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RESEARCH REPORT

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Trends in new psychoactive substance poisonings in the Netherlands: A 14-year retrospective analysis (2012–2025)

Johanna J. Nugteren-van Lonkhuyzen[1] | Irma S. van den Hengel-Koot[1] | Claudine C. Hunault[1] | Dylan W. de Lange[1,2] | Antoinette J. H. P. van Riel[1] | Laura Hondebrink[1]

[1]Dutch Poisons Information Center, University Medical Center Utrecht, Utrecht University, Utrecht, the Netherlands

[2]Intensive Care Department, University Medical Center Utrecht, Utrecht University, Utrecht, the Netherlands

Correspondence
Johanna J. (Annette) Nugteren-van Lonkhuyzen, Dutch Poisons Information Center (NVIC), University Medical Center Utrecht, Utrecht University, PO Box 85500, 3508 GA, Utrecht, the Netherlands.
Email: a.vanlonkhuyzen@umcutrecht.nl

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Abstract

Background and aims: Data on the presence of new psychoactive substances (NPS) mainly originate from drug-checking, law enforcement and wastewater analysis sources, while data on NPS poisonings are scarce. In Europe, the documented incidence rate of NPS poisonings is highest in the Netherlands. We investigated temporal trends in NPS poisonings reported to the Dutch Poisons Information Center (DPIC) between 2012 and 2025 and compared these trends across NPS categories.

Design: National observational study based on retrospective extraction of recreational drug poisonings (including NPS) from the DPIC database from 2012 to 2025. The DPIC is not accessible to the general public and reporting by healthcare professionals is voluntary.

Setting/cases: The DPIC database contains standardized case report forms with anonymous patient data and individually (self-)reported substance exposures (not ICD-coded, not analytically confirmed). All cases concerning human exposures to recreational drugs recorded in the DPIC database were included.

Measurements: Primary outcomes were the annual number and annual incidence rate of NPS poisonings reported to the DPIC, relative to the annual number of all recreational drug poisonings. Secondary outcomes were incidence rates of specific (categories of) NPS over time. Predictor was the year of report.

Findings: Between 2012 and 2025, healthcare professionals reported 19 316 recreational drug poisonings, including 4289 NPS-related poisonings, while seeking advice on patient management. The annual number of NPS poisonings increased from 32 in 2012 to 829 in 2025. Between 2012 and 2025 the annual incidence rate of NPS poisonings increased statistically significantly by 19% per year [incidence rate ratio = 1.19; 95% confidence interval (CI) = 1.15–1.23]. A higher incidence rate of NPS poisonings was observed in July and December. Cathinones, phenethylamines and benzodiazepines represented 83% of all NPS poisonings. Benzodiazepines were predominant in 2012 and 2024, phenethylamines from 2013 to 2018 and cathinones from 2019 to 2023 and in 2025. The total number of unique NPS notified to the DPIC increased from 17 in 2012 to 176 in 2025. Poisonings with 3-methylmethcathinone (3-MMC), bromazolam,

4-fluoroamphetamine (4-FA), 4-bromo-2,5-dimethoxyphenethylamine (2C-B) and 4-methylmethcathinone (4-MMC, mephedrone) were reported most frequently (5–22% of 4289 NPS poisonings). Poisonings with arylcyclohexylamines, cannabinoids, opioids, arylalkylamines, tryptamines (indolalkylamines), piperidines and pyrrolidines and other substances were rare (every category <5% of 4289 NPS poisonings). No poisonings with aminoindanes or piperazines were reported from 2012 to 2025.

Conclusions: The annual incidence rate of new psychoactive substances poisonings reported to the Dutch Poisons Information Center increased by 19% per year between 2012 and 2025. The predominant categories and specific substances involved changed markedly over time.

KEYWORDS
cathinones, designer benzodiazepines, designer drugs, phenethylamines, poisons center, toxicovigilance

INTRODUCTION

Over the past decade, the presence of new psychoactive substances (NPS) in Europe has evolved, as monitored by the European Union Drugs Agency (EUDA, formerly known as EMCDDA). The annual number of first-time notifications of NPS peaked at 101 new substances in 2014, and has stabilized at approximately 50 annually, with 1000 NPS currently being monitored [1]. The emergence of NPS is not confined to Europe; globally, over 1400 NPS have been reported across 153 counties and territories [2].

So far, surveillance of the European drug market primarily relies on data regarding NPS that are (newly) available on the consumer market and are detected in drug-checking programs, seized by law enforcement agencies or detected in wastewater. While data on NPS-related health incidents remain limited, several ongoing research initiatives provide insights into trends related to specific (categories of) NPS involved in acute poisonings, including clinical effects, and user demographics.

One such initiative is the Euro-DEN Plus project, which collects epidemiological data on drug-related emergency department (ED) visits. This project offers insights into acute health incidents related to drug use, including NPS [3, 4].

Another source of epidemiological data on NPS poisonings are Poison Control Centers (PCCs) [5–11]. PCCs provide 24/7 information services on the management of (suspected) poisonings. Most PCCs maintain detailed records of reported poisonings, including NPS poisonings. As a result, PCCs are among the first to document adverse health effects following NPS exposure, which are often unknown upon market entry. Additionally, PCC data often provide national coverage, and also include less severe poisonings not presenting to EDs, making them a valuable resource for toxicovigilance.

In Europe, the documented incidence rate of NPS poisonings is highest in the Netherlands [10]. The Dutch Poisons Information Center (DPIC) has monitored enquiries on NPS poisonings for over a decade now, as part of its toxicovigilance role in identifying potential public health threats. By registering symptoms reported during consultation and performing follow-up studies, the DPIC provided several signals of adverse health effects associated with NPS exposure [12–16]. However, long-term epidemiological data on NPS poisonings as a group are currently absent. To address this gap, we investigated temporal trends in NPS poisonings reported to the DPIC over a 14-year period (2012–2025) and compared these trends across NPS categories.

METHODS

Design

A national observational study was performed based on the retrospective extraction of poisoning cases from the DPIC database from 2012 to 2025.

Setting and cases

The DPIC operates a 24/7 telephone service, exclusive to healthcare professionals, providing information on the management of (suspected) poisonings. The reporting of poisonings is voluntary. All telephone consultations are digitally recorded, and during each inquiry, an electronic case report form (eCRF) is completed. These eCRFs contain anonymized data on the patient, exposure and clinical characteristics, which are stored in the DPIC database. Exposure data are based on self-reported substance exposures—not using International Classification of Diseases, Tenth Revision (ICD-10) codes or analytically confirmed—from the patient to their healthcare provider during anamnesis, and primarily addresses acute poisonings. In addition, routine follow-up is not performed, and thus clinical outcomes are generally unknown.

The DPIC database was searched retrospectively for cases involving NPS-related poisonings reported between 2012 and 2025, covering a 14-year period. Anonymized data on NPS exposure were

extracted from eCRFs. Both mono and mixed poisonings were included for analysis. In some cases, individual patients were exposed to more than one NPS, resulting in a higher number of NPS exposures than patients. In this study we analyzed reported NPS exposures, for which we use the term 'poisonings'.

Definitions

According to the EUDA definition, NPS are 'new narcotic or psychotropic drugs, in pure form or in preparation, that are not controlled by the United Nations drug conventions, but which may pose a public health threat comparable to that posed by substances listed in the conventions'. In this study, NPS were defined according to the EUDA definition, except for gamma-hydroxybutyric acid (GHB) and ketamine. These were considered established recreational drugs. Mixed poisonings of NPS with GHB or ketamine were included.

Benzodiazepines were defined as benzodiazepines not registered as medication in the Netherlands, including both benzodiazepines designed for recreational purposes and benzodiazepines registered as medication in other countries [12]. The term 'all recreational drugs' encompassed both established recreational drugs and NPS. Established recreational drugs included, but were not limited to: (meth)amphetamine, cocaine, GHB, heroin, ketamine, lysergic acid diethylamide (LSD), 3,4-methylenedioxymethamphetamine (MDMA), nitrous oxide, psilocybin-containing mushrooms and delta-9-tetrahydrocannabinol (THC).

Measurements

The primary outcomes of this study were the annual number and the annual incidence rate of NPS poisonings between 2012 and 2025. Rates were expressed relative to the annual number of all recreational drug poisonings (NPS + established recreational drugs) (shown as %). Secondary outcomes included overall and annual incidence rates of NPS categories and of specific substances. NPS were classified into the following categories according to the EUDA grouping system: aminoindanes, arylalkylamines, arylcyclohexylamines, benzodiazepines, cannabinoids, cathinones, opioids, phenethylamines, piperazines, piperidines and pyrrolidines, tryptamines and other substances. Poisonings involving NPS in the EUDA category 'Plants and extracts' were excluded from this study.

Data analysis

Descriptive statistics summarized the number and incidence rates of NPS poisonings by category. Temporal trends were assessed using a negative binomial (NB) model to handle overdispersion in the data, with the number of NPS poisonings as the outcome, the year as the predictor and all recreational drug poisonings as the offset, to adjust for annual variation. Additional checks were performed to further assess the NB model (deviance residuals plot, Q–Q plot of residuals, observed versus predicted plot and dispersion ratio). Results are reported as incidence rate ratios (IRRs) with 95% confidence intervals (95% CIs). The NPS poisoning incidence rate was plotted using monthly symbols. A time-series model was fitted to the 2012–2019 data (considered to be training data) using the *tbats()* function from the R 'forecast' package to capture trends and seasonal patterns. Forecasts were then produced for the period from 2020 to 2025, based on this model. Analyses were not pre-specified, and therefore findings should be considered exploratory. Statistical analysis was executed using IBM SPSS Statistics 26 (IBM, Armonk, NY, USA) and RStudio 2014.12.1 (R Foundation for Statistical Computing, Vienna, Austria).

The reporting of this study follows the recommendations of the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement for cohort studies (Table S3) [17]. A completed checklist is provided in the supporting information.

RESULTS

Total NPS poisonings reported to the DPIC (2012–2025)

From 2012 to 2025, 4289 NPS poisonings were reported to the DPIC and the annual number increased from 32 in 2012 to 829 in 2025 (Table 1). Over half of all NPS poisonings were reported in the last 3 years (n = 2291, 53% of all NPS poisonings). The annual NPS poisoning incidence rate increased from 4% in 2012 to 40% in 2024, and then declined to 38% in 2025 (Figure 1; Table S1). Between 2012 and 2025 the annual incidence rate increased significantly by 19% per year (IRR = 1.19; 95% CI = 1.15–1.23). A higher incidence rate of NPS poisonings was observed in July and December (Figure S1). The observed rate differed from the forecast based on the TBATS (trigonometric seasonality, Box–Cox transformations, autoregressive moving average error processes, trend and seasonal components) model, showing a higher NPS poisoning incidence rate than expected from 2020 onwards (Figure S2). In all, 62% of the NPS poisonings (n = 2651) involved mixed intoxications.

Classes of NPS poisonings reported to the DPIC (2012–2025)

From 2012 to 2025, cathinones, benzodiazepines and phenethylamines represented 83% of all NPS poisonings reported to the DPIC. Overall, most of the reported NPS poisonings involved cathinones, followed by benzodiazepines and phenethylamines (Table 1). The predominant category of NPS changed over the years. In 2012 and 2024, benzodiazepines were the leading category of NPS, whereas phenethylamines were the leading category of NPS from 2013 to 2018, and cathinones were the leading category of NPS from 2019 to 2023 and in 2025 (Figure 2; Table 1). Few poisonings with arylalkylamines, arylcyclohexylamines, cannabinoids, opioids, piperidines and

TABLE 1 Poisonings with the most prevalent (categories of) new psychoactive substances (NPS) reported to the Dutch Poisons Information Center (DPIC) from 2012 to 2025.

	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024	2025	Total
All NPS poisonings	***n* = 32**	***n* = 41**	***n* = 91**	***n* = 107**	***n* = 130**	***n* = 132**	***n* = 102**	***n* = 111**	***n* = 211**	***n* = 487**	***n* = 554**	***n* = 659**	***n* = 803**	***n* = 829**	***n* = 4289**
	n (%)	*n* (%)	*n* (%)	*n* (%)	*n* (%)	*n* (%)	*n* (%)	*n* (%)	*n* (%)	*n* (%)	*n* (%)	*n* (%)	*n* (%)	*n* (%)	*n* (%)
Cathinones (**% of year**)	6 (19)	8 (20)	10 (11)	10 (9)	23 (18)	23 (17)	33 (32)	42 (38)	84 (40)	205 (42)	223 (40)	300 (46)	280 (35)	326 (39)	1573 (37)
3-MMC (**% of category**)	0 (0)	1 (13)	2 (20)	1 (10)	4 (17)	8 (35)	10 (30)	25 (60)	64 (76)	158 (77)	119 (53)	202 (67)	158 (56)	213 (65)	965 (61)
4-MMC (**% of category**)	5 (83)	1 (13)	3 (30)	4 (40)	3 (13)	5 (22)	12 (36)	12 (29)	19 (23)	25 (12)	42 (19)	36 (12)	32 (11)	21 (6)	220 (14)
Benzodiazepines (**% of year**)	7 (22)	2 (5)	6 (7)	16 (15)	10 (8)	23 (17)	15 (15)	24 (22)	64 (30)	170 (35)	197 (36)	236 (36)	342 (43)	271 (33)	1383 (32)
Bromazolam (**% of category**)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	14 (8)	44 (22)	88 (37)	123 (36)	109 (40)	378 (27)
Pyrazolam (**% of category**)	0 (0)	0 (0)	0 (0)	1 (6)	0 (0)	1 (4)	0 (0)	0 (0)	0 (0)	7 (4)	35 (18)	34 (14)	48 (14)	43 (16)	169 (12)
Phenethylamines (**% of year**)	6 (19)	19 (46)	58 (64)	63 (59)	78 (60)	68 (52)	38 (37)	30 (27)	33 (16)	48 (10)	53 (10)	44 (7)	42 (5)	32 (4)	612 (14)
2C-B (**% of category**)	1 (17)	3 (16)	17 (29)	14 (22)	21 (27)	24 (35)	19 (50)	11 (37)	23 (70)	28 (58)	22 (42)	23 (52)	11 (26)	16 (50)	233 (38)
4-F-A (**% of category**)	3 (50)	11 (58)	27 (47)	44 (70)	50 (64)	39 (57)	14 (37)	16 (53)	5 (15)	4 (8)	1 (2)	3 (7)	3 (7)	4 (13)	224 (37)
Arylcyclohexylamines (**% of year**)	5 (16)	5 (12)	9 (10)	4 (4)	7 (5)	2 (2)	2 (2)	5 (5)	13 (6)	17 (3)	22 (4)	24 (4)	26 (3)	41 (5)	182 (4)
2-Fluorodeschloroketamine (**% of category**)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (50)	0 (0)	1 (20)	3 (23)	4 (22)	7 (32)	7 (29)	8 (31)	8 (31)	50 (27)
Methoxetamine (**% of category**)	5 (100)	5 (100)	9 (100)	4 (100)	7 (100)	0 (0)	1 (50)	1 (20)	1 (8)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	33 (18)
Cannabinoids (**% of year**)	1 (3)	2 (5)	1 (1)	5 (5)	1 (1)	2 (2)	2 (2)	2 (2)	2 (1)	5 (1)	2 (<1)	24 (4)	47 (6)	54 (7)	150 (3)
HHC (**% of category**)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	15 (63)	31 (66)	34 (63)	80 (53)
Opioids (**% of year**)	0 (0)	0 (0)	1 (1)	0 (0)	1 (1)	0 (0)	1 (1)	0 (0)	0 (0)	10 (2)	19 (3)	7 (1)	35 (4)	57 (7)	131 (3)
ODT (**% of category**)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	10 (100)	19 (100)	6 (86)	27 (77)	33 (58)	95 (73)
Arylalkylamines (**% of year**)	3 (9)	3 (7)	3 (3)	5 (5)	4 (3)	4 (3)	6 (6)	3 (3)	3 (1)	9 (2)	14 (3)	6 (1)	13 (2)	12 (1)	88 (2)
6-APB (**% of category**)	3 (100)	1 (33)	1 (33)	1 (20)	1 (25)	2 (50)	4 (67)	2 (67)	1 (33)	4 (44)	6 (43)	1 (17)	5 (38)	6 (50)	38 (43)
Tryptamines (indolalkylamines) (**% of year**)	4 (13)	2 (5)	3 (3)	4 (4)	5 (4)	7 (5)	1 (1)	4 (4)	4 (2)	6 (1)	11 (1)	6 (1)	7 (1)	21 (3)	85 (2)
DMT (**% of category**)	1 (25)	1 (50)	1 (33)	3 (75)	2 (40)	2 (29)	0 (0)	4 (100)	2 (50)	0 (0)	2 (18)	3 (50)	1 (14)	3 (14)	25 (29)
Piperidines and pyrrolidines (**% of year**)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (2)	0 (0)	0 (0)	3 (1)	5 (1)	4 (1)	6 (1)	5 (1)	4 (1)	29 (1)
4-F-MPH (**% of category**)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (50)	0 (0)	0 (0)	2 (67)	4 (80)	4 (100)	5 (83)	5 (100)	1 (25)	22 (76)
Other substances (**% of year**)	0 (0)	0 (0)	0 (0)	0 (0)	1 (1)	1 (1)	4 (4)	1 (1)	5 (2)	12 (2)	9 (2)	6 (1)	6 (1)	11 (1)	56 (1)
3-FPM (**% of category**)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (25)	0 (0)	3 (60)	1 (8)	1 (11)	3 (50)	2 (33)	0 (0)	11 (20)

Note: The incidence rate of specific NPS categories is shown as a percentage of the number of all NPS poisonings (**% of year**) reported to the DPIC annually or for all studied years (2012–2025). The incidence rate of individual NPS is shown as a percentage of the number of poisonings within a specific category of NPS (**% of category**) reported to the DPIC annually or for all studied years (2012–2025).
Abbreviations: 2C-B = 4-bromo-2,5-dimethoxyphenethylamine; 3-FPM = 3-fluorophenmetrazine; 3-MMC = 3-methylmethcathinone; 4-FA = 4-fluoroamphetamine; 4F-MPH = 4-fluoromethylphenidate; 4-MMC = 4-methylmethcathinone; 6-APB = 6-(2-aminopropyl)benzofuran; DMT = *N*,*N*-dimethyltryptamine; DPIC = Dutch Poisons Information Center; HHC = hexahydrocannabinol; ODT = *O*-desmethyltramadol; NPS = new psychoactive substances.

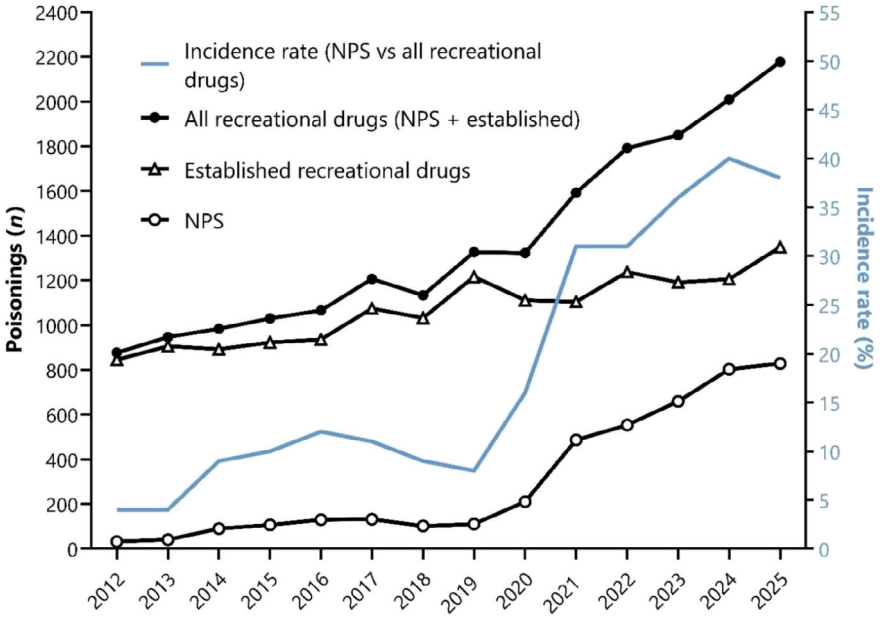

FIGURE 1 Epidemiology of new psychoactive substance (NPS) poisonings reported to the Dutch Poisons Information Center (DPIC) from 2012 to 2025. Shown are the annual number of NPS poisonings (○), the annual number of poisonings with established recreational drugs (△) and the annual number of all recreational drug poisonings (NPS and established recreational drugs) (●). The annual NPS poisoning incidence rate is expressed relative to the annual number of all recreational drug poisonings (shown as %, blue line).

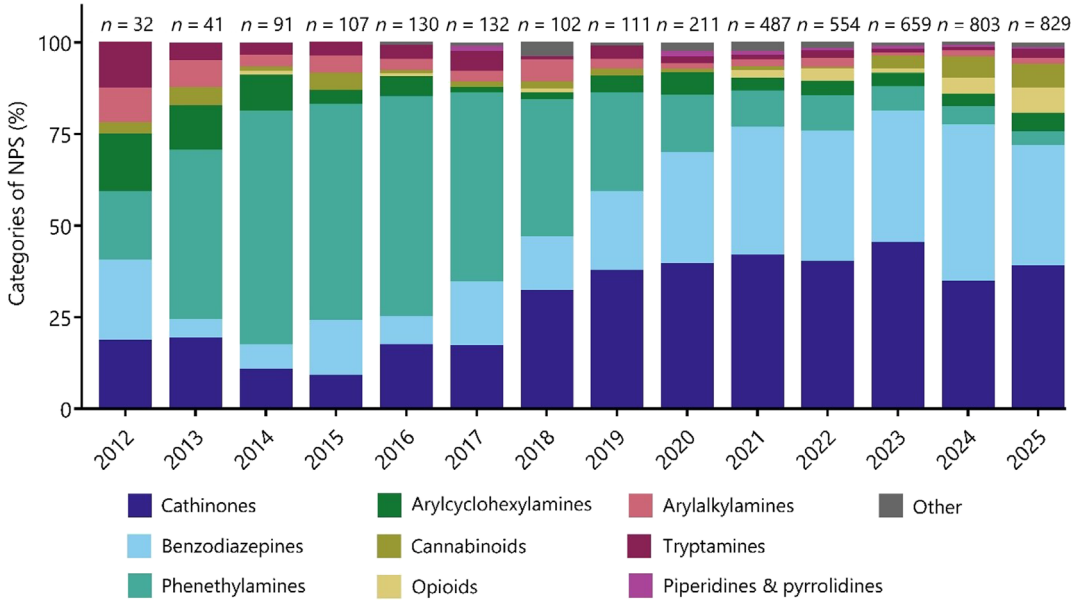

FIGURE 2 Poisonings with specific categories of new psychoactive substances (NPS) reported to the Dutch Poisons Information Center (DPIC) from 2012 to 2025. The annual incidence rate of poisoning with specific categories of NPS is shown as a percentage of the annual number of all NPS poisonings reported to the DPIC from 2012 to 2025.

pyrrolidines, tryptamines (indolalkylamines) and other substances were reported, with each category listed representing <5% of all NPS poisonings. No poisonings with aminoindanes or piperazines were reported from 2012 to 2025.

Poisonings with specific NPS reported to the DPIC (2012–2025)

The total number of NPS notified to the DPIC increased over the years, from 17 unique substances in 2012 up to 176 in 2025 (Table S2). Overall, poisonings with 3-methylmethcathinone (3-MMC, *n* = 965, 22%), bromazolam (*n* = 378, 9%), 4-fluoroamphetamine (4-FA, *n* = 224, 5%), 4-bromo-2,5-dimethoxyphenethylamine (2C-B, *n* = 233, 5%) and 4-methylmethcathinone (4-MMC/mephedrone, *n* = 220, 5%) (all percentages relative to all NPS poisonings) were reported most frequently (Table S2). In 2012, most NPS poisonings involved 4-MMC and methoxetamine (both representing 16% of annual NPS poisonings), followed by 4-FA from 2013 to 2017 (27%–41% of annual NPS poisonings) and 2C-B in 2018 (19% of annual NPS poisonings). From 2019 to 2025, 3-MMC was the most prevalent NPS (21%–32% of annual NPS poisonings) (Figure 3).

Poisonings with cathinones reported to the DPIC (2012–2025)

From 2012 to 2025, 1573 poisonings with cathinones were reported to the DPIC. The annual number of cathinone poisonings increased from six in 2012 to 326 in 2025 (Table 1). The most frequently involved cathinones were 3-MMC and 4-MMC (Table 1). From 2016 to 2021, in 2023 and in 2025, the annual number of 3-MMC poisonings increased. The incidence rate of 3-MMC poisonings peaked in 2021. A similar trend was observed for 4-MMC poisonings. The highest number of 4-MMC poisonings was reported in 2022, while the incidence rate peaked earlier, in 2018.

Poisonings with benzodiazepines reported to the DPIC (2012–2025)

From 2012 to 2025, 1383 poisonings with benzodiazepines were reported to the DPIC. From 2019 to 2024, the annual number of benzodiazepine poisonings increased, with a peak of 342 in 2024 (Table 1). The most frequently involved designer benzodiazepines were bromazolam and pyrazolam. Poisonings with bromazolam were first reported to the DPIC in 2021 (Figure 3). Since then, the annual number of bromazolam poisonings has increased nearly 10-fold, from 14 in 2021 to 123 in 2024. The incidence rate of bromazolam poisonings peaked in 2025. Prior to 2021, poisonings involving pyrazolam were rarely reported (0–1 poisonings/year). However, an upward trend was observed, resulting in 48 poisonings in 2024. The highest incidence rate of pyrazolam poisonings was observed in 2022.

Poisonings with phenethylamines reported to the DPIC (2012–2025)

From 2012 to 2025, 612 poisonings with phenethylamines were reported to the DPIC. The highest number of poisonings occurred in 2016 (Table 1). The most frequently involved synthetic phenethylamines were 4-FA and 2C-B. From 2012 to 2016, the number of 4-FA poisonings increased, peaking at 50 in 2016. Thereafter, the annual number declined and stabilized at approximately 1–5 poisonings/year. The incidence rate of 4-FA poisonings peaked in 2015. The annual number of 2C-B poisonings increased from one in 2012 to 28 in 2021. From 2016 to 2023, the annual number of 2C-B poisonings remained relatively constant at approximately 23 poisonings/year (range = 19–28 poisonings/year). Notably, temporary declines occurred in 2019 and in 2024 (both $n = 11$). In 2025, the number of 2C-B cases increased, but did not return to its previous level. The highest incidence rate of 2C-B poisonings was observed in 2020.

Poisonings with arylcyclohexylamines reported to the DPIC (2012–2025)

From 2012 to 2025, 182 poisonings with arylcyclohexylamines were reported to the DPIC. Until 2019, the annual number of arylcyclohexylamines poisonings remained <10. In 2025, 41 poisonings were reported (Table 1). From 2012 to 2016, all arylcyclohexylamine poisonings involved methoxetamine. However, the most commonly involved arylcyclohexylamine was 2-fluorodesketamine.

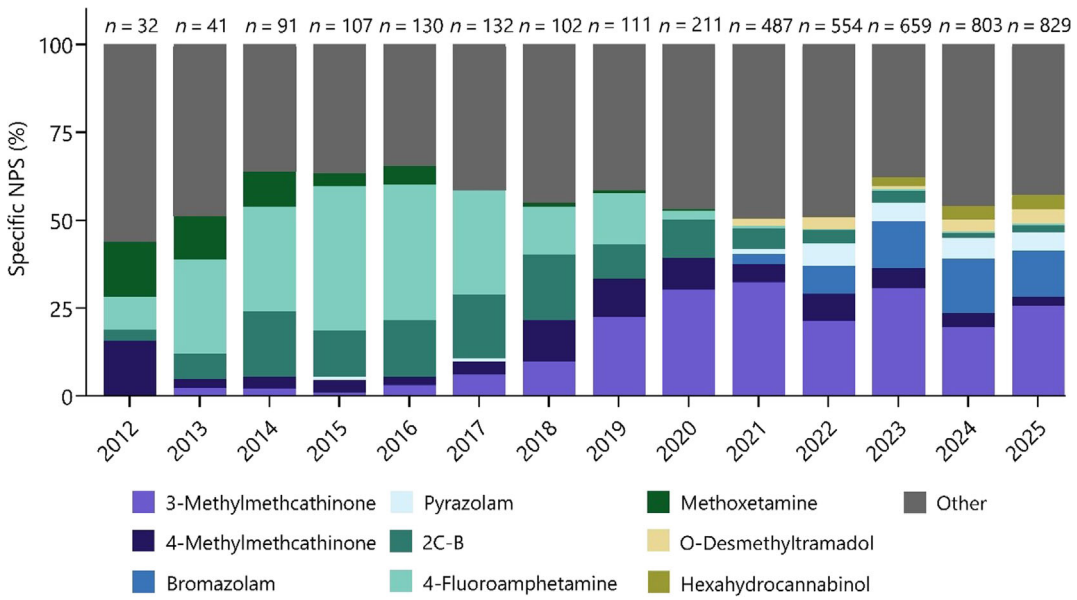

FIGURE 3 Poisonings with specific new psychoactive substances (NPS) reported to the Dutch Poisons Information Center (DPIC) from 2012 to 2025. The annual incidence rate of poisonings with specific NPS is shown as a percentage of the annual number of all NPS poisonings. 2C-B = 4-bromo-2,5-dimethoxyphenethylamine.

Poisonings with cannabinoids reported to the DPIC (2012–2025)

From 2012 to 2025, 150 poisonings with cannabinoids were reported to the DPIC (Table 1). Most poisonings involved the semi-synthetic cannabinoid hexahydrocannabinol (HHC), which was reported from 2023 onwards (Figure 3).

Poisonings with opioids reported to the DPIC (2012–2025)

From 2012 to 2025, 131 poisonings with opioids were reported to the DPIC (Table 1). The majority of opioid poisonings (70%) were reported in 2024 and 2025. Most poisonings involved *O*-desmethyltramadol (ODT), which was not reported prior to 2021 (Figure 3). Since 2024, multiple nitazene poisonings were reported, followed by methiodone (IC-26) poisonings in 2025 (Table S2).

Poisonings with arylalkylamines reported to the DPIC (2012–2025)

From 2012 to 2025, 88 poisonings with arylalkylamines were reported to the DPIC (Table 1). Most poisonings involved 6-(2-aminopropyl)benzofuran (6-APB), which were reported every year from 2012 to 2025.

Poisonings with tryptamines (indolalkylamines) reported to the DPIC (2012–2025)

From 2012 to 2025, 85 poisonings with tryptamines were reported to the DPIC (Table 1). The most commonly involved tryptamine was *N*,*N*-dimethyltryptamine (DMT), reported almost every year except for 2018 and 2021.

Poisonings with piperidines and pyrrolidines reported to the DPIC (2012–2025)

From 2012 to 2025, 29 poisonings with piperidines and pyrrolidines were reported to the DPIC (Table 1). The majority of piperidine and pyrrolidine poisonings involved 4-fluoromethylphenidate (4F-MPH).

Poisonings with other (combinations of) NPS reported to the DPIC (2012–2025)

From 2012 to 2025, 56 poisonings with other (combinations of) NPS were reported to the DPIC (Table 1). The most frequently reported NPS within the category of other NPS was 3-fluorophenmetrazine (3-FPM), with poisonings reported annually from 2018 to 2024 at a rate of 0–3 poisonings/year.

DISCUSSION

The annual number and incidence rate of NPS poisonings reported to the DPIC strongly increased from 2012 to 2025, representing approximately 4300 NPS poisonings. During a 14-year period the predominant categories of NPS, and the specific NPS involved in these poisonings, varied. A notable increase in health incidents involving NPS was also reported by Monitor Drug Incidents (MDI), a sentinel network tracking acute drug-related health incidents in the Netherlands, with details collected from medical services like emergency departments, ambulances, forensic physicians and first-aid posts at large events [18]. The national rise in NPS presence in the Netherlands is supported by various indicators, including data from the Dutch National Drug Monitor, drug-checking services and wastewater-based epidemiology. These sources point to a broad and evolving range of NPS, spanning multiple chemical classes and psychoactive profiles, and an increasing prevalence of use, especially among 'clubbers' [9, 19–25].

In other European countries, an increased number of NPS consumer samples submitted to drug-checking programs has also been reported [26, 27]. The available evidence indicates that most NPS samples do contain the expected substance, although reliability varies across years and for specific NPS. Some NPS appear more prone to substitution or adulteration than others. Data from the Dutch drug-checking service indicated that between 2018 and 2022, 90% of consumer-submitted samples (containing recreational drugs, including NPS) contained the expected substance [28]. The reliability of self-reported NPS use is further supported because the Dutch government generally does not prosecute individuals for the possession or use of small amounts of controlled substances [3], reducing a patient's likelihood of concealing drug use.

A systematic nationwide overview for NPS-related fatalities is currently lacking in the Netherlands. Therefore, the number of deaths attributable to the use of NPS is unknown [29]. Nevertheless, several case reports describing fatal intoxications involving NPS have been published over the years in our country [13, 30].

Not all available data sources show a continued increase in the presence of NPS on the drug market. Data from European law enforcement agencies showed that between 2017 and 2020 the number of NPS seizures declined, while the total quantity fluctuated. Seizures increased in 2021 and 2023, with seized quantities reaching a historical peak in 2023 [1]. In 2022, The highest seized volume was reported in the Netherlands (24 613 kg) [31]. In addition, the number of ED visits for NPS poisoning peaked in 2014–2015, possibly associated with an increased awareness of NPS amongst physicians and funded projects to analyze NPS exposures, but have declined more recently [4, 7]. However, identifying NPS poisonings in multi-center retrospective database research may be challenging, possibly leading to an underestimation of the prevalence of NPS poisonings.

From 2020 onwards, we observed a strong increase in the number of poisonings involving cathinones and benzodiazepines. Cathinones now dominate the European NPS market, as reflected by their position as the second-largest NPS category monitored by the EU Early Warning System and the percentage and overall quantity of material seized by law enforcement agencies [1]. The widespread availability and structural diversity of cathinones may contribute to an increase in associated health incidents, as supported by our data. Compared with cathinones, benzodiazepine-related NPS are a relatively small category (38 individual substances notified to the EUDA up to 2024), and the number and quantities seized are limited. As drug-checking programs only monitor samples offered by consumers, often involving 'party drugs', benzodiazepines are rarely detected [9]. However, the incidence of poisonings with benzodiazepine-related NPS is increasing globally [12, 32–36]. The under-reporting of poisonings involving these substances may be linked to the limited availability of validated analytical methods, misinterpretation of toxicological results or insufficient awareness regarding the existence of this NPS category [37]. Consequently, PCCs were among the first to report health incidents involving NPS of the benzodiazepine category [12, 32, 34].

In contrast to other NPS categories, we observed relatively few poisonings involving cannabinoids (n = 150) and opioids (n = 131), although the number of poisonings has increased in recent years. Cannabinoids are the largest NPS category monitored by the EU Early Warning System and are commonly involved in health incidents in many countries [38]. Their contrasting low presence in the Netherlands may be attributed to the easy accessibility of cannabis in Dutch coffeeshops, which likely reduces the use of (semi-)synthetic cannabinoids [39]. However, we recently observed an increase in the number of poisonings with edibles containing the semi-synthetic cannabinoids hexahydrocannabinol (HHC) and tetrahydrocannabiphorol (THCP) [40].

Poisonings with opioids were dominated by ODT (73% of all opioid poisonings), while exposures to other variants were only sporadically reported in earlier years. While deaths from ODT poisoning have only been reported in the context of polydrug use [41, 42], most cases still resulted in moderate to severe symptoms, often requiring hospitalization [43]. The low number of opioid poisonings contrasts with the broader European context, where 88 opioids have been identified since 2009 (EUDA, 2025). Opioid-related NPS pose a significant public health threat owing to their high potential for respiratory depression and associated mortality [44]. This mainly concerns fentanyl derivatives and benzimidazole (nitazene) opioids. In recent years, multiple deaths have been associated with these substances. In addition, we have observed poisonings with nitazenes since 2024, followed by poisonings with methiodone (IC-26) since 2025. Opioid-related NPS poisonings may be under-reported because these substances are increasingly present as adulterants in samples sold as prescription medication, leaving users and healthcare providers unaware of the true exposure [1].

We observed a temporal variation in both dominant NPS categories and the specific NPS involved in poisonings. For example, phenazepam poisonings were only reported between 2014 and 2018. Its scheduling in the Netherlands in 2017 likely contributed to the subsequent decline of reported health incidents. A similar pattern was seen with 4-FA that peaked in 2016 (n = 50) but nearly disappeared from 2020 to 2022. This decrease may be partly explained by its regulation in 2017, which was preceded by extensive media coverage of severe poisonings [16]. Negative media coverage likely discouraged 4-FA use, contributing to a decline in poisonings. However, media exposure may also increase PCC consultations by raising awareness among healthcare providers. This might have occurred with alpha-pyrrolidinovalerophenone (α-PVP), which received intense media attention in 2016 for causing extremely violent 'zombie-like' behavior. A peak in reported suspected poisonings (n = 10) was observed that year, followed by a decline thereafter. As most cases lacked analytical confirmation, clinical features could not be definitively linked to α-PVP. Moreover, excited delirium, commonly reported in these cases, can be caused by various psychoactive substances, including established recreational drugs and alcohol [45]. It is plausible that media narratives influenced clinical suspicion and reporting bias toward α-PVP.

Another factor influencing poisoning trends is NPS availability and composition. In 2019, most 2C-B samples analyzed by Dutch drug-checking services were adulterated or contained no 2C-B at all [46]. This may have negatively influenced consumer demand for 2C-B, resulting in a decline in overall use and associated poisonings. Conversely, adulterated NPS can increase health risks when users are unaware of the actual contents of pills or powders. Following the 2021 ban on 3-MMC, reported poisonings initially declined, but rose again in 2023. Data from Dutch drug-checking services revealed that many samples sold as 3-MMC actually contained other legal cathinones, like 3-chloromethcathinone (3-CMC) or 2-methylmethcathinone (2-MMC) [47], which may differ in their potency and pharmacokinetics, thereby potentially increasing overdose risk.

A significant increase in the annual incidence rate of NPS poisonings occurred in 2020, which was when the COVID pandemic started in the Netherlands. Whether this increase was caused by the pandemic is open to debate. Other possible causes include variables not included in the time series analysis, such as greater ease in obtaining NPS products on the market in terms of price, the number of websites and advertising on social networks. Evidence on the impact of the COVID pandemic on the Dutch NPS market is limited and heterogeneous. An analysis of online drug markets indicated shifts in substance availability during the first lockdown, with reduced activity for stimulants (e.g. amphetamine, cocaine, MDMA) and a relative increase for substances such as 2C-B, ketamine and LSD [48]. Other studies suggest that 3-MMC use increased among certain groups during the pandemic, while 2C-B use remained stable [49, 50], and 4-FA use declined and remained low thereafter [51]. In addition, data from drug-checking services showed a reduced number of sample submissions during 2020–2021, followed by a marked increase in 2022, particularly for 3-MMC [52–54]. Overall, these findings suggest that the pandemic influenced drug markets and use patterns, which may have resulted in an increase of NPS poisonings. Finally, a seasonal pattern was observed in the number of reported

NPS poisonings, being highest in July and December. A high incidence of drug-related health incidents during the summer months has been described previously [55, 56].

Limitations

The primary limitation of the PCC data is selection bias, as the DPIC is only contacted by healthcare providers, typically about patients already experiencing adverse effects, or when the healthcare provider is unfamiliar with the management of NPS poisonings. Changes in awareness, media attention and diagnostic practices may have increased the self-reported likelihood of NPS exposure. Most poisonings reported to the DPIC are not analytically confirmed and rely on self-reported information. This may result in misclassification when users do not receive the substance they intended to buy. Finally, the number of NPS poisonings presented here may be influenced by the DPIC service model, which includes an online platform for healthcare professionals (www.vergiftigingen.info), alongside its 24/7 telephone service. Monographs for most NPS are absent online. Monographs on 2C-B and 4-FA have been available since 2020, and for 3-MMC since February 2025, possibly lowering the call volume on these NPS.

CONCLUSION

The increased incidence of NPS poisonings reported to the DPIC underscores the relevance of toxicosurveillance by PCCs in monitoring the evolving epidemiology of NPS-related health incidents. The integration of PCC data with complementary data sources such as drug-checking programs, law enforcement seizures, wastewater analysis, drug-related deaths and ED presentations, can improve the overall monitoring of NPS. By extending this surveillance approach to other PCCs a more thorough insight into the European and worldwide drug markets could be provided, as well as a better understanding of the potential public health risks of NPS use.

AUTHOR CONTRIBUTIONS

Johanna J. Nugteren-van Lonkhuyzen: Conceptualization; methodology; investigation; formal analysis; writing—original draft; writing—review and editing; visualization. **Irma S. van den Hengel-Koot:** Investigation; formal analysis; writing—review and editing; visualization. **Claudine C. Hunault:** Formal analysis; writing—review and editing. **Dylan W. de Lange:** Supervision; writing—review and editing. **Antoinette J.H.P. van Riel:** Supervision; writing—review and editing; methodology; conceptualization. **Laura Hondebrink:** Conceptualization; methodology; investigation; formal analysis; writing—review and editing; visualization.

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DECLARATION OF INTERESTS

All authors have completed the International Committee of Medical Journal Editors (ICMJE) uniform disclosure form at http://www.icmje.org/coi_disclosure.pdf and declare: no support from any organization for the submitted work; no financial relationships with any organizations that might have an interest in the submitted work in the previous 3 years; no other relationships or activities that could appear to have influenced the submitted work.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

ORCID

Johanna J. Nugteren-van Lonkhuyzen https://orcid.org/0000-0002-4255-9158
Irma S. van den Hengel-Koot https://orcid.org/0000-0002-0370-7285
Claudine C. Hunault https://orcid.org/0000-0001-7843-6208
Dylan W. de Lange https://orcid.org/0000-0002-0191-7270
Antoinette J. H. P. van Riel https://orcid.org/0000-0002-2746-1371
Laura Hondebrink https://orcid.org/0000-0001-9823-008X

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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