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Risk factors for the need for advanced care among prescription and over-the-counter drug overdose patients

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Abstract

Aim: Prescription drug and over-the-counter (OTC) drug overdose is a major problem in emergency departments in Japan, and some need advanced care which is more than observation. We aimed to identify the prehospital risk factors for the need of advanced care among overdose patients.

Methods: This was a single-center retrospective cohort study. We included overdoses patients of prescription drugs or OTC drugs, who admitted to our hospital between 2016 and 2021. We grouped them into advanced care and non-advanced care. The main outcome was the need for advanced care. We performed a multiple logistic regression analysis, calculated the PAV score (**P**aracetamol use, **A**lcohol use, abnormal **V**ital signs on scene) and performed a receiver operating characteristic (ROC) analysis.

Results: There were 229 subjects. The logistic regression analysis revealed that alcohol, paracetamol, and the abnormal vital signs on scene were associated with advanced care (alcohol-odds ratio [OR]: 2.95; 95% confidence interval [CI]: 1.29–6.75; paracetamol-OR: 5.47; 95% CI: 2.18–13.71; abnormal vital signs-OR: 4.61, 95% CI: 2.07–10.27). The rate of advanced care in the high PAV score (2 and 3) group was statistically higher than that in the low PAV score (0–1) group ($p = 0.04$). Area under the ROC curve of the PAV score was 0.72 (95% CI, 0.65–0.80).

Conclusion: Alcohol, paracetamol use and abnormal vital signs on scene might be risk factors for advanced care among prescription drugs or OTC drugs overdose patients, and the PAV score may predict the need for advanced care.

KEYWORDS
acetaminophen, advanced care, alcohol, overdose, paracetamol

INTRODUCTION

Drug overdose is a major problem seen in emergency departments (ED) worldwide. It is commonly associated with mental illness or suicide attempts, and results in significant morbidity and mortality. Therefore, it is not only a health problem but a social and economic issue.[1,2] The severity of drug overdose varies from the patients who need care for just a short observational hospital stay to the patients who need advanced care.[3–5] In addition, the patients hospitalized for observation sometimes deteriorate into a critical illness due to complications from the drug overdose that occur after hospital admission. Therefore, it is important to judge the severity early in the course among drug overdose patients.

As drug overdose is an important social issue, there have been many studies on the prevalence and mortality of drug overdose,[1,5,6] and some of these studies focused on

the risk factors for a drug overdose.[7,8] Other previous studies demonstrated the risk factors for complications or death caused by drug overdose, and most of them reported on the specific type of drugs involved, such as paracetamol[9] or opioids,[10] which are common and highly toxic in large doses. Regarding grading the severity of drug overdoses, some studies, including the poisoning severity score developed by the International Programme on Chemical Safety and the Swedish Poisons Information Service, suggested that the clinical parameters and symptoms available in the ED could be used to predict which patients would require treatment in medium care units or intensive care units.[11–15]

Many kinds of prescription drugs and over-the-counter (OTC) drugs can be a cause of overdose, and we often encounter a situation where the types and amounts of the causative drugs are unknown in the ED. Frequently, the drugs involved in overdose are some combination of benzodiazepines, antipsychotics, antidepressants, and OTC drugs.[4] However, opioids are less commonly involved in overdose in Japan than in some other Western countries. Accordingly, a method to determine the severity of drug overdose regardless of the type and amount of medicines can be useful in the ED. Moreover, most previous attempts to create a severity grading scale used in-hospital information to predict mortality and the need for intensive care. In contrast, we tried to predict whether the overdose patient is severely ill or will require advanced care which is more than observation using prehospital factors in order to help the emergency medical service (EMS) providers in deciding which hospital the patient should be transported to. Using prehospital information to decide where patients should be transported to can patient overflows and lower medical costs.[4,11] We hypothesized that the vital sign on scene was the most important risk factor obtained by EMS providers to judge the severity of overdose patients. The aim of current study was to identify the prehospital risk factors for server overdose and the need of advanced care treatment for prescription drug and OTC drug overdoses.

MATERIALS AND METHODS

Ethics approval and consent to participate

The ethics committee of the Nippon Medical School Tama Nagayama Hospital approved the present study (committee reference number: No. F-2022-001). The requirement for written informed consent was waived since we analyzed anonymous data, so, participation of patients was obtained through an opt-out methodology. A detail information on the study and opt-out form was posted in front of the ED.

Study design

The current study was single-center retrospective cohort study using the medical records of the emergency and critical care medicine department of Nippon Medical School Tama Nagayama Hospital, which is a tertiary referral hospital in Japan and is a located at a rural area in the southwest of Tokyo.

Participants

We included all patients diagnosed as suffering an overdose of a prescription or OTC drug who were transported to our ED and admitted our hospital between 1 January 2016 and 31 December 2021, and they were followed up until hospital discharge. Overdose patients with other severe diseases or injuries were excluded.

Outcome measures

The main outcome measure was the need of the advanced care for drug overdose.

Definitions and data collection

The main outcome measure was the need of admission for advanced care which was more than that of medical admission for ongoing monitoring and follow up testing. In accordance with previous studies, the information on the following advanced care treatments for drug overdose were gathered: the use of vasopressor, flumazenil, antiarrhythmic agents, sedative drugs, N-acetylcysteine and vitamin C; as well as treatments for acute kidney injury, deep venous thrombosis, hypoglycemia, and rhabdomyolysis, the use of nasal airway, mechanical ventilation therapy, cricothyroid puncture, continuous hemodiafiltration, hemodialysis, direct hemoperfusion, hemodiafiltration, and cardiopulmonary resuscitation.[6,11,16] We defined the patients who were underwent the above cares during hospitalization as the advanced care group, and the patients who received an ongoing monitoring and an intravenous drip during the hospital stay as non-advanced care group.

Abnormality of vital signs on scene was judged present if the patients met any of the following criteria: 100, 200 or 300 on the Japan coma scale[17] (the patients could not be aroused with some stimuli), oxygen saturation under 90%, systolic blood pressure under 90 mmHg, respiratory rate under 10 or over 29, or pulse rate under 50 or over 120.

Determining the actual number of tablets ingested was a difficult task. Therefore, we classified the number of tablets into three groups using a roughly estimated number: under 50, from 50 to 99, and over 99. Similarly, we divided the patients into two groups according to age: under 65 years, and 65 years and over.

A simple score that consists of three factors were calculated: **P**aracetamol use, **A**lcohol intake, and abnormal **V**ital signs on scene. We called this the PAV score and possible scores range from 0 to 3.

Statistical analysis

The patients were divided into two groups: patients who needed advanced care and patients who did not need advanced care, and the backgrounds and the treatments were compared between two. We used the Chi-squared test or Fisher's test for categorical variables, and Student's *t*-test or Mann–Whitney *U* test for continuous variables, as appropriate. Since the data were not normally distributed, numerical values are expressed as median (interquartile range [IQR]).

Next, multiple imputations were performed in order to decrease the bias caused by incomplete data; each missing value was replaced with a set of 5 substitute plausible values, then the models were constructed for each imputed dataset and a single model was made by statistical inference with the 5 imputed datasets.[18–21] After multiple imputations, the risk factor for the advanced care was analyzed, using a logistic regression analysis on the advanced treatment adjusted for sex, age ≥65, abnormal of vital signs on the scene, alcohol intake with drugs, paracetamol use, and the number of tablets. These clinically suitable variables were selected in accordance with previous studies.[12–14]

Moreover, we added the PAV score, which consisted of the three factors that showed a strong relationship between drug overdose and advanced care, to the logistic regression analysis. Then, Receiver Operating Characteristic (ROC) analysis was performed with the estimation of the corresponding area under the curve (AUC) to evaluate the scores.

RESULTS

Among 6728 patients admitted to our ED during the study period, 231 were admitted for drug overdose. Two patients were excluded: one was admitted for drug overdose but subsequently died from cancer, and the other was diagnosed with a lumbar burst fracture due to a fall after ingesting drugs. The final study population was 229 patients (Figure 1). Among these 55 patients (24.0%) needed advanced care to treat drug overdose.

The patients' characteristics are shown in Table 1. There were statistically significant differences for abnormal vital signs on scene, and the patients who consumed alcohol with drugs between the non- advanced care group and the advanced care group (48.2% vs. 76.4%, $p < 0.01$; 11.5% vs. 25.5%, $p = 0.01$, respectively). However, the rates of recurrence episodes of overdose and a history of previous mental illness did not differ between the two groups (14.4% vs. 7.3%, $p = 0.17$; 81.6% vs. 76.4%, $p = 0.39$, respectively). The maximum dose was 600 tablets in the non- advanced care group, and 809 tablets in the advanced care group. The median number of the tablets was 86 (IQR: 67–132) in the non- advanced care group and 88 (IQR: 58–174) in the advanced care group and this was not significantly different ($p = 0.12$).

Regarding mortality, no one died in the non-advanced care group; however, two patients died in the advanced care group (0% vs. 3.6%, $p = 0.01$). The causative agents are shown

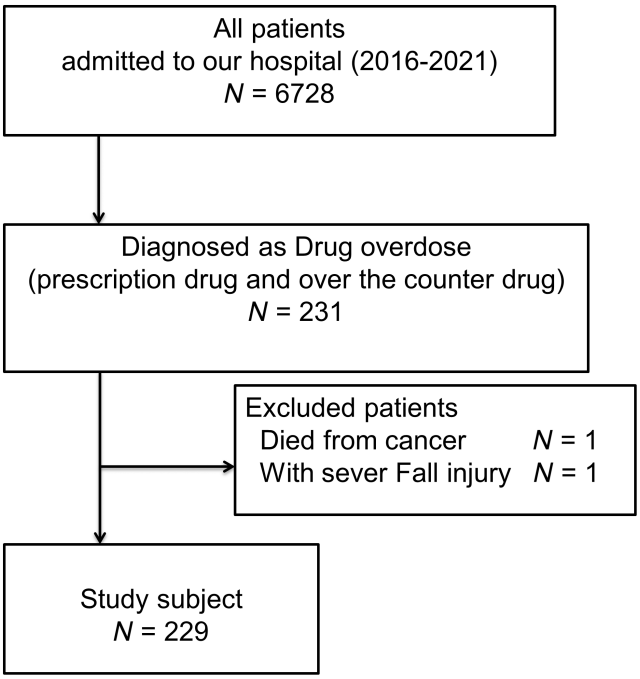

FIGURE 1 Patient selection.

in Table 2. Benzodiazepine was most often detected (49.3%) in the current study. Table 3 shows the details of advanced care. Charcoal was most often undergone (54.5%) and the mechanical ventilation therapy was performed for 32.7% of advanced care group.

In Table 4, the logistic regression analysis after multiple imputations revealed that alcohol, paracetamol, and the abnormal vital signs on scene with overdose were associated with the need for advanced care (alcohol-odds ratio [OR]: 2.95; 95% confidence interval [CI]: 1.29–6.75; paracetamol use-OR: 5.47; 95% CI: 2.18–13.71; abnormal vital signs-OR: 4.61, 95% CI: 2.07–10.27). Age over 65, sex, the number of tablets ≥100 and 50–99 compared with <50 were not associated with the need for advanced care (OR: 1.61, 95% CI: 0.41–6.29; OR: 0.93, 95% CI: 0.42–2.05; OR: 0.64, 95% CI: 0.16–2.49; OR: 0.29, 95% CI: 0.08–1.06).

The PAV score ranged from 0 to 3, and the rate of advanced care in the high PAV score (2 and 3) group was statistically higher than that in the low PAV score (0–1) group (57.1% vs 18.4%, $p = 0.04$) (Figure 2). We grouped PAV scores of 2 and 3 together because there was only one patient with a PAV score of 3. The ROC curve showed that the PAV score had an AUC of 0.72 (95% CI, 0.65–0.80; Figure 3).

DISCUSSION

The current study suggests that among patients who overdose on prescription or OTC drugs, paracetamol use, drinking alcohol with drugs, or having abnormal vital signs on scene (i.e., before admission to the hospital) might is correlated with the need for advanced care after admission to the hospital. On the other hand, advanced age, sex, and the dose

TABLE 1 Demographics and clinical characteristics of drug overdose patients.

Variables	Non-advanced care ($n = 174$)	Advanced care ($n = 55$)	p-value
Age, years	39 (24–47)	42 (30–54)	0.04
Age < 18, years	7/174 (4.0)	3/55 (5.5)	0.65
Age > 65, years	8/174 (4.6)	5/55 (9.1)	0.21
Male	43/174 (24.7)	16/55 (29.1)	0.52
Psychiatric disease	142/174 (81.6)	42/55 (76.4)	0.39
Recurrence episode of overdose	25/174 (14.4)	4/55 (7.3)	0.17
Abnormality of vital signs on scene	82/170 (48.2)	42/55 (76.4)	<0.01
Apparent suicide attempt	73/174 (42.0)	21/55 (38.2)	0.62
Alcohol use	20/174 (11.5)	14/55 (25.5)	0.01
Known number of the tablets	86 (67–132)	88 (58–174)	0.12
Unknown number of the tablets	13/173 (7.5)	9/53 (17.0)	0.04
Including over-the-counter drug	35/174 (20.1)	17/55 (30.9)	0.10
Including paracetamol	15/174 (8.6)	14/55 (25.5)	<0.01
Including benzodiazepine	91/174 (52.3)	22/55 (40.0)	0.12

Note: Data are shown as the number of positive observations/total number of observations (%) or as median (interquartile range).For each variable, the number of missing observations can be obtained as the difference between the total number of patients in each category and the total number of observations.

TABLE 2 List of causative drugs.

	$N = 229$	%
Benzodiazepine	113	49.3
Atypical antipsychotic	74	32.3
Antidepressant	42	18.3
Non-benzodiazepine	41	17.9
Thienodiazepine	38	16.6
Paracetamol	29	12.7
Anticonvulsant	29	12.7
NSAID	25	10.8
Typical antipsychotic	23	10.0
Caffeine	19	8.3
Other hypnotics	17	7.4
Lithium	11	4.8
Barbiturate	9	3.9
Pregabalin	7	3.1
Antihistamine	6	2.6
Anticholinergic agent	3	1.3
Bromovaleryl urea	3	1.3
Others	6	2.6

Abbreviation: NSAID, Non-steroidal anti-inflammatory drug.

TABLE 3 Details of advanced care.

Variables	Advanced care ($n = 55$)
Charcoal	30 (54.5)
Mechanical ventilation	18 (32.7)
Antibiotic agents	13 (23.6)
N-acetylcysteine	13 (23.6)
Vasopressor	6 (10.9)
Oxygenation	5 (9.1)
Sedative drugs for agitation	5 (9.1)
Continuous hemodiafiltration	4 (7.3)
Nasal airway	4 (7.3)
Treatments for rhabdomyolysis	4 (7.3)
Cardiopulmonary resuscitation	3 (5.5)
Treatments for hypoglycemia	3 (5.5)
Flumazenil	2 (3.6)
Hemodialysis	2 (3.6)
Antiarrhythmic agents	1 (1.8)
Cricothyroid puncture	1 (1.8)
Treatments for deep venous thrombosis	1 (1.8)
Direct hemoperfusion	1 (1.8)
Milk	1 (1.8)
Vitamin C	1 (1.8)

Note: Data are shown as the number of positive observations/total number of observations (%).

of medicines were not significantly related to the need for advanced care.

The novel point of the current study was our attempt to identify factors that predict the severity of prescription and OTC drug overdose using prehospital factors. Death from drug overdose has been steadily increasing and remains a major public health problem.[1,2,22] Therefore, many previous studies focused on the risk of suffering an overdose[7,8,23,24] or the epidemiological aspects of overdose a social viewpoint.[1,2,5,22] Around 70% of drug overdose deaths in the United States are related to opioids[25]; however, opioid overdose is very rare in Japan. Accordingly, we adopted the need

TABLE 4 Logistic regression analysis for the need of advanced care among drug overdose patients.

	Original data set			After multiple imputations		
	Odds ratio	95%CI	*p*-value	Odds ratio	95%CI	*p*-value
Age ≥ 65 years old	5.29	0.84–33.51	0.08	1.61	0.41–6.29	0.49
Age < 64 years old (Reference)	1			1		
Male	0.89	0.37–2.14	0.79	0.93	0.42–2.05	0.86
Female (Reference)	1			1		
Abnormal vital signs on scene	3.29	1.44–7.53	<0.01	4.71	2.12–10.47	<0.01
Normal vital signs on scene (Reference)	1			1		
Alcohol intake	2.86	1.15–7.08	0.02	3.32	1.43–7.73	0.01
Without alcohol intake (Reference)	1			1		
Paracetamol intake	5.91	2.29–15.25	<0.01	5.74	2.25–14.66	<0.01
Without paracetamol intake (Reference)	1			1		
Number of tablets ≥100	0.67	0.20–2.26	0.52	0.64	0.16–2.49	0.51
50–99	0.34	0.10–1.13	0.08	0.29	0.08–1.06	0.06
< 50 (Reference)	1			1		

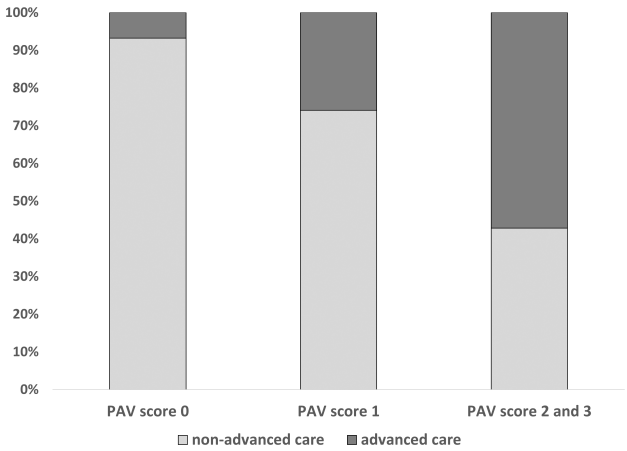

FIGURE 2 The rate of advanced care based on PAV score.

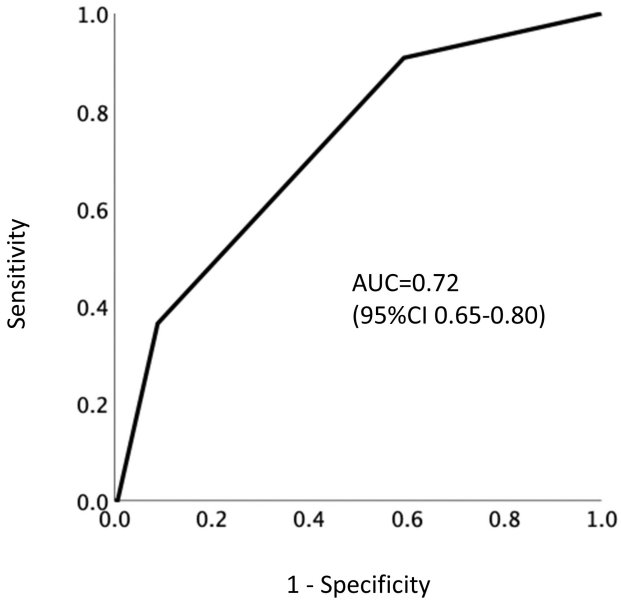

FIGURE 3 ROC curve for PAV score.

for critical care treatment as a severity marker instead of mortality. Shastry et al.[3] reported that almost one-fifth of low-risk drug overdose patients require additional medical management after the ED in observation units. That is to say, there is need for additional medical management for all overdose patients. Therefore, we focused on predicting the severity of drug overdose patients. In order to decrease in the burden incurred by overdose patients on ED, we created the PAV score, which is an assessment tool to judge the severity of an overdose on scene. We feel that this might help identify patients who will need advanced care and might help ambulance personnel to judge the appropriate hospital to which to transport the patient. The prehospital factors which make up the PAV score are easily assessed by ambulance staff, making it a useful and practical scoring system.

Another interesting result of this study was the effect of alcohol. Patients who took excessive doses of prescription medicines or OTC drugs along with alcohol received advanced care more frequently than those who did not consume alcohol. Votaw et al.[26] previously reviewed benzodiazepine misuse and found that alcohol use increase the risk of benzodiazepine misuse and benzodiazepine-related overdoses, and taking benzodiazepines along with alcohol resulted in reinforcement of the intoxicating effects of both substances. Around 50% of the patients consumed benzodiazepines and other hypnotics, suggesting that alcohol is consumed to heighten the side effect of these drugs.

The current study showed that paracetamol was a risk factor for the need for advanced care. Paracetamol, or

acetaminophen, is the most common non-prescription analgesic in the world, and frequently used for suicide attempts due to its easy availability.[9,27] A study performed by Jeong et al.[28] gave some insights into this situation. They reported that the ingested dose of paracetamol exceeds 150 mg/kg, then N-acetylcysteine treatment should be used to prevent hepatotoxicity is safe when the paracetamol concentration cannot be measured. In Japan, major OTC drugs and prescription drugs contain from 80 mg to 300 mg of paracetamol per tablet. The average adult body weight in Japan is around 50 kg for females and around 65 kg for males. When patients ingest 50 paracetamol tablets (200 mg of paracetamol), it probably results in over 150 mg/kg and they need N-acetylcysteine treatment and observation.

In the current study, the quantity of the tablets (≥100 and 50–99 compared with <50) was not associated with the need for advanced care. This may be attributed to the fact that the causative drugs involved included only a few with dose-dependent lethal side effects, such as lithium or tricyclic antidepressants. Although, the type of causative drugs could potentially influence the results of this study, this factor was not considered in our analysis.

LIMITATIONS

The current study has some limitations. First, this study was a single-center study with a small number of subjects. Therefore, it might have limited predictive power. For example, our study's findings regarding the lack of significant differences in recurrence episodes of overdose and history of previous mental illness between groups should be interpreted with caution due to the small sample size. This limitation restricts our ability to conduct a comprehensive analysis of these factors. Future research, ideally through multicenter studies with larger cohorts, is necessary to explore these important aspects more thoroughly. Second, our study did not include opioid overdose patients. So, the patients' backgrounds, the complications or the prognosis could be different from other countries. Third, the trends of prescription drugs have changed. For example, Selective Serotonin Reuptake Inhibitors are safer and more often used for depression than tricyclic antidepressants, and benzodiazepines are being replaced by non-benzodiazepine hypnotics. These changing trends could influence the outcomes of drug overdoses, but we did not account for this factor.

CONCLUSIONS

Our study suggests that prescription and OTC drug overdose patients who drink alcohol, take paracetamol, and have abnormal vital signs on scene are more likely to need advanced treatment. Moreover, our PAV (Paracetamol, Alcohol, and abnormal Vital signs on scene) score could be helpful to assess the severity of an overdose. Further large validation studies are needed to confirm our results.

ACKNOWLEDGMENTS

Not applicable.

CONFLICT OF INTEREST STATEMENT

The authors declare that they have no competing interests.

DATA AVAILABILITY STATEMENT

The dataset generated and analyzed during the current study are available from the corresponding author on reasonable request.

ETHICS STATEMENT

The ethics committee of the Nippon Medical School Tama Nagayama Hospital approved the present study (committee reference number: No. F-2022-001). The requirement for written informed consent was waived since we analyzed anonymous data, so, participation of patients was obtained through an opt-out methodology. A detail information on the study and opt-out form was posted in front of the ED.

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REFERENCES

1. Rudolph KE, Kinnard EN, Aguirre AR, Goin DE, Feelemyer J, Fink D, et al. The relative economy and drug overdose deaths. Epidemiology. 2020;31(4):551–8.
2. Hedegaard H, Fau-Miniño AM, Miniño Am Fau-Warner M, Warner M. Urban-rural differences in drug overdose death rates, by sex, age, and type of drugs involved, 2017. Vol 345. NCHS Data Brief; 2019. p. 1–8.
3. Shastry S, Yeo J, Richardson LD, Manini AF. Observation unit management of low-risk emergency department patients with acute drug overdose. Clin Toxicol (Phila). 2020;58(7):773–6. [published Online First: 20190925].
4. Okazaki Y, Shimojo N, Matsuishi Y, Hoshino H, Ouchi A, Kawano S, et al. Risk factors for prolonged intensive care unit and hospital stay among patients with acute drug overdose in Japan. Acute Med Surg. 2020;7(1):e482 [published Online First: 20200120].
5. Glei DA-O, Preston SH. Estimating the impact of drug use on US mortality, 1999-2016. PloS One. 2020;15(1):e0226732.
6. Mokhlesi B, Leiken JB, Murray P, Corbridge TC. Adult toxicology in critical care: part I: general approach to the intoxicated patient. Chest. 2003;123(2):577–92.
7. Lee EH, Park JO, Cho JP, Lee CA. Prioritising risk factors for prescription drug overdose among older adults in South Korea: a multimethod study. Int J Environ Res Public Health. 2021;18(11):5948.
8. Daly CA-O, Griffin E, McMahon E, Corcoran P, Webb RT, Witt K, et al. Repeat self-harm following hospital-presenting intentional drug overdose among young people-a National Registry Study. Int J Environ Res Public Health. 2020;17(17):6159. https://doi.org/10.3390/ijerph17176159
9. Popiolek I, Hydzik P, Jagielski PA-O, Zrodlowska M, Mystek K, Porebski G. Risk factors for hepatotoxicity due to paracetamol overdose in adults. Medicina (Kaunas). 2021;57(8):752. https://doi.org/10.3390/medicina57080752
10. Foglia R, Kline A, Cooperman NA-O. New and emerging opioid overdose risk factors. Curr Addict Rep. 2021;8:319–29.
11. van den Oever HLA, van Dam M, van 't Riet E, Jansman FGA. Clinical parameters that predict the need for medium or intensive care admission in intentional drug overdose patients: a retrospective cohort study. J Crit Care. 2017;37:156–61. [published Online First: 2016 Sep 28].

12. Persson HE, Sjöberg GK, Haines JA, Pronczuk de Garbino J. Poisoning severity score. Grading of acute poisoning. J Toxicol Clin Toxicol. 1998;36(3):205–13.
13. Meulendijks CF, van den Berg EF, Fortuyn HD, Fortuyn H, Verkes RJ, van der Wilt GJ, et al. Predicting the need for hospital admission in patients with intentional drug overdose. Neth J Med. 2003;61(5):164–7.
14. Eizadi Mood N, Sabzghabaee AM, Khalili-Dehkordi Z, Khalili-Dehkordi Z. Applicability of different scoring systems in outcome prediction of patients with mixed drug poisoning-induced coma. Indian J Anaesth. 2011;55(6):599–604.
15. Liisanantti JH, Ohtonen P, Kiviniemi O, Kiviniemi O, Laurila JJ, Ala-Kokko TI. Risk factors for prolonged intensive care unit stay and hospital mortality in acute drug-poisoned patients: an evaluation of the physiologic and laboratory parameters on admission. J Crit Care. 2011;26(2):160–5. [published Online First: 2010 Oct 30.].
16. Zimmerman JL. Poisonings and overdoses in the intensive care unit: general and specific management issues. Crit Care Med. 2003;31(12):2794–801.
17. Chikuda H, Yasunaga H, Takeshita K, Horiguchi H, Kawaguchi H, Ohe K, et al. Mortality and morbidity after high-dose methylprednisolone treatment in patients with acute cervical spinal cord injury: a propensity-matched analysis using a nationwide administrative database. Emerg Med J. 2014;31(3):201–6.
18. Little RJ, D'Agostino R, Cohen ML, Dickersin K, Emerson SS, Farrar JT, et al. The prevention and treatment of missing data in clinical trials. N Engl J Med. 2012;367:1355–60.
19. Janssen KJ, Donders AR, Harrell FE Jr, Vergouwe Y, Chen Q, Grobbee DE, et al. Missing covariate data in medical research: to impute is better than to ignore. J Clin Epidemiol. 2010;63(7):721–7.
20. Tanaka C, Tagami T, Kaneko J, Fukuda R, Nakayama F, Sato S, et al. Early versus late surgery after cervical spinal cord injury: a Japanese nationwide trauma database study. J Orthop Surg Res. 2019;14(1):302 [published Online First: 2019/09/07].
21. Tanaka C, Tagami T, Nakayama F, Kudo S, Takehara A, Fukuda R, et al. Association between mortality and age among mechanically ventilated COVID-19 patients: a Japanese nationwide COVID-19 database study. Ann Intensive Care. 2021;11(1):171.
22. Chihara I, Ae R, Kudo Y, Uehara R, Makino N, Matsubara Y, et al. Suicidal patients presenting to secondary and tertiary emergency departments and referral to a psychiatrist: a population-based descriptive study from Japan. BMC Psychiatry. 2018;18(112):112.
23. Yule AM, Carrellas NW, Fitzgerald M, McKowen JW, Nargiso JE, Bergman BG, et al. Risk factors for overdose in treatment-seeking youth with substance use disorders. J Clin Psychiatry. 2018;79(3):17m11678. https://doi.org/10.4088/JCP.17m11678 [published Online First: 17m11678].
24. Lyons RM, Yule AM, Schiff D, Bagley SM, Wilens TE. Risk factors for drug overdose in young people: a systematic review of the literature. J Child Adolesc Psychopharmacol. 2019;29(7):487–97.
25. Wilson N, Kariisa M, Kariisa M, Seth P, Smith HT, Davis NL. Drug and opioid-involved overdose deaths-United States, 2017-2018. MMWR Morb Mortal Wkly Rep. 2020;69(11):290–7.
26. Votaw VR, Geyer R, Rieselbach MM, McHugh RK. The epidemiology of benzodiazepine misuse: a systematic review. Drug Alcohol Depend. 2019;200:95–114. [published Online First: 20190507].
27. Chiew AL, Gluud C, Brok J, Brok J, Buckley NA. Interventions for paracetamol (acetaminophen) overdose. Cochrane Database Syst Rev. 2018;2(2):CD003328 [published Online First: CD003328.].
28. Jeong HH, Cha K, Choi KH, So BH. Evaluation of cut-off values in acute paracetamol overdose following the United Kingdom guidelines. BMC Pharmacol Toxicol. 2022;23(1):5.

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