Mortality, morbidity and follow-up after acute poisoning by substances of abuse: a prospective observational cohort study

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Abstract

Aims: Despite the excess mortality and morbidity associated with acute poisoning by substances of abuse, follow-up is frequently not organised. We assessed morbidity, including repeated poisoning, and follow-up after acute poisoning by substances of abuse through charting contacts with health services. We also charted short-term mortality.

Methods: Patients 12 years and older treated for acute poisoning by substances of abuse at a primary care emergency outpatient clinic in Oslo, Norway, were included consecutively from October 2011 through September 2012. We retrieved information from national registers on fatalities, hospital admissions, and contacts at outpatient specialist health services and with general practitioners (GPs), during the 90 days following a poisoning episode.

Results: We included 1731 patients treated for 2343 poisoning episodes. During the 90 days following the poisoning, 31% of the patients were treated at somatic hospitals, 9% admitted to psychiatric hospitals, 37% in treatment at outpatient psychiatric/addiction specialist health services, 55% saw their GP, while 34% had no follow-up. The short-term mortality rate was 2.0%, eight times higher than expected. Increasing age, suicidal intention, opioid poisoning, and severe mental illness were associated with increased risk of death. Increasing age, male gender, opioid poisoning, and severe mental illness were associated with repeated poisoning. Patients with increased risk of repeated poisoning were more likely to be in follow-up at outpatient specialist psychiatric/addiction services and in contact with their GP.

Conclusions: Follow-up measures seem targeted to those most in need, though one out of three had none. The mortality rate calls for concern.

Key words:

Poisoning, intoxication, overdose, substance abuse, substance use disorder, opioids, mortality, morbidity, follow-up, repetition

Word count: 3534 words

Background

Acute poisoning is a risk factor for excess mortality [1]. Among patients with mental disorders, excess mortality was highest among those with substance use disorders, ranging from five to 24 times higher than in the general population [2]. Long-term mortality rates among opioid users range from six to 54 times higher than expected [3, 4]. A tenfold increase in risk of death has been found among injecting heroin users the first month following an overdose [5]. The increased mortality rates are due to both natural and unnatural causes of death [1, 4, 6, 7]. Long-term morbidity is also increased, with raised prevalence of infections, mental illness, cardiovascular disease and respiratory conditions [6]. A Swedish study including 2000 adolescents treated for substance use disorder, found excess mortality over the next 30 years, and an increased risk of mental and physical illness, even when adjusted for continued substance use [8]. Similar findings were reported in a Swiss study of young adults treated for alcohol intoxication [9]. In two Norwegian studies, as many as 30 % of patients treated for acute poisoning repeated within a year, and nine percent of patients treated for acute poisoning by substances of abuse repeated within a week [10, 11]. Apart from studies on repetition rates, we have not found studies on morbidity in the immediate aftermath of an acute poisoning.

Despite the excess mortality and morbidity, follow-up is frequently not organised for patients with acute poisoning related to substance abuse [12, 13]. In a previous study, we found that the patient was referred to specialist psychiatric or addiction treatment services in only ten percent of the cases [14]. However, more patients than the ones referred at the time of the poisoning episode may have been treated in specialist health services, due to previously established contact or referral by other agencies. We are not aware of other studies of the extent of follow-up in specialist health services after acute poisoning by substances of abuse.

Many patients with substance use disorders are regularly in contact with their general practitioner (GP). In a study from the Netherlands, 83 % of patients with alcohol abuse or dependence were managed in primary care [15], while in a Swiss study of patients treated for opiate overdose, 58 % reported regular follow-up by their GP [16]. In contrast, only one out of four patients in our previous study saw their GP within a month of the poisoning episode [14]. However, the time frame may have been too short assess the extent of follow-up by GPs.

Aims

Our main aims were to assess morbidity, including repeated poisoning, and follow-up after acute poisoning by substances of abuse through charting contacts with health services during the first three months. We also charted short-term mortality. Furthermore, we looked for variations related to age, gender, toxic agents, intention, severe mental illness, and homelessness.

Methods

The study was a prospective observational cohort study. Patients were included consecutively from 1 October 2011 to 30 September 2012.

Setting

The study was done at the Oslo Accident and Emergency Outpatient Clinic (OAEOC) in Oslo, Norway. Oslo is the capital city of Norway and had a population of 613 285 as per 1 January 2012 [17]. The Norwegian medical emergency system has two levels. Patients have to be assessed in primary care or by ambulance services before presenting to a hospital. The

OAEOC is the main primary care casualty clinic in Oslo, serving the entire city at all hours. It has about 200 000 consultations a year. It comprises an emergency general practice service, a trauma clinic, a psychiatric emergency service and an emergency social service. Diagnostic resources are limited. The doctors are mostly registrars/residents. The majority of patients with acute poisoning by substances of abuse in Oslo are treated at the OAEOC [18, 19].

Inclusion

All patients 12 years and older treated at the OAEOC for an acute poisoning by substances of abuse were included. All potential substances of abuse were included, encompassing alcohol, prescription drugs, illegal drugs, and others. Patients treated for concomitant conditions were included if the poisoning in itself warranted treatment or observation. We systematically searched the electronic patient lists and included any missed eligible patients. There were 2733 eligible cases. In 174 cases the patient did not have a Norwegian national identity number and was excluded. In 216 cases the patient declined participation. In total, we included 2343 cases in 1731 patients.

Data collection and classification

For all included cases, the doctor treating the patient completed a pre-set registration form. Any information missing in the registration form was gathered, if available, from the electronic medical records. For each case we registered date, age, gender, main toxic agent, homelessness, suicidal intention, and previous history of severe mental illness. Diagnoses of toxic agents were made by the doctor treating the patient based on all available information. The main toxic agent was defined as the one considered most toxic in the doses taken. Main toxic agents were grouped as ethanol, opioids, benzodiazepines, stimulants, gamma-hydroxybutyrate (GHB) and others. In a previous study of the same data material, we found

two distinct groups of patients presenting with ethanol poisoning: Young patients presenting during weekends, usually only once during the inclusion period, and older patients with multiple presentations [18]. We divided the ethanol group accordingly (patients ≤ 30 years and > 30 years at the first presentation to the OAEOC). Suicidal intention was assessed by the doctor treating the patient. Severe mental illness encompassed mainly psychosis, but also bipolar disorder and severe personality disorders, and was assessed by the doctor treating the patient mainly based on information from local medical records and/or information from the patient or the patient's companions. Homelessness was defined as being registered with no permanent address in the National Registry.

Data on contacts with the specialist health services were retrieved from the Norwegian Patient Register (NPR). The NPR registers all patient contacts in Norwegian hospitals and specialist health services. Data on consultations with GPs and primary care casualty clinics were retrieved from the Control and Payment of Reimbursements to Health Service Providers (KUHR) database of the Norwegian Health Economics Administration (HELFO). Norwegian GPs and primary care casualty clinics report all their patient contacts to the KUHR database. Information on deaths during the study period was retrieved from the National Cause of Death Register. The study period was the inclusion period plus the following three months (1 October 2011 – 31 December 2012). As the patients were included consecutively from 1 October 2011 to 30 September 2011, the median potential observation time for fatalities was nine months, ranging from three to 15. All data from the national registers were extracted based on the patient's unique Norwegian national identity number.

From the national registers, we retrieved the number of outpatient consultations in somatic, psychiatric and addiction specialist health services during the 90 days following each

poisoning episode, as well as the number of days admitted to hospital (somatic and psychiatric) and to addiction treatment clinics. We also registered whether the patient was in contact with an opioid substitution treatment (OST) program. Furthermore, we retrieved the number of consultations with GPs and primary care casualty clinics during the same time period. Finally, we retrieved the main diagnosis for each contact/admission, coded in the International Classification of Diseases and Related Health Problems, tenth Edition, (ICD-10) from the NPR, and in the International Classification of Primary Care, second edition, (ICPC-2) from the KUHR database. We grouped the diagnoses as poisoning, substance abuse, psychiatric, infection, injury, and other. A psychiatric diagnosis was defined as any diagnosis of mental and behavioural disorder (ICD-10) or in the psychological chapter (ICPC-2), apart from acute poisoning and substance abuse related diagnoses.

Some patients were treated for poisoning by substances of abuse at the OAEOC several times. The information on contacts with health services was collated for each patient, and each contact was only recorded once. Main toxic agent for a patient was defined as the most frequently diagnosed main toxic agent in that patient's poisoning episodes. For even frequencies we chose the main toxic agent considered most serious, in the following order: opioids, stimulants, GHB, benzodiazepines, ethanol, others. Any overlap between 90-day periods was taken into account, and total time under observation was calculated. If the patient died, observation time was censored at the date of death. Number of contacts and days in hospital were re-calculated if necessary and given per 90 days.

Outcome measures

The main outcome measures were proportions of patients admitted to or in contact with health services during the observation time, number of days admitted or number of contacts during

the observation time, diagnoses at contacts/admissions, fatalities during the study period, and factors associated with death and repeated poisonings. We also calculated standardised mortality ratios (SMR). The number of fatalities in our cohort during the study period was compared to the expected number of fatalities in a group with similar age and gender distribution in the general population, derived from information on deaths in 2012 from Statistics Norway, using five-year age strata [17].

Statistics

Statistics were done in SPSS version 23. Chi-square test was used when comparing proportions. Fisher's exact test was used for expected cell counts less than five. Odds ratios for factors associated with repeated poisoning were estimated using logistic regression analysis. In the univariate analyses we included the following variables: gender, age, main toxic agent, severe mental illness, suicidal intention, homelessness, contact with GP, contact with outpatient psychiatric and/or addiction specialist health services, and enrolment in an OST program. Variables associated with repeated poisoning ($p < 0.20$), were included and adjusted for in the multiple regression analysis. Hazard ratios for factors associated with death during the study period were estimated using Cox regression analysis. In the univariate analyses we used the same variables as in the logistic regression analysis, adding repeated poisoning. Variables associated with death ($p < 0.20$), were included and adjusted for in the multiple regression analysis.

Ethics

The study was performed in accordance with the Helsinki declaration and approved by the Regional Committee South East for Medical and Health Research Ethics (REK nr 2010/1129-

1) and the Oslo University Hospital Information Security and Privacy Office. Participants provided informed verbal consent.

Results

During one year 1731 patients were treated for 2343 episodes of acute poisoning by substances of abuse. Thirty-four (2.0 %) patients died, 275 (16 %) presented with repeated poisoning (Table 1).

In total, 31 % (538/1731) of the patients were treated at somatic hospitals, and nine percent (162/1731) were admitted to psychiatric hospitals (Table 2). Admittance to psychiatric hospital was most frequent among patients with a history of severe mental illness and patients treated for poisoning with suicidal intention, 33 % (61/183) and 36 % (47/130) respectively. Significantly larger proportions among these patients also had contacts at psychiatric outpatient services, 49 % (90/183) and 52 % (67/130) respectively, compared to 17 % (300/1731) in the total material, and larger proportions saw their GP, 69 % (127/183) and 76 % (99/130), compared to 55 % (959/1731). Patients in the benzodiazepine and stimulant groups were also overrepresented among admissions to psychiatric hospital, 27 % (39/144) and 23 % (24/105) respectively, and spent more days admitted, median 10.0 per 90 days (interquartile range 2.0 – 25.0) and 5.9 (1.5 – 27.7), compared to 4.1 (1.0 – 15.1). Patients in the younger ethanol group were generally less in contact with health services than all the other groups. However, the small proportion of three percent (16/458) in the ethanol younger group admitted to psychiatric hospital, were admitted for a long time, 7.5 days (1.0 – 19.5).

Acute poisoning was the main reason for contacts/admissions at casualty clinics and somatic hospitals, 56 % (2913/5223) (Supplementary table 1). The most frequent reasons for GP consultations were substance abuse, 28 % (815/2876), and psychiatric 26 % (759/2876).

In total, 34 % (585/1731) had no follow-up (Table 3). Among the 36 % (629/1731) of patients enrolled in an OST program and/or in treatment at outpatient psychiatric and/or addiction specialist health services, 70 % (441/629) were also in contact with their GP. Among the patients in the opioid group, 56 % (204/364) were enrolled in an OST program, and/or had follow-up at outpatient psychiatric or addiction specialist health services.

Opioid poisoning was associated with multiple poisoning episodes, adjusted odds ratio (AOR) 2.9 (95 % CI 2.1 – 4.1), as was severe mental illness, AOR 2.1 (1.4 – 3.2), and follow-up at outpatient psychiatric and/or addiction specialist health services, AOR 2.4 (1.7 – 3.2), or by GP, AOR 1.7 (1.3 – 2.3) (Table 4).

Among the 34 fatalities during the study period, eleven patients died from unintentional poisoning by substances of abuse. Seven patients committed suicide, among whom three by poisoning. SMR was 7.6 overall, 7.4 among males and 7.9 among females. Risk of death during the study period was particularly increased among patients above the age of 40 years, adjusted hazard ratio (AHR) 5.8 (95 % CI 2.0 – 16.9), with suicidal intention, AHR 4.1 (1.6 – 10.7), treated for opioid poisoning, AHR 2.5 (1.1 – 5.4), and with severe mental illness, AHR 2.3 (1.0 – 5.1) (Table 5).

Discussion

Summary of main findings

During the first three months following an acute poisoning by substances of abuse, 31 % of the patients were treated at a somatic hospital. Nine percent were admitted to a psychiatric hospital. Thirty-six percent of the patients were in treatment at outpatient psychiatric and/or addiction specialist health services and/or enrolled in an OST program, while 55 % saw their GP. However, as many as 34 % of the patients had no follow-up.

The mortality rate among patients recently treated for poisoning by substances of abuse was eight times higher than in the general population. Age above 40 years, poisoning with suicidal intention, opioid poisoning, and a history of severe mental illness were factors associated with increased risk of death. Risk of death was not increased in itself for patients with repeated poisonings, though most factors associated with repeated poisoning also were associated with increased risk of death. Patients with increased risk of repeated poisoning were more likely to be in follow-up at outpatient psychiatric and/or addiction specialist health services and/or in contact with their GP.

Morbidity and mortality

There was considerable excess morbidity among our patients. Nine percent were admitted to a psychiatric hospital. In comparison, previous Norwegian studies have found admission rates in the range of 0.4–1.3 % per year in the general population [20, 21]. In a group of Oslo inhabitants of the same age and gender distribution as our patients, 32 % would be expected to be treated at a somatic hospital per year including outpatient contacts [17], compared to the 31 % per the shorter time frame of three months in our study. The expected proportion of 32 % per year would also include hospital treatment of patients with acute poisoning sent on from

the OAEOC. When including these, the proportion of patients in our study treated at a somatic hospital was 41 %. Furthermore, 31 % of our patients were treated at a primary care casualty clinic at least once during the first three months following the poisoning episode, compared to 14–21 % of Oslo inhabitants between the age of 16 and 66 years during the entire year of 2012 [17].

Acute poisoning was responsible for a large proportion of the somatic morbidity among our patients, measured as contacts with somatic hospitals and primary care casualty clinics. Sixteen percent were treated for acute poisoning by substances of abuse several times during the year of inclusion. Thus, repeated poisoning constitutes a major aspect of substance use related morbidity. Contrary to previous research [22, 23], we did not find an association between repeated poisoning and increased risk of death. Our study may have been underpowered in this respect, due to the short time of observation. However, there was a considerable overlap between the factors associated with increased risk of death and those associated with increased risk of repeated poisoning (Tables 4 & 5).

The SMR of 7.6 was increased in the same range as in previous studies [1, 6], emphasising the risk of substance use resulting in an acute poisoning. Patients treated for opioid poisoning or poisoning with suicidal intention, and patients with severe mental illness, were found to be particularly at risk, also in line with previous studies [2-5, 24].

Follow-up

Two out of three patients were in follow-up at psychiatric and/or addiction specialist health services, including OST programs, and/or by their GP. In at risk patient groups, the proportions in follow-up were even larger, reaching 86 % among patients with severe mental

illness and 91 % among patients treated for poisoning with suicidal intention. In comparison, 60–72 % of Oslo inhabitants between the age of 16 and 66 year saw their GP at least once in 2012 [17], probably including most patients also in follow-up at psychiatric and/or addiction specialist health services. Still, substantial numbers of patients at risk are not in follow-up, as was also the case for one out of four treated for opioid poisoning. The acute poisoning episode is a moment of crisis and an opportunity for initiating or re-establishing follow-up measures [25, 26]. Special effort should be made to reach patients at risk.

Being in contact with psychiatric and/or addiction specialist health services or a GP was associated with repeated poisoning. We find reason to believe that this is a result of follow-up measures reaching the patients in need, rather than of treatment not working. Previous research has found that being in treatment reduces hazardous substance use and hence the risk of excess morbidity and death [27-30].

On a larger scale, preventive measures beyond follow-up initiated at the time of acute poisoning seem necessary. The mortality and morbidity associated with acute poisoning by substances of abuse is a burden on the individual and his/her close relations. The cost to society is considerable. Easy access to treatment, including OST programs, improved housing and work opportunities, and accessible activity centres for youth, are societal measures that could be helpful.

Strengths and limitations

Our study included the majority of patients treated for acute poisoning by substances of abuse in a European capital city. However, about 200 patients with more severe acute poisoning by substances of abuse bypass the OAEOC every year, triaged for direct hospital treatment by

ambulance services [11]. Furthermore, in upwards of 700 cases per year, mostly opioid overdoses, the patient is left on scene after treatment by the ambulance service [19]. Thus, the number of opioid poisonings is underestimated in our study, as ambulance data are not included.

Our data on contacts with specialist health services, primary care casualty clinics and GPs probably are close to complete, as they are retrieved from national registers based on reports necessary for the funding of these services. However, there may be inaccuracies in the reported diagnoses. As we have no data from the ambulance services, the number of patients with repeated poisoning is probably underestimated in our study, especially in the opioid group. It is also possible that the patients declining to be brought to further treatment at the OAEOC are a group of patients with more hazardous substance use and less likely to be in follow-up. If so, our results underestimate the risks of the patients in the opioid group and overestimate the proportion in follow-up.

The SMRs were calculated from deaths during the inclusion period and deaths in the general population in 2012. The median observation time concerning death among included patients was nine months. Accordingly, the SMRs are probably somewhat underestimated.

Previous history of severe mental illness encompassed a number of different diagnoses and was based on the information available there and then. Thus, the prevalence of severe mental illness among our patients is probably underestimated. Diagnoses of toxic agents and suicidal intention were made by the doctor treating the patient. No toxicological laboratory analyses were done, and only one percent of cases were seen by the psychiatric emergency service at

the OAEOC [14]. However, the diagnoses stem from real clinical situations, and the management of the patients was based on them.

We have no data from social services or municipal outreach services. Contact with assertive community treatment teams would show up in our data as outpatient contacts, if run by the specialist health services. Similar teams run by the municipalities do not report to the national registers we used. Some of the patients without follow-up, as defined in our study, probably had follow-up from such municipal agencies, as they aim to take care of patients who for various reasons are unable to attend at outpatient clinics or GP appointments. Social services, however, mainly address problems of daily living and not health problems. On the other hand, GPs or psychiatric and/or addiction specialist health services may be involved also with these patients, as managing patients with complex conditions often requires the involvement of several agencies. Consequently, we do not know how many patients were completely without follow-up.

Conclusion

Patients treated for acute poisoning by substances of abuse had significant excess mortality and morbidity. Though it seems that follow-up measures were targeted to the patients most in need, one out of three had no follow-up, including substantial proportions of at risk patients.

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Conflict of interest

The authors declare that there is no conflict of interest.

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Table 1. Characteristics of patients – main toxic agent groups

	Ethanol younger n (%)	Ethanol older n (%)	Opioids n (%)	Stimulants n (%)	GHB n (%)	Benzodiazepines n (%)	Other n (%)	Total n (%)
Males	239 (52)	361 (70)	281 (77)	78 (74)	67 (79)	74 (51)	36 (59)	1136 (66)
Age[a]	21 (19 – 24)	49 (41 – 58)	36 (28 – 44)	34 (26 – 41)	30 (24 – 37)	35 (25 – 48)	27 (22 – 42)	33 (23 – 46)
Severe mental illness	25 (5)	50 (10)	39 (11)	20 (19)	5 (6)	34 (24)	10 (16)	183 (11)
Suicidal intention[b]	4 (1)	10 (2)	23 (6)	5 (5)	1 (1)	80 (56)	7 (11)	130 (8)
Homeless	3 (1)	16 (3)	52 (14)	4 (4)	3 (4)	4 (3)	1 (3)	83 (5)
Repeated poisoning[c]	19 (4)	87 (17)	121 (33)	22 (21)	11 (13)	13 (9)	2 (3)	275 (16)
Died during study period	0 (-)	13 (3)	14 (4)	2 (2)	1 (1)	4 (3)	0 (-)	34 (2)
Total	458 (100)	514 (100)	364 (100)	105 (100)	85 (100)	144 (100)	61 (100)	1731 (100)

[a]Median (IQR)
[b]Suicidal intention in one or more poisoning episodes at the OAEOC.
[c]Treated more than once for poisoning by substances of abuse at the OAEOC during the inclusion period.
GHB: gamma-hydroxybutyrate. IQR: interquartile range. OAEOC: Oslo Accident and Emergency Outpatient Clinic

Table 2. Contacts with health services – proportions of patients

	GP n (%)	Primary care casualty clinic n (%)	Somatic hospital n (%)	Admitted psychiatric hospital n (%)	Psychiatric outpatient clinic n (%)	Addiction outpatient clinic n (%)	Admitted addiction institution n (%)	Opioid substitution treatment n (%)	Total n (%)
Gender									
Males	576 (51)***	352 (31)	359 (32)	95 (8)	153 (13)***	282 (25)	190 (17)	79 (7)	1136 (100)
Females	382 (64)	186 (31)	176 (30)	67 (11)	147 (25)	129 (22)	86 (14)	34 (6)	595 (100)
Age									
12-30	382 (51)**	203 (27)**	169 (22)***	70 (9)	146 (19)	130 (17)***	82 (11)***	25 (3)***	754 (100)
≥ 31 years	576 (59)	335 (34)	366 (37)	92 (9)	154 (16)	281 (29)	194 (20)	88 (9)	977 (100)
Toxic agent groups[a]									
Ethanol younger	200 (44)	83 (18)	82 (18)	16 (3)	67 (15)	36 (8)	12 (3)	0 (-)	458 (100)
Ethanol older	308 (60)	164 (32)	180 (35)	23 (4)	53 (10)	106 (21)	99 (19)	5 (1)	514 (100)
Opioids	220 (60)	159 (44)	144 (40)	50 (13)	61 (17)	169 (46)	102 (28)	82 (23)	364 (100)
Stimulants	56 (53)	34 (32)	29 (28)	24 (23)	29 (28)	26 (25)	17 (16)	8 (8)	105 (100)
GHB	46 (54)	29 (34)	34 (40)	6 (7)	13 (15)	25 (29)	17 (20)	3 (4)	85 (100)
Benzodiazepines	104 (72)	58 (40)	54 (38)	39 (27)	63 (44)	43 (30)	27 (19)	11 (8)	144 (100)
Other	24 (39)	11 (18)	12 (20)	4 (7)	14 (23)	6 (10)	2 (3)	4 (7)	61 (100)
Severe mental illness									
Yes	127 (69)***	80 (44)***	74 (40)**	61 (33)***	90 (49)***	61 (33)**	47 (26)***	14 (8)	183 (100)
No	831 (54)	458 (30)	461 (30)	101 (7)	210 (14)	350 (23)	229 (15)	99 (6)	1548 (100)
Suicidal intention[b]									
Yes	99 (76)***	54 (42)*	46 (35)	47 (36)***	67 (52)***	39 (30)	27 (21)	10 (8)	130 (100)
No	859 (54)	484 (30)	489 (31)	115 (7)	233 (15)	372 (23)	249 (16)	103 (6.)	1601 (100)
Homeless									
Yes	36 (43)*	36 (43)*	40 (48)**	7 (8)	9 (11)	35 (42)***	21 (25)*	16 (19)***	83 (100)
No	922 (56)	502 (30)	495 (30)	155 (9)	291 (18)	376 (23)	255 (15)	97 (6)	1648 (100)
Repeated poisoning[c]									
Yes	192 (70)***	175 (64)***	145 (53)***	49 (18)***	63 (23)*	138 (50)***	113 (41)***	39 (14)***	275 (100)
No	766 (53)	363 (25)	390 (27)	113 (8)	237 (16)	273 (19)	163 (11)	74 (5)	1456 (100)
Died during study period									
Yes	18 (53)	11 (32)	18 (53)**	7 (21)*	5 (15)	10 (29)	5 (15)	2 (6)	34 (100)
No	940 (55)	527 (31)	517 (30)	155 (9)	295 (17)	401 (24)	271 (16)	111 (7)	1697 (100)
Total	958 (55)	538 (31)	535 (31)[d]	162 (9)	300 (17)	411 (24)	276 (16)	113 (7)	1731 (100)
Number of contacts/days admitted[e]	2.0 (1.0 – 3.0)	1.0 (1.0 – 2.0)	1.5 (1.0 – 3.2)[f]	4.1 (1.0 – 15.1)	3.1 (1.0 – 7.9)	3.0 (1.0 – 6.0)	8.0 (3.0 – 17.0)		

*p < 0.05, **p < 0.01, ***p < 0.001. Comparisons within contact groups.

[a]p < 0.001 for all comparisons across toxic agent groups

[b]Suicidal intention in one or more poisoning episodes at the OAEOC.
[c]Treated more than once for poisoning by substances of abuse at the OAEOC during the inclusion period.
[d]Patients admitted and/or with outpatient contact, excluding admissions/contacts for acute poisoning episodes initially treated at the OAEOC. If these admissions/contact were included, 702/1731 (41%) patients had admissions/contacts at somatic hospitals.
[e]Median (IQR) numbers per 90 days of contacts or days admitted for patients in contact or admitted.
[f]Days admitted. Median number of outpatient contacts 1.0 (IQR 1.0 – 2.0).
GHB: gamma-hydroxybutyrate. GP: general practitioner. IQR: interquartile range. OAEOC: Oslo Accident and Emergency Outpatient Clinic

Table 3. Level of follow-up

	Opioid substitution program n (%)	Outpatient psychiatric/addiction specialist health services n (%)	GP n (%)	None n (%)	Total n (%)
Died during study period	2 (6)	10 (29)	11 (32)	11 (32)	34 (100)
Repeated poisoning[a]	39 (14)	127 (46)	64 (23)	45 (16)	275 (100)
Admitted somatic hospital[b]	55 (11)	200 (39)	138 (27)	115 (23)	508 (100)
Admitted psychiatric hospital	15 (9)	115 (71)	19 (12)	13 (8)	162 (100)
Contact at casualty clinic	51 (9)	226 (42)	160 (30)	101 (19)	538 (100)
Gender					
Females	34 (6)	202 (34)	202 (34)	157 (26)	595 (100)
Males	79 (7)	314 (28)	315 (28)	428 (38)	1136 (100)
Age					
12-30 years	25 (3)	222 (29)	209 (28)	298 (40)	754 (100)
> 30 years	88 (9)	294 (30)	308 (32)	287 (29)	977 (100)
Toxic agent groups					
Ethanol younger	0 (0)	89 (19)	142 (31)	227 (50)	458 (100)
Ethanol older	5 (1)	133 (26)	204 (40)	172 (33)	514 (100)
Opioids	82 (23)	122 (34)	77 (21)	83 (23)	364 (100)
Stimulants	8 (8)	40 (38)	23 (22)	34 (32)	105 (100)
GHB	3 (4)	31 (36)	23 (27)	28 (33)	85 (100)
Benzodiazepines	11 (8)	86 (60)	31 (22)	16 (11)	144 (100)
Other	4 (7)	15 (25)	17 (28)	25 (41)	61 (100)
Severe mental illness	14 (8)	115 (63)	29 (16)	25 (14)	183 (100)
Suicidal intention[c]	10 (8)	82 (63)	26 (20)	12 (9)	130 (100)
Homelessness	16 (19)	23 (28)	12 (14)	32 (39)	83 (100)
Total	113 (7)[d]	516 (30)[e]	517 (30)	585 (34)	1731 (100)

[a]Treated more than once for poisoning by substances of abuse at the OAEOC during the inclusion period.
[b]Including patients admitted from the OAEOC at acute poisoning episode, excluding patients with outpatient contacts only.
[c]Suicidal intention in one or more poisoning episodes at the OAEOC.
[d]110 of these patients were also in contact with outpatient psychiatric/addiction specialist health services, 84 patients had contact with their GP.
[e]357 of these patients also had contact with their GP.
GHB: gamma-hydroxybutyrate. GP: general practitioner. OAEOC: Oslo Accident and Emergency Outpatient Clinic

Table 4. Factors associated with multiple poisonings during the inclusion period – logistic regression analysis

	Cases total n	Multiple poisonings n (%)	Crude			Adjusted		
			Odds ratio	95 % CI	p-value	Odds ratio	95 % CI	p-value
Gender								
Females	595	72 (12)	1			1		
Males	1136	203 (18)	1.6	1.2 – 2.1	0.002	**1.4**	1.0 – 2.0	0.025
Age								
12-30 years	754	78 (10)	1			1		
31-40 years	354	69 (19)	2.1	1.5 – 3.0	< 0.001	1.4	0.98 – 2.1	0.065
> 40 years	623	128 (21)	2.2	1.7 – 3.0	< 0.001	**1.9**	1.4 – 2.7	< 0.001
Main toxic agent								
Ethanol	972	106 (11)	1			1		
Opioids	364	121 (33)	4.1	3.0 – 5.5	< 0.001	**2.9**	2.1 – 4.1	< 0.001
Stimulants	105	22 (21)	2.2	1.3 – 3.6	0.003	1.7	0.98 – 2.9	0.062
GHB	85	11 (13)	1.2	0.63 – 2.4	0.57	1.2	0.59 – 2.4	0.63
Benzodiazepines	144	13 (9)	0.81	0.44 – 1.5	0.50	**0.47**	0.25 – 0.88	0.019
Other	61	2 (3)	0.28	0.07 – 1.2	0.077	0.26	0.06 – 1.1	0.068
Severe mental illness[a]	183	55 (30)	2.6	1.8 – 3.7	< 0.001	**2.1**	1.4 – 3.2	< 0.001
Homelessness[a]	83	27 (33)	2.7	1.7 – 4.4	< 0.001	1.5	0.90 – 2.6	0.11
GP contact[a]	958	192 (20)	2.1	1.6 – 2.8	< 0.001	**1.7**	1.3 – 2.3	0.001
Specialist health services[a,b]	626	165 (26)	3.2	2.5 – 4.2	< 0.001	**2.4**	1.7 – 3.2	< 0.001
Enrolled in OST[a]	113	39 (35)	3.1	2.0 – 4.7	< 0.001	0.91	0.55 – 1.5	0.69
Total	1731	275 (16)						

Odds ratios adjusted for the variables in the table. Adjusted odds ratios for significant associations are shown in bold types.
In the univariate analysis, no association was found between multiple poisonings and suicidal intention in one or more poisonings ($p \geq 0.20$).
[a]Reference groups were no history of severe mental illness, not being homeless, no contact with GP, no contact with outpatient psychiatric and/or addiction specialist health services, and not being enrolled in an OST program.
[b]Contact with outpatient psychiatric and/or addiction specialist health services.
CI: confidence interval. GHB: gamma-hydroxybutyrate. GP: general practitioner. OST: opioid substitution treatment program.

Table 5. Factors associated with death during the study period – Cox regression analysis

	Cases total	Death	Crude			Adjusted		
	n	n (%)	Hazard ratio	95 % CI	p-value	Hazard ratio	95 % CI	p-value
Gender								
Females	595	8 (1.3)	1					
Males	1136	26 (2.3)	1.7	0.78 – 3.8	0.18	1.6	0.72 – 3.8	0.24
Age								
12-30 years	754	4 (0.5)	1			1		
31-40 years	354	7 (2.0)	3.7	1.1 – 12.7	0.036	2.5	0.72 – 8.8	0.15
> 40 years	623	23 (3.7)	6.9	2.4 – 19.9	< 0.001	**5.8**	2.0 – 16.9	0.001
Main toxic agent								
Ethanol	972	13 (1.3)	1			1		
Opioids	364	14 (3.8)	3.0	1.4 – 6.4	0.004	**2.5**	1.1 – 5.4	0.025
Stimulants	105	2 (1.9)	1.5	0.33 – 6.6	0.61	1.4	0.31 – 6.3	0.67
GHB	85	1 (1.2)	0.92	0.12 – 7.0	0.94	1.4	0.17 – 11.3	0.75
Benzodiazepines	144	4 (2.8)	2.1	0.68 – 6.4	0.20	0.77	0.20 – 2.9	0.70
Other	61	0	< 0.001	-	0.98	< 0.001	-	0.98
Severe mental illness[a]	183	8 (4.4)	2.5	1.2 – 5.6	0.021	**2.3**	1.0 – 5.1	0.049
Suicidal intention[a,b]	130	8 (6.2)	3.6	1.6 – 8.0	0.001	**4.1**	1.6 – 10.7	0.004
Total	1731	34 (2.0)						

Hazard ratios adjusted for the variables in the table. Adjusted hazard ratios for significant associations are shown in bold types.
Median time under observation was 267 days, range one to 456 days.
In the univariate analysis, no association was found between death and homelessness, repeated poisoning, contact with GP, contact with outpatient psychiatric and/or addiction specialist health services, or enrolment in an OST program ($p \geq 0.20$).
[a]Reference groups were no history of severe mental illness, and no suicidal intention in any poisoning.
[b]Suicidal intention in one or more poisonings.
CI: confidence interval. GHB: gamma-hydroxybutyrate. GP: general practitioner. OST: opioid substitution treatment program.

Supplementary table 1. Main diagnosis at contacts and admissions

Diagnosis	GP contacts	Primary care casualty clinic contacts	Somatic hospital admissions and outpatient contacts	Psychiatric hospital admissions and outpatient contacts	Addiction treatment admissions and outpatient contacts
Poisoning	43 (1)	2475 (67)	438 (29)	22 (1)	2 (0.1)
Substance abuse	815 (28)	251 (7)	80 (5)	446 (21)	2364 (82)
Psychiatric[a]	759 (26)	196 (5)	13 (1)	1154 (53)	237 (8)
Infection	199 (7)	154 (4)	153 (10)	-	-
Injury	91 (3)	269 (7)	134 (9)	-	-
Other	969 (34)	366 (10)	694 (46)	552 (25)[b]	288 (10)
Total	2876 (100)	3711 (100)[c]	1512 (100)[d]	2174 (100)[e]	2891 (100)

[a]Any diagnosis of mental and behavioural disorder (ICD-10, chapter F) or in the psychological chapter P of ICPC-2, apart from substance abuse related diagnoses and acute poisoning.
[b]The majority of these were Z00.4 (ICD-10) General psychiatric examination.
[c]Including 2343 poisoning episodes treated at the OAEOC.
[d]Including 342 poisoning episodes treated at the OAEOC in which the patient was sent on to somatic hospital.
[e]Including 49 poisoning episodes treated at the OAEOC in which the patient was sent on to psychiatric hospital.
GP: general practitioner. ICD-10: International Classification of Diseases and Related Health Problems, tenth edition. ICPC-2: International Classification of Primary Care, second edition.
OAEOC: Oslo Accident and Emergency Outpatient Clinic