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eReferences

This supplementary material has been provided by the authors to give readers additional information about their work.

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eMethods

eMethod 1. Baseline and in-hospital characteristics collection

Baseline characteristics

- Baseline data included the date of birth, gender, height, weight, temperature, systolic and diastolic blood pressures, heart rate, Glasgow score, Killip class, oxygen saturation and ventilation mode, presence of symptoms, list of medications at admission, history of cardiovascular disease, psychiatric illness (including major depressive disorder, bipolar disorder or schizophrenic disorder) or other significant clinical histories and main admission diagnosis.
- Regarding the drug addiction surveys, we assessed: i) declaration of psychoactive drug use (cannabinoids, cocaine, amphetamines, MDMA, heroin or other opioids); ii) smoking history (daily or nondaily smoker, cigarettes smoked per day by daily smokers, age started smoking, years smoked and e-cigarette use); iii) declaration of alcohol use.
- Of note, history of cardiovascular disease (CVD) was defined by the presence of: known MI, previous PCI, previous CABG, peripheral atheroma with revascularization, stroke, history of heart failure, history of atrial fibrillation, history of surgery for valvular heart disease, pacemaker or ICD, and cardiomyopathies.

Hospital clinical characteristics

- Electrocardiogram (ECG) and transthoracic echocardiography (TTE) with left ventricular ejection fraction (LVEF) were performed systematically within the first 24 hours of admission for all patients. Need for revascularization [percutaneous coronary intervention (PCI) or coronary artery bypass surgery (CABG)], ventricular arrhythmia (sustained

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ventricular tachycardia or fibrillation), cardiogenic shock, need for haemodynamic support, and urgent repeat revascularization were recorded.

- Laboratory results were also collected systematically upon admission, including hemoglobin, potassium, creatinine, the maximum peak of troponin (hsTNI), the N-terminal prohormone of B-type natriuretic peptide (NT-proBNP) or B-type natriuretic peptide (BNP).
- All the diagnostic procedures of cardiovascular imaging or invasive angiography reports were collected. All treatment introduced during hospitalisation and the procedures performed were collected.
- The COVID status of each patient was systematically assessed at ICCU admission using RT-PCR, following current World Health Organization guidelines.

eMethod 2. Definition of main admission diagnosis

- The medical reasons for admission and the main admission diagnosis were adjudicated by a committee of two experts at the end of the hospitalisation in each centre.
- Main admission diagnosis was categorized into different subgroups: i) ST elevation myocardial infarction (STEMI), including mechanical complication of acute coronary syndrome; ii) non-ST elevation myocardial infarction (NSTEMI); iii) acute heart failure; iv) myocarditis; v) pericarditis; vi) pulmonary embolism; vii) atrial arrhythmia; viii) ventricular arrhythmia; ix) cardiac conduction abnormalities; x) coronary spasm; xi) Takotsubo; xii) aortic dissection; xiii) spontaneous coronary dissection, xiv) chest pain without identified cardiac cause, and xv) other cardiovascular or non-cardiovascular diagnosis.
- Of note, other cardiovascular diagnoses included: infectious endocarditis, acute hypertensive crisis without heart failure, prosthetic valve dysfunction without heart failure, vagal discomfort or orthostatic hypotension without severe cardiac conduction abnormality detected, and monitoring after electrocution.
- Of note, other non-cardiovascular diagnoses included: gastric ulcer, pancreatitis, acute cholecystitis, anemia, exacerbation of COPD, severe asthma, lung or systemic infection, severe COVID-19, migraine crisis, palpitations or dyspnea without a cardiovascular diagnosis.

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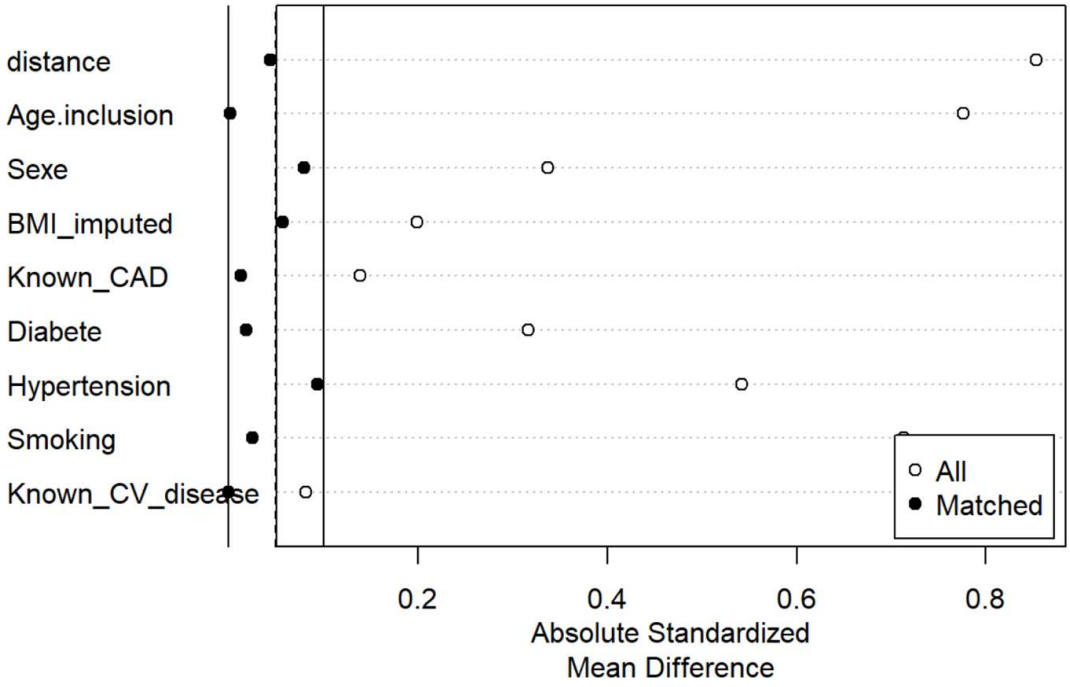
Main admission diagnosis	Definition
Acute coronary syndrome	Acute coronary syndrome will be defined by typical angina of ≥ 20 min duration, ECG changes, and a rise in troponin or creatine kinase level above the 99th percentile of the upper reference limit after elimination of the differential diagnosis (myopericarditis, Takotsubo syndrome, Tachyarrhythmias, acute heart failure…).[1] Acute coronary syndrome will be classified as ST-segment elevation and non ST-segment elevation categories.[2]
Acute heart failure	An hospitalization for heart failure (HF) will be defined by symptoms and/or signs of HF with evidence of diastolic or systolic dysfunction by echocardiography and elevated levels of natriuretic peptide (BNP >35 pg/ml and/or NT-proBNP >125 pg/ml).[3]
Myocarditis, pericarditis, Takotsubo syndrome	Myocarditis will be defined by chest pain, a rise in troponin or creatine kinase level above the 99 percentile of the upper reference limit and confirmation by cardiovascular magnetic resonance (CMR) using the Lake Louis criteria.[4] Pericarditis will be defined when two out of the four following criteria are fulfilled: a) chest pain b) pericardial rubs c) ECG changes d) pericardial effusion. Takotsubo syndrome will be defined using the clinical expert consensus statement on takotsubo syndrome.[5]
Pulmonary Embolism	Symptoms of pulmonary embolism (dyspnea, chest pain…) confirmed by imaging tests.[6]
Acute supraventricular arrythmias	Symptoms of tachycardia (palpitations, dyspnea…) leading to hospitalization in ICCU and 12-lead ECG confirming the supraventricular arrhythmia
Ventricular arrhythmias	Symptoms of tachycardia (palpitations, dyspnea…) leading to hospitalization in ICCU and 12-lead ECG confirming sustained ventricular tachycardia.
Other	The subgroup "other diagnosis" includes all diagnoses not eligible for the above categories, including aortic dissection, coronary spasm, unstable angina, endocarditis, hypertensive emergency, acute chest pain without etiology

eMethod 3. Absolute standardized mean differences and the propensity matched population (Recreational drug users vs. No recreational drug users)

Absolute standardized mean differences calculated using Yang and Dalton's method <0.2 were used as a proxy of covariate balance.



eMethod 4. Reasons for failure to perform drug urine assay

Among the 76 patients without drug urine assay performed, 38 (50%) patients had urine leakage in a diaper without the possibility of performing the drug urine assay efficiently, 28 (36.8%) patients did not urinate during the first 12 hours of hospitalisation, and for 10 (13.2%) patients the drug urine assay was not performed by the paramedical team due to having prioritized the therapeutic management in emergency, or due to an oversight, especially at night.

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eTables

eTable 1. Detailed list of participating centers

This table reports all participating centers with the respective number of patients recruited.

Centers	Patients recruited (n)
Amiens, University Hospital Center	6
Annecy, Hospital Center	51
Avignon, Hospital Center	58
Bobigny, Avicenne University Hospital Center, APHP	9
Boulogne Billancourt, Hôpital Ambroise Pare, University Hospital Center, APHP	10
Bordeaux, University Hospital Center	45
Brest, University Hospital Center	63
Caen, University Hospital Center	32
Chartres, Hospital Center	30
Créteil, Henri Mondor University Hospital Center	52
Dijon, University Hospital Center	69
Fréjus, Hospital Center	26
Grenoble, University Hospital Center	76
La Réunion, University Hospital Center	54
Lille, University Hospital Center	43
Limoges, University Hospital Center	6
Lyon, University Hospital Center	42
Marseille, La Timone University Hospital Center, APHM	51
Martinique, Fort de France University Hospital Center	33
Montfermeil, Hospital Center	40
Montpellier, University Hospital Center	46
Montreuil, Hospital Center	32
Neuilly sur Seine, Ambroise Paré Private Hospital	42
Nîmes, University Hospital Center	56
Orléans, Regional Hospital Center	50
Paris, Hôpital Bichat, University Hospital Center, APHP	35
Paris, Hôpital Cochin, University Hospital Center, APHP	30
Paris, Hôpital Européen Georges Pompidou, University Hospital Center, APHP	12
Paris, Hôpital Lariboisiere, University Hospital Center, APHP	60
Paris, Hôpital Saint-Antoine, University Hospital Center, APHP	27
Percy-Clamart, Hôpital d'Instruction des Armées	10

Poitiers, University Hospital Center	73
Rennes, University Hospital Center	42
Rouen, University Hospital Center	25
Saintes, Hospital Center	25
Strasbourg, University Hospital Center	84
Toulouse, University Hospital Center	83
Tours, Clinique Saint Gatien Alliance (NCT+), Saint-Cyr-sur-Loire	17
Versailles, Hôpital Mignot, Hospital Center	30
Total	**1575**

Abbreviations : AP-HM: Assistance publique – Hôpitaux de Marseille; AP-HP: Assistance publique – Hôpitaux de Paris.

eTable 2. Reliability parameters of the urine drug assay

A) Technical methodology to perform the NarcoCheck® urine drug assay

The following recreational drugs were evaluated for all consecutive patients by urine drug assay using a cartridge-based system (NarcoCheck®, Kappa City Biotech SAS, Montluçon, France) as soon as possible at most within two hours of admission to the ICCU: i) cannabinoids (tetrahydrocannabinol [THC]), including cannabis and hashish; ii) cocaine and metabolites, including crack; iii) amphetamines; iv) MDMA; and v) heroin and other opioids. The test was performed using a urine jar or a urinary catheter by nurses who were trained following a standardised protocol just before the recruitment period to ensure maintenance of clinical accuracy of the procedure. The test is immersed directly into the urine sample, which prevents any liquid handling. Of note, morphine and other opioid administration for pain sedation during the initial management of patients before admission to the ICCU was recorded, and their urine tests for opioids were considered negative.

B) Reliability of the NarcoCheck® urine drug assay

To assess the reliability of the NarcoCheck® urine drug assay, a comparative analysis between NarcoCheck® and the findings of the regional reference Laboratory in Biological Toxicology was performed on a random sample of 60 patients. NarcoCheck® urine drug assay had a sensitivity of 91.7% and specificity of 97.9%.

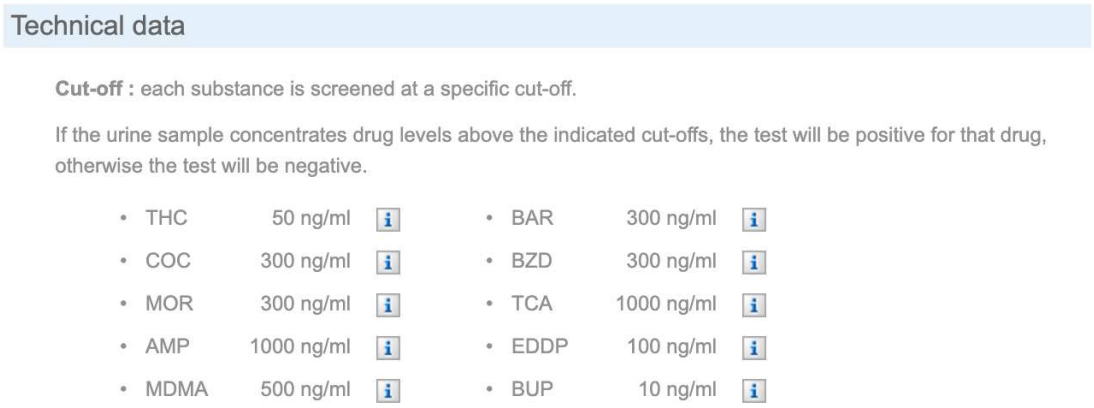
		Reference Laboratory in Biological Toxicology	
		Positive	Negative
NarcoCheck® urine drug assay	Positive	11	1
	Negative	1	47

C) Technical methodology to perform the reference test in the Laboratory

The reference test for the presence of drugs in the regional reference Laboratory in Biological Toxicology is based on radioimmunoassay or enzyme immunoassay depending on the substance. Of note, the comparative analysis was performed for all patients with a positive NarcoCheck® urine drug assay with the indication to the reference laboratory to assess the presence of all the recreational drugs evaluated in the study regardless of the initial result using NarcoCheck®.

D) Detection limit of the method for each drug

The detection limit of the method for each drug is depicted just below (*website of Kappa City Biotech SAS: https://www.narcocheck.com/en/multi-drugs-urine-tests/multi-drugs-medicines-urine-test-10in1.html*):



Technical data

Cut-off : each substance is screened at a specific cut-off.

If the urine sample concentrates drug levels above the indicated cut-offs, the test will be positive for that drug, otherwise the test will be negative.

• THC	50 ng/ml	• BAR	300 ng/ml
• COC	300 ng/ml	• BZD	300 ng/ml
• MOR	300 ng/ml	• TCA	1000 ng/ml
• AMP	1000 ng/ml	• EDDP	100 ng/ml
• MDMA	500 ng/ml	• BUP	10 ng/ml

eTable 3. Sensitivity analysis between the baseline characteristics of the overall population screened (N=1,499) and the final population analysed (N=1,411).

	Number of data available	Overall population screened (N=1,499)	Final population analysed (N=1,411)	p-value
Age, years	1499	63.3 ± 14.9	63.3 ± 14.9	1.00
Men, n (%)	1499	1043 (69.6)	981 (69.5)	0.89
BMI, kg/m²	1499	27.3 ± 5.5	27.2 ± 5.5	0.78
CV risk factors, n (%)				
Diabetes	1499	326 (21.7)	305 (21.6)	0.89
Hypertension	1499	795 (53.0)	759 (53.8)	0.71
Dyslipidaemia	1499	582 (38.8)	545 (38.6)	0.81
Current or previous smoking	1499	956 (63.8)	908 (64.4)	0.31
Family history of CAD	1499	247 (16.5)	235 (16.7)	0.87
Medical history of CV disease, n (%)				
Known MI	1499	234 (15.6)	218 (15.5)	0.78
Previous PCI	1499	482 (32.2)	459 (32.5)	0.56
Previous CABG	1499	51 (3.4)	46 (3.3)	0.71
Stroke	1499	5 (0.3)	3 (0.2)	0.61
Peripheral arterial disease	1499	57 (3.8)	55 (3.9)	0.82
Known chronic kidney disease †	1499	155 (10.3)	145 (10.3)	0.98
History of HF hospitalisation	1499	88 (5.9)	79 (5.6)	0.68
Known LVEF <50%	1499	102 (6.8)	96 (6.8)	0.96
History of atrial fibrillation	1499	175 (11.7)	166 (11.8)	0.73
Pacemaker or ICD	1499	92 (6.1)	92 (6.5)	0.71

Cardiomyopathies	1499	78 (5.2)	72 (5.1)	0.79
Medical history of non-CV disease, n (%)				
Cancer	1499	151 (10.1)	140 (9.9)	0.62
HIV	1499	13 (0.9)	12 (0.9)	0.93
COPD	1499	67 (4.5)	61 (4.3)	0.61
Asthma	1499	22 (1.5)	22 (1.6)	0.82
Psychiatric history, n (%)	1496	154 (10.3)	143 (10.1)	0.71
Recreational drug detected (multiple possible), n (%)				
Cannabis	1499	136 (9.1)	128 (9.1)	0.94
Heroin and other opioids	1499	28 (1.9)	25 (1.8)	0.77
Cocaine	1499	25 (1.7)	23 (1.6)	0.61
Amphetamines	1499	10 (0.7)	10 (0.7)	0.82
MDMA	1499	9 (0.6)	9 (0.6)	0.91
Alcohol use, n (%)	1499	799 (53.3)	766 (54.3)	0.71
Current smoker, n (%)	1499	382 (25.5)	362 (25.7)	0.63
Clinical data on admission				
Systolic blood pressure, mmHg	1495	136 [118-153]	134 [118-153]	0.87
Heart rate, bpm	1493	79 [67-95]	79 [67-95]	0.77
Oxygen saturation, %	1485	98 [96-99]	98 [96-99]	0.91
Killip class ≥ 2	1492	235 (15.8)	235 (16.7)	0.98
Laboratory results				
Hemoglobin (g/dL)	1491	13.7 [12.5-14.9]	13.7 [12.5-14.9]	1.00
Creatinemia (micromol/L),	1492	80 [67-99]	80 [67-99]	0.71
High-sensitivity cardiac troponin peak	1375	266 [40-3,962]	279 [40-4,055]	0.44

NTproBNP	676	734 [175-2,677]	700 [169-2,675]	0.51
BNP	582	141 [39-452]	141 [39-453]	0.83
TTE data				
LV ejection fraction, %	1468	55 [45-60]	55 [45-60]	0.89
Systolic pulmonary artery pressure, mmHg	936	30 [25-42]	30 [24-41]	0.62
TAPSE, %	1301	21 [10-34]	21 [18-24]	0.41

Values are n (%), mean ± SD, or median [interquartile range].

Abbreviations: BMI: body mass index; BNP: brain natriuretic peptide; CABG: coronary artery bypass grafting; CAD: coronary artery disease; COPD: chronic obstructive pulmonary disease; CV: cardiovascular; HF: heart failure; HIV: human immunodeficiency virus; ICD: implantable cardioverter-defibrillator; LVEF: left ventricle ejection fraction; MI: myocardial infarction; NSTEMI: non ST-elevation myocardial infarction; NTproBNP: NT-proB-type natriuretic peptide; PCI: percutaneous coronary intervention; SD: standard deviation; STEMI: ST-elevation myocardial infarction; TAPSE: tricuspid annular plane systolic excursion.

eTable 4. Difference in duration (days) of ICCU hospitalisation according to recreational drug detected

Variable	Mean difference estimated (95% CI)	p-value
Cannabis	1.6 (5.4-2.2)	0.403
Cocaine	0.7 (10.4-9.0)	0.891
Heroine and other opioids	0.7 (3.8-2.5)	0.677
Amphetamine	4.8 (18.4-8.9)	0.495
MDMA	1.8 (16.3-12.7)	0.809
Recreational drug detected	1.7 (5.3-1.9)	0.358

The median (IQR) duration of hospitalisation in ICCU was 5.0 (3.0–7.0) days.

Abbreviations: CI, confidence interval ; IQR, interquartile range ; ICCU, intensive cardiac care unit ; MDMA, methylene dioxymethamphetamine.

eTable 5. Univariable analysis of each baseline characteristics for in-hospital MAEs (N=1,411).

Variable	Odds-ratio (95% CI)	p-value
Age	1.02 (1.00-1.04)	0.076
Men	0.85 (0.50-1.46)	0.553
BMI	0.98 (0.93-1.03)	0.361
Hypertension	1.38 (0.82-2.32)	0.228
Dyslipidaemia	1.00 (0.60-1.69)	0.989
Diabetes	2.23 (1.31-3.80)	**0.003**
Current or previous smoking	0.54 (0.27-1.08)	0.083
Family history of CAD	0.33 (0.12-0.93)	**0.036**
Cannabis	2.05 (1.05-4.02)	**0.036**
Cocaine	4.27 (1.42-12.8)	**0.010**
Heroin and other opioids	1.46 (0.78-2.72)	0.236
Amphetamines	2.40 (0.30-19.2)	0.411
MDMA	28.8 (7.55->100)	**<0.001**
Alcohol use	0.42 (0.24-0.71)	**<0.001**
Recreational drug detected	5.73 (3.33-9.84)	**<0.001**
Known MI	1.64 (0.89-3.02)	0.115
Previous PCI or CABG	0.78 (0.44-1.37)	0.381
Stroke	1.12 (0.42-14.8)	0.81
Peripheral arterial disease	1.62 (0.76-4.91)	0.41
Known chronic kidney disease	2.19 (1.14-4.22)	**0.019**
History of HF hospitalisation	4.06 (2.03-8.15)	**<0.001**
Known LVEF <50%	2.46 (1.18-5.16)	**0.017**
History of atrial fibrillation	1.86 (0.97-3.57)	0.062

Known cardiomyopathy	3.99 (1.94-8.23)	**<0.001**
History of CVD	1.07 (0.64-1.79)	0.783
PM or ICD	0.57 (0.14-2.36)	0.435
Cancer	2.55 (1.35-4.83)	**0.004**
HIV	1.99 (0.25-15.69)	0.512
COPD	2.52 (1.04-6.10)	**0.040**
Asthma	2.21 (0.51-9.70)	0.291
Prior COVID19 vaccination	1.24 (0.72-2.15)	0.438
Haemoglobin	0.78 (0.69-0.88)	**<0.001**
Creatinine	1.00 (1.00-1.01)	**0.015**
High-sensitivity cardiac troponin peak	1.00 (1.00-1.02)	**0.011**
NTproBNP	1.02 (1.01-1.04)	**<0.001**
Systolic blood pressure	0.97 (0.96-0.98)	**<0.001**
Diastolic blood pressure	0.96 (0.94-0.97)	**<0.001**
Temperature	1.00 (0.64-1.58)	0.988
Heart rate	1.02 (1.01-1.02)	**0.002**
Oxygen saturation	0.99 (0.96-1.02)	0.331
Killip class	3.90 (2.10-7.27)	**<0.001**
Glasgow score	0.08 (0.03-0.21)	**<0.001**
LV ejection fraction	0.94 (0.93-0.96)	**<0.001**
LV end-diastolic volume indexed	1.01 (1.00-1.01)	**0.003**
Systolic pulmonary artery pressure	1.04 (1.02-1.05)	**<0.001**
TAPSE	0.89 (0.84-0.94)	**<0.001**
Anticoagulant or anti-platelet aggregation	2.79 (1.62-4.81)	**<0.001**

Antihypertensive treatment	1.94 (1.12-3.37)	**0.018**
Statins	1.11 (0.65-1.89)	0.701

Abbreviations: BMI: body mass index; BNP: brain natriuretic peptide; CABG: coronary artery bypass grafting; CAD: coronary artery disease; COPD: chronic obstructive pulmonary disease; CV: cardiovascular; HF: heart failure; HIV: human immunodeficiency virus; ICD: implantable cardioverter-defibrillator; LVEF: left ventricle ejection fraction; MI: myocardial infarction; NSTEMI: non ST-elevation myocardial infarction; NTproBNP: NT-proB-type natriuretic peptide; PCI: percutaneous coronary intervention; SD: standard deviation; STEMI: ST-elevation myocardial infarction; TAPSE: tricuspid annular plane systolic excursion.

eTable 6. Sensitivity analysis: univariable and multivariable analysis of recreational drug detected for composite outcome including stroke.

Variables	Unadjusted		Model 1 (comorbidities)*		Model 2 (clinical severity)†	
	OR (95%CI)	**p-value**	**OR (95%CI)**	**p-value**	**OR (95%CI)**	**p-value**
Recreational drug detected						
No recreational drug	1.0	-	1.0	-	1.0	-
Single recreational drug	3.01 (1.89-5.80)	**<0.001**	6.31 (2.63-12.4)	**<0.001**	6.02 (2.79-11.8)	**<0.001**
Multiple recreational drug	7.36 (2.84-14.1)	**<0.001**	12.0 (4.00-30.0)	**<0.001**	11.5 (4.34-32.9)	**<0.001**

Univariable and multivariable analysis of recreational drug detected for another composite outcome defined by all-cause death, resuscitated cardiac arrest, cardiogenic shock requiring medical or mechanical hemodynamic support, and stroke.

* Covariates in the **model 1**: age, men, diabetes mellitus, current smoking status, history of cardiovascular disease (CVD), main admission diagnosis, known chronic kidney disease with glomerular filtration rate <90 ml/min, history of cancer, and recreational drug detected (divided into 3 categories: no recreational drug detected, single recreational drug, and multiple recreational drug defined by at least two recreational drugs detected).

† Covariates in the **model 2**: age, men, main admission diagnosis, systolic blood pressure, baseline Killip class, heart rate, and recreational drug detected (divided into 3 categories: no recreational drug detected, single recreational drug, and multiple recreational drug defined by at least two recreational drugs detected).

‡ CVD defined by the presence of: known MI, previous PCI, previous CABG, peripheral atheroma with revascularization, stroke, history of heart failure, history of atrial fibrillation, history of surgery for valvular heart disease, pacemaker or ICD, and cardiomyopathies.

Abbreviations: same as Table 1; OR, odds-ratio; CI, confidence interval.

eTable 7. Univariable and multivariable analyses of multiple recreational drugs detected for in-hospital MAEs.

Variables	Unadjusted		Model 1 (comorbidities)*		Model 2 (clinical severity)†	
	OR (95%CI)	**p-value**	**OR (95%CI)**	**p-value**	**OR (95%CI)**	**p-value**
Age	1.02 (1.00-1.04)	0.076	1.02 (1.00-1.04)	0.093	1.03 (1.01-1.05)	**0.013**
Men	0.85 (0.50-1.46)	0.553	0.81 (0.45-1.45)	0.472	0.85 (0.47-1.52)	0.41
Diabetes mellitus	2.23 (1.31-3.80)	**0.003**	2.23 (1.20-4.12)	**0.008**	-	-
Current smoking status	0.74 (0.48-1.30)	0.812	0.73 (0.46-1.27)	0.781	-	-
History of CVD‡	1.07 (0.64-1.79)	0.783	0.91 (0.48-1.72)	0.761	-	-
Known CKD§	2.19 (1.14-4.22)	**0.019**	1.40 (0.67-2.93)	0.376	-	-
Cancer	2.55 (1.35-4.83)	**0.004**	2.36 (1.15-4.85)	**0.020**	-	-
Systolic blood pressure	0.97 (0.96-0.98)	**<0.001**	-	-	0.97 (0.95-0.99)	**<0.001**
Killip class	3.90 (2.10-7.27)	**<0.001**	-	-	3.65 (2.00-6.89)	**<0.001**
Heart rate	1.02 (1.01-1.02)	**0.002**	-	-	1.03 (1.01-1.05)	**0.001**
Admission diagnosis						
Acute coronary syndrome	1.0	-	1.0	-	1.0	-
Chest pain without CV diagnosis‖	-	-	-	-	-	-
Acute heart failure	2.86 (1.60-5.11)	**<0.001**	2.56 (1.30-5.05)	**0.007**	2.66 (1.34-5.28)	0.005
Myocarditis / Pericarditis	0.34 (0.05-2.54)	0.294	0.45 (0.06-3.57)	0.448	0.45 (0.05-3.69)	0.457
Pulmonary embolism‖	-	-	-	-	-	-
Arrythmia	0.76 (0.10-5.75)	0.790	0.85 (0.10-7.29)	0.879	0.79 (0.09-6.73)	0.830
Cardiac conduction abnormalities‖	-	-	-	-	-	-

Others	0.59 (0.14-2.51)	0.473	0.51 (0.11-2.33)	0.382	1.91 (0.65-5.63)	0.240
Recreational drug detected						
No recreational drug	1.0	-	1.0	-	1.0	-
Single recreational drug	3.51 (2.01-6.17)	**<0.001**	6.31 (3.01-12.8)	**<0.001**	6.20 (2.97-12.0)	**<0.001**
Multiple recreational drug	8.02 (3.19-15.7)	**<0.001**	12.7 (4.80-35.6)	**<0.001**	12.8 (4.92-36.9)	**<0.001**

* Covariates in the **model 1**: age, men, diabetes mellitus, current smoking status, history of cardiovascular disease (CVD), main admission diagnosis, known chronic kidney disease with glomerular filtration rate <90 ml/min, history of cancer, and recreational drug detected (divided into 3 categories: no recreational drug detected, single recreational drug, and multiple recreational drugs defined by at least two recreational drugs detected).

† Covariates in the **model 2**: age, men, main admission diagnosis, systolic blood pressure, baseline Killip class, heart rate, and recreational drug detected (divided into 3 categories: no recreational drug detected, single recreational drug, and multiple recreational drugs defined by at least two recreational drugs detected).

‡ CVD defined by the presence of: known MI, previous PCI, previous CABG, peripheral atheroma with revascularization, stroke, history of heart failure, history of atrial fibrillation, history of surgery for valvular heart disease, pacemaker or ICD, and cardiomyopathies.

§ defined by history of chronic kidney disease with glomerular filtration rate <90 ml/min.

‖ no in-hospital MAE in this subgroup of patients.

Abbreviations: same as Table 1; OR, odds-ratio; CI, confidence interval.

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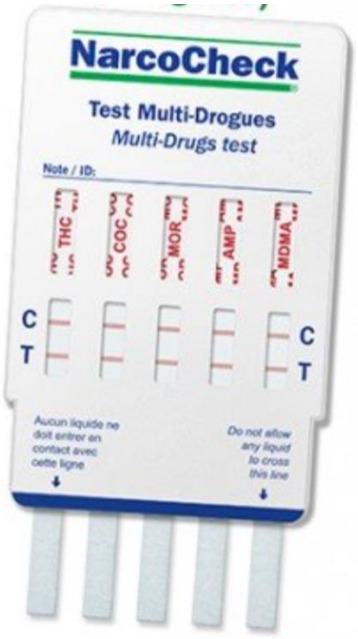
eFigures

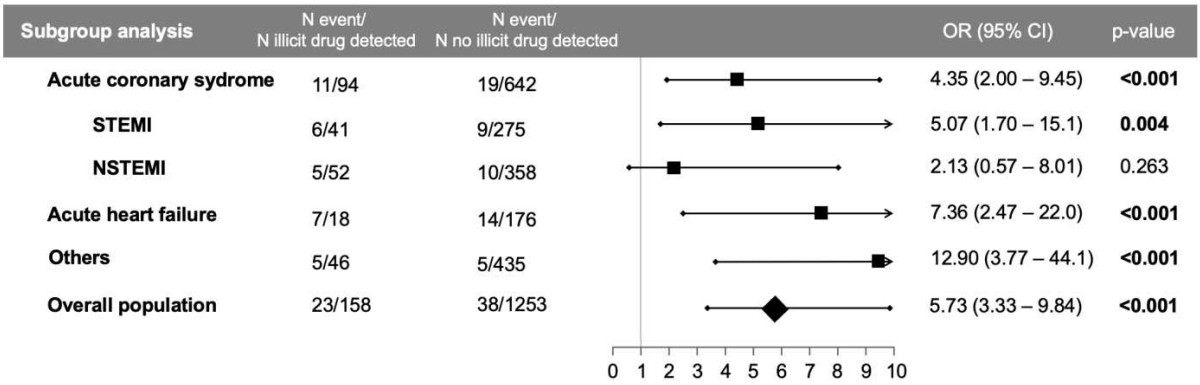
eFigure 1. Presentation of the urine drug test

The following psychoactive drugs were detected using a multidrug test (NarcoCheck®, Kappa City Biotech SAS, Montluçon, France): i) cannabinoids (tetrahydrocannabinol [THC]), including cannabis and hashish; ii) cocaine and metabolites, including cocaine and crack; iii) amphetamines; iv) MDMA; and v) heroin and other opioids.



eFigure 2. Forest plot: subgroup analysis of the effect of recreational drug detected on in-hospital MAEs according to the main admission diagnosis.

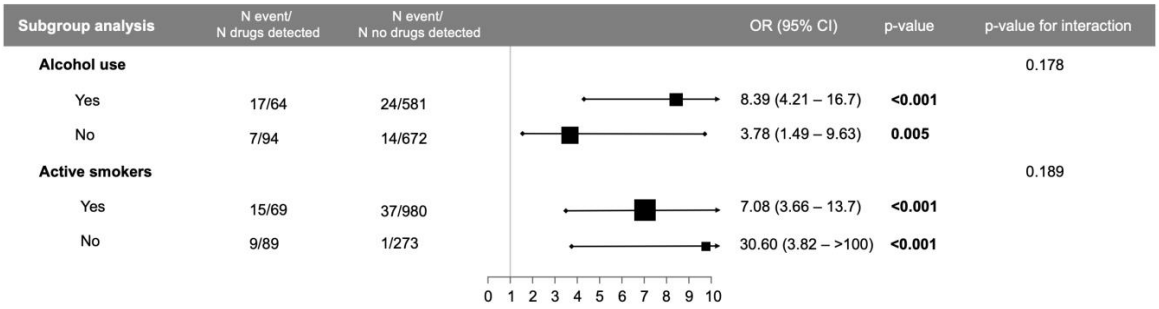
Forest-plot with unadjusted odd-ratio (OR; black squares) and 95% confidence interval (CI, horizontal lines) of recreational drug detection effects for the occurrence of in-hospital MAEs according to the main admission diagnosis.



eFigure 3. Forest plot: subgroup analysis of the effect of recreational drug detected on in-hospital MAEs by current smoking status and alcohol use at least once a week.

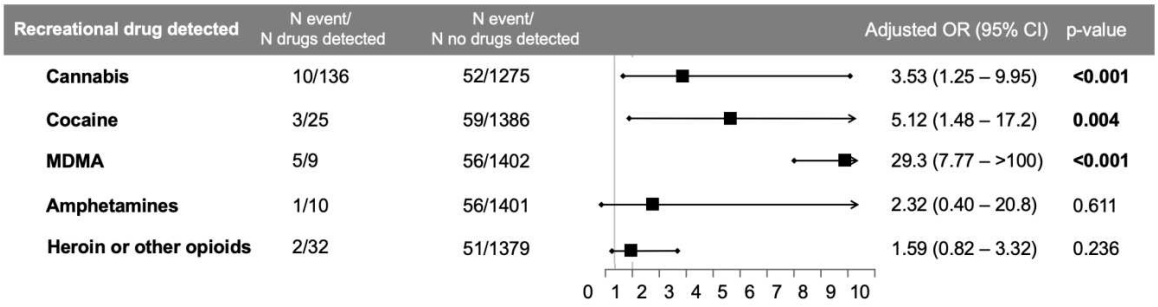
Forest-plot with unadjusted odd-ratio (OR; black squares) and 95% confidence interval (CI, horizontal lines) of recreational drug detection effects for the occurrence of in-hospital MAEs according to the tobacco or alcohol use at least once a week.

Interactions between the tested variables and the effects of recreational drug detection on in-hospital MAEs were determined using the heterogeneity test with p-value interaction.



eFigure 4. Forest plot: Multivariable analysis of each recreational drug detected for in-hospital MAEs.

Forest-plot with adjusted odd-ratio (OR; black squares) and 95% confidence interval (CI, horizontal lines) on in-hospital MAEs according to each recreational drug detected. after adjustment for model 1.



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