatric and medical admissions: laboratory based identification of prevalence and drug influence. Gen Hosp Psychiatry 2008, 30: 55-60.

II. Mordal J, Holm B, Gossop M, Romoren M, Morland J, Bramness JG: Psychoactive substance use among patients admitted to an acute psychiatric ward: Laboratory findings and associations with clinical characteristics. Nordic Journal of Psychiatry (accepted for publication).

III. Mordal J, Holm B, Mørland J, Bramness JG. Recent substance intake among patients admitted to acute psychiatric wards: physician's assessment and on-site urine testing compared with comprehensive laboratory analyses. J Clin Psychopharmacol. 2010 Aug;30(4):455-9.

IV. Mordal J, Medhus S, Holm B, Mørland J, Bramness JG: Influence of drugs and alcohol upon patients admitted to acute psychiatric wards: Physician’s assessment compared to blood drug concentrations. Submitted.

List of abbreviations

ADH	Alcohol dehydrogenase method
ASI	Addiction Severity Index
AUDIT	Alcohol Use Disorder Identification Test
CTI	Clinical Test for Impairment
DSM-IV	Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition
DUDIT	Drug Use Disorder Identification Test
DUDIT-E	Drug Use Disorder Identification Test – Extended
EMIT	Enzyme multiplied immunoassay technique
GAF	Global assessment of functioning
GC-MS	Gas chromatography-mass spectroscopy
H-SCL 10	Hopkins Symptom Checklist, 10 item version
HS-GC-FID	Headspace gas chromatographic flame ionisations detection
ICD-10	International Classification of Diseases, Tenth Edition
LC-MS	Liquid chromatography-mass spectroscopy
LSD	Lysergic acid diethylamide
MAP	Multicenter study of Acute Psychiatry (performed in Norway 2005)
MINI	MINI International Neuropsychiatric Interview
PANSS	The positive and negative syndrome scale
SCID	Structured Clinical Interview for DSM-IV
TLC	Thin-layer chromatography
WHO	World Health Organization

Definitions

In literature dealing with mental health and substance use, there is a wide variation in phenomenology, methodology and terminology. In this thesis, the following definitions are used:

"Mental disorders" and "substance use disorders" are defined according to the standard nomenclature of the International Classification of Diseases (ICD-10), chapter F0-F9 (1). The criteria for the main substance use disorders are given in Table 1.

"Comorbidity" refers to a person having co-occurring mental disorder and substance use disorder.

"Severe mental illness" refers to major mental disorders such as schizophrenia, severe bipolar disorder and severe depression, with loss of daily function and persistence over time (2).

"Acute psychiatric admission" will refer to persons being admitted for inpatient assessment and treatment in acute psychiatric wards for adults. Many of these patients have severe mental illnesses. The patient may, however, present with a wide range of problems and does not necessarily fulfill the criteria for any mental disorder.

"Psychiatric emergency department" will refer to an out-patient department for the assessment and treatment of patients with acute psychiatric conditions.

The words "substance" and "drug" are used as synonyms, and will both refer to psychoactive substances including benzodiazepines, opioids, alcohol, amphetamines, cocaine, cannabis and hallucinogens. The study is laboratory based, and all the specific substances that were included in the analyses are described in chapter 4.1. These substances can be classified on the basis of their primary effect (sedatives, stimulants and hallucinogens) or on their legal status (medicinal drugs, alcohol and illegal drugs), and may be used recreationally to purposefully alter one's consciousness or therapeutically as medication.

"Recent substance intake" will mostly refer to substances taken during the previous few days before admission, and is not necessarily a part of a substance use disorder.

"Drug influence" will refer to the acute and impairing effects of substance intake, as measured by clinical assessment or by blood drug analyses.

Table 1 Selected substance use disorders according to ICD-10 (condensed) (1). The criteria are applied for substances individually.

ICD-10 diagnoses
Acute intoxication
There must be clear evidence of recent use at sufficiently high doses
Symptoms or signs of intoxication compatible with the known actions of the particular substance
Not accounted for by a medical disorder or by another mental disorder
Harmful use
Substance-induced psychological or physical harm
Pattern of use persisted for at least 1 month or has occurred repeatedly within 1 year
Dependence (at least 3)
Compulsion to use
Impaired control
Withdrawal state when substance use is reduced or ceased
Tolerance development
Substance use prioritized over other activities
Continued use despite harmful consequences
Withdrawal state
Recent cessation or reduction of substance use after repeated and prolonged use
Symptoms and signs compatible with the known features of a withdrawal state from the particular substance
Not accounted for by a medical disorder or by another mental disorder
Substance-induced psychotic disorders
Onset of psychotic symptoms must occur during or within 2 weeks of substance use
Psychotic symptoms must persist for more than 48 hours
Must not exceed 6 months

ICD-10; International Classification of Diseases.

1. Introduction

About 450 million people worldwide are affected by mental disorders (3). In 2005, mental disorders comprised 14% of the global burden of disease (4). The figure includes substance use disorders and is likely to increase by 2030. This burden has substantial social and economic consequences for individuals, families and governments. There is a wide international and interregional variation in the organization of mental health services, and many developing countries lack such services (3).

In many European countries and in the USA, mental health services have been de-institutionalised over the last decades. This has resulted in a shift from inpatient care to community care (5). Still, inpatient units play an important role in the treatment of many psychiatric patients, and hospitals are an essential part of modern psychiatric services, demanding significant human and economic resources (6). In most countries, acute wards represent a key component of the overall network of mental health services, being the only part of the system that cannot refuse to accept a referral (7). Despite the importance of acute inpatient care, its quantitative and qualitative features remain largely unexplored (7, 8).

This thesis focuses on the use and influence of drugs and alcohol among patients admitted to acute psychiatric wards in two Norwegian hospitals. Different measurements are applied and compared, with an emphasis on comprehensive laboratory analyses and physician assessment. The study emerged from clinical practice, and the background was two-fold. First, there was a lack of studies documenting the rates of substance use among acute psychiatric admissions in Norway. Second, few studies had used comprehensive toxicology analyses internationally, and in particular, quantitative blood drug analyses were previously unproven.

1.1. Acute psychiatric admissions

System characteristics:

Countries vary widely with regard to the initial assessment and caretaking of persons with acute mental and/or behavioural disturbances. Several institutions can be involved, such as primary health care, emergency departments, psychiatric outpatient clinics, substance abuse facilities and police. In psychiatric emergency departments, for example, the staff will need to determine if the patient needs to be admitted to a psychiatric inpatient facility or if they can be

safely discharged to the community after a period of observation and/or brief treatment. Acute psychiatric teams, crisis hostels and community health centre beds may also provide alternatives to hospitalization (9-11). The decision to hospitalize from emergency departments may be related to contextual factors such as site and bed availability (12), but patient factors such as suicide potential, danger to others and symptom severity comprise the strongest predictors of hospital admission (13, 14).

Procedures and criteria for hospital admission vary across regions and countries (14). Rates of involuntary placement or treatment of people with mental illness are considered to be an indicator for the characteristics of national mental health care laws. Among 13 European countries not including Norway, the percentage of involuntary admissions in relation to all admissions ranged from 3% - 30%, with a median value of 13% (15). In a national study in Norway, the rate was 42% and differed greatly across regions (16), and there was also a substantial between-ward variance in the use of seclusion, restraint and involuntary medication (17). European and US studies also find geographical variations with regard to the numbers of admissions and acute beds per 1000 inhabitants, staff/patient ratio and assessment and treatment strategies (5, 6, 16, 18-20). These variables may also differ across public and private inpatient facilities (21). Mean length of hospital stay has been reported in a few national studies, being 10 days in Norway, 12 in Italy and median 15 days in England (5, 6, 16). Readmissions are common, and in Norway, 57% of patients admitted to acute psychiatric wards had at least one other psychiatric admission during the previous year (16). During the period of de-institutionalisation, the overall length of stay has declined and the rates of admission and pressure on beds have increased (7), and this has raised serious concerns on the quality of care (22).

Patient characteristics:

Variation across studies and countries is also observed with regard to patient characteristics. Multicentre studies in different countries including Norway have reported similar rates of men and women (50%) (16, 21, 23), whereas others found that men were admitted more frequently than women (5, 24). Mean age of all patients varied from 34 to 42 years (16, 21, 24). Main clinical diagnoses at discharge were reported in a few of these studies. According to ICD-10, the most common diagnostic groups were F3 affective disorders (range 21%-33%), F2

schizophrenia (24% - 36%), F4 neurotic disorders (4%-14%) and F1 substance use disorders (7% - 13%) (16, 21, 23).

The Norwegian setting:

As in other Scandinavian countries, the Norwegian health care system is catchment area based and publicly funded and provided. Services for alcohol and substance abuse are organized as a part of mental health services. In 2005, there were 23 acute psychiatric departments in Norway (17). A person may be referred for voluntarily or for compulsory observation of up to 10 days or for compulsory treatment for a prolonged period of time. There are psychiatric emergency departments in Bergen and Oslo (Psykiatrisk Legevakt), and the latter is open daily from 16-23 hrs and has a close cooperation with the somatic emergency department which also has an inpatient observational unit.

1.1.1. Initial assessment of acute psychiatric conditions

Patients admitted to psychiatric wards may present with a wide range of socioeconomic problems, mental and somatic symptoms and use of psychoactive substances. These possibilities deserve careful assessment and differential diagnostic considerations, which are some of the key roles of the acute ward and comprise the focus of this thesis.

The initial assessment of psychiatric patients has been studied by several authors in US emergency departments (25-28), and a clinical policy has been developed (29). In a focused medical assessment, a medical etiology for the patient's symptoms is excluded and other illness or injury in need for acute care is detected and treated (29). The evaluation involves obtaining a history, performing an appropriate physical and mental status examination, and testing, when indicated (28). Patients with acute intoxication and withdrawal states must be identified and treated. A recent review among emergency department patients concluded that on-site urine screening tests were unlikely to have a significant impact on the management of the presenting condition (30).

Less is known about the initial assessment of patients admitted to acute psychiatric wards. The need for a medical approach in the psychiatric ward is demonstrated by studies reporting unrecognized medical emergencies among psychiatric inpatients (31), as well as high prevalences of metabolic syndromes and infectious diseases (32), that also commonly go

undetected (33). The utility of routine laboratory screening among acute psychiatric admissions has been under debate (34, 35), and there are currently no specific guidelines about which somatic or toxicological tests should be routinely done. Electro cardiography and chest radiography should not be performed on a routine basis (36, 37), and the utility of neuroimaging is under debate (38, 39).

1.1.2. Initial treatment of acute psychiatric conditions

For acute psychiatric conditions, there is a scarcity of controlled clinical trials. Conditions like acute psychosis and agitated behaviour are difficult to study and co-operation from the study population is rare. Also, pharmacological studies may not be considered ethical, as many are funded by commercial companies and report outcomes that are difficult to interpret for routine clinical care (40). Still, selected pharmacological therapies for acute psychosis or agitated behaviour have been reviewed (e.g. benzodiazepines and/or antipsychotics), and patients have been recruited both in emergency departments and in acute wards (40-42). In clinical practice, several psychotropic drugs are commonly combined, despite limited empirical evidence for greater effectiveness or safety of such polypharmacy (43, 44). Little is also known about the use of pharmacological and physical restraints, seclusion and combination therapies (42), and practice guidelines for initial inpatient treatment are lacking. There are, however, comprehensive text books for emergency and inpatient psychiatry (45, 46), as well as practice guidelines for the assessment and treatment (acute and long-term) for various psychiatric conditions. For example, the American Psychiatric Association has guidelines for schizophrenia, bipolar disorders, substance use disorders and suicidal behaviours (47).

The case presentation (Box 1) refers to an actual person and may illustrate some typical challenges in the assessment and treatment of acute psychiatric conditions.

Box 1 Case presentation

In December 2004, a 21-year old man ("Joe") was admitted for the first time to the acute psychiatric ward. He was referred from an outpatient clinic for compulsory observation of up to 10 days because of substance use, aggressive behaviour and increasing psychotic symptoms. Joe was brought to the ward by police officers.

At the time of admission, Joe had incoherent speech and disorganized thoughts. He confirmed paranoid ideas, use of amphetamines and lack of sleep, but there were no signs of hallucinations. Little was known about his background, premorbid functioning and somatic health. Joe was verbally aggressive and did not accept any somatic assessment. After a while, he accepted antipsychotic medication and hypnotics, per os, and he soon fell asleep. The physician on call noted that this could possibly be a substance induced psychosis.

After a few days in the locked ward and with a lot of sleep, Joe seemed much calmer and was not aggressive any more. He said that he had a difficult childhood, as both his parents had severe substance problems, and that he for many years was taken care of by the child protection services. Joe started to smoke cannabis at the age of 13, and later he started using amphetamines and flunitrazepam. He did not complete primary school and now he was unemployed and lived with his mother again. There had been no previous contact with mental health services.

During hospital stay, Joe abstained from substance use and his psychotic symptoms weakened. He said he wanted to cut down his substance use and to start outpatient treatment, for which he was referred. At discharge after one week, he received the diagnosis of F12.5, cannabis induced psychosis. The clinician noted that attention deficit hyperactivity disorder could not be excluded. The diagnosis was based on routine clinical practice, and questionnaires, structured interviews or laboratory analyses for psychoactive substances were not used. Somatic assessment and brain imaging had not been performed, but blood samples were drawn three days after admission, and somatic laboratory analyses were all within the normal ranges.

1.2. Mental disorders and co-occurring substance use disorders

The thesis focuses on substance use among patients admitted to acute psychiatric wards. Although such use is not necessarily a part of a substance use disorder, it will here be discussed in the context of mental disorders and co-occurring substance use disorders.

1.2.1. Prevalence and consequences of co-occurring substance use disorders

There is a growing use of psychoactive substances worldwide. In year 2000, there were an estimated 2 billion alcohol users, 1.3 billion tobacco users and 185 million drug users, causing major global public health problems (48). Alcohol consumption alone comprised nearly 5% of the global burden of disease in 2004 (49). Among patients with mental disorders, substance use is even more common than in the general population (50, 51). The relation between substance use and mental disorders is complex and has been object of extensive research over the last two decades, and most studies have focused on substance use disorders.

The large population of persons with co-occurring disorders is heterogeneous in regard to type and severity of mental illness and substance use disorder and cognitive and psychosocial skills (2). Patients with severe mental illness in outpatient settings have been particularly studied, and a 50% lifetime prevalence of substance use disorders are commonly reported (52). Substance use disorders have been associated with several adverse consequences among these patients, such as a more severe symptom burden, more frequent hospital admissions, poor treatment outcome and increased risk of violent and suicidal behaviour (53-57). It has also been suggested that even small amounts of drugs or alcohol may pose problems for patients with severe mental illness (58, 59). In contrast, some studies of substance using patients with schizophrenia have reported fewer negative symptoms and better social functioning (60, 61). Substance use disorders are also highly prevalent among patients with less severe mental disorders, and may induce or exacerbate psychiatric symptoms and affect treatment outcome negatively (62, 63). For these co-morbid conditions, knowledge on etiology and pathophysiology is still limited (52).

Acute psychiatric admissions

With regard to substance use disorders among patients admitted to acute psychiatric wards, a review of studies published 1989 - 2009 is shown in Table A1 (Appendix) (16, 21, 24, 64-91).

In summary, these studies find that current substance use disorders are highly prevalent (commonly 40 - 50%) and have adverse clinical implications, such as poorer outcome, higher rates of admission and shorter length of hospital stay (73, 77, 79). There are, however, many methodological differences between these studies, with regard to study population, sample size and definition and measurement of substance use disorders (Table A1).

1.2.2. Assessment of co-occurring substance use disorders

The large and heterogeneous population of persons with co-occurring mental disorders and substance use disorders comprise challenges to diagnostic and treatment strategies. In the traditional system of parallel substance abuse treatment and mental health services, few patients were able to access needed treatments for both disorders, and the services were rarely addressing the common interactive elements of co-occurrence (2). Over the last decades, there has been an overall tendency towards assessment and treatment strategies that integrate mental health and substance abuse interventions. A comprehensive psychiatric evaluation is essential to guide the treatment of a patient with a substance use disorder, as is an evaluation of substance use for a patient with a psychiatric disorder (92). For patients with severe mental illness and substance use disorders, it has been stated that "assessment is the cornerstone of effective treatment" (93).

Acute psychiatric admissions

In studies of substance use disorders among patients in acute psychiatric wards, different methods have been used (Table A1). Diagnostic interviews are based on the diagnostic criteria for mental and substance use disorders and examples are Structured Clinical Interview for DSM-IV (SCID) (94) , Psychiatric Research Interview for Substance and Mental Disorders (PRISM) (95) and MINI International Neuropsychiatric Interview (96). Non-diagnostic interviews may also be used, such as the Addiction Severity Index (ASI) (97), and may be used to define "problem substance use". Clinician rated scales (e.g. the Drake scale (98)) and self-report questionnaires (e.g. Alcohol Use Disorder Identification Test, AUDIT (99)) have been used in several inpatient studies to indicate problem substance use or substance use disorders (Table A1).

There are, however, several challenges and limitations with these measurements in acute psychiatric settings. Little is known about their actual validity and reliability. Structured interviews and questionnaires may not be feasible for all patients in an acute psychiatric ward (100, 101). Also, diagnostic interviews ideally presuppose that substances were not used during the four previous weeks, which rarely is the case among acute admissions with high rates of substance use and short length of hospital stay. Few instruments are tailored for acute care settings (102), which partly may explain why many studies reported routine clinical diagnoses only (Table A1).

The impact of misdiagnosis has been debated. Under detection of substance use disorders have commonly been reported, and the possibility for adequate intervention and follow-up for patients with problematic substance use may therefore be lost (73). On the other hand, when substance use and psychotic symptoms co-occur, premature use of the label drug induced psychosis may obscure the diagnosis of an emerging serious mental illness (82, 103).

1.2.3. Treatment of co-occurring substance use disorders

Interventions for mental illness and substance use disorder include different treatments and rehabilitation (104). Treatments are medications or psychosocial strategies aimed at controlling or eliminating the symptoms or causes of illness or disorder; rehabilitation interventions are intended to improve skills and supports to enable persons to overcome the disabilities associated with illness or disorder. Treatment and rehabilitation overlap considerably and are often performed by multidisciplinary teams.

The effect of pharmacological management among patients with co-occurring disorders is not widely evaluated (2). Some medications that are effective for the treatment of alcohol use disorders in the general population, such as disulfiram and naltrexone, are probably also effective in persons with severe mental illness (105). Also, some medications that treat mental illnesses may lead to a reduction of substance use. Antidepressants appear to reduce alcohol use among patients with major depression and alcohol disorder (106), as mood stabilizers do among patients with bipolar and alcohol use disorder (107). Among persons with schizophrenia, atypical antipsychotics may offer some benefit in reducing craving or substance use, but research is preliminary (105).

Psychosocial treatments for people with co-occurring severe mental illness and substance misuse has recently been reviewed, and the results indicate that motivational interviewing can be effective for reducing substance use (58). To date, psychosocial treatments for other psychiatric populations with substance misuse have not been reviewed. In primary care settings, a recent review concluded that brief interventions can reduce alcohol consumption in men, with benefit at a year after intervention, but they are unproven in women for whom there is insufficient research data (108). The evidence for brief interventions delivered to heavy alcohol users admitted to general hospital is also inconclusive (109). A large US study performed in various medical settings, however, found that screening and brief interventions proved feasible and effective in reducing self-reported use of both alcohol and illegal drugs at six months follow-up, along with improved general and mental health and social functioning (110).

Acute psychiatric admissions

Psychopharmacology, different forms of psychotherapy and a therapeutic milieu are cornerstones of the treatment in the acute psychiatric ward. With regard to substance use disorders, objectives are e.g. to motivate the patient to change, to reduce the morbidity and sequelae of problematic substance use, to provide psycho education to patients and relatives and to refer for further treatment in adequate services (104). Motivational interviewing appears feasible among psychiatric inpatients, but randomized trials report mixed results. One study found that brief motivational interviewing during hospital stay reduced alcohol use at six months follow-up (111), whereas another recommended more extensive interventions, continuing on an outpatient basis, particularly for cannabis use (112).

1.3. Methods for assessing recent substance intake and drug influence

Of the methods assessing *substance use disorders*, few assess recent intake and drug influence. Typically, drug use is assessed for the previous 30 days (ASI), 6 months (Drake) and one year (AUDIT and MINI), and may therefore not be relevant in assessing acute conditions. In previous studies, however, recent substance intake and drug influence have been assessed by using patient report, physician assessment and laboratory tests.

1.3.1. Patient self-report

We are not aware of any validated self-report questionnaire that specifically assesses recent substance intake. Many studies have therefore included self-made questions addressing recent intake as part of questionnaires or interviews in emergency departments (113), acute medical settings (114), drug treatment settings (115) and acute psychiatric settings (69, 81, 116, 117). Drug use may then be assessed for the previous 6 or 24 hours (118), two days (69), one week (117), two weeks (51) or one month (113). However, some validated instruments have an indirect measure of recent intake, by assessing the frequency of drug use; for example by "every day last month" (ASI).

1.3.2. Physician assessment

In studies from psychiatric acute care settings, physicians have been asked to judge if the patient had been taking any substances recently (76, 90). Clinical assessment of recent drug intake is a challenging task, and when compared with laboratory drug findings, these studies report significant discrepancies. In a few studies, physicians have assessed whether the acute psychiatric admission was related to substance use (119) or substance induced (120, 121). "Drug intoxication" in acute psychiatric settings has been defined in different ways, such as by any intake of substances last 24 hours (122), by an intentional drug overdose to attempt suicide (119) and by an overall clinical judgement (70). "Drug influence" has previously been reported in one study only, by using an overall physician assessment (16, 87).

Also in studies from medical acute care settings, physicians have been asked to judge if the patient had been taking any substances recently (123-125). When compared with laboratory findings, most studies report significant discrepancies, whereas a few reported better

agreement (126, 127). Physicians have also assessed whether the acute medical condition was related to substance use (128). In addition, the severity of acute poisoning has been evaluated as "not severe, moderate or severe" (123) and consciousness as "awake, somnolent or coma" (124). The Glasgow Coma Scale is also widely used as a measure of consciousness in studies of acute poisonings (129). We are not aware of any study comparing these clinical assessments with quantitative blood drug findings.

In forensic toxicology, the ability of police physicians to assess recent substance intake and drug influence among apprehended has also been studied, using for example the Standardized Field Sobriety Test (130) and the Norwegian Clinical Test for Impairment (131). The latter test consists of three parts: Substance use history (alcohol and other drugs), clinical examination (with simple physical and cognitive tests) and a conclusion on the estimated degree of drug influence.

1.3.3. Toxicology methods

Toxicology methods are widely used for assessing recent substance intake. A comparison of some of the different techniques is shown in Table 2 (129). Gas and liquid chromatography-mass spectroscopy (GC-MS and LC-MS) are the reference standards with high sensitivity and specificity. They are useful for quantitation and can have a broad analyte range. These methods are however expensive and do not provide immediate, on-site results.

Table 2 Relative comparison of toxicology methods

Method	Sensitivity	Specificity	Quantitation	Analyte range	Speed	Cost
On site test	+	+/-	No	Few	Fast	£
Immunoassay	++	++	Yes	Moderate	Medium	££
TLC	+	++	No	Broad	Slow	££
GC	++	++	Yes	Broad	Medium	££
GC-MS, LC-MS	+++	+++	Yes	Broad	Slow	£££

TLC, thin-layer chromatography; GC, gas chromatography; GC-MS, gas chromatography-mass spectroscopy; LC-MS, liquid chromatography-mass spectroscopy.

These toxicological methods can be applied on different biological matrices. Urine has been most commonly used both in psychiatric clinical settings and in research. Most drugs can be detected in urine for some days after last intake, whereas cannabis can be detected in up to several weeks (132). Drug analyses may also be performed in blood, saliva and breath (with generally shorter detection times than urine) and hair (detection times up to a year) (129).

On-site urine tests are widely used in clinical settings and provide results within 5-10 minutes. Many institutions offer immunoassay urine testing for the most commonly abused drugs, and results are generally available in 30 minutes. More comprehensive analyses may take up to hours or days and are usually performed off-site.

In clinical toxicology, quantitative blood drug analyses can be used to assess the type and severity of intoxications (129), and in forensic toxicology, such analyses are also used to estimate the degree of drug influence or impairment (133). Toxicological methods used in acute psychiatric settings will be discussed in the next chapter.

1.4. Toxicological findings among patients in acute psychiatric services: A literature review

In the following, we will describe studies using toxicological methods among outpatients in psychiatric emergency departments and among patients admitted to acute psychiatric wards.

1.4.1. Psychiatric emergency departments

Among studies of emergency psychiatry and substance use, many have been performed in US psychiatric emergency departments (134-141). These studies report urine detection rates of "any drug" ranging from 21% - 62%. Most of these studies have reported substance specific detection rates by using both immunoassay screening and chromatographic confirmation. We have identified one study using blood drug analyses, but quantitative results were not presented (122). The latter study concluded that the impact of substance abusing patients was substantial; they presented often with acutely suicidal conditions, required high levels of behavioural management, spent more time in the emergency department, but had less need for psychiatric hospitalization. When laboratory findings were compared with patient and physician reports, significant discrepancies were reported in most studies, and better agreement in some (141). Some studies concluded in favor of the routine use on-site urine screening tests (134, 140), whereas others did not (141). A recent review, however, concluded not in favor of using on-site urine tests among emergency department patients (30).

1.4.2. Acute psychiatric admissions

Detection rates and methodological considerations

Through a literature review, we identified 20 studies using toxicological analyses among patients admitted to acute psychiatric wards from 1970 - 2009 (69, 70, 72, 76, 81, 84-87, 90, 116, 117, 142-149). These studies report urine detection rates of "any drug" ranging from 15% - 72% and of "illegal drugs" ranging from 6% - 62% (Table A2, Appendix). These broad ranges are partly due to methodological differences. In many studies, sample sizes were small and biological specimens were often obtained only for a subgroup of included patients (Table A2). All studies were performed in urban settings, but some studies have selected groups of patients, such as men (81) or psychotic patients (142). Studies also exhibit variation in the

methods used for substance detection. Most studies used qualitative immunological urine analyses, whereas five studies did not report which methods were used (76, 85, 87, 145, 146). Only four previous studies have used gas or liquid chromatography-mass spectroscopy (81, 90, 117, 142), of which two included immunological screening (81, 117). Many studies lacked detailed information on recent substance intake and polydrug use, and substance specific detection rates were reported in about half of the studies (Table A2). Urine samples were obtained within 2, 24 or 48 hours after admission, if information about this was reported, and blood samples were used in three studies only (87, 116, 142). At the time of admission, clinical drug intoxication due to cocaine was reported among 50% of the patients in one study (70), and clinical drug influence among one-third of the patients in another (87), but these results were not compared with blood drug findings.

Sociodemographic and clinical associations

Sociodemographic and clinical associations of biological confirmed substance use among psychiatric inpatients have not been widely studied. On the basis of urine drug findings, stimulant drug use has been associated with schizophrenia (81) and illegal drug use has been associated with men, younger age and precarious housing (116). In three other studies, drug users could not be differentiated from non-users on the basis of urine drug findings (69, 76, 86). Another study used blood drug analyses and found that the methamphetamine concentration was partly related to more severe psychotic symptoms (150).

Under detection

Studies comparing urine analysis to routine clinical practice, structured interviews and patient self-reports have reported under-detection of recent substance intake (65, 66, 81, 116, 117). These studies focused on the initial assessment at the time of psychiatric admission. Studies among inpatients in a sub-acute phase have reported better agreement between urine findings and structured interviews, partly explained by the fact that these patients knew that their reports were compared with urine tests (69, 142).

1.4.3. Knowledge gaps

Reviewing previous research among psychiatric inpatients, it seems generally accepted that assessment of recent substance intake is important. However, there is no consensus on how this assessment should be performed. The utility of laboratory analyses has not been widely evaluated, and few previous studies have used comprehensive laboratory methods, including both screening and confirmation, for substance detection. On-site urine tests are widely used, but few studies have compared them with chromatographic results in an acute psychiatric setting. Also, few previous studies have reported data on quantitative blood drug analyses and acute drug influence among patients admitted to acute psychiatric wards.

2. Objectives

This cross-sectional study was performed among patients admitted to acute psychiatric wards in two Norwegian hospitals. The main objectives were:

- To identify the rates of psychoactive substance use and drug influence among patients admitted to acute psychiatric wards
- To investigate associations between substance use and various clinical variables
- To compare physician assessment and on-site urine testing with the results of comprehensive toxicological analyses

The specific research aims were:

1) To identify rates of recent substance intake among patients admitted to acute psychiatric wards by using comprehensive laboratory methods (papers I and II)
2) To identify the rates of substance-related admissions, as measured by both physicians and patients, and to assess the rate of self-perceived need for substance-related treatment (paper II).
3) To study associations between laboratory verified substance intake and sociodemographic variables, clinical characteristics and patient self-report (paper II)
4) To compare physician assessment of recent substance intake with laboratory drug analyses (paper III)
5) To compare on-site urine testing with laboratory drug analyses (paper III)
6) To estimate the rate of drug influence as assessed by physicians and blood drug concentrations (paper I and IV)
7) To investigate the relationship between drug influence as assessed by physicians and blood drug concentrations (paper IV)

3. Material

3.1. Setting

The study was conducted in a 27-bed acute psychiatric ward at Lovisenberg Diakonale Hospital, Oslo, Norway and in an 18-bed acute psychiatric ward in Sørlandet Hospital, Arendal, Norway. Both are public hospitals and serve approximately 100.000 inhabitants each. From Lovisenberg, patients were also recruited among acute medical admissions, as a comparison group in paper I (Table 3).

3.2. Study samples

All papers comprise data collected among acute, consecutive admissions. Paper I consists of data collected in a pilot project at Lovisenberg Diakonale Hospital in 2003 (Table 3). Of 116 acute psychiatric admissions, 100 (86%) were included in the study and 16 (14%) were excluded due to lack of biological specimens for drug analysis. Of 253 eligible medical admissions, 118 (47%) were randomly selected and informed about the study. Of these, 106 (90%) were included and 12 (10%) declined.

Papers II-IV comprise data collected in the main study during 2006 and 2007. At Lovisenberg, 309 (88%) of 351 psychiatric admissions were included, 33 (9%) declined, and 8 (2%) were excluded due to dementia. In Arendal, 47 (42%) of 111 acute admissions were included, 50 (45%) declined, 8 (7%) were excluded due to dementia and 6 (5%) were not asked to participate. Numbers included in the different papers are shown in Table 3.

Table 3 Number of admissions included in the study and in the different papers (N).

Setting	Consecutive admissions in the study period	Included in study (%)	Paper I	Paper II	Paper III	Paper IV
Pilot study Lovisenberg 2003						
Psychiatric admissions	116	100 (86%)	100			
Medical admissions	258	106 (41%)	106			
Main study 2006-2007						
Lovisenberg psychiatric admissions	351	309 (88%)		298	284	236
Arendal psychiatric admissions	111	47 (42%)			41	35

Thus, a total of 456 (79%) of 578 consecutive psychiatric admissions were included in the study. Overall, the mean age of included patients was 39 years (SD 15) and 47% were males. Sociodemographic variables, hospital stay characteristics and discharge diagnoses for the patients included in the main study from Lovisenberg and Arendal are given in Table 4. For comparison, we have also included data from a national survey of patients admitted to acute psychiatric wards (n = 3572) conducted at 19 acute psychiatric wards in 2005 (16). These figures will be further discussed in paragraph 6.1.1.

In this study, some patients with readmissions were included more than once, but we will mostly study each admission *per se*, as also seen in other studies (16, 76).

3.3. Inclusion and exclusion criteria

For the main study (papers II-IV), consecutively admitted patients who were willing to participate in the study provided written informed consent. If patients were readmitted in the project period, they were asked to participate again. Additional inclusion criteria were applied for the different papers, according to their specific aims, and these criteria were based on the type and time of biological sampling (as described in the papers). Exclusion criteria were dementia or mental retardation, as diagnosed by the ward psychiatrist.

For the pilot study (paper I), patients admitted to the medical ward aged 18-67 who were willing to participate in the study provided written informed consent. Exclusion criteria were dementia or mental retardation or acute intoxication. For the psychiatric admissions, informed consent was not obtained (see ethical considerations, chapter 4.6).

Table 4 Sociodemographic and clinical variables for included admissions at Lovisenberg (n = 309) as compared to Arendal (n = 47) and a national sample (n = 3572) (16, 17).

	Lovisenberg N = 309	Arendal N = 47	National sample N = 3572	P - value
Age, mean (SD)	39 (14)	38 (13)	41 (16)	-[a]
Men	47%	51%	50%	0.538
Non - Norwegian origin	20%	0%	10%	<0.001
Living alone	69%	62%	52%	<0.001
Homeless	10%	4%	4%	<0.001
Care for children	8%	21%	12%	0.022
Married	7%	19%	17%	<0.001
Employed	12%	2%	13%	0.088
On welfare	12%	6%	9%	0.180
Disability pension	39%	60%	38%	0.010
Any psychiatric admission previous year	55%	70%	57%	0.146
Referral from general practitioner	5%	17%	21%	
Emergency department (”legevakt”)	23%	46%	38%	
Psychiatric emergency department	27%	0%	2%	<0.001
Outpatient clinics	26%	15%	9%	
Somatic clinics (inpatient or outpatient)	11%	6%	8%	
Prison	1%	0%	1%	
Admitted at day-time (7-16)	51%	57%	47%	0.538
Followed by police	15%	4%	25%	<0.001
In voluntary admission	57%	28%	42%	<0.001
Suicidal plans or self-harm at admission	33%	21%	27%	0.068
Use of belts	7%	0%	4%	0.022
Seclusion	21%	9%	20%	0.130
Transfer to long-term inpatient care	17%	34%	15%	0.001
Admission GAF-F, mean (SD)	36 (11)	40 (9)	37 (-)[a]	-[a]
Admission GAF-S, mean (SD)	35 (12)	38 (11)	35 (-)[a]	-[a]
Discharge GAF-F, mean (SD)	45 (12)	47 (11)	45 (-)[a]	-[a]
Discharge GAF-S, mean (SD)	49 (11)	49 (10)	47 (-)[a]	-[a]
Length of stay in days	9.2 (11.7)	4.5 (11.9)	9.5 (12.5)	-[a]
Main discharge diagnoses (ICD-10)				
F1 Substance use disorders	29%	21%	7%	<0.001
F2 Schizophrenia	22%	19%	24%	0.606
F3 Affective disorders	25%	32%	29%	0.279
F4 Neurotic disorders	8%	13%	10%	0.360
F6 Personality disorders	10%	11%	8%	0.294
Any drug use disorder (F1)	45%	36%	22%	<0.001

GAF; Global Assessment of Functioning. The Lovisenberg data are studied in paper II, in relation to findings of psychoactive substances (298 admissions with biological samples for drug analyses). Values < 0.002 remain significant with Bonferroni correction.

[a] Not computable because of incomplete data from the national sample

4. Methods

4.1. Measurements

4.1.1. Laboratory analyses

Blood and urine samples were collected as soon as possible after admission. Samples of whole blood for drug analyses were collected by laboratory staff using 5 mL Vacutainer® tubes containing fluoride and heparin (BD Diagnostics, Franklin Lakes, NJ, USA). Additional blood for routine laboratory analyses was obtained simultaneously. Urine samples were collected with 200 mL vacuum containers, which were distributed by ward staff, and patients were not observed while sampling. To ensure anonymity, all samples were given a unique project number in a research protocol. The samples were refrigerated as soon as possible and brought on a weekly basis to the Division of Forensic Toxicology and Drug Abuse, Norwegian Institute of Public Health. In a biobank established for the project, samples of blood and urine were then frozen at about -20°C within a few days after arrival. Finally, within a few weeks, samples were analyzed for drugs by using routine toxicological methods.

Using the enzyme multiplied immunoassay technique (EMIT® II Plus Assay, Microgenics, USA), all urine samples were screened for a wide range of substances and their metabolites, as shown in Table 5. Blood samples were screened with EMIT for opiates, amphetamines, cocaine and cannabis (151), and by high-performance liquid chromatography-mass spectrometry (LC-MS) for other drugs (152). Blood samples were screened for alcohol with an enzymatic dehydrogenase method, as were the urine samples of patients who did not provide blood (153). All positive screening results in urine and blood were confirmed by GC-MS or LC-MS (154-156). A headspace gas chromatographic flame ionization detection (HS-GC-FID) method was used for ethanol determination in blood (157). Cut-off values are presented in Table 5. Urine samples were also analyzed for creatinine and pH. The laboratory had been accreditated since 1996 according to ISO 17025 for performing these confirmation and quantification methods for forensic toxicology purposes by the Norwegian body for accreditation of laboratories (Norsk Akkreditering, Kjeller, Norway).

Substances were reported as present if they were detected in urine or blood, except in the cases of benzodiazepines or opiates that had been administered after admission but before sampling. The laboratory results were only used for research purposes and were available for the researchers some weeks after admittance. In papers I-III both blood and urine drug results

were used, in paper IV only blood analyses were used. In paper I, we described a method to estimate the degree of drug influence, which is based on blood drug concentrations.

For a subsample of included patients, oral fluid (N = 98) and hair samples (N = 30) were also collected for drug analyses. These results will not be described in this thesis, but the samples of oral fluid have been included in a separate paper (158).

Table 5 Substances included in the study with analytic methods and cut-off values (ng/ml) for screening and confirmation in blood and urine[a]

	Blood[b]				Urine[b]			
	Screening		Confirmation		Screening		Confirmation	
Substance	Method	Cut-off	Method	Cut-off	Method	Cut-off	Method	Cut-off
Benzodiazepines	-	-	-	-	EMIT	200	-	-
Diazepam	LC-MS	57	LC-MS	57	-	-	LC-MS	150
Oxazepam	LC-MS	287	LC-MS	287	-	-	LC-MS	144
Flunitrazepam	LC-MS	2	LC-MS	2	-	-	LC-MS	28
Clonazepam	LC-MS	9	LC-MS	9	-	-	LC-MS	32
Nitrazepam	LC-MS	14	LC-MS	14	-	-	LC-MS	25
Alprazolam	LC-MS	9	LC-MS	9	-	-	LC-MS	31
Zopiclone	LC-MS	19	LC-MS	19	-	-	-	-
Opiates	EMIT	85	-	-	EMIT	300	-	-
Morphine	-	-	GC-MS	15	-	-	LC-MS	29
Codeine	-	-	GC-MS	32	-	-	LC-MS	60
Methadone	LC-MS	62	LC-MS	62	EMIT	300	LC-MS	62
Dextropropoxyfen	LC-MS	68	LC-MS	68	EMIT	300	LC-MS	200
Buprenorphine	-	-	-	-	EMIT	5	LC-MS	4
Barbiturates[c]	LC-MS	4640	LC-MS	4640	EMIT	200	-	-
Alcohol[d]	ADH	0.002	HS-GC-FID	0.004	ADH	0.01	HS-GC-FID	0.01
Amphetamines	EMIT	54	-	-	EMIT	300	-	-
Amphetamine	-	-	GC-MS	41	-	-	LC-MS	135
Methamphetamine	-	-	GC-MS	45	-	-	LC-MS	150
Ecstasy	-	-	GC-MS	58	-	-	LC-MS	77
Cannabis	EMIT	9	GC-MS	1	EMIT	20	LC-MS	10
Cocaine	EMIT	91	GC-MS	60	EMIT	300	LC-MS	60

LC-MS indicates liquid chromatography-mass spectrometry; GC-MS, gas chromatography-mass spectrometry; EMIT, enzyme multiplied immunoassay technique; ADH, alcohol dehydrogenase method for alcohol; HS-GC-FID, Headspace gas chromatographic flame ionisations detection.

[a] Due to conversion from molar units, some of the numbers in the table may seem odd. Blood concentrations are given and plasma/blood concentration ratios for some drugs are markedly above 1. Cut-off values are given for analyses performed in 2006-7 (papers II-IV). Values for blood analyses performed in 2003 are given in paper I.

[b] Analyses in blood and urine also included lorazepam, ethylmorphine, isopropanol, methanol and 6-monoacetylmorphine (6-MAM, a metabolite of heroine), and, in blood; carbamazepine, meprobamate, carisoprodol, phenazepam, midazolam, zolpidem, and, in urine; pholcodin, phencyclidine, lysergic acid diethylamide (LSD) and 2-ethylidene-1.5-dimethyl-3.3-diphenylpyrrolidine (EDDP, a metabolite of methadone). Urine gammahydroksybutyrat (GHB) was analyzed only on special request and urine creatinine and pH were analyzed for all samples.

[c] Phenobarbital.

[d] Values given in %.

4.1.2. On-site urine testing

In paper III, we used data from the routine performance of "Clearview 6 panel Drug Screen Card" (Inverness Medical International, Bedford, UK). This specific device was chosen because it was routinely used at the Lovisenberg ward at the time of the project. Cut-off values are presented in the paper. Results of the on-site test were routinely documented in case notes.

4.1.3. Physician assessment

Data from the physician assessment described here were used in papers II-IV. At admission, all patients underwent a routine clinical interview by the physician on call. Subsequently, the physician completed a study form including the following four questions (see Appendix):

Based on all available data at the time of assessment:

1) During the last week and at the time of assessment; to which extent has the patient had positive symptoms? (The positive subscore of the positive and negative syndrome scale, PANSS: Delusions, conceptual disorganization, hallucinatory behaviour, hyperactivity/agitation, grandiosity, suspiciousness and hostility, as assessed on a scale from 0-7, with increasing severity) (159) (papers II and IV)

2) Is there any information on recent substance intake (tick off): Benzodiazepines, opiates, amphetamines, cannabis, cocaine, alcohol, others or none? (paper III)

3) In your opinion, is this patient under drug influence at admission: Not at all, mildly, moderately, markedly or uncertain? (paper IV)

4) Do you think that the current admission was related to substance use: Not at all, partly or totally? (paper II)

The assessment was meant to be overall judgments by the physician on call, based on all available information from patients, companions, clinical manifestations, referring physician and routine laboratory analyses. Questions 2 and 3 were derived from the Clinical Test for Impairment (131).

4.1.4. Patient self-report

In paper II, we used data obtained by a patient self-report questionnaire which was obtained in 230 (77%) of the 298 admissions and included a question on tobacco use, the Hopkins Symptom Checklist 10-item version (HSCL-10) (160) and the questions "Do you think that the current admission was related to substance use?", "Do you think you need professional help to change your alcohol use?" and "Do you think you need professional help to change your drug use (tick off): Not at all, partly or totally? (see appendix). The latter question is part of the Drug Use Disorders Identification Test-Extended (DUDIT-E), which includes both medicinal and illegal drug use (161). The self-reports also included the 10-item Alcohol Use Disorder Identification Test (AUDIT) (99), the 11-item Drug Use Disorder Identification Test (DUDIT) (162) and the 2-item Lie/Bet Questionnaire for screening for pathological gamblers (163). The results of the self-report questionnaires were documented in medical records and were available for the clinicians. The results of the Lie/Bet Questionnaires are not presented in this thesis.

4.1.5. Review of medical records and clinical diagnoses

For papers II-IV, sociodemographic and clinical characteristics for the included patients were obtained by review of medical records and are shown in Table 4. The review was performed by the first author for all patients at Lovisenberg and by research assistants in Arendal. Most variables were gathered and coded with similar methods as in the national survey performed in 2005 (16), including the Global assessment of functioning and symptoms (GAF, split version) (164, 165) and an assessment of suicidal risk at admission by rating patients on a scale from 1 to 6, where 1 = 'no risk' and 6 = 'recent severe self-harm with obvious intention to die' (121). The researchers also obtained additional information about prescribed medication before and during hospitalization. On this basis, we could exclude laboratory findings that could only be explained by substances prescribed after admission (papers II-IV), and we could estimate the rate of nonprescribed use of medicinal drugs before admission (paper II).

Clinical diagnoses were also obtained from medical records. These diagnoses were routinely stated at discharge and always controlled by a ward psychiatrist. During the hospital stay, most patients at Lovisenberg (66%) were interviewed with the Norwegian 16-item version of

the Mini-International Neuropsychiatric Interview (MINI) (96) and the 7-item Iowa Personality Disorder Screen (166). These results were documented in medical records and were available for the clinician performing the diagnostic assessment at discharge. The use of MINI has been described in a separate paper (101).

4.2. Ethical considerations

The study was approved by The Regional Committee for Medical Research Ethics and the Norwegian Data Inspectorate. Blood sampling did not result in any dangerous episodes, and laboratory results were only used for research purposes. The results of patient self-report and of the MINI interviews were documented in medical records, with the consent of the patients. This information was available for the clinicians and could therefore possibly have influenced treatment and referral strategies. For example, a MINI interview revealed previous hypomanic episodes for a patient with the clinical diagnosis of recurrent depression, and this information altered treatment strategies.

In the main study, patients were given written and oral information about the study during the first days of their admission. If the patient understood the nature of the research and was willing to participate, he or she was asked to sign a consent form (see appendix). If patients were unable to give informed consent during the first days, they were approached again when their mental state improved. Blood and urine samples were sent for drug analyses only if the patient wanted to participate in the study. When samples were collected from patients who did not want to participate in the study, these were destroyed. Included samples were only analyzed with regard to psychoactive substances, and they were destroyed by the end of the project period.

For data collected in 2003, medical patients were given written and oral information about the study as part of the initial assessments. If the patient understood the nature of the research and was willing to participate, they were asked to sign a consent form. For the psychiatric patients, informed consent was not asked for or obtained. We argued that many patients would be severely ill at the time of admission, and that it would not be possible to obtain consent before sampling. With this exception, the study was conducted in accordance with the declaration of Helsinki (167). Other recent studies have also been performed without informed consent of the patients (80, 90), and some previous studies performed drug analyses

under the guise of other somatic tests (143, 148). We experienced in the main project that informed consent very well can be obtained, within a few days after admission, and we recommend future studies to do so.

4.3. Statistical analyses

The Statistical Package for the Social Sciences versions 12 – 16 were used for all statistical analyses (SPSS, Chicago, USA). A list of variables included in the different papers is shown in Table 6. Count data were presented as numbers (%). Continuous data with approximate normal distributions were presented as means (SD) and non-normal data as medians (range). For comparison of two groups, a chi square test was used for dichotomous dependent variables, and Student's t-test or Mann Whitney U-test for continuous dependent variables. All tests were two-tailed and we used a significance level of 0.05. For comparison of multiple groups, χ^2 tests were used for dichotomous dependent variables and post-hoc pairwise comparisons between all subgroups were Bonferroni corrected (paper II). Group differences between multiple groups in normally distributed continuous variables were analyzed with one-way analysis of variance (ANOVA), and post-hoc comparisons were performed using the Tukey HSD test. Kruskall-Wallis tests were used for non-normal data with Mann-Whitney tests and Bonferroni corrections for post-hoc pairwise comparisons. Also, the physician's ability to detect recent substance intake was characterized by sensitivity and specificity (paper III). To investigate the impact of various factors on the clinical assessment of drug influence, we used a binary logistic regression model generating odds ratios (OR) with 95% confidence intervals (95% CI) (paper IV). For further details on the statistical analyses, the reader is referred to each paper.

Table 6 List of variables included in Papers I-IV

Variables	Paper I	Paper II	Paper III	Paper IV
Age	(X)[a]	X	X	X
Gender	(X)[a]	X	X	X
Education etc		X		
Involuntary admission		X	X	X
Suicidal risk score		X		
Length of stay in days	(X)[a]	X	X	X
Discharge diagnoses (ICD-10)	(X)[a]	X	X	X
Physician on call				
Psychotic symptoms		X		X
Global assessment of functioning		X		
Admission related to substance use		X		
Recent drug intake			X	X
Drug influence				X
Patient self-report				
Hopkins symptom checklist-10		X		
Use of tobacco		X		
Admission related to substance use		X		
Perceived treatment need		X		
Laboratory data				
Blood	X	X	X	X
Calculation of blood drug concentration scores	X			X
Urine	X	X	X	
On-site tests			X	

ICD-10; International Classification of Diseases.

[a] Obtained on group-level for psychiatric patients, on individual level for medical patients.

5. Results

5.1. Summary of the results

This chapter presents findings in line with the seven research aims:

Aim 1: To identify rates of recent substance intake among patients admitted to acute psychiatric wards by using comprehensive laboratory methods.

In a pilot study in 2003, urine and blood samples were collected from 100 psychiatric admissions at Lovisenberg Diakonale Hospital (paper I). With chromatographic methods, psychoactive substances were found in 63% (95% CI 54%-73%) of the admissions; medicinal drugs in 47% (37%-57%), alcohol in 8% (3%-13%) and illegal drugs in 36% (18%-26%). At the same ward, in 2006/2007, the same methods were applied among another 298 acute psychiatric admissions (paper II). Psychoactive substances were detected in 63% (57%-68%) of the admissions, medicinal drugs in 46% (41%-52%), alcohol in 12% (9%-16%) and illegal drugs in 28% (23%-33%). A total of 20 different substances were detected, with up to ten in a single patient. In both studies, amphetamines were particularly commonly detected; 22% (14%-30%) and 16% (12%-20%). The laboratory findings are summarized in Table 7, which also includes the figures from Arendal and separate figures for blood and urine (see additional results, chapter 5.2). As compared with most previous studies, these detection rates are high and may partly be explained by the use of comprehensive laboratory methods

Aim 2: To identify the rates of substance-related admissions, as measured by both physicians and patients, and to assess the rate of self-perceived need for substance-related treatment.

At 298 psychiatric admissions in 2006/2007, both patients and physicians were asked if they thought that the admission was related to substance use, and patients were also asked if they needed professional help for substance use (paper II). Substance use was seen as being related to the admission by 42% (36%-48%) of patients and 45% (39%-51%) of physicians on call, and a need for professional help for substance use was reported by one-third of patients. Also by using non-laboratory methods, these results confirm the major impact of recent substance use in acute psychiatric wards, and demonstrate that many patients want professional help to change their substance use behaviour.

Aim 3: To study associations between laboratory verified substance intake and sociodemographic variables, clinical characteristics and patient self-report.

Urine and blood samples were collected from 298 psychiatric admissions and extensively analyzed for medicinal drugs, alcohol and illegal drugs (paper II). Sociodemographic and clinical variables were obtained by a review of medical records. Psychotic symptoms at the time of admission were assessed by the physician on call using the positive subscale of the Positive and Negative Syndrome Scale (PANSS). Patients with negative tests and with medicinal drugs only did not differ significantly from the other groups on any variable in the post-hoc analyses. Patients using alcohol had a high suicidal risk score at admission and the shortest length of stay (median one day). Use of illicit drugs was associated with psychotic symptoms and readmission. Given the high rates of substance use and the important clinical associations, drug screening seems warranted in acute psychiatric settings. Interventions designed for substance-using patients should be developed and integrated.

Aim 4: To compare physician assessment of recent substance intake with laboratory drug analyses.

The sample comprised 325 consecutive admissions from two acute psychiatric wards (paper III). Physicians on call were asked to judge if the patient had recently taken benzodiazepines, opiates, alcohol, amphetamines, cannabis or cocaine. Blood and urine samples were obtained and analyzed with chromatographic laboratory methods for a wide range of substances. Physicians' assessments were compared with the reference standard of laboratory analyses. The sensitivity of the physician's assessment was highest for amphetamines (76%) (95%CI 64%-88%), followed by benzodiazepines (61%) (53%-68%), opiates (57%) (37%-75%), cannabis (55%) (42%-68%) and cocaine (50%) (10%-90%), whereas specificity was above 90% for all substances. The study indicates clinical under-detection of recent substance intake among acute psychiatric admissions.

Aim 5: To compare on-site urine testing with laboratory drug analyses.

Of 325 included admissions, a routine on-site urine screening test was performed in 92 (paper III). The results of the on-site urine tests were compared with the reference standard of laboratory urine analyses. The sensitivity of the on-site test ranged from 76% (58%-94%) for amphetamine to 97% (91%-100%) for cannabis, and specificity ranged from 82% (72%-92%) for cannabis to 100% (100%) for cocaine. On-site urine testing identified substance use that was not recognized by the physician's initial assessment, although specificity for cannabis and benzodiazepines was low. Chromatographic methods, which offered important supplementary information about substance use, should be considered for the routine screening of acutely admitted psychiatric patients.

Aim 6: To estimate the rate of drug influence as assessed by physicians and blood drug concentrations.

In 2003, 100 psychiatric admissions were included (paper I). On the basis of blood drug concentrations, drug influence was estimated in 26% (18%-26%) of admissions. From the data collection in 2006/2007, 271 acute admissions were included (paper IV). At admission, the physician on call performed an overall judgment of drug influence. Psychotic symptoms were assessed with the positive subscale of the Positive and Negative Syndrome Scale. Quantitative results from blood analyses were used to calculate blood drug concentration scores. Patients were judged as being under the influence of drugs and/or alcohol in 28% (95% CI 23%-34%) of the 271 admissions. Markedly elevated blood drug concentration scores were estimated for 15% (11%-20%) of patients. These findings demonstrate that many are under the influence of drugs or alcohol at the time of admission.

Aim 7: To investigate the relationship between drug influence as assessed by physicians and blood drug concentrations.

Among 271 admissions, physician assessment showed a moderate positive relationship to the blood drug concentration scores ($r = 0.52$, $p < 0.001$) and related also independently to symptoms of hyperactivity/agitation and to the detection of alcohol, cannabis and amphetamines (paper IV).

5.2. Additional results

The illustrations below were not published in the papers, but are included here because of their relevance for the thesis. In a summary of laboratory findings from the two data collection periods at Lovisenberg and the one in Arendal, there were no significant differences (Table 7). Because the sample size in Arendal was small, the confidence intervals were wide.

Paper II was based on the laboratory findings in blood and/or urine from the second data collection period in Lovisenberg (N = 298). Detection of more than one drug was common, and the overlap of different drug groups can be illustrated by a Venn diagram (Figure 1). When comparing specific detection rates in blood and urine, no significant differences were found, with the exception of morphine that was more commonly detected in urine (Table 7). When comparing findings in blood and/or urine with physician assessment, laboratory rates were higher for benzodiazepines and lower for alcohol.

Detection rates from paper II were further stratified on age and gender (Table 8). Nitrazepam was more commonly detected among women (17% vs. 5%, $p < 0.01$) and amphetamines among men (25% vs. 8%, $p < 0.001$), and benzodiazepines (diazepam) were most common in the highest age group and illegal drugs (cannabis) were most common in the lowest age group ($p < 0.01$ for all). Illegal drugs were detected among 38 (59%) of 64 men in the lowest age group; 36% were positive for amphetamines and 38% for cannabis.

The moderate positive relationship between physician assessment and blood drug concentration scores described in paper IV can also be illustrated by a column chart (Figure 2). In this chart there were five blood drug concentration groups; low concentrations (1 point), mildly elevated (2-3 points), moderately elevated (4-5) and markedly elevated (6 and above). In the paper, we merged the two first groups into “moderately elevated” and the two latter into “markedly elevated”.

Table 7 Summary of laboratory findings in blood and/or urine among patients studied in Arendal in 2007 and in Lovisenberg in 2003 and 2006-7. From the latter data collection, separate results are also shown for blood, urine and physician assessment. Values are given in % (95% CI).

	Arendal 2007 Blood and/or urine N = 43	Lovisenberg 2003 Blood and/or urine N = 100	Lovisenberg 2006-2007 Blood and/or urine N = 298	Lovisenberg 2006-2007		
				Blood N = 287	Urine N = 257	Physician assessment N = 295
Any drug	74 (61-87)	63 (54-73)	63 (57-68)	58 (53-64)	58 (52-64)	61 (56-67)
≥ 3 drugs	23 (11-36)	19 (11-27)	17 (13-21)	11 (8-15)	19 (14-24)	-[a]
Medicinal drugs	61 (46-73)	47 (37-57)	46 (41-52)	40 (34-45)	40 (34-46)	33 (28-39)
Benzodiazepines	58 (43-73)	40 (30-50)	43 (38-49)	32 (27-38)	37 (31-42)	29 (24-34)
Diazepam or met	54 (39-68)	34 (25-43)	34 (29-39)	24 (19-29)	31 (25-36)	-[a]
Flunitrazepam	5 (0-11)	5 (1-9)	6 (4-9)	4 (1-6)	5 (3-8)	-[a]
Clonazepam	9 (1-18)	10 (4-16)	11 (8-15)	8 (5-11)	9 (5-12)	-[a]
Nitrazepam	9 (1-18)	5 (1-9)	11 (8-15)	9 (6-13)	9 (5-12)	-[a]
Opiates	7 (0-15)	8 (3-13)	9 (6-12)	4 (2-7)	11 (7-14)	9 (6-12)
Morphine	7 (0-15)	7 (2-12)	8 (5-11)	3 (1-5)	10 (7-14)	-[a]
Codein	5 (0-11)	5 (1-9)	5 (3-8)	4 (2-6)	7 (4-11)	-[a]
Opioids	7 (0-15)	9 (4-15)	4 (2-6)	4 (2-6)	4 (2-6)	-[a]
Methadone	2 (0-7)	9 (4-15)	3 (1-5)	4 (2-6)	3 (1-5)	-[a]
Alcohol	14 (4-24)	8 (3-13)	12 (9-16)	12 (8-16)	18 (4-41)[b]	26 (21-31)
Illegal drugs	30 (17-44)	36 (27-45)	28 (23-33)	21 (16-26)	28 (23-34)	22 (18-27)
Amphetamines	21 (9-33)	22 (14-30)	16 (12-20)	11 (7-14)	16 (11-20)	14 (11-19)
Cannabis	23 (11-36)	17 (10-24)	18 (14-23)	12 (8-16)	20 (15-25)	12 (9-16)
Cocaine	0 (0)	2 (0-5)	2 (0-4)	1 (0-2)	2 (0-4)	2 (0-3)

[a] These variables were not assessed by the physicians.

[b] Alcohol in urine was detected in 2 of 11 patients where blood samples were not obtained.

Table 8 Laboratory findings in blood and/or urine among 298 patients studied in Lovisenberg in 2006-7, according to age and gender. Values are given in % (95% CI).

	Gender		Age groups		
	Men N = 138	Women N = 160	18-34 years N = 148	35-50 years N = 87	51-80 years N = 63
Any drug	66 (58-74)	60 (52-68)	61 (53-69)	59 (48-69)	73 (62-84)
≥ 3 drugs	20 (13-26)	16 (10-21)	18 (11-24)	20 (11-28)	14 (6-23)
Medicinal drugs	43 (35-51)	49 (42-57)	39 (31-47)	46 (36-56)	64 (52-75)[c]
Benzodiazepines	38 (30-46)	48 (40-56)	37 (29-44)	40 (30-51)	64 (52-75)[b]
Diazepam or met	29 (21-36)	38 (31-46)	27 (20-34)	32 (22-42)	52 (40-65)[b]
Flunitrazepam	7 (3-12)	6 (2-9)	7 (3-11)	7 (2-12)	5 (0-10)
Clonazepam	12 (7-18)	10 (5-15)	12 (6-17)	14 (7-21)	6 (0-12)
Nitrazepam	5 (1-9)	17 (11-23)[b]	9 (4-13)	12 (5-18)	18 (8-17)
Opiates	11 (6-16)	7 (3-11)	6 (2-10)	14 (7-21)	8 (1-15)
Morphine	10 (5-15)	6 (3-10)	6 (2-10)	13 (6-20)	6 (0-12)
Codein	7 (3-12)	4 (1-7)	2 (0-4)	9 (3-15)	8 (1-15)
Opioids	4 (1-8)	4 (1-8)	4 (1-7)	7 (2-12)	2 (0-5)
Methadone	4 (1-7)	3 (0-6)	3 (0-5)	7 (2-12)	0 (0)
Alcohol	12 (7-18)	13 (7-18)	11 (6-16)	13 (6-20)	16 (7-25)
Illegal drugs	40 (32-48)	18 (12-24)[a]	38 (30-46)	20 (11-28)	18 (8-27)[b]
Amphetamines	25 (18-33)	8 (3-12)[a]	20 (14-27)	13 (6-20)	10 (2-17)
Cannabis	23 (16-30)	14 (9-20)	26 (19-33)	12 (5-18)	10 (2-17)[b]
Cocaine	2 (0-5)	2 (0-4)	4 (1-7)	0 (0)	0 (0)

[a] $p < 0.001$, [b] $p < 0.01$, [c] $p < 0.05$.

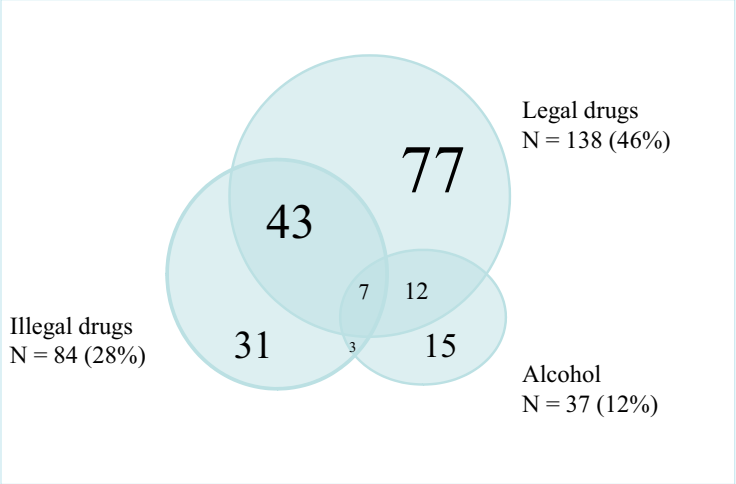

Figure 1 Laboratory findings as illustrated by a Venn diagram. Legal drugs, alcohol or illegal drugs were detected among 187 (63%) of 298 psychiatric admissions. Values are given in n (%).

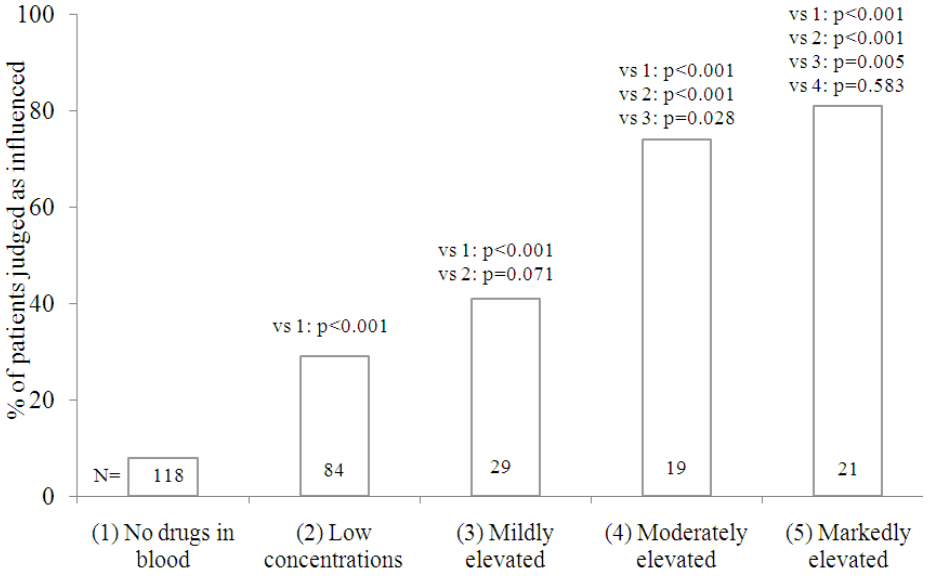

Figure 2 The percentage of patients being clinically judged as influenced by drugs, as related to blood drug concentrations. The total numbers of patients in each group are indicated at the bottom of each column. The differences between the groups are shown above the columns (total N = 271).

6. Discussion

6.1. Methodological considerations

6.1.1. Study design

We used a cross-sectional design to determine the rates of substance use and to compare clinical assessment and laboratory findings. A cross-sectional design does not enable conclusions about cause and effect. However, this type of observational study is well suited and commonly used to identify prevalence, risk factors for disease, and to evaluate diagnostic procedures. The method provides a description of the population only at the time when information is collected. At Lovisenberg, data was collected both in 2003 and 2006, which enables a study of possible changes in substance use patterns over time.

The following limitations of the study design should also be acknowledged. First, paper I was limited by the lack of informed consent and individual data on sociodemographic and clinical characteristics. Second, our definition of nonprescribed use of medicinal drugs may be questioned, and we could rather have included validated instruments such as the Benzodiazepine Dependence Questionnaire (168). Third, alcohol is rapidly removed from the body, and additional biomarkers with longer detection times, such as ethyl glucoronide (169) or carbohydrate deficient transferrin (116), could have added valuable information and increased the estimates of recent alcohol users. Fourth, with regard to the characteristics of the participating physicians, we only obtained data on name and gender. Additional information, such as on their previous experience, could have been valuable in exploring the relationships between physician assessment and laboratory findings. Finally, in paper IV, the physicians were not asked to specify which drugs were the probable cause of influence and neither why some patients were impossible to evaluate with regard to drug influence. These aspects could potentially have given valuable information. In addition, abstinence or withdrawal syndromes could have been one of the alternatives, also according to the comments made by some of the physicians.

6.1.2. Internal validity

Internal validity is usually discussed with regard to selection bias, information bias and statistical validity / confounding.

Selection bias

Selection bias refers to errors that may have influenced participation in the study and the selection of participants. These errors could cause the results to be non-representative of the target population. If the non-participants carry characteristics which are associated with the outcome results, selection bias may have occurred.

In the Lovisenberg sample of 2006-7, 309 (88%) of 351 admissions were included (Table 3). We found no difference between those who were included and not, with regard to age, gender, substance related diagnoses at discharge and readmissions in the study period ($p > 0.2$). Non-participants were, however, more often admitted on an involuntary basis (81% vs. 57%, $p = 0.003$) and more often receiving a diagnosis of schizophrenia at discharge (41% vs. 25%, $p = 0.037$). We have no reason to believe that the substance use patterns of non-participants differed significantly from the participants, and we therefore assume that the overall detection rates were representative for patients admitted to this ward.

In Arendal, we aimed at including 100 admissions, but this did not succeed due to several practical obstacles. A total of 47 (42%) of 111 admissions were included, and because of the small sample size, these data have only been used in papers III and IV having a methodological focus. When comparing participants and non-participants, no difference was found with regard to age, gender, involuntary admissions, discharge diagnoses and readmissions in the study period ($p > 0.2$). For the Lovisenberg admissions included in paper I, only a limited number of clinical data was obtained at group level, and participants could therefore not be compared with non-participants.

Information bias

Information bias refers to systematic errors in data collection or analysis. In this thesis, misclassification of respondents into either “case” or “not case” is such a possible error. For example, in paper II, laboratory results were used as the basis for dividing admissions into four groups. Relatively large and heterogeneous groups may increase the risk of losing relevant information. Among patients placed in the illegal drug group, for example, possible

differences between the users of cannabis and amphetamines may not have been discovered. In addition, the grouping was based on a single laboratory test, which may be insensitive for the severity of substance use problems. Furthermore, most patients do not belong to one specific drug group over time. The use of cut-off values for ordinal variables (e.g. the clinical assessment of drug influence) and continuous variables (e.g. blood drug concentrations and AUDIT) also introduces the possibilities of misclassifications. Some other aspects of information bias (e.g. reporting bias and recall bias) will be discussed in chapter 6.1.3., with regard to physician assessment and patient self-report.

Statistical validity / confounding

Although the main sample size is large compared to many other studies, subgroup analyses were challenged by small groups. For example, in paper II, there were few admissions in the alcohol group, which reduced the statistical power of subgroup analyses and could cause Type II errors. The use of confidence intervals reduces the uncertainties in detection rates related to sample size and increases the generalization of the results (Tables 7 and 8). Also, the multiple testing performed in papers II and IV was Bonferroni corrected, but this method may be too conservative (170).

Confounding occurs when a covariate is associated with both the outcome variable of interest and a selected independent variable resulting in an incorrect association. Controlling for known confounding factors may be done during analyses by either stratification of the data or by multivariate analyses. In this thesis, confounding has been addressed by both these methods. In chapter 5.2, detection rates were stratified on age and gender (Table 8), and in paper IV, binary logistic regression analyses were performed. However, there may be confounders for which we have not controlled because of a lack of appropriate data and small sample size. For example, we lack data on previous discharge diagnoses, which is a potential confounder when comparing physician assessment and laboratory results.

6.1.3. Validity and reliability of measurements

Laboratory analyses

Both screening and confirmation analyses are required to provide a robust laboratory finding of a given substance (30). As opposed to most previous research in the area, this two-step

procedure was applied throughout the present study and ensures high reliability and validity. The laboratory methods are used in forensic toxicology and the risk of false positive results is very low. However, false negative laboratory results could occur with substances having concentrations below screening cut-off values. False negative findings could also have occurred because of urine tampering (171). Creatinine and pH were, however, within recommended ranges for all samples, which indicate that tampering was not common.

The use of laboratory results as the reference standard of recent drug intake may be questionable, due to several reasons. For substances with short half-lives, clinicians may have revealed significant use that was not confirmed by analyses – either because the intake had occurred some days earlier or because of the test delay of up to 24 hours. On the other hand, findings of substances with long half-lives could be due to intake that was not considered "recent" by the physician.

The use of blood drug findings as the basis for estimation of acute drug influence is also subject of methodological concerns. The method described in paper I does not take account of the facts that blood concentrations related to intake of a given dose of a drug will vary between individuals, and for a given blood concentration, the degree to which a drug influences behaviour or symptoms will also vary. Also, the calculation of blood drug concentration scores (papers I and IV) was based on an assumption of additive effects of psychoactive substances (172, 173). Substances may, however, interact in different ways; it may be that e.g. sedating benzodiazepines may reduce the chances of observing the drug influence effects of more stimulating drugs. Finally, with regard to blood drug concentrations, the laboratory has estimated measurement uncertainties of up to +/- 30% (174). However, these analytical variations have not been included in the papers, as we did not believe that they would bias our findings.

On-site urine testing

We wanted to evaluate the routine on-site urine testing as performed by clinical staff, but we have no data about these persons. Little competence and experience with the test could have caused low reliability and validity. Also, the choice of screening device should be based upon knowledge of which substances are being abused in the population. In this study, the on-site test device was designed to detect ecstasy and cocaine, for which there were a total of 0 and 6

confirmed findings, respectively. The device was not designed to detect zopiclone, methadone and metamphetamine, for which there were 22, 10 and 50 confirmed findings. Hence, another on-site test could have been chosen to have a better match with the observed drug panorama.

Physician assessment

The assessment was performed by 39 different physicians. The study questions may have been interpreted differently by different persons, and the inter-rater variability was not examined or known. To possibly enhance reliability, all physicians had received oral and written information about the study form and the project, and a detailed instruction for the PANSS positive subscale was attached to the form. Hence, physicians were sensitized to the issue of substance use, and reporting bias could have occurred by the physicians over-reporting both recent intake at admission and substance use disorders at discharge.

The PANSS was developed to assess psychotic symptoms among patients with schizophrenia (159), and there is no published data on the reliability and validity in acute psychiatric settings. There are, however, studies using PANSS among acute admissions and among patients with bipolar disorders, for example, and serious validity problems have not been reported (80, 175). Also, its face validity was good, and in unpublished material from a psychiatric intensive care unit, excellent inter-rater reliability was found in assessing 12 consecutively admitted in-patients (102).

The question on recent substance intake was ambiguous in at least two ways which could reduce its reliability and validity: 1. Medicinal drugs were not mentioned explicitly. 2. Recent intake was not defined with regard to time frame.

1. It was not specified explicitly that the assessment also included medicinal drugs, as it is in the Clinical Test for Impairment (131). This may have contributed to the fact that benzodiazepines and opiates seldom were ticked off by the physicians. To obtain additional data on medicinal drug use, a retrospective review of medical records was performed by the researchers. Reviewed documents included the admission case notes and the inpatient prescription form, both provided by the physician on call, and all use of medicinal drugs was documented. By using this method, many additional users of medicinal drugs were identified. The physician assessment of recent intake of medicinal drugs was therefore based on the combined results of the study form and the review of medical records. The physician assessment of recent intake of alcohol and illegal drugs was based solely on the study form.

2. No definition was given on recent intake, and this could therefore be interpreted differently by different physicians. However, additional comments were given by most physicians, and for only 8 patients, the intake of substances was less recent than one week. For the assessments with no details on time and dose of substance intake, there is a risk of including an intake that was weeks or months ago. For the assessment of recent substance intake, alternative instruments could have been used, and one option is the Time line follow back (176).

Patient self-report

Acute psychiatric patients may have limited ability for self rating scales due to their psychiatric conditions and affected cognitive functions (100). Memory loss could especially be a problem for the AUDIT and DUDIT questionnaires in assessing substance use over the last year. This recall bias may lead to inaccuracies in the data registered and to misclassifications and inaccurate results. However, AUDIT and DUDIT have recently been used and validated among persons with severe mental disorders (177). Also, self-report has proved a reliable way of assessing tobacco use among acute psychiatric admissions (116). The HSCL-10 has demonstrated good sensitivity and specificity as compared with the widely used HSCL-25 (178). These questionnaires were however developed for measuring psychological distress in the general population, and their psychometric properties among acutely hospitalized patients have, to our knowledge, not been studied. Also, few previous studies have used self-report questions on substance-related admissions and self-perceived treatment needs, and their reliability and validity are therefore not known.

Review of medical records and clinical diagnoses

Review of medical records was performed by unblinded researchers, and the information was not confirmed or controlled by other persons, which may reduce the reliability and validity of this review. Clinical variables such as GAF, suicidal risk and discharge diagnoses were obtained. It is known that the routine use of GAF may suffer from low reliability, and group consensus has been suggested as a better alternative (179). Clinical diagnoses may also suffer from low reliability and validity. During the project period, however, results from self-report questionnaires (AUDIT and DUDIT) and structured interviews (MINI and IOWA) were documented in medical records for most patients. This could possibly enhance the reliability and validity of clinical diagnoses, although we do not know to what degree the clinicians took

this information into their diagnostic considerations. A comprehensive diagnostic interview such as SCID could have further enhanced the diagnostic validity, but we found that even a short diagnostic interview (MINI) was only feasible for two thirds of these patients (101).

6.1.4. External validity

Generalization of results should always be made with caution, and this applies to our results. In order to claim external validity, a study requires internal validity. There are several aspects in our methodology, discussed above, which may have resulted in inaccuracies and bias. In papers I and II, we identified the detection rates of psychoactive substances among patients admitted to the acute psychiatric wards at Lovisenberg. The internal validity of these laboratory results is high, and this calls for an evaluation of external validity. For the admissions included in paper I, however, only a limited number of clinical data was obtained at group level. These data could therefore not be analyzed with regard to representativity.

For the Lovisenberg admissions recruited in 2006-7 (paper II), we have a number of relevant patient background variables. This sample of 309 admissions was compared with data from all admissions at Lovisenberg during 2006 (n=1133) (obtained from computerized records), and no difference was found with regard to age, gender, involuntary admissions, length of stay and discharge diagnoses ($p > 0.2$ for all). The sample was also compared with included admissions in Arendal (n = 47) and data from a national survey of patients admitted to acute psychiatric wards (n = 3572) conducted at 19 acute psychiatric wards in 2005 (16). No differences were found between the groups for age, gender, GAF – scores, length of stay and disorders not related to substance use ($p > 0.5$) (Table 4). Lovisenberg participants were, however, more often of non – Norwegian origin (20% vs. 0% and 10%), homeless (10% vs. 4% and 4%), unmarried (93% vs. 81% and 83%) and having a substance use disorder as discharge diagnosis (45% vs. 36% and 22%) ($p < 0.001$ for all).

Some of these differences are also described for the general population. The special position of being the largest city and the capital of Norway may lead to an accumulation in Oslo of marginalized groups with high levels of substance use and mental symptoms. Substance use is more common among young people in Oslo than elsewhere in Norway (180), and many psychiatric disorders are more prevalent than in rural areas (181). In Oslo, 18% of the population has non-western origin, as compared with 5% in Bergen and Trondheim and only

3% in Tromsø (182), but whether this affects the epidemiology of substance use is not known. We found that non-western participants commonly had drug-negative urine and blood samples (paper II), and it has been shown that substance related disorders are less common among patients with non-western origin (183). This indicates that the high proportion of non-western participants in our sample is likely to minimize the rates of current substance use.

Acute psychiatric admission practices vary across regions (15), but it is not known whether Oslo differs from other Norwegian cities with regard to the pre-hospital treatment of psychiatric patients with acute substance use or intoxications, for example in the use of psychiatric, medical or substance abuse inpatient facilities. Oslo has a specialized psychiatric emergency department, however, from which almost every third Lovisenberg admission was referred for admission (Table 4). Psychiatrists can be more reluctant to admit patients than less experienced physicians (184), and this may result in a more selected group of severely ill patients among acute admissions in Oslo than elsewhere in Norway. In comparing Lovisenberg admissions with the national sample, however, no differences were found with regard to GAF-scores, use of restraints, length of stay or discharge diagnoses other than substance use disorders (Table 4). The national survey represents an important comparison group for our sample, although it was conducted one year before our study. Its reliability and validity is not known and we did not have access to the specific data obtained in other acute wards in cities like Oslo, Bergen and Trondheim.

In conclusion, the study sample seems representative for patients admitted to the psychiatric unit at Lovisenberg, but not representative at a national level with regard to various background variables and substance use patterns. Still, we assume that our findings were representative for “big city” - hospitals in Norway. Generalizability to foreign cities should be made with caution, however, as both substance use patterns, acute psychiatric services and inpatient characteristics differ across regions and countries.

6.2. Discussion of main results

The main findings of the present study were presented in chapter 5.3 and will now be discussed one by one. First, however, we will return to the case presentation (Box 2).

Box 2 Case presentation, 2 years later

In December 2006, Joe had his 17th admission to the acute psychiatric ward. Again, he was referred for compulsory observation of up to 10 days because of substance use, aggressive behaviour and psychotic symptoms. His previous admission was only a few weeks ago, which lasted for 5 days and he had received the discharge diagnosis of F.19.5 substance induced psychosis, due to use of multiple substances. His mother and some care-givers were increasingly worried for Joe and afraid that he was suffering from a severe mental illness. He had not been able to follow any voluntary outpatient treatment, which repeatedly had been offered him. He was homeless, unemployed, lived on social welfare and both his mental and somatic health had clearly worsened since his first admission, two years ago.

At admission, he was clinically judged as being drug influenced, but he did not co-operate with regard to somatic evaluation or laboratory tests. He accepted antipsychotic medication and hypnotics, and after a few days in the locked ward he seemed much calmer and free for psychotic symptoms. On the 9th day, however, he had some disturbed behaviour and expressed paranoid ideas. A urine sample was obtained, and the on-site test was positive for cannabis. It was not clear when this cannabis was taken, and it was decided to prolong the compulsory observation for ten more days. During these days, he was closely observed and abstained from drugs, and he was functioning quite well.

On the 20th day after admission, he was offered a voluntary stay for further treatment and help with his socioeconomic situation, but he chose to leave the ward against medical advice. He was still homeless, as his mother did not want him to live with her because of his threatening behaviour, and again, he was offered outpatient treatment on a voluntary basis. After an extensive diagnostic evaluation, he received the diagnosis of F19.5 substance induced psychosis, due to use of multiple substances.

During this admission, clinical staff members were discussing several questions, such as:

• To what extent did Joe actually use substances? How was his motivation to change his drug use patterns?

• Was this a primary or secondary psychotic disorder? How could these assessments possibly be performed?

• If his condition really was substance induced: How could we possibly help Joe from now on?

• Suppose instead he was suffering from a severe mental disorder: Would then the treatment strategies differ?

1. High rates of recent substance intake

We found that almost two-thirds of the sample was positive for at least one psychoactive substance, and a total of 20 different substances were detected, with up to ten in a single patient. The high detection rates from Lovisenberg in the pilot study of 2003 were replicated in the main study three years later. Amphetamines were, for example, detected in about one in five admissions in both studies. This indicates a relatively stable substance use pattern in the admitted population over a three year period. In the same period, there was a continuous overload on the ward capacity with a mean bed occupancy of 130% and above (185), and our findings suggest a stable and substantial percentage of substance-related admissions. We also found that substances were more commonly detected among acute psychiatric than among acute medical admissions (paper I).

Bearing in mind the geographical differences in acute psychiatric services (6, 15) and methodological differences across studies, detection rates of specific substances were compared with those of previous studies (paper II). Comparison was also challenged by the lack of confidence intervals in previous studies. As compared with most previous studies, the present detection rates are high and may partly be explained by the use of comprehensive laboratory methods (Table 5). Our study sample is not representative in a national perspective, but we assume that our findings are representative for other big city hospitals in Norway. In Oslo, high detection rates of amphetamines have also been reported from psychotic inpatients previously (142), whereas psychotic outpatients have high rates of self-reported use (51). High detection rates of amphetamines and other substances were also observed among the admissions in Arendal, and this strengthens the assumption that the Lovisenberg findings are not unique in Norway.

In the papers, we have compared our results with studies from Europe and the USA. Recent studies among acute psychiatric admissions in Israel and South Africa report on-site urine detection rates of any drug of 17% and 44%, respectively (Table A2) (84, 85). In South Africa, “Mandrax” was detected among 5% of the admissions, which is a locally produced amphetamine, and illustrates that substance use patterns vary across regions and countries. Both studies underline that substance use is common and needs to be taken into consideration.

In line with previous studies, we found that detection rates were associated with age and gender. Illegal drugs were detected among the majority of men aged 18-35 years, and this

calls for an increased clinical suspiciousness of illegal drug use when assessing young men in an acute psychiatric ward.

As stated in paper III, use of psychoactive substances is not necessarily of clinical significance, and benzodiazepines and opiates are commonly prescribed for therapeutic reasons. Still, recent intake of substances may result in severe medical conditions (31) and increase the risk of violence and suicide (57, 186). Even small amounts of a drug may pose problems for people with mental illness (59). Also, for patients using multiple substances, the risk of side effects caused by drug interactions is further increased by the trend toward polypharmacy in psychiatric inpatient treatment (44).

2. Every second admission was related to substance use and every third patient reported a need for professional help

It is noteworthy that a similar percentage of physicians and patients saw the admission as being related to substance use. In previous studies, patients often tended to deny substance use and its negative effects (116, 117). Our finding indicates that patients in this study sample were not under-communicating their recent substance use and its relation to the current admission.

It is also an interesting finding that one third of patients reported a need for professional help for their substance use. Self-perceived treatment need among patients admitted to acute psychiatric wards is not widely evaluated, and our finding suggests that two simple questions may rapidly identify patients with problematic substance use and perceived treatment need. On the other hand, these questions may also identify patients with a clinically problematic substance use and with no perceived treatment need. According to the theories of motivational interviewing and the stages of change, these patients may be in a “pre contemplation stage” with regard to their substance use, and comprise specific challenges for health care providers (187, 188). The questions were a part of the DUDIT-E questionnaire, which includes 66 questions on substance use patterns, motivation to change and perceived need for professional help (161). Such instruments have a potentially high value in providing rapid information of relevance for acute psychiatric treatment and referral strategies.

In general, lack of motivation for treatment is a common phenomenon among severely mentally ill patients seen by emergency psychiatric services. Lack of motivation has been associated with danger and paranoid symptoms, and motivational techniques and involuntary treatment have been recommended for these patients (189). The evidence for substance specific intervention in acute psychiatric settings is limited, however.

3. Recent alcohol intake was associated with suicidal behaviour and short hospital stay, and illegal drugs were associated with psychosis and readmission

The identification of risk factors of substance use can contribute to improved detection strategies. Little is known, however, about the sociodemographic and clinical associations of toxicological findings among patients admitted to acute psychiatric wards. Our findings suggest that acutely admitted patients with both substance use and suicidal behaviour require specialized focus (121). The short hospital stays for substance users comprise a major challenge for proper assessment and treatment, and underline the importance of the initial assessments and the potential for toxicological analyses. Our findings also state that patients using illegal drugs constitute a large and marginalized group which calls for clinical concern. Amphetamines, which were were detected in one-sixth of patients, are particularly associated with serious negative health effects (190), and have a major and increasing impact on emergency services (128).

4. Recent substance intake was commonly under detected by the physician on call

There is a large variation in the asassessment and treatment strategies of acutely admitted psychiatric patients. Strategies may depend on local traditions and on available resources, and no consensus exists about the most appropriate or cost-effective methods. In this thesis, we have compared different methods for assessing recent substance intake. Some of our findings on sensitivity, specificity and feasibility are summarized in Table 9. The table also shows the approximate costs of these methods and their ability to provide on-site test results and to assess the frequency and severity of drug use (i.e. to distinguish between use and abuse).

Table 9 Relative comparison of different methods for assessing recent drug intake and drug use

Method	Sensitivity, recent intake	Specificity, recent intake	Feasibility, acute ward	Cost	On-site results	Frequency of drug use	Severity of drug use
Physician's assessment	+/-	+/-	+++	0	Yes	Yes	Yes
Patient questionnaire	(+/-)	(+/-)	++	0	Yes	Yes	Yes
Blood GC-MS	+++	+++	++(+)[a]	+++	No	No	No
Urine GC-MS	+++	+++	+(+)	+++	No	No	No
Urine on-site	+/-	+/-	+(+)	+	Yes	No	No

GC-MS, gas chromatography-mass spectroscopy.
[a] If performed by trained staff.

As illustrated in the table, physician's assessments are feasible, cheap and provide on-site results which may include an evaluation of both frequency and severity of drug use. The sensitivity and specificity of recent drug intake is moderate, however. We found that many substances were under detected by the physician on call; in particular cannabis and benzodiazepines. False positive evaluations were also observed.

The impact of clinical misdiagnosis of recent substance intake among patients admitted to acute psychiatric wards is not widely evaluated. Psychoactive substance use is not always considered to be of clinical significance, and benzodiazepines and opiates are commonly prescribed for therapeutical reasons. Still, unrecognized substance use leads to the risk of overlooking severe acute intoxications and withdrawal syndromes (31). Second, even small amounts of a drug may pose problems for people with mental illness (59). Third, the possibility for adequate intervention and follow-up for patients with problematic substance use may be lost.

5. On-site urine testing identified cannabis use that was not recognized by the physician's assessment, although specificity for cannabis and benzodiazepines was low

The value of on-site urine screening tests among acute psychiatric admissions has not been widely evaluated, and although this specific on-site test is widely used, its properties are previously unreported. Our findings confirm the shortcomings of on-site urine testing in a clinical setting (30, 191) and demonstrate the additional information obtained by comprehensive laboratory screening (90, 191) (Table 9).

Among patients admitted to acute psychiatric wards, previous studies have contradictory findings with regard to the value of toxicological screening. With the use of immunological urine methods, some previous studies conclude that routine urine screening is useful (84, 90, 116), especially among psychotic patients who may be unwilling or unable to provide a proper history (66, 70, 117). Another study recommends the use of routine toxicological screening as a supplement to structured assessment (72), whereas other studies recommend the use of structured interviews rather than routine screening (65, 69, 142). This study suggests that chromatographic methods could be considered for routine toxicological screening.

6. One-fourth of the patients were under drug influence

This study is one of the few studies on drug influence among patients admitted to acute psychiatric wards (70, 87). It is also the first study presenting detailed results of quantitative blood drug analyses in this setting. In paper I, we estimated the degree of drug influence (26%) solely based on blood concentrations of various drugs. In paper IV, a similar rate was estimated by the physicians on call. We will now return to the case presentation (Box 3).

Box 3 Case presentation and study findings.

Joe was admitted five times during the project period, and he consented to study inclusion in all of them.

• At all admissions, the physicians suspected recent intake of amphetamines and cannabis. Joe was judged as markedly impaired at 4 admissions and moderately at one. However, he was not able to give any detailed substance use history and he did usually not cooperate with regard to toxicological tests at the time of admission. Initial somatic evaluation was performed in two admissions.

• At only one admission, he cooperated with regard to immediate blood sampling (15 minutes after admission), and he was then clinically judged to be under moderate drug influence. Afterwards, he accepted medication with antipsychotics and benzodiazepines (olanzapine 20 mg and zopliclone 7.5 mg per os). However, after two hours with a gradually less agitated behaviour, **he was found unconscious in his bed**, with pupillary miosis and intact breathing and circulation. He was immediately brought to the acute medical department for further observation. He was hypotensive (81/41 mm Hg), and he was given intravenous fluid management. After an hour, he awakened and his blood pressure was normalized and he was brought back to the psychiatric ward. The reason for this condition remained uncertain, but there were two main differential diagnoses: Either he had intoxicated immediately before admission (e.g. opiates), or he had a hypotensive reaction on the medication that he had received in the ward.

• The blood sample was immediately analyzed for somatic parameters, where all results were within normal ranges. The sample was later analyzed for the purpose of this study, and the only positive finding was oxazepam at a very low concentration (172 ng/ml, whereas a maximum concentration at therapeutic use is 1150). This means that he was *not* under drug influence at the time of admission, and that his condition was probably a hypotensive reaction to the medication that he had received in the ward.

Lovisenberg and Arendal, blood samples for these analyses are not routinely collected immediately after admission, but usually within 1-3 days. In the project period, ward staff seemed pleased with having these results available sooner than normal, and, anecdotically, there were some examples of low blood sugar and of high C-reactive protein (an indicator of acute infection), that resulted in immediate medical interventions. Previous studies among psychiatric inpatients have discussed the use of such somatic laboratory analyses (34) and the high prevalence of undetected medical disease (31-33). This thesis was not designed to evaluate these questions further, but focuses on psychoactive substance use, which is known to have a substantial and negative impact on somatic health (48).

The feasibility of immediate blood sampling among acute psychiatric admissions is previously unreported. As compared to urine sampling, blood samples were collected sooner and more frequently in both the pilot and the main studies, although some patients did not cooperate with regard to sampling at the time of admission (Box 3). This project thereby demonstrates that patients can be reluctant or not able to provide urine samples in clinical settings. Still, as most substances have longer detection times in urine than in blood (132), urine may be the sample of choice for a broader assessment of recent intake. A positive urine test, however, does not provide any information on drug influence.

7. Clinical drug influence was positively related to the blood drug concentration scores, to symptoms of hyperactivity/agitation and to the detection of alcohol, cannabis and amphetamines.

Although there were some discrepancies between physician assessment and blood drug findings, there was no indication that any of these cases were severe unrecognized intoxications. The discrepancies could partly be explained by the many regular substance users in this sample that could have developed tolerance for high blood concentrations, or that they were misinterpreted as being influenced at the time of admission because of their general appearance (Box 3).

Our findings could also indicate that physicians misinterpreted specific psychotic symptoms (hyperactivity/agitation) as drug related behaviour. The impact of the initial assessment on the discharge diagnosis in this study is not known. At discharge, however, many patients (10%) received the diagnosis of drug induced psychosis, although the length of hospital stay was

short and the etiology of psychosis is difficult to determine in the acute phase (192). Premature use of the label drug induced psychosis may obscure the diagnosis of an emerging serious mental illness (82, 103) (Box 4). Thus, the detection of recent substance intake and drug influence may have implications for immediate interventions (31), and may also have long-term implications: In busy acute wards, initial assessments may comprise the basis for diagnostic assessments at discharge and thereby influencing future treatment and referral strategies.

Box 4 Case presentation, with status per 2010.

During 2007, Joe's health and socioeconomic situation were deteriorating further. He was repeatedly admitted to the acute ward, discharged after some days, and still unable or unwilling to take part in outpatient treatment or in-patient treatment elsewhere. Both staff in the social welfare office and in the acute ward agreed that his behaviour was now life-threatening and that immediate action was needed. In November, he was admitted for his 27th stay to the acute ward. As his condition was still supposed to be substance-induced, it was not possible to establish long-term compulsory assessment and treatment under the mental health law. However, it was decided to use the laws of social welfare, to transfer him with police for a long-term compulsory hospital stay in a locked ward for dual diagnosis patients.

During a 4 months' stay in the dual diagnosis unit and in the absence of drugs and alcohol, Joe was still having psychotic symptoms. At discharge, the main diagnosis was F20 Schizophrenia, and the secondary diagnosis was F10.9 Harmful use of multiple substances.

With the diagnosis of a severe mental disorder, the treatment strategies were changed dramatically. Since February 2008 and to date (August 2010), Joe has lived in a well-staffed outpatient treatment centre, he has been under close supervision and compulsory long-term treatment with antipsychotic medication injected every second week. During these 30 months, his life has stabilized and he was admitted to the acute ward only once.

6.3. Clinical implications and future research

The case presentation illustrates how challenging the *initial assessments* at the time of acute admissions can be (Box 3). A natural question for clinicians would be: Should comprehensive blood and urine analyses have priority among patients admitted to the acute psychiatric ward? The study has demonstrated some of the advantages of comprehensive laboratory testing, and when moderate or high prevalence of substance use is known or suspected, chromatographic methods could be considered for routine screening. In this project, the comprehensive laboratory analyses were rather slow and expensive. Now, by 2010, there are chromatographic methods providing quicker results for a lower cost, thus being more feasible in clinical settings. In assessing *recent substance intake*, urine analyses seem better than blood drug analyses because substances normally have longer detection times in urine than in blood. We

used quantitative blood drug analyses for the study of *drug influence*. In some cases, such analyses may provide useful diagnostic information at the time of acute psychiatric admission (Box 3). However, we do not see any reason to include blood drug screening as routine assessments in acute psychiatric wards. Drug influence should rather be included in the clinical assessments at the time of admission.

During initial assessments, physician's assessment, patient self-report and laboratory tests can be used in conjunction and have complementary roles. The different methods have their advantages and disadvantages as summarized in Table 9, and future studies are needed to define the proper way of combining these measures in acute psychiatric settings. The clinical utility and cost-efficiency of laboratory analyses could then be explored in greater detail, and different devices and methods should be tested simultaneously.

The case presentation also illustrates how challenging the *diagnostic evaluation at discharge* can be (Boxes 2 and 4). Ever since his first admission, Joe was diagnosed with drug induced psychosis, and this may have obscured the diagnosis of an emerging serious mental illness. For substance-using patients admitted with first episode psychotic symptoms, the diagnosis of acute and transient psychotic disorder, unspecified, should be preferred (F23.9) (82). With regard to the important differential diagnosis of amphetamine induced psychosis and primary psychotic disorders, we are now planning another data collection. In a longitudinal multi-centre study, patients with amphetamine-use and psychosis will be recruited in the acute ward, and assessed with several measures including laboratory methods and comprehensive diagnostic interviews, to possibly enhance the diagnostic accuracy.

In this thesis, one-third of patients wanted help with their substance use behaviour. Obviously, there is a need for more evidence on effective interventions for substance using patients in acute care settings. A service program including screening, brief interventions and referral to treatment has shown very promising results with regard to substance use and related problems in a wide range of medical settings (110). Similar programs could be implemented and evaluated in acute psychiatric services as well.

In an editorial on current issues in Scandinavian acute psychiatric wards, Ruud et al concludes that there is a need for development of higher standards of care and further research (8). It is our hope, that this study can contribute in improving the standards of care for patients admitted to acute psychiatric wards.

7. Conclusions

The main results of the present study can be summarised in the following points:

1. Patients acutely admitted to an inner city psychiatric ward in Oslo had high rates of recent substance intake. Amphetamines were especially common.

2. Both patients and the physicians on call saw the current admission as being related to substance use in nearly half of the cases. One-third of the patients reported a need for professional help with regard to substance use.

3. Recent alcohol intake was associated with suicidal behaviour and short hospital stay. Recent intake of illegal drugs was associated with psychosis and readmission.

4. Recent substance intake was commonly under detected by the physician on call. This was especially pronounced for cannabis.

5. On-site urine testing identified cannabis use that was not recognized by the physician's initial assessment, although specificity for cannabis and benzodiazepines was low.

6. Drug influence was present in one-fourth of the patients, both as assessed by the physician on call and by blood drug concentrations.

7. Physician assessment showed a moderate positive relationship to the blood drug concentration scores and related also to symptoms of hyperactivity/agitation and to the detection of alcohol, cannabis and amphetamines.

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9. Appendices

Table A1 A selection of studies documenting prevalence rates of current co-occuring substance use disorders among patients consecutively admitted to acute psychiatric wards.

Reference	Country	N	Method for diagnosis	Substance	Any diagnosis of abuse or dependence (%)
Ananth (1989)	USA	75	DIS	Any	72
Brady (1991)	USA	100	SCID	Any	29
Wilkins (1991)[a]	USA	56	Clinical diagnosis	Any	23[d]
Chen (1992)	USA	104	Clinical diagnosis	Any	30[d]
Lehman (1994)	USA	435	SCID	Any	54
Albanese(1994)[b]	USA	89	SCID	Any	30
Appleby (1997)	USA	375	Drake scale	Any	45
Dixon (1998)	USA	268	SCID	Any	41
Reid (2004)[c]	Trinidad	123	Clinical diagnosis	Any	43
Wheeler (2005)	New Zealand	1232	Clinical diagnosis	Any	27
Galletly (1993)	Australia	121	Clinical diagnosis	Any	7
Acuda (1997)	Zimbabwe	194	AUDIT	Alcohol	28
Katz (2008)	Israel	470	SCID	Any	17
Weich (2009)	South Africa	298	Clinical diagnosis	Any	51
Soyka (1993)[b]	Germany	447	Clinical diagnosis	Any	29
Modestin(1997)	Switzerland	417	Clinical diagnosis	Any	48
Bonsack (2006)	Switzerland	266	Clinical diagnosis	Any	39
Ley (2002)	UK	112	Clinical diagnosis	Any	18[d]
Barnaby (2003)	UK	200	AUDIT	Alcohol	49
Sinclair (2008)	UK	178	AUDIT	Alcohol	51/29[e]
Preti (2008)	Italy	1316	Clinical diagnosis	Any	8[d]
Xafenias (2008)	Greece	313	ASI	Any	33
Nitschke (1995)	Denmark	70	Clinical diagnosis	Alcohol	39
Hansen (2000)	Denmark	376	SCAN	Any	50
Cruce (2007)[b]	Sweden	241	AUDIT, DUDIT	Any	25
Møller (2004)[b]	Norway	48	SMAST, DAST	Any	56
Øydna (2006)	Norway	1533	Drake scale	Any	47
Ruud (2006)	Norway	3572	Clinical diagnosis	Any	7[d]
Vaaler (2006)	Norway	118	ICD-10-R	Any	36
Fløvig (2008)	Norway	227	ICD-10-R	Any	32
Helseth (2009)[b]	Norway	60	ASI, SCID	Any	50

DIS, Diagnostic Interview Schedule; SCID, Structured Clinical Interview for DSM-IV; ASI, Addiction Severity Index (ASI); AUDIT, Alcohol Use Disorder Identification Test; SCAN (Schedules for Clinical Assessment in Neuropsychiatry); SMAST, Short Michigan Alcohol Screening Test; DAST, Drug Abuse Screening Test; ICD-10-R, International Classification of Diseases 10th edition, diagnostic criteria for research.

[a] Study of male inpatients only.

[b] Study of inpatients with psychotic disorders only.

[c] Study of first time admissions only.

[d] Stated as primary diagnosis at discharge.

[e] Rates given for men / women.

Table A2 Studies using laboratory methods in urine to document rates of substance use among consecutive, acute psychiatric admissions, across diagnostic groups.

Reference	Country	N total	N with urine sample	Laboratory method urine	Any drug (%)	Any illegal drug (%)	Poly drug info	Benzo diaze-pines (%)	Opiates (%)	Alcohol (%)	Amph etami nes (%)	Cocaine (%)	Cannabis (%)	Methad one (%)	Others (%)
Robinson (1970)	USA	146	54	GC	-	-	-	-	-	-	15	-	-	-	-
Blumberg (1971)[a]	USA	332	271	TLC	-	32	-	-	-	-	-	-	-	-	-
Crowley (1974)	USA	50	50	GC	40	6	-	24	-	10	0	-	-	-	-
Razani (1975)	USA	44	44	TLC	41	-	-	-	-	-	34	-	-	-	-
Wilkins (1991)	USA	56	56	IA + LC	62	62	>1d 30%	-	14	-	0	50	32	-	PCP 5
Brady (1991)	USA	100	28	IA	43	32	-	7	4-	-	-	29	14	-	
Shaner (1993)[b]	USA	108	100	IA + LC	-	-	-	-	-	-	-	31	-	-	-
Sanguineti (1992)	USA	247	247	Ns	34	-	-	-	-	-	-	-	-	-	-
Sanguineti (1993)	USA	401	401	Ns	15	-	-	-	-	-	-	-	-	-	-
Galletly (1993)	Australia	121	121	IA + TLC	-	10	-	22	-	8	-	-	-	-	-
Katz (2008)	Israel	470	470	On site test	17	-	>1d 5%	-	4	-	2	1	6	-	-
Weich (2009)	South Africa	298	298	Ns	44	-	-	-	6	-	7	1	24	-	Mdrx 5
Mathers (1991)	UK	908	496	IA	-	-	-	-	-	-	-	-	13	-	-
Ley (2002)	UK	112	112	IA	23	16	-	6	3-	-	1	1	14	-	Brb 3
Modestin (1997)	Switzerland	417	354	Ns	54	27	>1d 25%	40	19	-	0	15	10	12	LSD 0
Bonsack (2006)	Switzerland	266	240	IA	-	20	-	-	4	-	0	4	11	6	-
De Beaur. (2007)	France	486	486	IA[c]	-	26	>1d 4%	-	5	41[c]	5	1	19	-	Brb 3
Nitschke (1995)	Denmark	70	70	Ns[c]	-	-	-	36	1	41[c]	0	-	10	-	-
Helseth (2005)[b]	Norway	65	65	LC-MS[d]	72	34	-	42	8	2	17	0	23	2	Zop23
Fløvig (2008)	Norway	227	196	LC-MS	56	15	-	45	8	6	5	0	10	-	-

GC, gas chromatography; TLC, thin-layer chromatography; IA, immunoassay; LC, liquid chromatography; LC-MS, liquid chromatography-mass spectroscopy; Ns, not specified; >1d, more than one drug; PCP, phencyclidine; Brb, barbiturates; Mdrx, mandrax; LSD, lysergic acid diethylamide; Zop, zopiclone.

[a] Patients aged 15-25 years.

[b] Patients with psychotic disorders.

[c] In addition, blood samples were used for assessment of CDT (carbohydrate deficient transferrin).

[d] In addition, blood samples were used for substance detection with LC-MS.

Vil du delta i forskningsprosjektet

"Rus i akuttpsykiatrien"?

Kjære nyinnlagte pasient!
Mange psykiatriske pasienter bruker eller har brukt rusmidler. Sammenhengen mellom rus og psykisk helse er et viktig og komplisert felt hvor det ønskes mer kunnskap. Derfor spør vi om du vil bli med i et forskningsprosjekt hvor vi skal undersøke dette nærmere. Vi ønsker å kartlegge psykisk helse og rusvaner hos alle nyinnlagte pasienter ved akuttpsykiatrisk avdeling. Det er viktig at både pasienter som bruker og ikke bruker rusmidler deltar. Ved din deltakelse vil du gi et verdifullt bidrag til et forskningsprosjekt som ønsker å bidra til bedre utredning og behandling i akuttpsykiatrien.

Studieinnhold

1) Vi ber om tillatelse til å hente opplysninger fra din journal til bruk i forskningsprosjektet.
2) Vi ber om tillatelse til å intervjue deg om din psykiske helse og dine rusvaner. Intervjuene varer cirka en time og gjøres i løpet av oppholdet her.
3) Ved innleggelsen ble det rutinemessig tatt blodprøve og urinprøve. Vi ber om tillatelse til å analysere prøvene med hensyn til rusmidler.

Datasikkerhet

1) Medarbeiderne i prosjektet har taushetsplikt, og all informasjon om deg vil bli behandlet konfidensielt. Personlige opplysninger vil kun brukes til forskning og vil ikke kunne kobles til deg.
2) Blodprøvene og urinprøvene analyseres og oppbevares ved Nasjonalt Folkehelseinstitutt. Der opprettes det en egen biobank for dette prosjektet, som divisjonsdirektøren er ansvarlig for. Prøvene er ikke tilgjengelig for noen andre. Analysene tar noe tid, og svarene vil kun brukes til forskning. Prøvesvarene blir derfor ikke tilgjengelig for deg, din behandler eller din journal.
3) Intervjuene med deg vil også gi viktig informasjon. Du har rett til å få innsyn i disse opplysningene og til å få noe endret hvis det er feil. Denne informasjonen legges i journalen din, og kan være nyttig for din behandling.

Informasjon og samtykke

Risiko og nytte
Det er ingen risiko eller ubehag ved å delta i prosjektet. Mange pasienter vil oppleve utredningen som nyttig.

Frivillighet
Deltakelsen er frivillig og du behøver ikke bestemme deg med det samme. Du kan trekke deg fra prosjektet når som helst uten å oppgi grunn og uten at det får noen følger for behandlingen din. Da vil det biologiske materialet bli destruert og opplysningene om deg vil bli slettet, så lenge de ikke allerede er inngått i vitenskapelige arbeider.

Prosjektslutt
Noen pasienter vil bli kontaktet om et halvt år for en etterundersøkelse. Prosjektet avsluttes 31.12.2009. Da vil alle prøvene bli destruert og alle sensitive persondata slettet. Resultatene av studien vil bli publisert som gruppedata, uten at den enkelte kan gjenkjennes.

Prosjektledelse
Prosjektet er et samarbeid mellom Lovisenberg Diakonale Sykehus og Nasjonalt Folkehelseinstitutt. Det er finansiert av Helse Øst, og har ingen kommersielle formål. Forsker er lege Jon Mordal. Avdelingen kan formidle kontakt med ham når som helst ved spørsmål eller uklarheter.

Bjørn Holm	Vibeke Lie	Jørg Mørland
Sjefslege	Avd. overlege, psyk.	Divisjonsdirektør
Lovisenberg D. Sykehus	Lovisenberg D. Sykehus	Nasjonalt Folkehelseinstitutt

Prosjektet er tilrådd av Regional komité for medisinsk forskningsetikk og av Personvernombudet for forskning, Norsk samfunnsvitenskapelig datatjeneste AS.

Samtykkeerklæring – prosjektet "Rus i akuttpsykiatrien":

Jeg har mottatt skriftlig og muntlig informasjon om prosjektet og sier meg villig til å delta.

Oslo, dato: _____

Signatur: _____

Plassér pasientetiketten her

Innkomst-skjema

"Rus i akuttpsykiatrien 2006"
Lovisenberg Diakonale Sykehus
Nasjonalt folkehelseinstitutt

Spørsmål til mottagende lege:
Skal besvares for alle nyinnlagte pasienter

(Se viktig informasjon helt nederst)

Plasser pasientetikett her

Eventuelt skriv med blokkbokstaver:

Pas. navn: _____

F. nummer: _____

Dato og tidspunkt for innkomstundersøkelse

_____

På bakgrunn av alle tilgjengelige data ved innkomstvurdering

1) I løpet av den siste uken og ved innkomstvurdering: I hvilken grad har pasienten hatt positive symptomer?
(Markér høyeste score i denne perioden, se PANSS –veil. på baksiden)

Vrangforestillinger	1	2	3	4	5	6	7
Tankemessig desorganisering	1	2	3	4	5	6	7
Hallusinasjoner	1	2	3	4	5	6	7
Uro / agitasjon	1	2	3	4	5	6	7
Storhetsidéer	1	2	3	4	5	6	7
Mistenksomhet / forfølgelsesidéer	1	2	3	4	5	6	7
Fiendtlighet	1	2	3	4	5	6	7

2) Opplysninger om aktuelt inntak av rusmidler (kryss av)

□ Alkohol □ Amfetamin □ Organisk løsemiddel
□ Benzodiazepiner □ Kokain □ Annet rusmiddel:____
□ Cannabis □ Morfin / heroin □ Ingen opplysninger

Hvis opplysninger om dette:
Stoff, mengde, tidspunkt, inntaksmåte: _____

3) I hvilken grad opplever du at pasienten er påvirket av rusmidler ved innkomst? (kryss av)

□ Ikke påvirket □ Moderat påvirket
□ Lett påvirket □ Tydelig påvirket □ Ikke mulig å bedømme

4) Hvordan vurderer du rusmidlers betydning for innleggelsen?

□ Ingen betydning □ Stor betydning
□ Moderat betydning □ Ikke mulig å bedømme

Dato og tidspunkt: _____
Signatur, mottakende lege: _____

Rekvirere blodprøver så snart som mulig (ø-hjelp, "prosjekt"). Obs! Trengs suppl. undersøkelser? Du skal ikke informere om prosjektet i innkomstsituasjonen. Dette gjøres senere. Legg ferdig utfylt skjema i medisinkardex for aktuelle pasient, og kryss av i "sjekkliste". TAKK FOR SAMARBEIDET!

PANSS positiv subskala

Det kan lønne seg å lese skalaene nedenfra og oppover før du scorer

Vrangforestillinger

1 **Mangler** - Symptomet, slik det er definert, er ikke tilstede.
2 **Minimale** - Tvilsomt patologisk. Kan være en ekstrem normalvariant.
3 **Lette** - Forekomst av en eller to vrangforestillinger som er vage, ikke utkrystalliserte og som ikke fastholdes iherdig. Vrangforestillingene påvirker ikke pasientens tenkning, sosiale relasjoner eller atferd.
4 **Moderate** - Forekomst av en brokete samling av diffuse, vagt utformede, ikke stabile vrangforestillinger eller av noen vel utformede som av og til påvirker tenkning, sosiale relasjoner eller atferd.
5 **Middels alvorlige** - Forekomst av tallrike vel utformede vrangforestillinger som pasienten iherdig fastholder og som av og til påvirker tenkning, sosiale relasjoner eller atferd.
6 **Alvorlige** - Forekomst av en stabil samling vrangforestillinger som er utkrystalliserte, muligens systematiserte og som pas. iherdig holder fast ved og som klart påvirker tenkning sosiale relasjoner og atferd.
7 **Ekstreme** - Forekomst av en stabil samling vrangforestillinger som enten er uttalt systematiserte eller meget tallrike og som dominerer viktige områder av pasientens liv. Dette resulterer ofte i upassende, ansvarsløse handlinger som også kan medføre risiko for pasientens eller andres sikkerhet.

Tankemessig desorganisering

1 **Mangler** - Symptomet, slik det er definert, er ikke tilstede.
2 **Minimale** - Tvilsomt patologisk. Kan være en ekstrem normalvariant.
3 **Lette** - Tenkningen er omstendelig, på siden av temaet eller med tvilsom logikk. Der er til dels vanskeligheter med å bruke tenkningen målrettet, og springende assosiasjoner kan komme frem når pas. blir utsatt for press.
4 **Moderate** - Klarer å fokusere tankene når kommunikasjonen er kortfattet og strukturert, men tankeprosessen blir til dels usammenhengende eller irrelevant ved en mer komplisert samtale, eller ved minimalt press.
5 **Middels alvorlige** - Har stort sett vanskelig for å organisere sine tanker, slik at dette blir tydelig pga. ofte forekommende irrelevante svar, manglende sammenheng, løse assosiasjoner selv når pas. ikke er under press.
6 **Alvorlige** - Tenkningen er i stor grad sporet av med manglende indre sammenheng, som resulterer i påtagelig irrelevant og usammenhengende tenkning som finnes nesten hele tiden.
7 **Ekstreme** - Tankeprosessen er helt usammenhengende. Høy grad av tankeflukt som umuliggjør kommunikasjon (ordsalat eller mutisme).

Hallusinasjoner

1 **Mangler** - Symptomet, slik det er definert, er ikke tilstede.
2 **Minimale** - Tvilsom patologisk. Kan være en ekstrem normalvariant.
3 **Lette** - En eller to klart uttrykte, men ikke ofte forekommende hallusinasjoner eller flere diffuse unormale perseptuelle opplevelser som ikke forvrenger tenkningen eller atferden.
4 **Moderate** - Hallusinasjonene opptrer ofte, men ikke hele tiden og pasientens tanker og atferd påvirkes bare i mindre grad.
5 **Middels alvorlige** - Hallusinasjonene forekommer ofte, kan omfatte mer enn en sansemodalitet og har tendens til å forvrenge tenkningen og/eller påvirke atferden. Pas. kan svare på dem emosjonelt og av og til også verbalt.
6 **Alvorlige** - Hallusinasjoner forekommer nesten hele tiden, og forårsaker stor forstyrrelse av tenkning og atferd. Pas. oppfatter disse som virkelige sanseopplevelser, og funksjonsnivået er preget av hyppige emosjonelle og verbale reaksjoner på dem.
7 **Ekstreme** - Pas. er så og si fullstendig opptatt av hallusinasjoner, som nesten helt dominerer tenkning og atferd. Hallusinasjonene tolkes gjennom fastlåste vrangforestillinger og kommer til uttrykk gjennom tale og atferd, også slik at pas. adlyder imperativ hallusinose.

Uro / agitasjon

1 **Mangler** - Symptomet, slik det er definert, er ikke tilstede.
2 **Minimale** - Tvilsomt patologisk. Kan være en ekstrem normalvariant.
3 **Lette** - Pas. er noe agitert med økt aktsomhet, dvs. med økt tendens til raskt å innrette seg på nye inntrykk, eller med tendens til lett uro gjennom hele intervjuet, men uten klare agitasjonsepisoder eller påtagelige humørsvingninger. Noe økt taletrengthet.
4 **Moderate** - Pas. er klart agitert og urolig under hele intervjuet, og dette påvirker tale og motorikk eller pas. har sporadiske utbrudd som kommer av og til.
5 **Middels alvorlige** - betydelig hyperaktivitet eller ofte forekommende utbrudd av motorisk aktivitet som kan observeres, og dette gjør det vanskelig for pas. å sitte stille i lengre tid enn noen minutter av gangen.
6 **Alvorlige** - Uttalt uro dominerer intervjuet, og begrenser pasientens oppmerksomhet og påvirker til en viss grad naturlige funksjoner som spising og søvn.
7 **Ekstreme** - Uttalt uro som i stor grad hindrer pas. fra å spise og sove, og som gjør kontakt med andre personer nesten helt umulig. Økt talestrøm og økt motorisk aktivitet som resulterer i manglende sammenheng og utmattelse.

Storhetsidéer

1 **Mangler** - Symptomet, slik det er definert, er ikke tilstede.
2 **Minimale** - Tvilsomt patologisk. Kan være en ekstrem normalvariant.
3 **Lette** - Virker noe ekspansivt eller skrytende, men uten storhetsideer.
4 **Moderate** - Urealistisk følelse av påtagelig overlegenhet i forhold til andre. Noen diffust formulerte vrangforestillinger om å ha en spesiell posisjon eller spesielle evner kan forekomme uten at det fører til handlinger.
5 **Middels alvorlige** - Pas. uttrykker klare vrangforestillinger som gjelder spesielle evner, posisjon eller styrke som påvirker holdningen men ikke atferd.
6 **Alvorlige** - Pas. uttrykker klare vrangforestillinger om bemerkelsesverdig overlegenhet som involverer mer enn et område (rikdom, kunnskap, berømmelse o.l.), som påtagelig påvirker samspillet med andre og som kan føre til utagering fra pasientens side.
7 **Ekstreme** - Tenkningen og samspillet med andre og atferden domineres av multiple vrangforestillinger om fantastiske evner, helse, kunnskap, berømmelse, styrke og/eller moralsk høyverdighet som kan få bisarre uttrykk.

Mistenksomhet / forfølgelsesidéer

1 **Mangler** - Symptomet, slik det er definert, er ikke tilstede.
2 **Minimale** - Tvilsomt patologisk. Kan være en ekstrem normalvariant.
3 **Lette** - Fremtrer med en forsiktig eller åpen mistenksom holdning, men tenkning og samspill med andre og atferd er minimalt påvirket.
4 **Moderate** - Uttalt mistenksomhet er klart fremtredende og forstyrrer intervjuet og/eller atferden, men det er ikke tegn på vrangforestillinger om å bli forfulgt. Alternativt kan det finnes løst formulerte vrangforestillinger om å bli forfulgt, men de synes ikke å påvirke pasientens holdninger eller forhold til andre.
5 **Middels alvorlige** - Pas. viser uttalt mistenksomhet som fører til store problemer i forhold til andre mennesker eller det finnes klare vrangforestillinger om å bli forfulgt som har begrenset innflytelse på forholdet til andre og atferd.
6 **Alvorlige** - Klare og mer varige vrangforestillinger om å bli forfulgt som kan være systematiserte og som i betydelig grad påvirker pasientens forhold til andre.
7 **Ekstreme** - Et nettverk av systematiserte vrangforestillinger om å bli forfulgt som dominerer pasientens tenkning, forhold til andre og atferd.

Fiendtlighet

1 **Mangler** - Symptomet, slik det er definert, er ikke tilstede.
2 **Minimale** - Tvilsomt patologisk. Kan være en ekstrem normalvariant.
3 **Lette** - Indirekte eller kontrollert sinne slik som sarkasmer, manglende respekt, fiendtlighet og perioder med irritabilitet.
4 **Moderate** - Pas. fremviser en klart fiendtlig holdning, blir ofte irritabel og gir direkte uttrykk for sinne.
5 **Middels alvorlige** - Pas. er svært irritabel og bruker av og til ukvemsord Eller er truende.
6 **Alvorlige** - Er ikke samarbeidsvillig, bruker ukvemsord eller truer, og dette forstyrrer i stor grad intervjuet og påvirker i stor grad forhold til andre. Pas. kan bli voldsom og destruktiv, men er ikke fysisk voldsom mot andre.
7 **Ekstreme** - Uttalt raseri som resulterer i ekstrem uvilje til samarbeid, utelukker kontakt med andre eller resulterer i episoder med fysisk vold mot andre.

Velkommen til Lovisenberg Diakonale Sykehus!

Spørsmål til alle pasienter ved akuttpsykiatrisk avdeling

Vi ønsker i størst mulig grad å forstå din situasjon og dine eventuelle helseproblemer. Derfor håper vi du kan samarbeide om å svare på noen spørsmål om dette. Utfyllingen tar cirka 15 minutter, og vil være til stor hjelp for oss. Bare spør personalet ved behov. Takk for hjelpen!

Navn: _____

Fødselsdato: _____

Dato i dag: _____

Under finner du en liste over ulike problemer.
Har du opplevd noe av dette den siste uken (til og med i dag)?

Sett et kryss på hver linje	Ikke plaget	Litt plaget	Ganske mye	Veldig mye
1. Plutselig frykt uten grunn	☐	☐	☐	☐
2. Føler deg redd og engstelig	☐	☐	☐	☐
3. Matthet eller svimmelhet	☐	☐	☐	☐
4. Føler deg anspent eller oppjaget	☐	☐	☐	☐
5. Lett for å klandre deg selv	☐	☐	☐	☐
6. Søvnproblemer	☐	☐	☐	☐
7. Nedtrykt, tungsindig	☐	☐	☐	☐
8. Følelse av å være unyttig, lite verd	☐	☐	☐	☐
9. Følelse av at alt er et slit	☐	☐	☐	☐
10. Følelse av håpløshet mht. framtida	☐	☐	☐	☐
11. Har tanker om å ta ditt eget liv	☐	☐	☐	☐

Om alkohol og stoff/narkotika	Slett ikke	Delvis	Svært mye
12. Tror du bruk av alkohol eller stoff har hatt betydning for innleggelsen her?	☐	☐	☐
13. Synes du at du trenger profesjonell hjelp for å forandre din alkoholbruk?	☐	☐	☐
14. Synes du at du trenger profesjonell hjelp for å forandre ditt stoffbruk?	☐	☐	☐

Om pengespill (eks. spilleautomater og tipping)	Ja	Nei
15. Har du noen gang følt behov for å spille for mer og mer penger?	☐	☐
16. Har du noen gang løyet for mennesker som er viktige for deg, om hvor mye du spiller?	☐	☐

Om tobakk	Ja	Nei
17. Røyker du sigaretter eller bruker du snus?	☐	☐
18. Hvis ja: Hvor mange sigaretter røyker du vanligvis per dag? ____ Evnt. snusdoser per dag? ____		

Her er noen spørsmål om din bruk av alkohol siste 12 måneder

1. Hvor ofte drikker du alkohol?	Aldri	Månedlig eller sjeldnere	2-4 ganger i måneden	2-3 ganger i uken	4 ganger i uken eller mer
	☐	☐	☐	☐	☐
2. Hvor mange alkoholenheter tar du på en typisk drikkedag? (En alkoholenhet er: 1 glass vin, 1 drink, en liten flaske pils, 0,33 l)	1-2	3-4	5-6	7-9	10 eller flere
	☐	☐	☐	☐	☐
3. Hvor ofte drikker du seks alkoholenheter eller mer på en gang?	Aldri	Sjeldnere enn månedlig	Noen ganger i måneden	Noen ganger i uken	Daglig eller nesten daglig
	☐	☐	☐	☐	☐
4. Hvor ofte har du i løpet av det siste året ikke vært i stand til å stoppe og drikke alkohol etter at du hadde begynt?	Aldri	Sjeldnere enn månedlig	Noen ganger i måneden	Noen ganger i uken	Daglig eller nesten daglig
	☐	☐	☐	☐	☐
5. Hvor ofte har du i løpet av det siste året unnlatt å gjøre ting du skulle gjort på grunn av drikking?	Aldri	Sjeldnere enn månedlig	Noen ganger i måneden	Noen ganger i uken	Daglig eller nesten daglig
	☐	☐	☐	☐	☐
6. Hvor ofte har du i løpet av det siste året trengt en drink om morgenen for å komme i gang etter sterk drikking dagen før?	Aldri	Sjeldnere enn månedlig	Noen ganger i måneden	Noen ganger i uken	Daglig eller nesten daglig
	☐	☐	☐	☐	☐
7. Hvor ofte har du i løpet av det siste året hatt skyldfølelse eller samvittighetsnag på grunn av drikking?	Aldri	Sjeldnere enn månedlig	Noen ganger i måneden	Noen ganger i uken	Daglig eller nesten daglig
	☐	☐	☐	☐	☐
8. Hvor ofte har du i løpet av det siste året ikke husket hva som hendte kvelden før på grunn av drikking?	Aldri	Sjeldnere enn månedlig	Noen ganger i måneden	Noen ganger i uken	Daglig eller nesten daglig
	☐	☐	☐	☐	☐
9. Har du eller noen andre blitt skadet som følge av drikkingen din?	Nei		Ja, men ikke det siste året		Ja, det siste året
	☐		☐		☐
10. Har en slektning eller venn, lege eller sykepleier, eller noen andre engstet seg over drikkingen din, eller antydet at du burde redusere?	Nei		Ja, men ikke i løpet av siste år		Ja, i løpet av siste år
	☐		☐		☐

Her er noen spørsmål om stoff

1. Hvor ofte bruker du andre stoff enn alkohol? Se listen over stoff på neste side, og kryss av.	Aldri	1 gang i måneden eller sjeldnere	2-4 ganger i måneden	2-3 ganger i uken	4 ganger i uken eller mer
2. Bruker du flere enn ett stoff ved ett og samme tilfelle?	Aldri	1 gang i måneden eller sjeldnere	2-4 ganger i måneden	2-3 ganger i uken	4 ganger i uken eller mer
3. Hvor mange ganger i løpet av en typisk dag tar du stoff, når du tar stoff?	0	1-2	3-4	5-6	7 eller flere
4. Hvor ofte blir du kraftig påvirket av stoff?	Aldri	Sjeldnere enn en gang i måneden	Hver måned	Hver uke	Daglig eller nesten daglig
5. Har du det siste året opplevd at lengselen etter stoff har vært så sterk at du ikke kunne stå imot?	Aldri	Sjeldnere enn en gang i måneden	Hver måned	Hver uke	Daglig eller nesten daglig
6. Har det hendt at du i løpet av siste året ikke kunne slutte å ta stoff når du først hadde begynt?	Aldri	Sjeldnere enn en gang i måneden	Hver måned	Hver uke	Daglig eller nesten daglig
7. Hvor ofte i løpet av det siste året har du tatt stoff og så latt være å gjøre noe som du burde ha gjort?	Aldri	Sjeldnere enn en gang i måneden	Hver måned	Hver uke	Daglig eller nesten daglig
8. Hvor ofte i løpet av det siste året har du hatt behov for å starte dagen med å ta stoff etter stort stoffinntak dagen før?	Aldri	Sjeldnere enn en gang i måneden	Hver måned	Hver uke	Daglig eller nesten daglig
9. Hvor ofte i løpet av det siste året har du hatt skyldfølelse eller dårlig samvittighet fordi du har brukt stoff?	Aldri	Sjeldnere enn en gang i måneden	Hver måned	Hver uke	Daglig eller nesten daglig
10. Har du eller noen andre blitt skadet (psykisk eller fysisk) på grunn av din bruk av stoff?	Nei		Ja, men ikke i løpet av det siste året		Ja, i løpet av det siste året
11. Har en slektning eller venn, lege eller sykepleier, eller noen andre vært urolige for din bruk av stoff, eller sagt til deg at du bør slutte med stoff?	Nei		Ja, men ikke i løpet av det siste året		Ja, i løpet av det siste året

LISTE OVER STOFF (ikke alkohol)

Sett et kryss ved de stoffene du eventuelt har brukt

Cannabis	Amfetaminer	Kokain	Opiater	Hallusinogener	Løsningsmidler	GHB og andre
Marihuana Hasj Cannabisolje	Amfetamin Metamfetamin Khat Ritalin Dexamin	Crack Kokablad	Heroin Røyke-heroin Opium	Ecstasy (MDMA) LSD Meskalin PCP (englestøv) Fleinsopp	Tynner Bensin Gass Løsemidler, lim Trikloretylen	GHB Anabole steroider Lystgass Amylnitritt

Ved ett eller flere kryss:
Hvilket stoff har du brukt mest det siste året? _____
Når tok du dette stoffet sist? _____
Hvilke stoff har du eventuelt brukt den siste uken? _____

TABLETTER – LEGEMIDLER

Tabletter regnes som stoff når du tar:

- legemidler mer eller oftere enn legen har foreskrevet
- tabletter for å ha det moro, føle deg bra, bli "høy", eller prøve ut effekten
- tabletter som du har fått en slektning eller en venn
- tabletter som du har kjøpt "svart" eller stjålet

Sett et kryss ved de tablettene du eventuelt har brukt som beskrevet over

Beroligende legemidler / sovetabletter			Smertestillende legemidler		
Alopam Alprazolam Apodorm Barbital Dormicum Fenemal Flunipam Heminevrin	Imovane Mogadon Rivotril Rohypnol Sobril Somadril Stesolid	Stilnoct Valium Vival Xanor Xanor dep. Zolpidem Zopiklon **Andre:** Disipal Akineton	Actiq Aporex Anervan Buprenorfin Cosylan Dolcontin Durogesic Etylmorfin Fentanyl Fortralin Hydrokon	Ketalar Ketamin Ketogan Ketorax Kodein Metadon Modiodal Morfin Morfin-skopolamin	Nobligan OxyContin OxyNorm Paralgin Petidin Pinex Subutex Temgesic Tradolan Tramadol Tramagetic

Husk at tabletter regnes ikke som stoff når de er foreskrevet av lege, og du tar dem slik legen sier at du skal (både mengde og hyppighet).

Takk for at du har besvart våre spørsmål!

I

II

Original article to Nordic Journal of Psychiatry

Psychoactive substance use among patients admitted to an acute psychiatric ward: Laboratory findings and associations with clinical characteristics

Running title: Substance use among psychiatric admissions

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Abstract

Background: Estimates of psychoactive substance use among acutely admitted psychiatric patients vary among studies, and few have used comprehensive laboratory methods. *Aims:* This study used chromatography-based analyses of blood and urine to identify the rates of substance use among acute psychiatric admissions, and to study the associations with sociodemographic variables, clinical characteristics and patients' reports of symptoms, substance use and need for treatment. *Methods:* A cross-sectional study was conducted in 2006/2007 in Oslo, Norway. Blood and urine samples were collected from 298 acute psychiatric admissions and extensively analyzed for alcohol, medicinal and illicit drugs. Psychotic symptoms were assessed with the positive subscale of the Positive and Negative Syndrome Scale. Patient self-report questionnaires included the Alcohol and Drug Use Disorder Identification Tests. Patients were also asked if they needed professional help for substance use. *Results:* Psychoactive substances were detected in 63% of the 298 admissions, medicinal drugs in 46%, alcohol in 12% and illicit drugs in 28%. Patients using alcohol had a high suicidal risk score at admission and the shortest length of stay (median one day). Use of illicit drugs was associated with psychotic symptoms and readmission. Self-report questionnaires indicated harmful use of alcohol for half of the patients and of other substances for one-third. A need for professional help for substance use was reported by one-third of patients. *Conclusion:* Given the high rates of substance use and the important clinical associations, drug screening seems warranted in acute psychiatric settings. Interventions designed for substance-using patients should be developed and integrated.

Keywords: Substance use, alcohol, illicit drugs, toxicology, psychiatric inpatients.

Background

Recent intake of alcohol and medicinal or illicit drugs is common among patients in acute psychiatric settings, and may influence symptoms, treatment and prognosis (1, 2). Substance-using patients constitute a heterogeneous group. Some have primary substance-induced disorders, whereas others have primary mental disorders complicated by substance use (3), and patients' awareness of illness and perceived need for treatment vary (4). Such distinctions have clear implications for treatment (2). Identifying substance-using patients may be difficult in the acute phase, however, as symptoms of substance use can mimic many psychiatric disorders. Substance use detection is commonly undertaken through clinical interviews, patients' self-reports or toxicological tests.

European and US studies using toxicological analyses among acutely admitted psychiatric patients report frequencies ranging from 20% to 72% (5-14). Most of these studies were conducted in urban clinics, but the broad range may be partly explained by different substance use patterns across regions and countries. In addition, there are methodological differences that make comparisons across studies problematic. Many studies have included only a limited number of drugs, such as benzodiazepines (12) and cocaine (13). Some have studied groups of patients known to have high rates of substance use: men (14) or young psychotic patients (9), for example. Studies also exhibit variation in the methods used for substance detection. Urine samples have commonly been screened with immunoassay techniques, which have limited sensitivity and specificity, and not all substances can be detected (15). Thus, many studies lack detailed information on recent substance intake and polydrug use.

Identification and adequate management of substance-related conditions are critical in the clinical setting, and precise measures are required for epidemiological, surveillance and planning purposes. In acute psychiatric settings, few studies have used comprehensive

laboratory methods for assessing substance use, and little is known about the sociodemographic and clinical associations of toxicological findings among patients admitted to acute psychiatric wards.

Aims

This study investigates recent intake of alcohol and medicinal and illicit drugs among patients hospitalized in an urban Norwegian acute psychiatric ward. The study uses chromatography-based laboratory analyses of blood and urine to identify a wide range of psychoactive substances, and to estimate the level of nonprescribed use of medicinal drugs. Admissions were divided into four groups according to laboratory findings (no drugs detected, medicinal drugs only, alcohol and illicit drugs). These groups were compared with regard to sociodemographic variables, clinical characteristics and patients' reports of symptoms, substance use and need for treatment.

Material and methods

Participants

This cross-sectional study was conducted between September 2006 and February 2007 in a public hospital in Oslo, Norway, serving approximately 100,000 inner-city inhabitants. Consecutively admitted patients who were willing to participate in the study provided written informed consent. Of the 351 acute admissions, 298 (85%) were included in the study, 33 (9%) declined, 12 (3%) did not provide biological specimens for drug analysis and 8 (2%) were excluded because of dementia. The study sample comprised 220 patients admitted once and 32 patients admitted twice or more. The mean age of included patients was 39 years (SD 15); 47% were males, and 44% were admitted to the ward for the first time. The median length of hospital stay was 5 days (range 0-111). We found no difference between those included and those not included in the study sample on age ($P = 0.94$), gender ($P = 0.91$) and length of stay ($P = 0.57$), but nonparticipants were more often admitted on an involuntary basis (82% vs. 56%, $P < 0.001$). To evaluate the representativeness further, participants were compared with all 1133 admissions to the same Oslo unit during 2006 and with a national sample of more than 3500 acute psychiatric admissions from a multicentre study performed in 2005 (16). In these comparisons, no differences were found in age, gender or length of stay ($P > 0.2$). As compared with the national sample, however, participants were more often of non-Norwegian origin (20% vs. 10%), homeless (10% vs. 4%), involuntarily admitted (55% vs. 42%) and had a substance use disorder as discharge diagnosis (45% vs. 22%) ($P < 0.001$ for all).

Laboratory measures

Blood and urine samples were collected as soon as possible after admission. Admissions during which at least one sample was obtained within 48 hours were included in this study. Samples were brought on a weekly basis to the Division of Forensic Toxicology and Drug Abuse, Norwegian Institute of Public Health. Using the enzyme multiplied immunoassay technique (EMIT), all urine samples were screened for substances and their metabolites: benzodiazepines, opiates, amphetamines (amphetamine, methamphetamine and ecstasy), cocaine, cannabis, methadone, buprenorphine, dextropropoxyphene, barbiturates, phencyclidine and lysergic acid diethylamide (LSD) (Table 1). Blood samples were screened with EMIT for opiates, amphetamines, cocaine and cannabis, and by liquid chromatography-mass spectrometry for benzodiazepines, hypnotics, carisoprodol, meprobamate and methadone. Blood samples were screened for alcohol with an enzymatic dehydrogenase method, as were the urine samples of patients who did not provide blood. All positive screening results in urine and blood were confirmed by gas or liquid chromatography-mass spectrometry, with cut-off values presented in a previous paper (11).

Laboratory results were used only for study purposes, and were available for the researchers at the end of the data collection period. Both blood and urine analyses were used to increase the number of detectable substances (e.g. zopiclone was detected only in blood and LSD only in urine). It also increased the inclusion rate, as some patients provided only blood or only urine specimens. Except for benzodiazepines or opiates that had been prescribed after admission, substances were reported as present if they were detected in the blood or urine. Only one finding was counted if both the parent drug and its metabolites were detected. Morphine and codeine were defined as medicinal drugs unless the heroin metabolite 6-monoacetylmorphine (6-MAM) was also found. The benzodiazepine, phenazepam, was defined as an illicit drug, as it was neither registered nor sold in Norway.

To study the associations between laboratory findings and sociodemographic and clinical variables, we divided the study sample into four groups; 1) no drugs detected, 2) medicinal drugs only, 3) alcohol without illicit drugs (with or without medicinal drugs) and 4) illicit drugs (with or without alcohol and medicinal drugs). A retrospective review of medical records assessed whether or not findings of medicinal drugs represented prescribed use before admission. Reviewed documents included notes from the admitting physician and the nurse and physician on call, as well as the inpatient prescription form. If the specific laboratory finding could be explained by a prescription that was documented in the medical records, it was defined as "prescribed use". Other positive findings not documented were defined as "nonprescribed use", as were findings in which patients reported non-therapeutic use at the time of admission.

Sociodemographic variables, clinical characteristics and patient self-report

Sociodemographic and clinical variables for the study sample were also obtained by the review of medical records. The variables included age, gender, education level, accommodation type, employment status, number of previous psychiatric admissions, and the legal status of the admission, suicidal risk at admission, use of coercion (seclusion, coercive medication and manual restraints) and ICD-10 discharge diagnoses (Table 2). Suicidal risk at admission was assessed by rating patients on a scale from 1 to 6, where 1 = 'no risk' and 6 = 'recent severe self-harm with obvious intention to die' (17). Symptom severity and social and occupational functioning were measured by clinicians using the split version of the Global Assessment of Functioning (GAF) scale (18, 19). Psychotic symptoms at the time of admission were assessed by the physician on call using the positive subscale of the Positive and Negative Syndrome Scale (PANSS) (20). Standardized questionnaires were administrated

to the patients. The 10-item Hopkins Check List (HSCL-10) was used to measure symptoms of anxiety and depression during the last week (21). This instrument has demonstrated good sensitivity and specificity as compared with the widely used HSCL-25 (22). The 10-item Alcohol Use Disorder Identification Test (AUDIT) (23) and the 11-item Drug Use Disorder Identification Test (DUDIT) (24) were used to measure substance use patterns during the last year. All items were scored from zero to four. AUDIT scores of 8 for men and 5 for women were used as cut-off scores for harmful alcohol use, and DUDIT scores of 6 for men and 2 for women were used as cut-off scores for harmful use of medicinal or illicit drugs (24, 25). Patients were also asked about their tobacco use and asked, "Do you think you need professional help to change your alcohol use?" and "Do you think you need professional help to change your drug use?" (Not at all / partly / totally). The latter question is part of the Drug Use Disorders Identification Test-Extended (DUDIT-E) (26). Patients and physicians on call were also asked "Do you think that the current admission was related to substance use?" (Not at all / partly / totally). The results of patient self-reports and physician assessments were documented in medical records. The study was approved by The Regional Committee for Medical Research Ethics and the Norwegian Data Inspectorate.

Statistical analyses

Count data are presented as numbers (%), and the overall detection rates are presented with 95% confidence intervals (CI). Continuous data with approximate normal distributions are presented as means (SD) and non-normal data as medians (range). For comparisons of two groups, a χ^2 test was used for dichotomous dependent variables, and Student's t-test or Mann Whitney U-test for continuous dependent variables. We used a significance level of 0.05.

The four drug groups (no drugs, medicinal drugs only, alcohol without illicit drugs and illicit drugs) were compared with regard to sociodemographic and clinical variables, using Bonferroni corrections for multiple comparisons ($P < 0.002$). For dichotomous dependent variables, post-hoc pairwise comparisons among all subgroups were Bonferroni corrected with a significance level of 0.009. Normally distributed continuous variables were analyzed with one-way analysis of variance (ANOVA), and post-hoc comparisons were performed using the Tukey HSD test. Kruskall-Wallis tests were used for non-normal data, with Mann-Whitney tests and Bonferroni corrections for post-hoc pairwise comparisons.

Results

Urine and blood samples were obtained from patients in 246 (83%) of the 298 admissions. Blood samples only were obtained from 41 (14%) and urine only from 11 (4%). Blood samples were taken at a median of 30 minutes after admission (range 0-48 hours) and urine samples after 7 hours (0-95 hours). In 284 admissions (95%), either blood or urine was obtained within 24 hours. Physician assessments were performed for 285 (96%) admissions after a median of 30 minutes (range 0-6 hours). Of the 252 patients included in the study, self-report questionnaires were completed by 230 (91%), usually at the day of admission (median 0, range 0-30 days).

Psychoactive substances were detected in 187 (63%) (95% CI 57 - 68%) of the 298 admissions, medicinal drugs in 46% (41 - 52%), alcohol in 12% (9 - 16%) and illicit drugs in 28% (23 - 33%) (Table 1). Altogether, 20 different substances were detected, with two or more drug findings in 135 (42%) of the admissions. Up to 10 substances were found in specimens from one patient. Of the medicinal drugs, diazepam was the most common (34%) (95% CI 29 - 39%). Of the illicit drugs, cannabis was found in 18% (14 - 23%) and amphetamines in 16% (12 - 20%) of the admissions. Cocaine was rare (2%) (0 - 4%), and barbiturates, ecstasy, phencyclidine, GHB, and LSD were not detected in this population.

Admissions were divided into four groups according to laboratory findings. Patients positive for illicit drugs had a median of 2 detected substances, including 16 of the 19 cases with flunitrazepam, and 9 of the 10 cases with methadone (Table 1). Nonprescribed use of medicinal drugs was estimated for a total of 108 admissions (36%), with 66% in the medicinal drug group, 44% in the alcohol group and 55% in the illicit drug group. Flunitrazepam, methadone and morphine were used without prescription in more than 80% of the positive cases, all with median numbers of drug findings 4 or above (data not shown).

< Table 1 about here >

Drug groups were compared with regard to clinical characteristics (Table 2) and sociodemographic variables. No significant relationships were found with HSCL-10 scores, previous psychiatric admission and employment status (data not shown). Patients with negative tests and with medicinal drugs only did not differ significantly from the other groups on any variable in the post-hoc analyses. The current admission was seen as being partly or totally related to substance use by 42% of patients completing the questionnaire and by 45% of physicians on call, with the highest percentages found in the alcohol group and the illicit drug group. Harmful use of alcohol was reported by half of all patients; by all patients in the alcohol group and by 44% of the patients in the other groups. Harmful use of other substances was reported by one-third of all patients; by 78% in the illicit drug group and by 19% of the other patients. A need for professional help with regard to substance use was reported by 31% of patients (alcohol use 12%, drug use 12% and both 7%), with the highest percentages found in the alcohol group and the illicit drug group.

< Table 2 about here >

Patients in the alcohol group had the shortest hospital stay (median 1 day) and the highest percentage of alcohol use disorders (59%), compared to all other groups ($P < 0.002$). Patients positive for alcohol also had a higher suicidal risk score than did patients in groups of no

drugs ($P = 0.022$) and illicit drugs ($P = 0.006$), but not significantly higher than those with medicinal drugs only ($P = 0.57$).

Patients who were positive for illicit drugs had the lowest GAF score at admission ($P < 0.03$ in post-hoc ANOVA) and the highest percentages of disorders due to multiple substance use (56%) ($P < 0.001$), compared to all other groups. Compared to patients in the medicinal drugs and alcohol groups, patients who were positive for illicit drugs had the highest scores for positive psychotic symptoms (PANSS scores) ($P < 0.002$), and were more often admitted on an involuntary basis ($P < 0.009$). Compared to patients in the no drugs and medicinal drugs groups, patients positive for illicit drugs were more often men (66% vs. 42% and 32%), homeless (24% vs. 5% and 4%), tobacco users (95% vs. 64% and 59%), and had less education (76% had primary school or less, vs. 41% and 47%) ($P < 0.009$ for all post-hoc tests). When these variables were compared with patients in the alcohol group, the same tendencies were observed ($P = 0.02$ - 0.05), but the differences were not significant after Bonferroni correction.

The 32 patients with readmissions did not differ from other patients with regard to age ($P = 0.70$) and gender ($P = 0.41$), whereas detection of illicit drugs (39% vs. 25%, $P = 0.019$) and drug-related discharge diagnoses (65% vs. 37%, $P < 0.001$) were more common among readmitted patients (data not shown). Twelve patients had different laboratory findings upon readmission, and were therefore represented in two drug groups.

Discussion

Recent intake of psychoactive substances with potentially impairing effects was widespread among patients acutely admitted to this inner city psychiatric hospital in Oslo. Almost two-thirds of the sample was positive for at least one psychoactive substance. A total of 20 different substances were detected, with up to ten in a single patient. Both patients and the physicians on call saw the current admission as being related to substance use in nearly half of the cases. Self-report questionnaires indicated harmful alcohol use for half of the patients and harmful use of other drugs for one-third. A need for professional help for substance use was reported by one-third of patients. All these findings demonstrate the major impact of both recent and long-term substance use and the need for tailored interventions for substance-using patients in acute psychiatric wards.

The identification of risk factors of substance use can contribute to improved detection of substance-using patients. Patients positive for illicit drugs at admission, as compared to patients with drug-free samples, were more often men, homeless, less educated and tobacco users. These results correspond with previous inpatient studies using urine toxicology (7) and self-reports (5, 10). The use of illicit drugs was also associated with lower levels of general functioning (low GAF scores) and increased problems with psychosis and readmissions. These patients constitute a large and marginalized group calling for clinical concern. Amphetamines, which were detected in one-sixth of patients, are particularly associated with serious negative health effects (27) and may have a major impact on emergency services (28).

Alcohol-positive patients had a high suicidal risk score at admission. The relationship between acute alcohol intake and suicidal risk has been described previously (29). Taken together, these studies suggest that acutely admitted patients with both substance use and suicidal behaviour require specialized focus (17). Our results support the association between

substance use and shorter hospital stay (5, 8), and this finding may be especially the case for patients who are admitted under the influence of alcohol. Due to rapid elimination of alcohol, patients may leave the unit because of rapid recovery or unpleasant withdrawal symptoms.

We found that benzodiazepines and other medicinal drugs were often nonprescribed, and that nearly all patients with findings of flunitrazepam and methadone also tested positive for illicit drugs. Even if the rate of nonprescribed use may have been overestimated due to omissions or inadequacies in the medical records, this finding suggests a widespread abuse of medicinal drugs among these patients. Use of benzodiazepines and opiates should be carefully monitored in the treatment of psychiatric patients, and toxicological screening tests may help in detecting undeclared use of these drugs (30).

The percentage of included admissions was high (85%), and we assume that our findings are representative for patients admitted to this hospital. The substance use in this sample is not nationally representative, because of its higher rate of substance use disorders (16). This finding may be explained partly by higher rates of substance use in the general population of Oslo than in other parts of Norway (31), and in the inner city population in particular. Bearing in mind the geographical differences in acute psychiatric services (32) and methodological differences across studies, detection rates of specific substances are compared in the following paragraph with those of other studies from urban clinics in Europe and USA. Comparison is also challenged by the lack of confidence intervals in previous studies.

High detection rates were found for most substances in this study. The benzodiazepine rate of 43% (95% CI 38 - 49%) is in the upper range of previous reports (7% - 45%) (6, 8-12), which may be partly explained by our use of comprehensive and sensitive laboratory methods. Detection of alcohol in blood or urine indicates recent consumption (most likely during the last 12 hours), and the rate of 12% (95% CI 9 - 16%) seems higher than the few

previous figures available from other studies (2% and 6%) (8, 9). The rate of illicit drugs (28%, 95% CI 23 - 33%) is similar to recent reports from Switzerland and France (20% and 26%) (5, 7). For amphetamines, the rate of 16% corresponds with previous studies among inpatients in Oslo (17% and 22%) (9, 11), whereas others have reported frequencies of 5% or less (7, 8, 14). In contrast, cocaine was rarely found in this sample (2%) as compared to US samples (29% - 50%) (6, 13, 14), probably reflecting differences in substance use across countries.

An interpretation of our results should take the limitations of the study design into account. First, the study was conducted in a busy ward with many severely ill patients, and the quality of such non-laboratory data as the assessment of suicidal risk and perceived treatment need was suboptimal. For example, the assessment of prescribed medication was based on a review of medical records. Although medication history taking is mandatory at acute admissions, it may be limited by patients' memory problems, poor record-keeping, and, especially for patients admitted for the first time, a general lack of information. Second, for some patients, only blood samples were obtained. As most substances are rapidly eliminated from blood (33), it is likely that a few cases of recent substance use were not detected. Third, alcohol is rapidly removed from the body, and additional biomarkers with longer detection times, such as ethyl glucoronide or carbohydrate deficient transferrin, could have added valuable information and increased the estimates of recent alcohol users. Few admissions in the alcohol group reduced the statistical power of subgroup analyses. Finally, the division of the patients into four drug groups raised several methodological concerns. To distinguish users of alcohol and illicit drugs is common, whereas classifying patients with medicinal drugs only into one group has not previously been done. Relatively large and heterogeneous groups may increase the risk of losing relevant information. Among patients placed in the illicit drug group, for

example, possible differences between the users of cannabis and amphetamines may not have been discovered. In addition, the grouping was based on a single laboratory test, which may be insensitive for the severity of substance use problems. Among patients with no drugs detected, for example, nearly half had AUDIT scores above cut-off. Furthermore, most patients do not belong to one specific drug group over time, as illustrated by readmitted patients who were represented in two different groups.

The greatest strength of this study was the comprehensive laboratory analyses used for the identification of substances in the blood and urine of these patients. This enabled a thorough investigation of detection rates, polydrug use and nonprescribed use of medicinal drugs. The use of advanced laboratory methods identifies cases of substance use missed by less sensitive tests (15) or by patients' under-reporting (7, 30).

Given the high rates of substance use and the important clinical associations, drug screening seems warranted in acute psychiatric settings. Biometric and psychometric measures of substance use have complementary roles, and future studies are needed to define the proper way of combining these measures in acute psychiatric settings. Even a short hospitalization provides an excellent opportunity for identifying patients with or at risk for substance-related problems that may benefit from tailored interventions.

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Disclosure of interest

None of the authors have any commercial conflicts of interest.

Table 1. Substances detected in blood and/or urine among 298 acute psychiatric admissions and according to different drug groups.

			Admissions with positive findings, *n* = 187		
	All admissions *n* = 298 (100%)	(95% CI)	Medicinal drugs only *n* = 76 (100%)	Alcohol without illicit drugs *n* = 27 (100%)	Illicit drugs *n* = 84 (100%)
Median number of drugs (range)	1 (0-10)	-	1 (1-5)	1 (1-4)	2 (1-10)
Medicinal drugs*	138 (46%)	(41-52%)	76 (100%)	12 (44%)	50 (60%)
Benzodiazepines	129 (43%)	(38-49%)	72 (95%)	12 (44%)	45 (54%)
Diazepam or metabolites	101 (34%)	(29-39%)	55 (72%)	10 (37%)	36 (43%)
Flunitrazepam	19 (6%)	(4-9%)	3 (4%)	0 (0%)	16 (19%)
Clonazepam	34 (11%)	(8-15%)	12 (16%)	3 (11%)	18 (21%)
Nitrazepam	33 (11%)	(8-15%)	19 (25%)	2 (7%)	13 (16%)
Opiates or opioides	34 (11%)	(8-15%)	12 (16%)	1 (4%)	21 (25%)
Morphine	24 (8%)	(5-11%)	8 (11%)	1 (4%)	15 (18%)
Methadone	10 (3%)	(1-5%)	1 (1%)	0 (0%)	9 (11%)
Nonprescribed medicinal drugs†	108 (36%)	(31-42%)	50 (66%)	12 (44%)	46 (55%)
Benzodiazepines (nonprescr.)	91 (31%)	(25-36%)	42 (55%)	11 (41%)	38 (45%)
Diazepam (nonprescr.)	58 (20%)	(15-24%)	25 (33%)	10 (37%)	23 (27%)
Flunitrazepam (nonprescr.)	16 (5%)	(3-8%)	2 (3%)	0 (0%)	14 (17%)
Alcohol	37 (12%)	(9-16%)	0 (0%)	27 (100%)	10 (12%)
Illicit drugs‡	84 (28%)	(23-33%)	0 (0%)	0 (0%)	84 (100%)

Values given in *n* (%) for dichotomous variables and median (range) for continuous variables.
*Including hypnotica (zopiclone or zolpidem, *n* = 19), alprazolam (*n* = 3), carisoprodol (*n* = 1), meprobamate (*n* = 5), codeine (*n* = 16), buprenorphine (*n* = 2) and dextropropoxyfene (*n* = 1).
†Detection of one or more nonprescribed medicinal drug (25 patients admitted nonprescribed use and in another 83 admissions, the laboratory findings could not be documented in medical records).
‡Amphetamines (*n* = 47), cannabis (*n* = 55), cocaine (*n* = 6) phenazepam (*n* = 3), 6-MAM (metabolite of heroin) (*n* = 2).

Table 2. Clinical characteristics according to different drug groups among 298 acute psychiatric admissions.

		Admissions with positive findings, *n* = 187				
	No drugs detected *n* = 111 (100%)	Medicinal drugs only *n* = 76 (100%)	Alcohol w/o illicit drugs *n* = 27 (100%)	Illicit drugs *n* = 84 (100%)	χ^2	*P*
Data from medical records (*n* = 298)						
Involuntary admission	70 (63%)	27 (36%)	11 (41%)	57 (68%)	22.407	<0.001
Suicidal risk score	2.5 (1.5)	3.0 (1.6)	3.4 (1.2)	2.3 (1.5)	5.294*	0.001
Coercive measures‡	30 (27%)	5 (7%)	1 (4%)	32 (39%)	29.745	<0.001
Length of stay in days	9 (0-95)	10 (0-111)	**1 (0-51)**	4 (0-69)	22.878†	<0.001
Transfer to long-term inpatient care	30 (27%)	14 (18%)	1 (4%)	6 (7%)	17.092	0.001
Discharge diagnoses (ICD-10)§						
F1 Substance use disorders	16 (14%)	25 (33%)	20 (74%)	72 (86%)	112.093	<0.001
F10 Alcohol	9 (8%)	12 (16%)	**16 (59%)**	11 (13%)	43.032	<0.001
F19 Multiple substances	5 (5%)	4 (5%)	4 (15%)	**47 (56%)**	94.808	<0.001
F2 Schizophrenia	43 (39%)	17 (22%)	1 (4%)	16 (19%)	19.042	<0.001
F3 Affective disorders	39 (35%)	34 (45%)	10 (37%)	19 (23%)	8.892	0.031
Readmission in project period	18 (16%)	21 (28%)	9 (33%)	30 (36%)	10.452	0.015
Physician on call (*n* = 285)						
Positive symptoms (PANSS)¶	18 (9)	14 (7)	12 (5)	20 (9)	9.082*	<0.001
GAF – symptoms	36 (12)	37 (12)	39 (11)	32 (11)	3.291*	0.021
GAF – functioning	37 (13)	37 (9)	42 (10)	**32 (9)**	6.922*	0.001
Substance-related admission	22 (21%)	18 (25%)	24 (92%)	65 (80%)	110.311	<0.001
Patient self-report (*n* = 230)						
Substance-related admission	20 (23%)	10 (16%)	20 (87%)	47 (76%)	78.965	<0.001
≥ cut-off on AUDIT	39 (45%)	19 (31%)	**23 (100%)**	34 (59%)	34.755	<0.001
≥ cut-off on DUDIT	16 (19%)	9 (15%)	7 (30%)	**46 (78%)**	68.966	<0.001
Need for help with alcohol use	12 (14%)	6 (10%)	**13 (57%)**	14 (24%)	26.184	<0.001
Need for help with drug use	4 (5%)	8 (13%)	3 (14%)	**29 (48%)**	44.606	<0.001

Values given in *n* (%) for dichotomous variables and mean (SD) or median (range) for continuous variables. χ^2 tests were performed unless otherwise indicated, df = 3. *P*-values are given for comparisons among all drug groups. Values < 0.002 remain significant with Bonferroni correction. Variables that differed significantly after post-hoc pair wise comparisons are **bold**.

*F-value from analysis of variance (ANOVA), †Kruskal-Wallis test.

‡Seclusion (*n* = 61), coercive medication (*n* = 23) and manual restraints (*n* = 19).

§Stated as primary or secondary diagnosis at discharge. Other diagnostic groups were F4 neurotic disorders (*n* = 39) and F6 personality disorders (*n* = 53), whereas F0, F7 and F9 were rare (*n* < 10).

¶Positive and negative syndrome scale, positive subscale: Agitation, hostility, suspiciousness, delusions, thought disturbances, hallucinations and grandiosity; assessed on a scale from 0 - 7, with increasing severity.

III

IV