NIEUWE PSYCHOACTIEVE STOFFEN: KLINISCHE UITDAGINGEN ANNO 2025

Avondlezing St-Hiëronymus
20 februari 2025

Dr. Frederick Van Der Sypt
DOC & ACG De Sleutel

INHOUD VAN DEZE LEZING

- Inleiding NPS
- Cathinonen
- Ketamine
- Opioïden
- Benzo's
- Cannabinoïden
- Beleid?

EUDA
EUROPEAN UNION DRUGS AGENCY

EU EARLY WARNING SYSTEM ON NPS

The EU Early Warning System monitors 1000 NPS

In 2024, the EU Early Warning System (EWS) on new psychoactive substances (NPS) marks a significant milestone by formally notifying delta-9-THC-methylcarbonate, its 1000th substance. Amongst the monitored NPS, nitazene opioids account for 23 substances, while 24 are semi-synthetic cannabinoids.

EU Early Warning System on NPS

Established in 1997, the EU Early Warning System was the first regional mechanism set up to monitor and respond to uncontrolled new drugs in Europe.

Improved preparedness to NPS in the new EUDA mandate

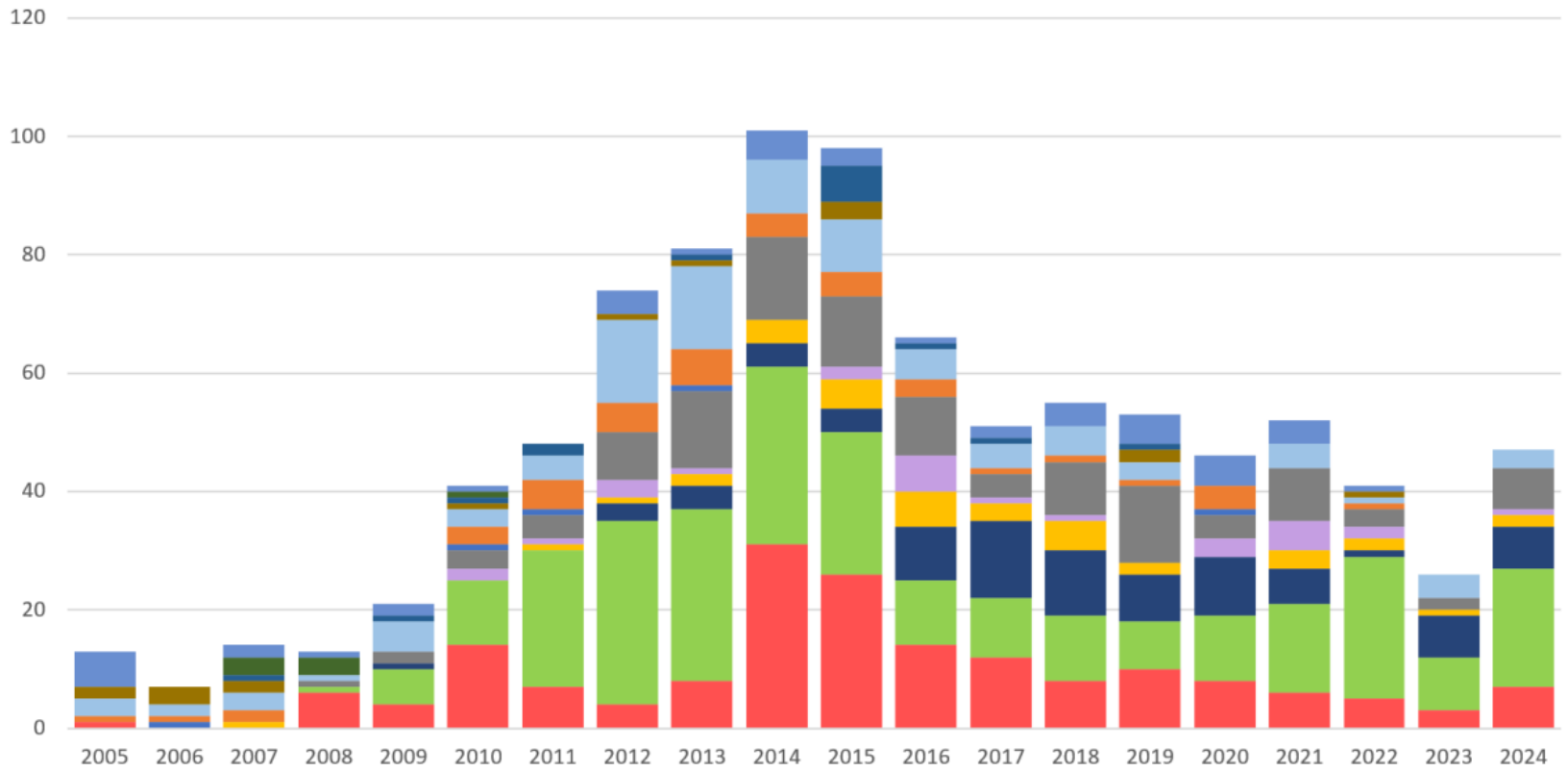
In addition to the EWS and risk assessment, the new European Drug Alert System and Network of Forensic and Toxicological Laboratories will strengthen EU preparedness on NPS.

Number of NPS notified for the first time by EWS (EU+2)

1000 NPS currently under monitoring

47 NPS reported for the first time in 2024

185 public health risk communications were issued by the EUDA until 2024



Category	Monitored NPS
Cathinones	177
Cannabinoids	277
Opioids	88
Benzodiazepines	38
Arylcyclohexylamines	30
Others	127
Aminoindanes	6
Arylalkylamines	42
Phenethylamines	114
Piperazines	19
Piperidines	15
Plants and extracts	9
Tryptamines	58

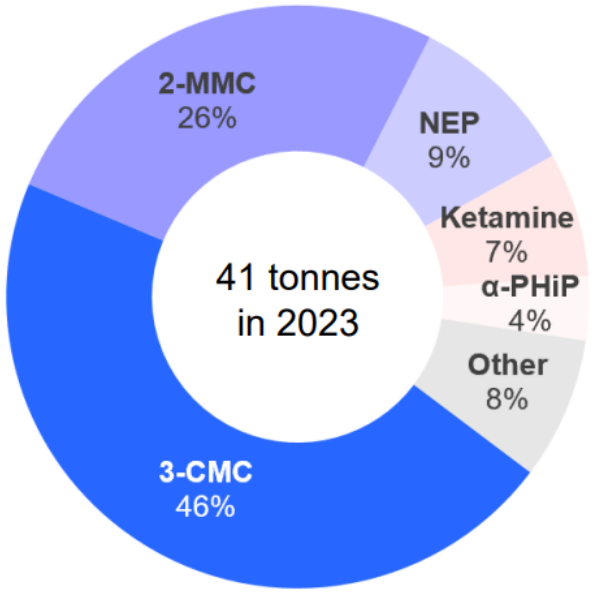
Number of seizures and quantity of NPS seized (EU)

341 NPS different detected in seizures in 2023

37 NPS risk-assessed by the EUDA

41 tonnes of NPS in Europe in over 34 000 seizures in 2023

Quantity seized by substance, 2023 (EU)



EU Drug Market: New psychoactive substances — In-depth analysis

EUDA
EUROPEAN UNION DRUGS AGENCY

EUROPOL

EU Drug Market: New psychoactive substances describes the European NPS market from production and trafficking to distribution and use. It details the processes, materials and players involved at various stages and levels of the market. The module takes a threat assessment approach, identifying key issues and defining recommendations for action at EU and Member State level.

This resource is a module of EU Drug Markets: In-depth analysis, the fourth comprehensive overview of illicit drug markets in the European Union by the EMCDDA and Europol.

Last update: *27 June 2024*

https://www.euda.europa.eu/publications/eu-drug-markets/new-psychoactive-substances_en

sciensano

HEALTH INFORMATION

THE DRUG SITUATION IN BELGIUM IN 2022

Annual report from the Belgian REITOX network

JEROME ANTOINE · MARGOT BALCAEN · MAARTEN DEGREEF · KIM FERNANDEZ · LIES GREMEAUX · ELS PLETTINCKX · LUK VAN BAELEN


afmps
fagg
Belgian Early Warning
System on Drugs
by Sciensano
NICC
INCC
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eurotox
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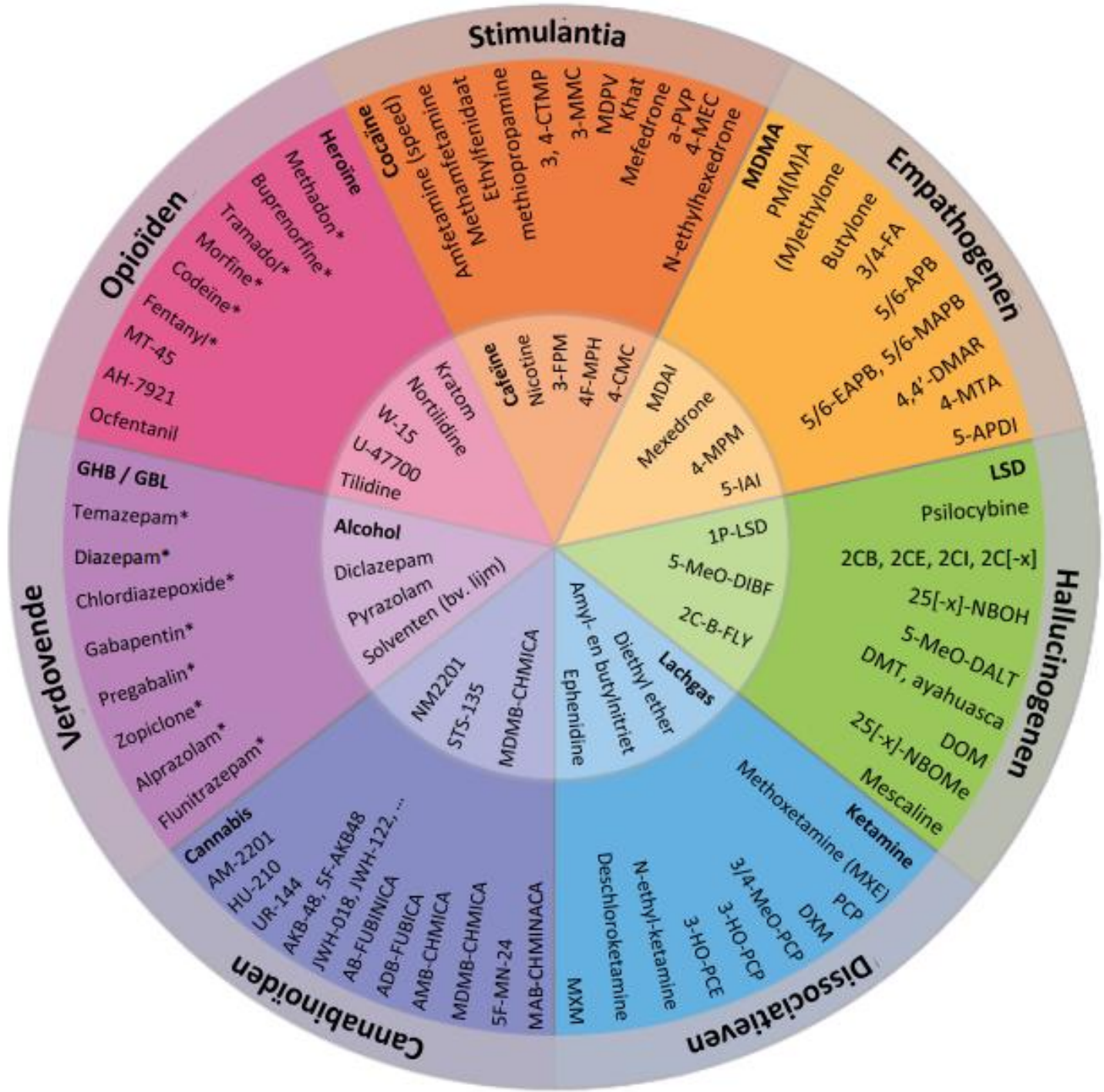
emcdda


Stimulantia
Cocaïne
Cocaïne (speed)
Amfetamine
Methamfetamine
Ethylfenidaat
methiopropamine
3, 4-CTMP
3-MMC
MDPV
Khat
Mefedrone
a-PVP
4-MEC
N-ethylhexedrone
Empathogenen
MDMA
PM(M)A
(M)ethylone
Butylone
3/4-FA
5/6-APB
5/6-EAPB, 5/6-MAPB
4,4'-DMAR
4-MTA
5-APDI
Hallucinogenen
LSD
Psilocybine
2CB, 2CE, 2CI, 2C[-x]
25[-x]-NBOH
5-MeO-DALT
DMT, ayahuasca
DOM
25[-x]-NBOMe
Mescaline
Dissociatieven
Ketamine
Methoxetamine (MXE)
PCP
DXM
3/4-MeO-PCP
3-HO-PCP
3-HO-PCE
N-ethyl-ketamine
Deschloroketamine
MXM
Cannabinoïden
Cannabis
AM-2201
HU-210
UR-144
AKB-48, 5F-AKB48
JWH-018, JWH-122, ...
AB-FUBINICA
ADB-FUBICA
AMB-CHMICA
MDMB-CHMICA
5F-MN-24
MAB-CHMINACA
Verdovende
GHB / GBL
Temazepam*
Diazepam*
Chlordiazepoxide*
Gabapentin*
Pregabalin*
Zopiclone*
Alprazolam*
Flunitrazepam*
Opioïden
Heroïne
Methadon*
Buprenorfine*
Tramadol*
Morfine*
Codeïne*
Fentanyl*
MT-45
AH-7921
Ocfentanil
Kratom
Nortilidine
W-15
U-47700
Tilidine
Cafeïne
Nicotine
3-FPM
4F-MPH
4-CMC
MDAI
Mexedrone
4-MPM
5-IAI
1P-LSD
5-MeO-DIBF
2C-B-FLY
Lachgas
Diethyl ether
Amyl- en butylnitriet
Ephenidine
NM2201
STS-135
MDMB-CHMICA
Alcohol
Diclazepam
Pyrazolam
Solventen (bv. lijm)

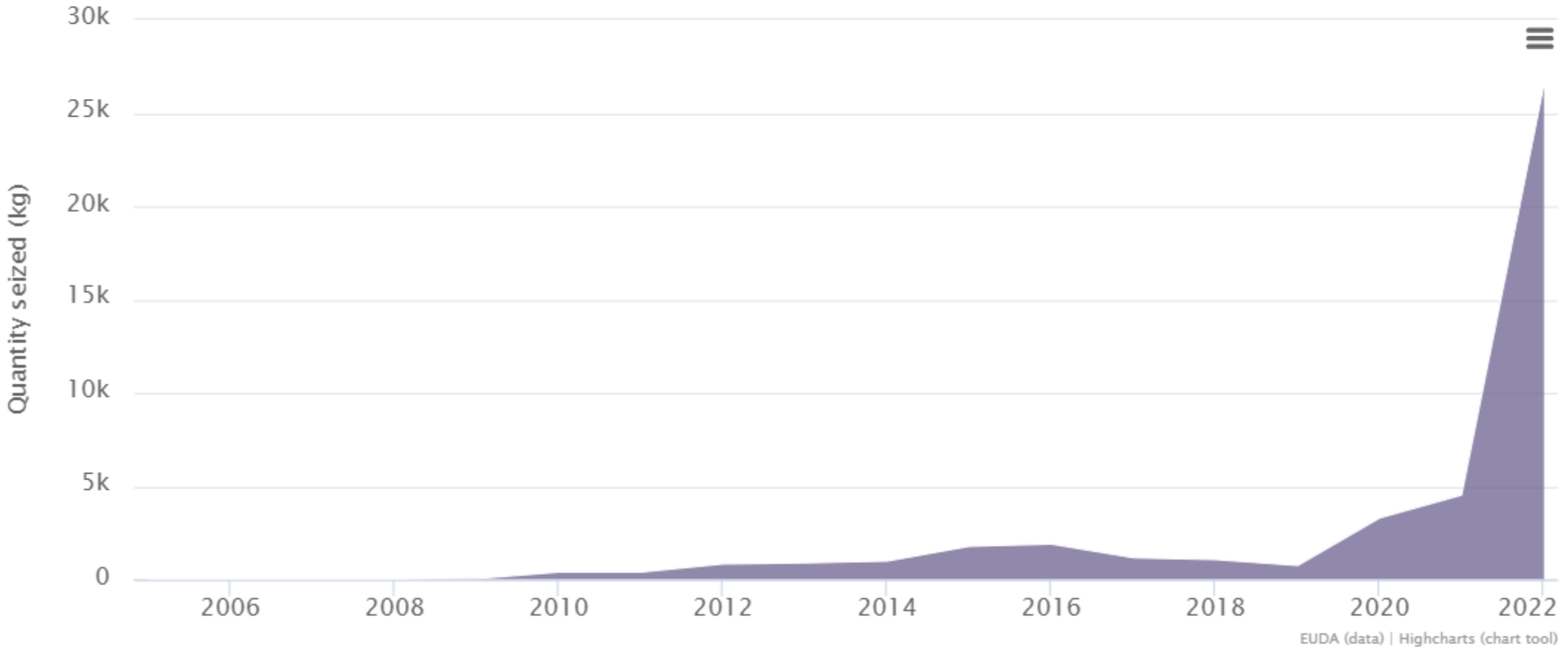
CATHINONES: VAN CATHA TOT FLAKKA

Synthetic cathinones becoming more significant in Europe's stimulant market

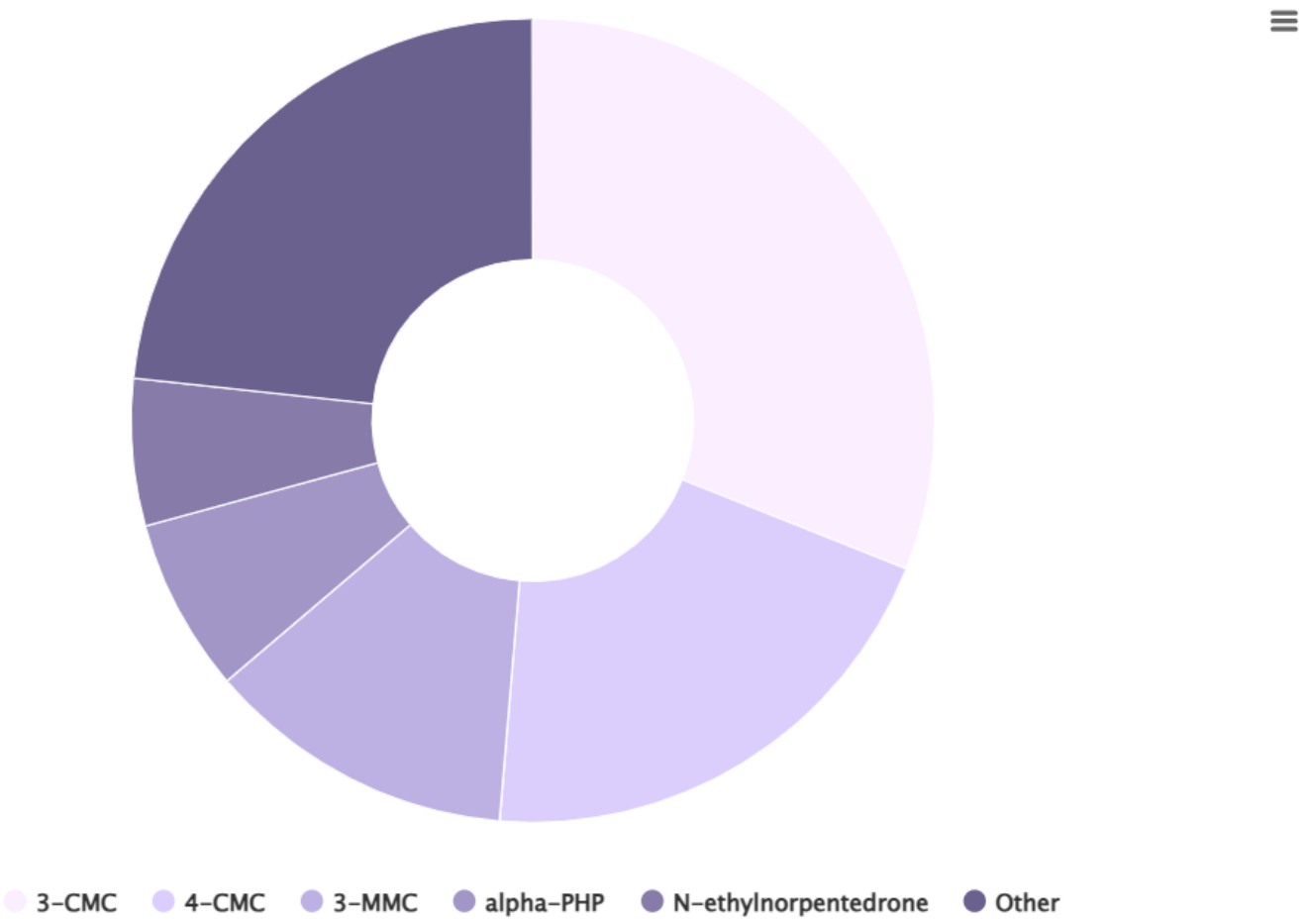
Synthetic cathinones have appeared and become established as replacements for stimulants such as amphetamine in some parts of Europe.

In 2022, large quantities of cathinones such as 3-CMC and 3-MMC, mostly trafficked from India, continued to be seized in Europe, indicative of the important role these drugs now play in some countries. This is a cause for concern, compounded by information suggesting that cathinones are also now increasingly being produced in Europe. Cathinones are also sold alongside or as other drugs, potentially increasing the risk of harm. In 2022 and 2023, the EU Early Warning System noted an increase in reports of synthetic cathinones mis-sold as MDMA or used to adulterate MDMA.

Seizures of synthetic cathinones reported to the EU Early Warning System: quantity of material seized for all forms reported in weight, European Union, 2005-2022 (kg)



Top five synthetic cathinones seized by number of seizures reported to the EU Early Warning System, European Union, 2022 (9 661 seizures)



Dismantled site associated with 4-CMC production in Poland, seized in 2022 with approximately 2 400 litres of 4-CMC seized. Source: Central Police Investigation Bureau, Polish Police

Price of cathinones in the Netherlands, 2022

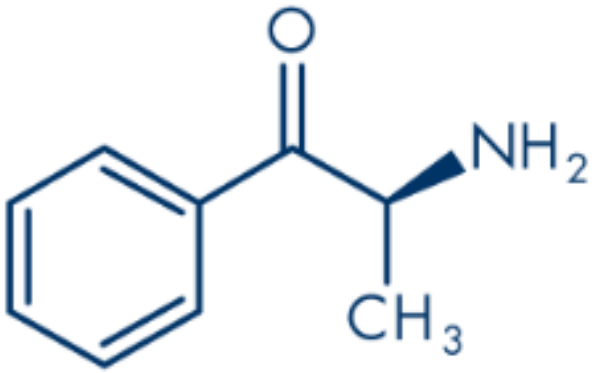
Cathinone	Location in the supply chain	Price
4-MMC powder	Wholesale	EUR 2 125 per kilogram
3-MMC powder	Wholesale	EUR 2 469 per kilogram
4-CMC powder	Wholesale	EUR 2 400 per kilogram
3-CMC powder	Wholesale ([1])	EUR 2025 per kilogram
4-MMC powder	Street price	EUR 22.50 per gram
3-MMC powder	Street price	EUR 18.00 per gram

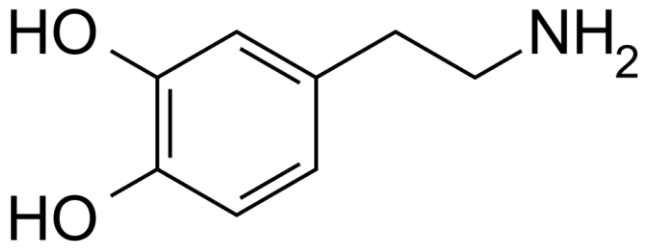
Source: Central Criminal Investigations Division, Dutch Police, Netherlands.
([1]) Price based on one information source. The wholesale and street prices for tablets containing these cathinones are not available. Information on the street price of 4-CMC powder and 3-CMC powder is not available.

Een greep uit de cathinones…

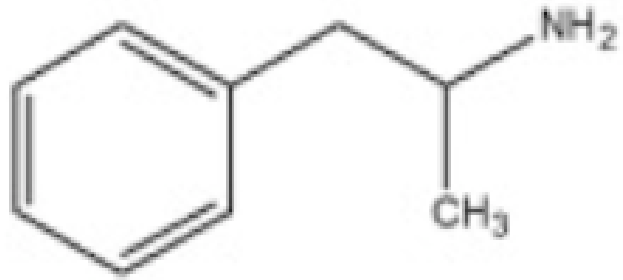
- N-Ethylbuphedrone (*NEB*)
- N-Ethylheptedrone(*HEP*)
- N-Ethylhexedrone (*HEX-EN*)
- MBDP (*Methyl-K*)
- MDPHP
- MDPV
- MPHP
- Mephedrone (*4-MMC*)
- Methcathinone (*M-CAT*)
- Methylone (*βk-MDMA*)
- Mexedrone (*4-MMC-MeO*)
- Naphyrone
- NEP (*N-Ethylpentedrone*)
- Pentedrone
- Pentylone (*βk-MBDP*)
- UWA-101 (*α-cyclopropyl-MDMA*)
- 3-CMC (*Clophedrone*)
- 3-MMC (*Metaphedrone*)
- 3-MEC
- 3-FMC (*3-Fluoromethcathinone*)
- 4-CMC (*Clephedrone*)
- 4-FMC (*4-FMC*)
- 4-MBC (*Benzedrone*)
- 4-MEC
- 4-MeMABP (*4-Methylbuphedrone*)
- 4-MPD (*4-Methylpentedrone*)
- α-PBP
- α-PHP
- α-PPP
- α-PVP
- α-PVT
- Butylone (*βk-MBDB*)
- Buphedrone (*MABP*)
- Bupropion (*Wellbutrin*)
- Cathinone (*Khat*)
- EBDP (*Ethyl-K*)
- EBDB (*Ethyl-J*)
- Ephylone (*βk-EBDP, N-Ethylpentylone*)
- Ethcathinone (*ETH-CAT*)
- Ethylone (*βk-MDEA*)
- Eutylone (*bk-EBDB*)
- Hexedrone

Figure 1: Cathinone



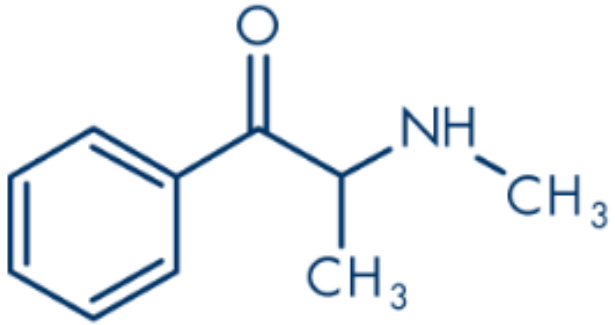


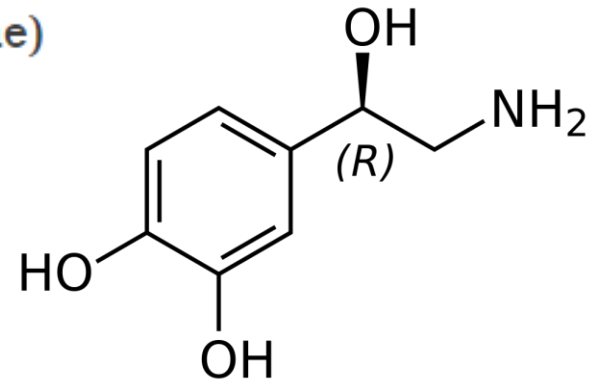
Dopamine



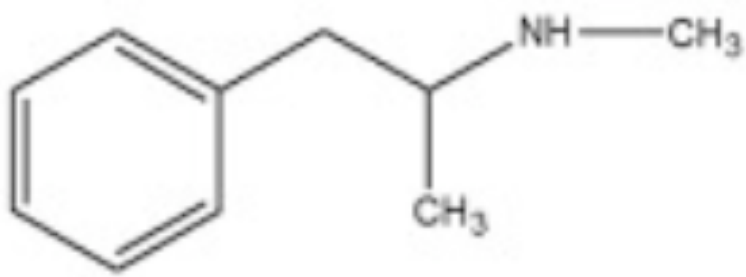
amphetamine

Figure 5: Methcathinone (ephedrone)



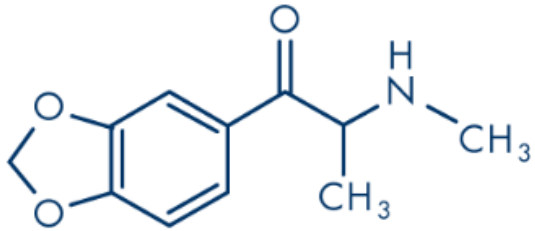


Noradrenaline



methamphetamine

Figure 4: Methylone (βk-MDMA, 3,4-methylenedioxy-N-methylcathinone)



Methylone

Summary sheet: Methylone

3,4-Methylenedioxy-N-methcathinone (also known as **M1**, **MDMC**, **βk-MDMA**, and **Methylone**) is a novel stimulant-entactogen substance of the cathinone class.

Methylone was first synthesized by chemists Peyton Jacob III and Alexander Shulgin in 1996 as a potential antidepressant.[1]

Methylone is sometimes used as a substitute for MDMA due to similarities in their effects. Alexander Shulgin commented that the substances has "almost the same potency of MDMA, but it does not produce the same effects." He also stated that it "has an almost antidepressant action, pleasant and positive, but not the unique magic of MDMA."[2]

The toxicity of methylone has not been well-studied, although it likely does not exceed that of MDMA, and it has a limited history of human usage. It is highly advised to use harm reduction practices if using this substance.

A-PVP

(Redirected from Apvp)

Not to be confused with A-PHP.

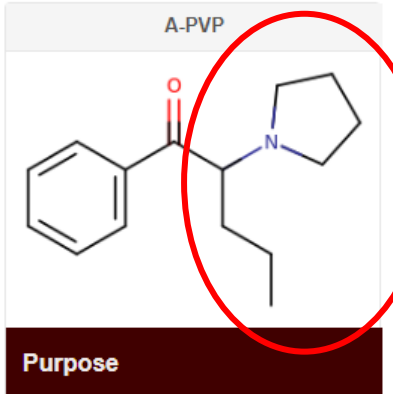
Summary sheet: A-PVP

alpha-Pyrrolidinovalerophenone (also known as **α-PVP**, **A-PVP**, **alpha-PVP**, and **flakka**) is a novel stimulant substance of the cathinone and pyrrolidinophenone classes. α-PVP is chemically related to prolintane and belongs to a group called the substituted cathinones, which includes compounds like MDPV, hexen, and a-PHP. It acts as a norepinephrine-dopamine reuptake inhibitor.

α-PVP was patented in the 1960s by Boehringer Ingelheim,[1] although it was never marketed. Reports of its use began to appear in the early 2010s. α-PVP has been subject to much scrutiny by the media as one of the ingredients found in "bath salts" or "legal highs" products.[*citation needed*] It has been mass produced in China and sold online as a research chemical.[*citation needed*] It has been linked to numerous hospitalizations and overdose deaths.[2]

User reports indicate that α-PVP produces powerful but short-lived stimulant effects comparable to those of methamphetamine and cocaine when insufflated or vaporized. Commonly reported effects include stimulation, disinhibition, increased libido, compulsive redosing, and euphoria. Like other synthetic cathinones, α-PVP is associated with compulsive use and addiction.

Very little data exists about the pharmacological properties, metabolism, and toxicity of a-PVP. Due to its potent psychostimulant effects and unknown toxicity profile, it is highly advised to use harm reduction practices if using with this substance.

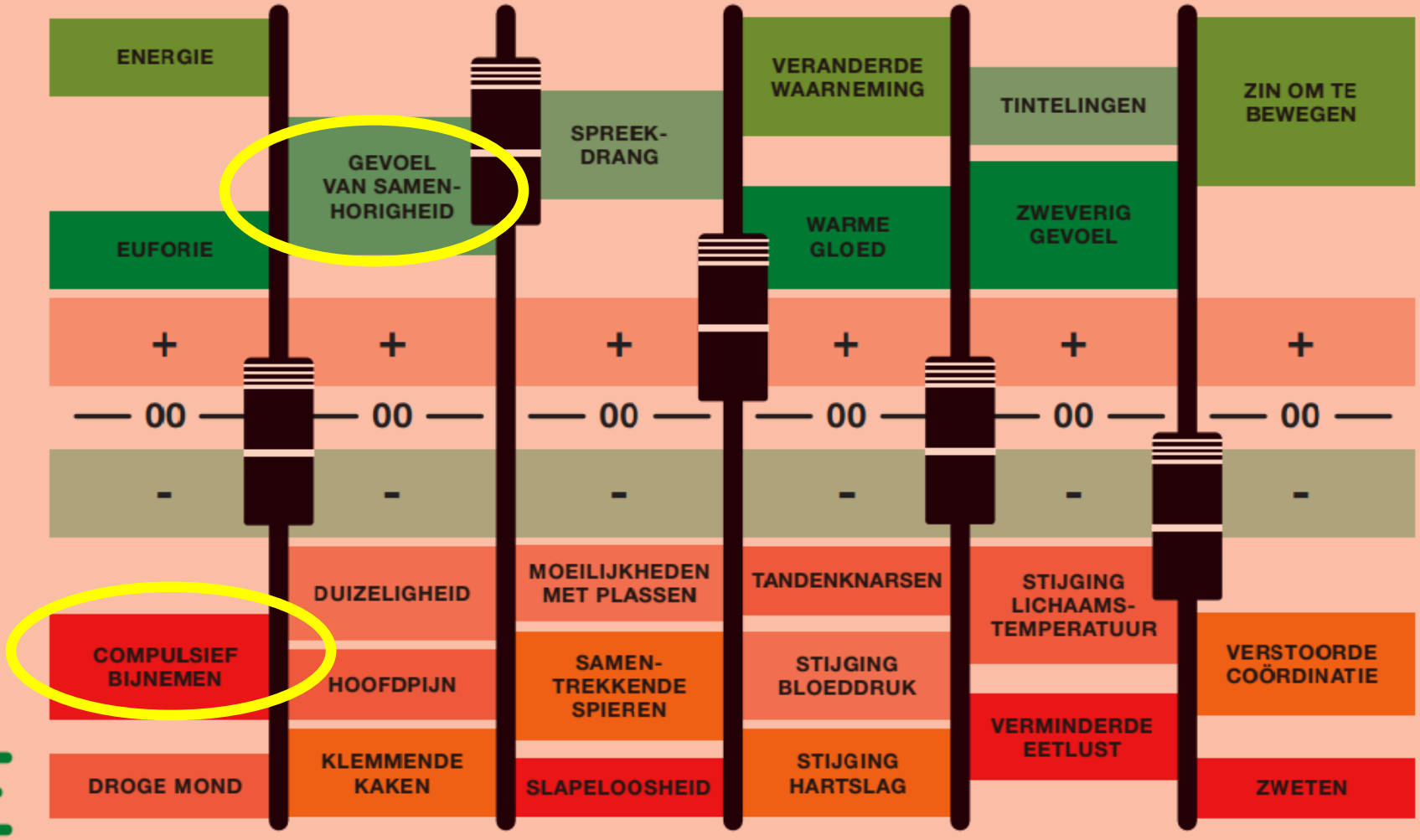


SAFE'N SOUND

MEPHEDRONE

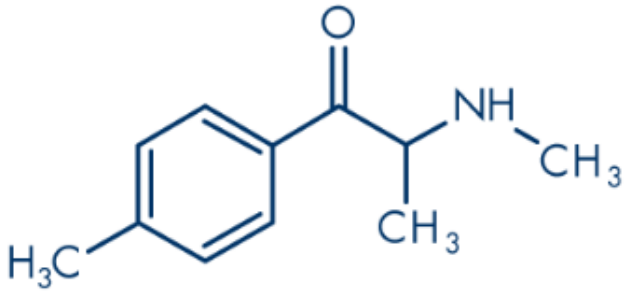
→EFFECTEN

De effecten worden sterk beïnvloed door de samenstelling van het product, de gebruiker en de omgeving waarin gebruikt wordt.



MEFEDRONE 4-MMC

Figure 3: Mephedrone (4-methylmethcathinone, 4-MMC)



- Gesynthetiseerd in 1929
- Op de markt in Europa sinds 2007
- Stimulans met subjectief cocaïne/MDMA-like effect (entactogeen volgens 78% van geïnterviewden) < populariteit?
- Functies bij chemseks: ontremming, lustverhogend (79%), langere duur van de seks, drempelverlagend naar andere vormen van seksueel contact

MEFEDRONE 4-MMC

- Duurtijd bij snuiven of peroraal: 2-3uur
- Kortdurend effect bij IV-gebruik (15-30 minuten) wat leidt tot compulsief gebruik en meer naaldcontacten!
- Gesnoven, peroraal, rectaal, injectie (slamming)
- Toxidroom vergelijkbaar met andere stimulantia
- Snelle tolerantie met escalerend compulsief gebruik

3-MMC

The substance appears to be used by existing stimulant users, such as those who use cocaine, amphetamines, ecstasy, and other cathinones, who either add it to their existing repertoire or use it as a replacement substance. This includes recreational use, and, in some cases high risk use, such as injecting. In the latter case, this may be part of chemsex practices including men who have sex with men. In addition, information from one Member State shows that 3-MMC may also be used by vulnerable groups such as young people, including inexperienced drug users. At least in part this is because it was reported to be easily available, not controlled, and having a relatively low cost. It appears that 3-MMC is used in private spaces (such as homes and domestic parties), as well as recreational settings (such as nightclubs, bars/pubs, music festivals), and as part of chemsex settings.

3-MMC

- Voor het eerst in 2012 op de Europese markt
- Vanaf 2020 meer aanwezig op de markt
- Geïmporteerd vanuit China, nu Indië
- Serotonine, noradrenaline en dopamine reuptake-inhibitor
- Chemseks
- Jongeren (goedkoop, beschikbaar, ~~legaal~~ ->3-CMC)
- Kortwerkend, frequente toediening, CAVE IV!

Cathinone Kopen

Deze producten zijn alleen bestemd voor onderzoeksdoeleinden en dus niet voor menselijke consumptie. Bewaar deze 4MMC alternatieven op een koele en droge plaats. Stabiliteit van research chemical 3-MMC kan tot 2 jaar duren onder goede opslag omstandigheden.

3-CMC KRISTAL, 3-CMC POEDER, 2-MMC, 3-CEC

ALLEMAAL | 2-MMC KOPEN | SOLID | 3-CEC KOPEN | 3-CMC KOPEN | POWDER | 3-CMC KOPEN | SOLID | 3.4-DMMC KOPEN | 3.4-DMMC KOPEN | PELLETS | 40MG | 3.4-DMMC KOPEN | POWDER | 4-ME-MABP KOPEN | A-PIHP KOPEN | BK-MDDMA / M11 KOPEN | 3-CMC KOPEN

2-MMC kopen | 1 gram

~~€16,95~~ €12,50

2-MMC kopen | 5 gram

~~€65,00~~ €50,00

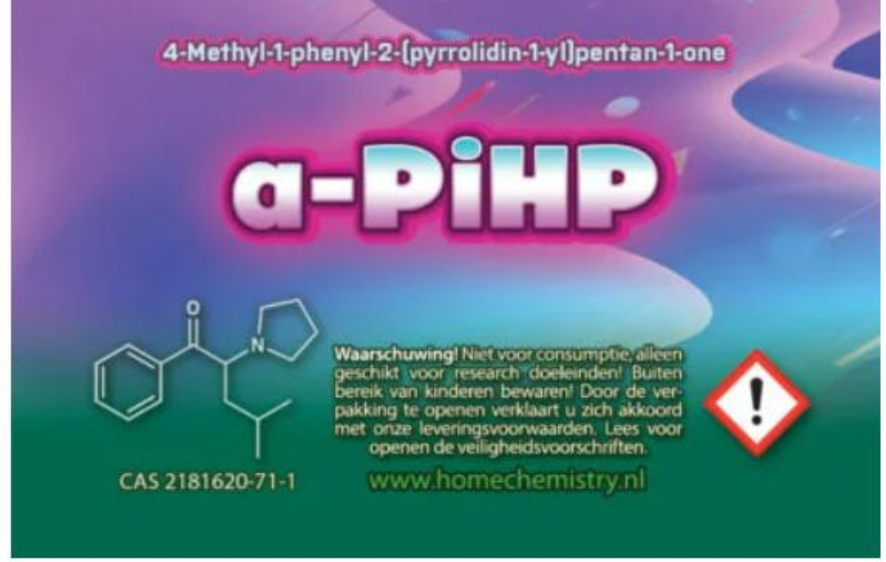
3.4-DMMC Kopen | 5 Pellets | 40mg

Synthetic cathinones drug profile

Pharmacology

As with phenethylamines, in the absence of ring-substitution, cathinones behave as central nervous system (CNS) stimulants, although invariably with a lower potency than the corresponding phenethylamine analogue. The lower potency is caused by the β-keto group creating a more polar molecule less able to cross the blood–brain barrier. Studies on the metabolism of methcathinone

The pyrrolidine ring and the tertiary amino group in MDPV could lead to a more lipophilic, i.e. more potent, molecule; Internet user-forums suggest that the dose is as low as 5–10 mg. Furthermore, it should be noted that p-methoxyphenethylamines (e.g. PMA, PMMA) are known to have a particularly high toxicity, and this property might translate to their βk-analogues. For example, methedrone (p-methoxymethcathinone) has been detected in a few fatalities.



a-PiHP Poeder (1gr)

Niet meer leverbaar

Dit product is verboden sinds 16 april 2024 en verkopen we daarom niet meer!

a-PiHP alternatief aanwezig!

Wij hebben alweer een alternatief gereed voor A-PiHP, genaamd MDPiHP.

MDPiHP komt uit dezelfde cathinone klasse en is uiteraard ook bedoeld voor onderzoeksdoeleinden.

Talk:A-PiHP

(Redirected from A-PiHP)

Not to be confused with A-PHP.

This page has not been fully approved by the PsychonautWiki administrators.

*It may contain **incorrect information**, particularly with respect to dosage, duration, subjective effects, toxicity and other risks. It may also not meet PW style and grammar standards.*

Summary sheet: A-PiHP

alpha-Pyrrolidinohexiophenone (also known as **α-PihP**, and **4-methyl-alpha-pyrrolidinopentanophenone**) is a lesser-known novel stimulant substance of the cathinone and pyrrolidinophenone classes. It is structurally related to MDPV and A-PHP and is one of the latest successors to the designer drug cathinone analog A-PVP|α-PVP].

Subjective effects such as euphoria, thought acceleration, disinhibition and ego inflation. It generally comes in the form of either a fine powder or crystallized shards that can produce powerful but short-lived euphoric stimulant effects reported to be more compulsive in nature (and strength) to vaporized methamphetamine. Like its cathinone predecessors, it is has gained notoriety for its tendency to induce compulsive redosing and addictive behaviors as well the ability to produce delusional states and psychosis when abused. The compulsivity induced in A-PiHP seems to be stronger compared to similar substances in this class, as reported by online anecdotal reports.

Very little data exists about the pharmacological properties, metabolism, and toxicity of α-PiHP. It has recently become commonly marketed as a legal, grey-market alternative to a-PHP, 3-MMC, and A-PVP, and commercially distributed through online research chemical vendors.

It is highly advised to use harm reduction practices if using this substance.

1 unit bestaat uit **1 Gram**

Aantal	Prijs per unit	Totaalprijs	Prijs per Gram
1 Unit	16,950	16,95	16,950
2 Units	15,980	31,96	15,980
3 - 4 Units	15,830	47,49	15,830
5 - 9 Units	15,000	75,00	15,000
10 - 24 Units	13,750	137,50	13,750
25 - 49 Units	13,000	325,00	13,000
50 Units	11,980	599,00	11,980

3 + - IN WINKELWAGEN

Reddit

https://www.reddit.com › mdpihp... · Vertaal deze pagina

MDPiHP research report, part 2. Dosage and duration ...

18 jul 2024 — Previously my **dosage** was 28mg intranasally, after which I did not continue dosing. The effects seemed present at a good level for 3 - 5 hours.

Br J Clin Pharmacol. 2020 Mar; 86(3): 410–419. PMCID: PMC7080616
Published online 2020 Feb 3. doi: 10.1111/bcp.14132 PMID: 31674690

The clinical challenges of synthetic cathinones

Fabrizio Schifano,[1] Flavia Napoletano,[2] Davide Arillotta,[1] Caroline Zangani,[1,3] Liam Gilgar,[4] Amira Guirguis,[5] John Martin Corkery,[1] and Alessandro Vento[6,7,8]

4 EFFECT-CATEGORIEËN BINNEN DE CATHINONES

Gemengd Cocaïne/MDMA effect: 4-MMC, mexedrone

MDMA-like effect: methedrone, 4-trifluoro-MMC

Methamfetamine-like: cathinone, ephedrone (methcathinone)

Pyrovalerones a-PVP, MDPV: meer uitgesproken effecten, zowel in goede als slechte zin; gevoelens van almacht, desoriëntatie, agressie, compulsiviteit, tachycardie, agitatie, hypertensie, hallucinaties, delier, hyperthermie, coma

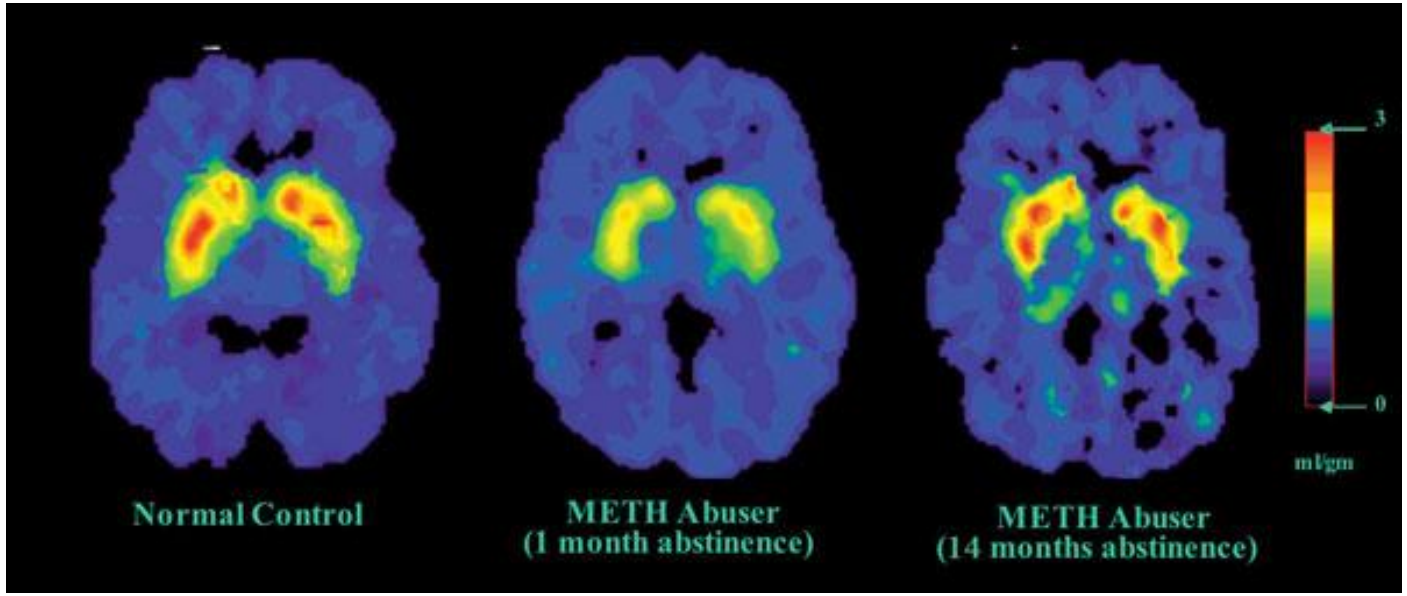
Clinical ill-health consequences following consumption of synthetic cathinones are overall consistent with their neuropsychopharmacological characteristics. After intake, initial stimulant effects e.g. euphoria, improved psychomotor speed, alertness and talkativeness[37] are typically observed. Acute psychiatric effects may, however, also include: low mood, loss of appetite, difficulty sleeping, a degree of paranoid ideation, cognitive impairment, changes in perception, agitation, hallucinations, delusions, amnesia, confusion, violence, suicidal thoughts[37, 38] and excited delirium.[39] With synthetic cathinones, suicides by hanging and deaths from firearm injuries have frequently been reported.[40, 41, 42]

Like amphetamine, synthetic cathinones result in medical side-effects consistent with sympathomimetic toxicity.[43, 44, 45] Hence, acute intoxication issues include hypertension, tachycardia, cardiac, kidney and liver failure, rhabdomyolysis, electrolyte imbalance, metabolic toxicity, paradoxical hypoglycaemia,[46] and cerebral oedema.[47, 48, 49] Flushing, sweating, chills, restlessness, shortness of breath, dry mouth, abdominal pain, anorexia, vomiting, erectile dysfunction and discolouration of the skin have also been reported.[6] Le Roux et al.[50] analysed some 105 amphetamine-like (including synthetic cathinones; 10% of the total) drug poisoning cases. The most frequently reported symptoms included anxiety and hallucinations (49%), mydriasis and headache (41%), tachycardia (40%), and hypertension (15%). Complications such as seizures (7%), cardiac arrest (5%), toxic myocarditis (1%) and haemorrhagic stroke (1%) were also observed. Cathinone-induced acute intoxication may be characterized as well by symptoms/signs of the serotonin syndrome, which is associated with hyperthermia, psychotic disorders, catatonia and hyperactive delirium.[51, 52]

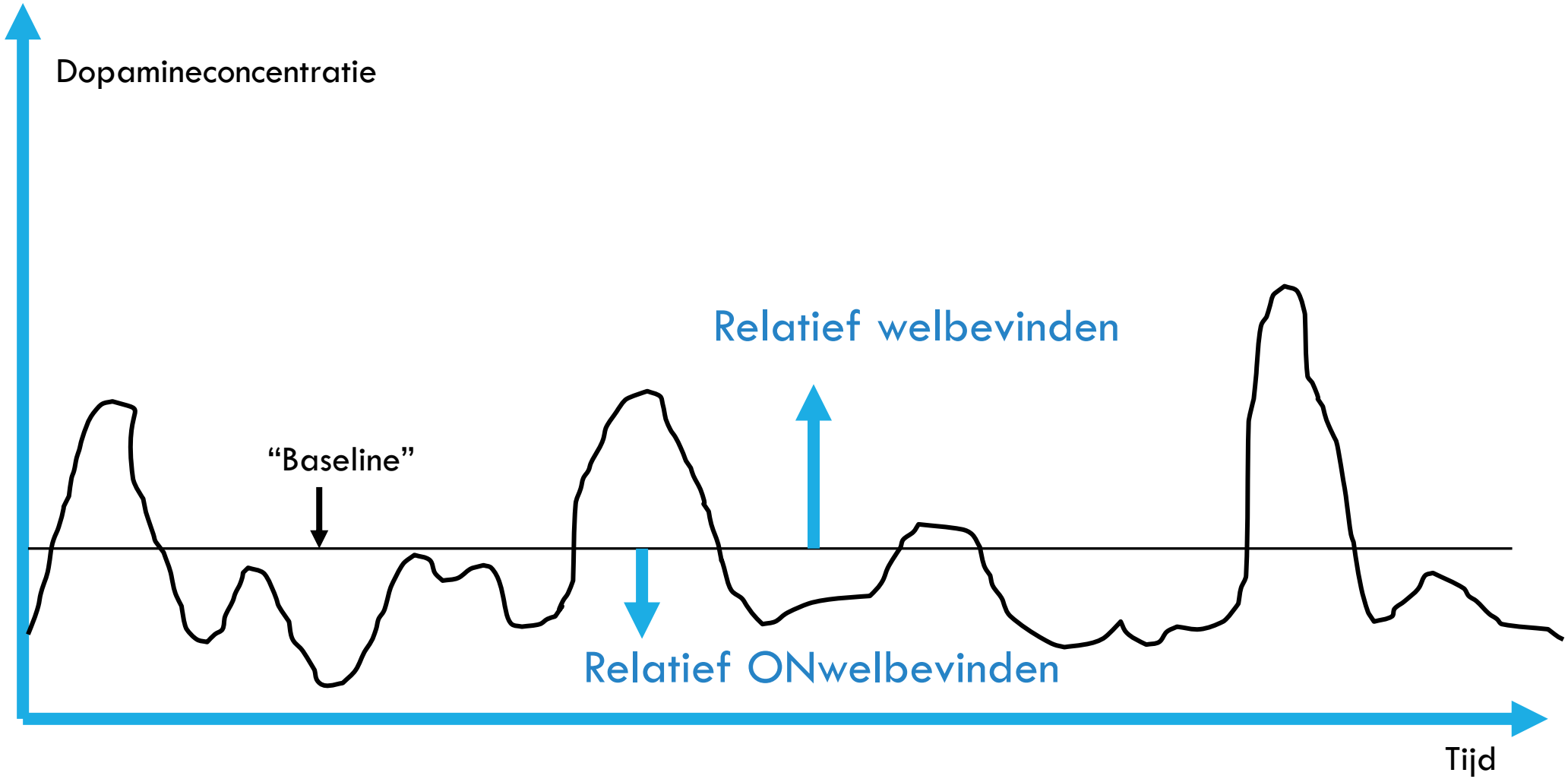
Some clients may simply need reassurance, support and medical monitoring. Management of cathinone, and indeed of any NPS/unknown psychotropics' ingestion, is typically directed at dealing with adverse effects as they arise.[83] Due to the similarity of cathinones with other stimulants, management strategies similar to those recommended for intoxication with those drugs might be useful.[84] For example, if a diagnosis of cathinone-induced delirium is suspected, treatment efforts should focus on controlling agitation and then treating medical complications such as metabolic acidosis.[43] Symptom-directed supportive care may also include the management of convulsions, hypertension/hypotension and rhabdomyolysis. Treatment of the cathinone-associated serotonin syndrome, which is often associated with agitation, may be managed using both benzodiazepines and cyproheptadine.[81] The observation of asymptomatic patients should continue for a few hours (for a review, see also[83]).

DE DOPAMINE-VALKUIL VAN STIMULANTIA

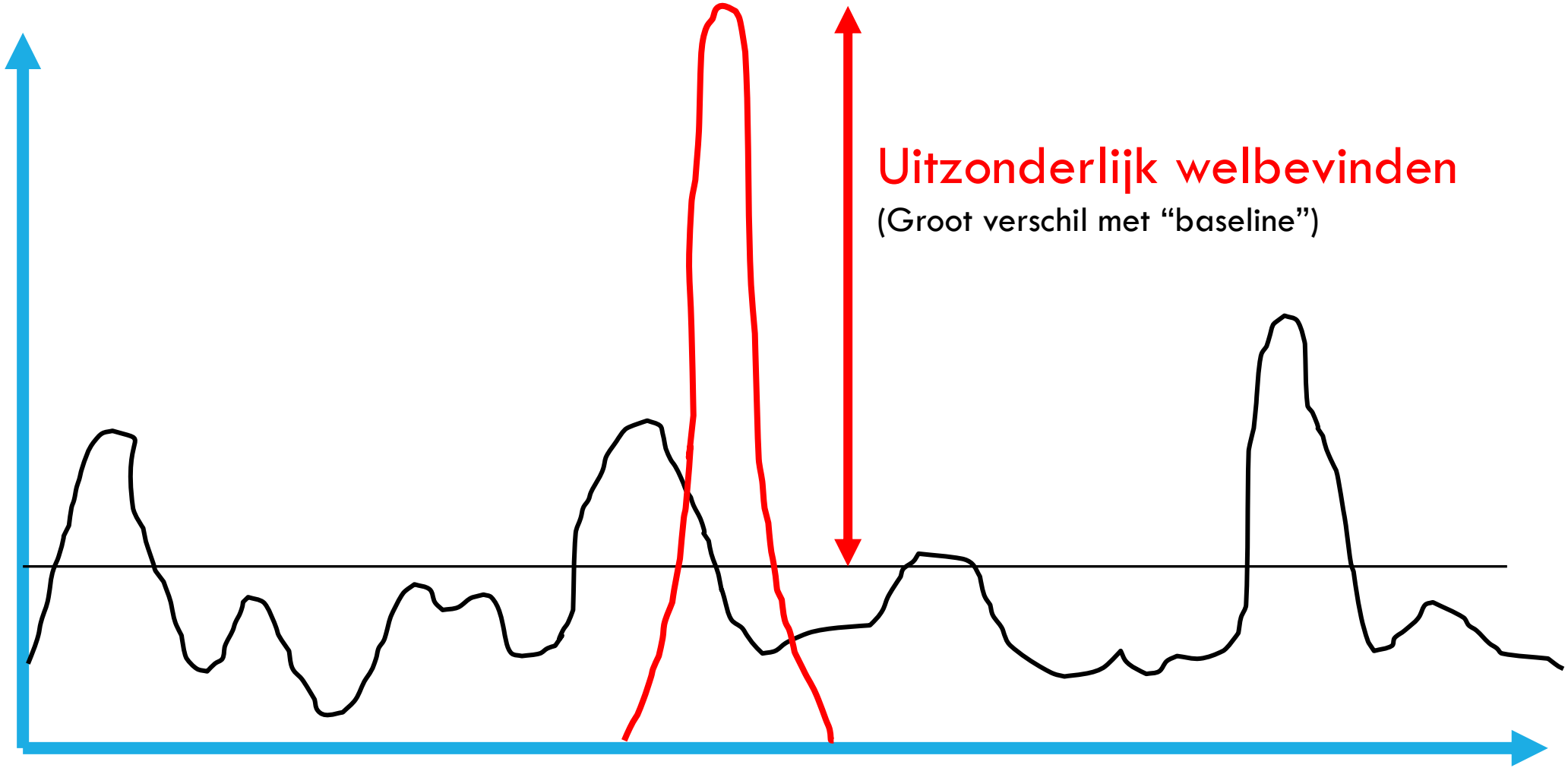
Onbekend maakt onbehandeld…



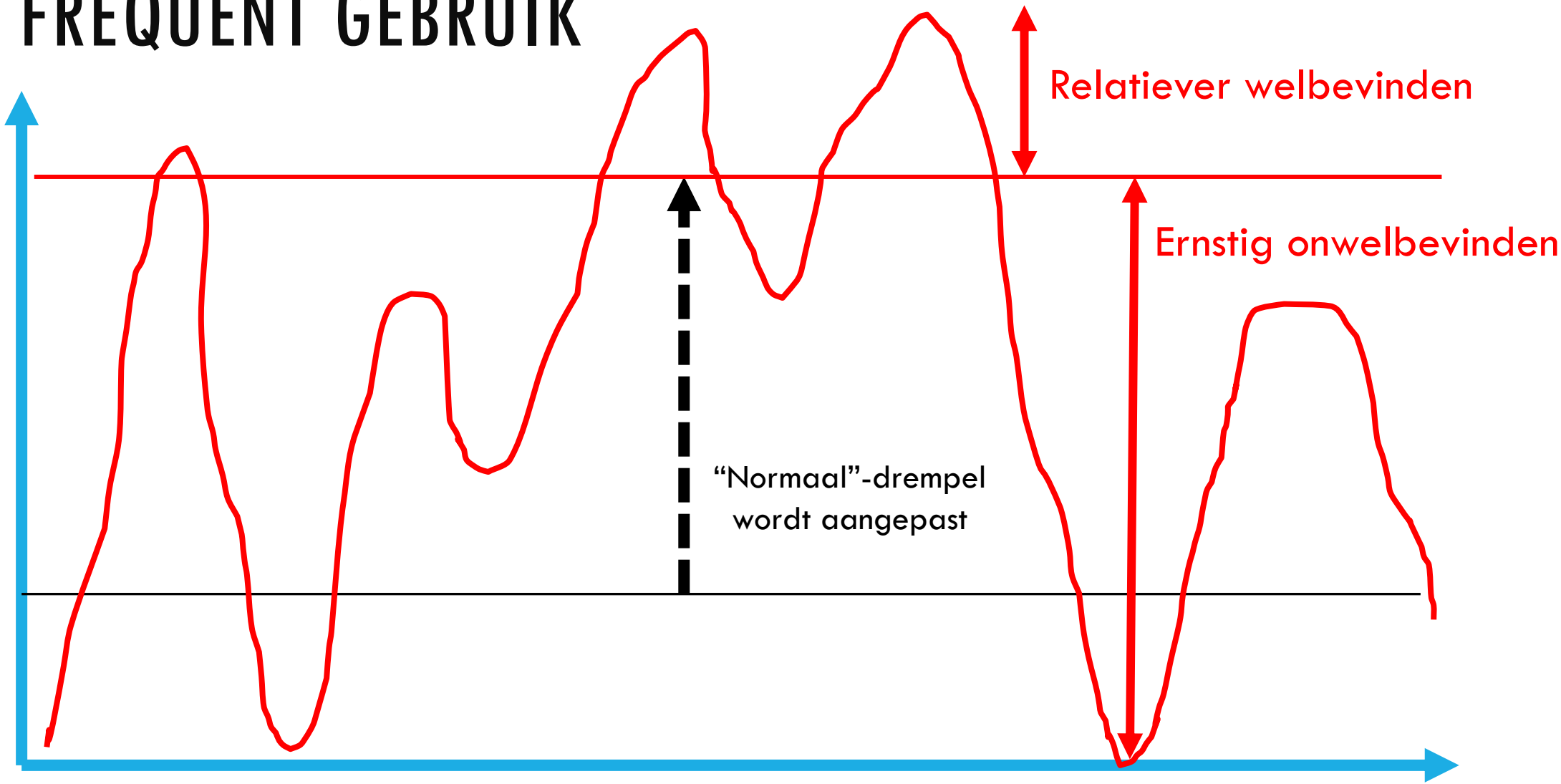
DE DOPAMINE-VALKUIL: NORMALE SITUATIE



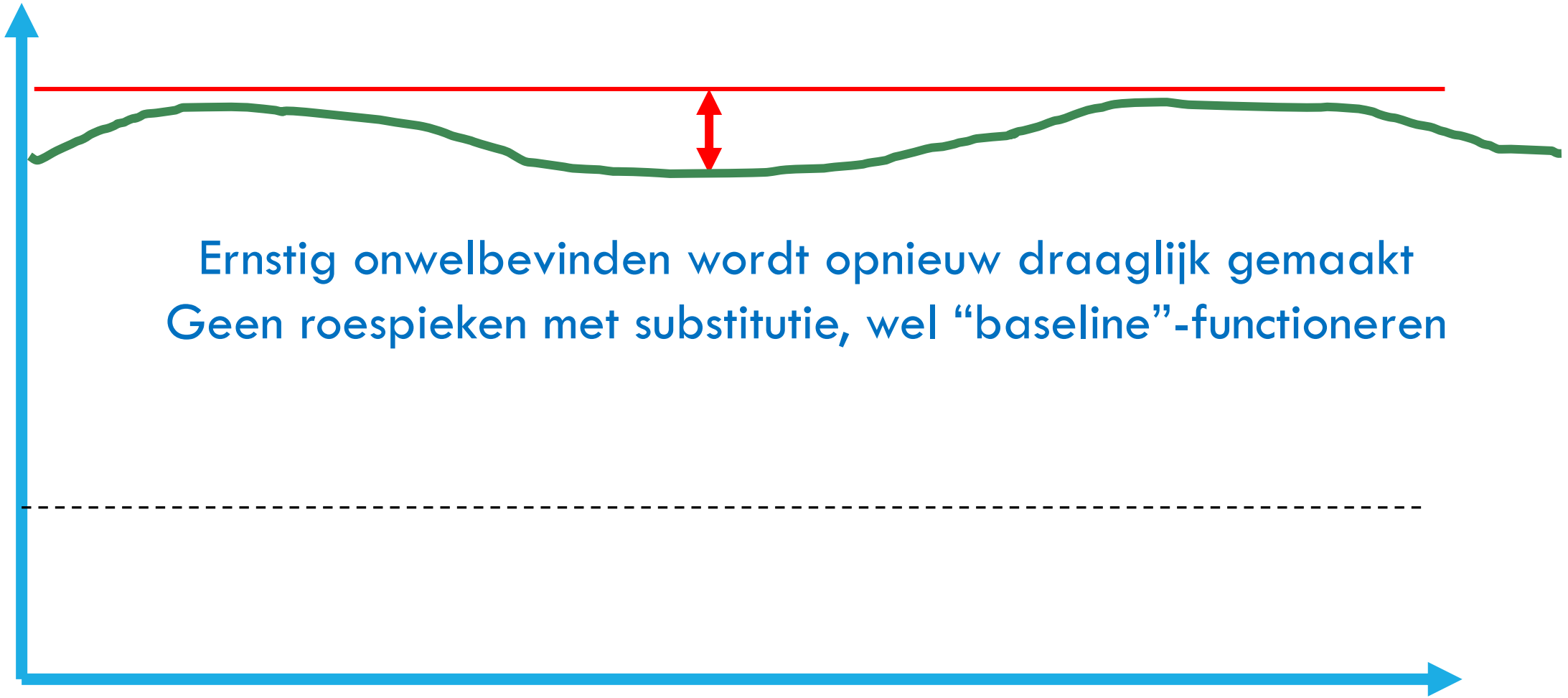
DE DOPAMINE-VALKUIL: SPORADISCH GEBRUIK



DE DOPAMINE-VALKUIL: AANPASSING AAN FREQUENT GEBRUIK



DE DOPAMINE-VALKUIL: SUBSTITUTIE



Ernstig onwelbevinden wordt opnieuw draaglijk gemaakt

Geen roespieken met substitutie, wel “baseline”-functioneren

Novel Psychoactive Treatment UK Network

NEPTUNE

Guidance on the Clinical Management of Acute and Chronic Harms of Club Drugs and Novel Psychoactive Substances

https://www.drugsandalcohol.ie/24292/1/NEPTUNE-Guidance_on_clinical_managemen_of_club_drugs_and_nove_%20psychoactive_substances.pdf

ACUTE EN SUBACUTE ONTWENNING

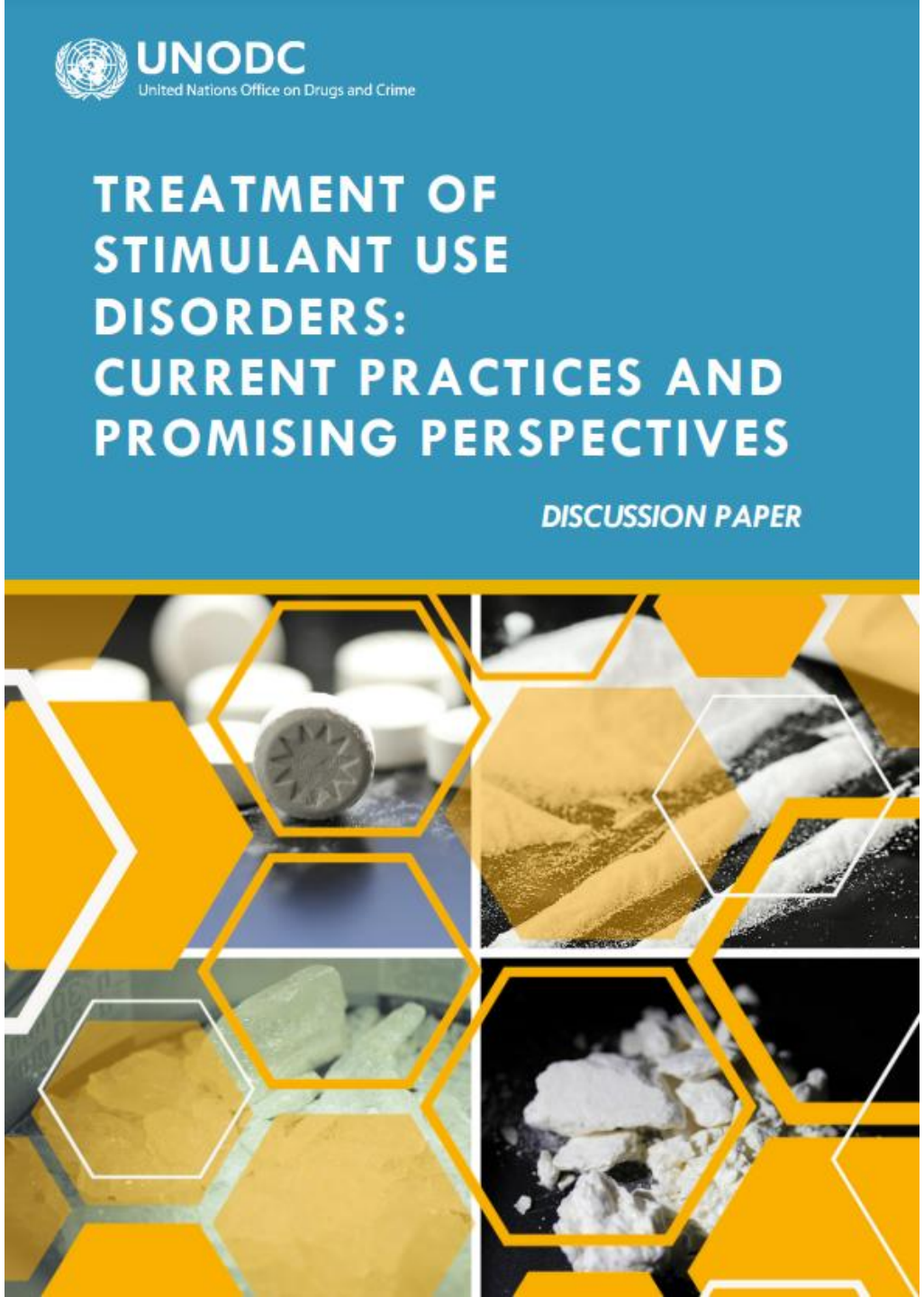
Table 8.2. *The two phases of methamphetamine withdrawal.*

Acute withdrawal symptoms	Longer-term withdrawal symptoms (can last up to 12 months)
Severe dysphoria	Anhedonia
Irritability	Impaired social functioning
Melancholia	Intense craving
Anxiety	Hyper-arousal
Hypersomnia and marked fatigue,	Vegetative symptoms
Intense craving	Anxiety-related symptoms
Paranoia	Severe dysphoria
Intensity of post-binge dysphoria can lead to suicide ideation and attempts have also been linked to withdrawal[56,197] (for more information on the withdrawal syndrome see Chapter 7)	Mood volatility
Akathisia/restless legs	Irritability
	Sleep pattern disruption

ACUTE EN SUBACUTE ONTWENNING

- In de eerste 3 maanden van ontwenning testen ex-gebruikers cognitief slechter dan chronische gebruikers: problemen van aandacht, begrip en geheugen, hierdoor minder vatbaar voor therapie
- Ontwenning: acute fase 7-10 dagen (dysforie+++ (cave suïcide), prikkelbaarheid, vermoeidheid, paranoia, rusteloze benen), daarna subacute fase van 2 weken tot 1 jaar (anhedonie, verstoord sociaal functioneren, intense craving, dysforie, stemmingswisselingen, onrust)
- Ernstigere ontwenning bij oudere gebruikers, langer gebruik en frequenter gebruik

https://www.unodc.org/documents/drug-prevention-and-treatment/Treatment_of_PSUD_for_website_24.05.19.pdf



It is proposed that symptoms encountered in patients in early abstinence may be associated with the decrease or "deficit," in the functioning of the dopaminergic system. A medication that will "normalize" the functioning of the dopaminergic system may decrease craving and other symptoms of prolonged withdrawal and will minimize the risk for relapse (Volkow and Boyle, 2018). The strategy that had the most support to date involve the use of medications that enhance the dopaminergic neurotransmission counteracting the dopaminergic deficit. This strategy includes numerous cocaine and amphetamine analogues as medications and is often referred to as "agonist therapy" or "replacement therapy," in parallel to methadone or buprenorphine treatment in opioid use disorder.

Drug and Alcohol Dependence
Volume 241, 1 December 2022, 109692

Lisdexamfetamine for the treatment of acute methamphetamine withdrawal: A pilot feasibility and safety trial

Liam S. Acheson [a b c], Nadine Ezard [a b c d], Nicholas Lintzeris [d e f], Adrian Dunlop [d g h], Jonathan Brett [i j], Craig Rodgers [b], Anthony Gill [b], Michael Christmass [k l], Rebecca McKetin [a], Michael Farrell [a], Steve Shoptaw [m], Krista J. Siefried [a b c]

Highlights

- There is no approved pharmacotherapy option for methamphetamine withdrawal.
- This is the first clinical trial of lisdexamfetamine for methamphetamine withdrawal.
- Lisdexamfetamine is safe and feasible for treating acute withdrawal.
- Participants found this treatment highly acceptable.
- More work is needed to determine the efficacy of this treatment.

2.3. Intervention

Tapering dose of LDX, beginning at 250mg oral once daily (OD), reducing by 50mg per day to 50mg OD on Day 5. LDX at a dose of 250mg (about three times higher than approved for other indications) is equivalent to approximately 74mg of dexamphetamine (Dolder et al., 2017), and similar doses of sustained release dexamphetamine (60–110mg) have previously been demonstrated to decrease MA withdrawal severity and cravings, and increase retention in care (Galloway et al., 2011, Longo et al., 2010). This dose of LDX has previously been shown to be safe in methamphetamine dependent people in a community setting (Ezard et al., 2021a), and is closer to recreational amphetamine doses. LDX was formulated in 50mg capsules and dispensed each morning under supervision of nursing staff. All participants received inpatient treatment as usual, consisting of symptom management and supportive care.

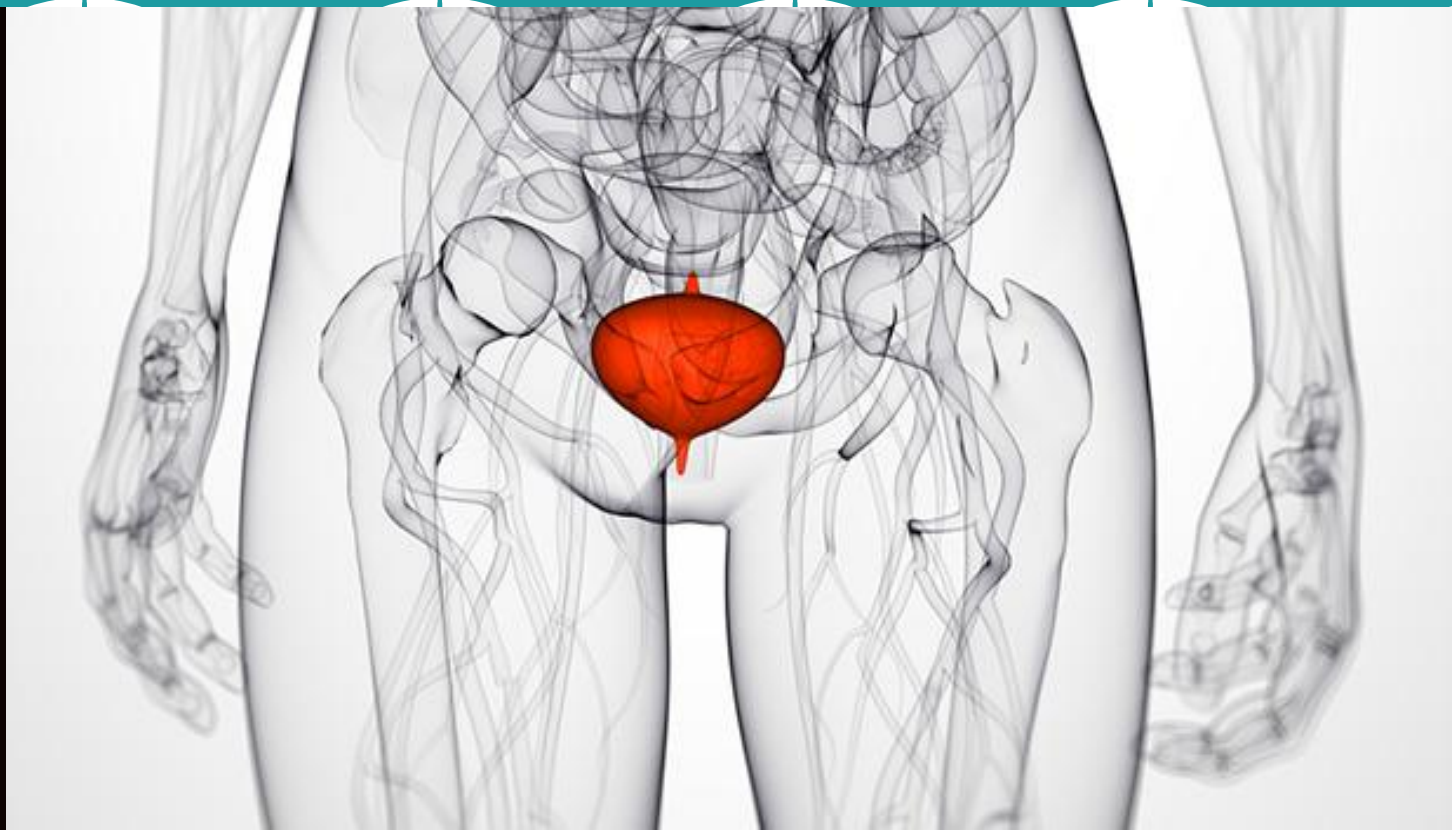
taken as prescribed, psychostimulants may have a normalizing effect, reversing the underlying deficits in the functioning of the dopaminergic system without further dysregulating the system. As a result, patients have less craving, have less impulsivity, and can abstain from illicit stimulants. In support of this approach, brain imaging studies showed that psychostimulant medications can normalize the function of the brain centres affected by the chronic exposure to stimulants and in turn diminish symptoms of the disorder (Zilverstand *et al.*, 2018).

The same pharmacological principle, sometimes referred to as a "replacement" or "substitution therapy," is used in treatment of opioid dependence, where opioidergic medications methadone and buprenorphine eliminate withdrawal and craving helping to reduce or stop heroin use. Similarly, nicotine or a nicotine receptor agonist varenicline, medications that have pharmacological effects similar to the effects of tobacco, are useful in treatment of tobacco dependence.

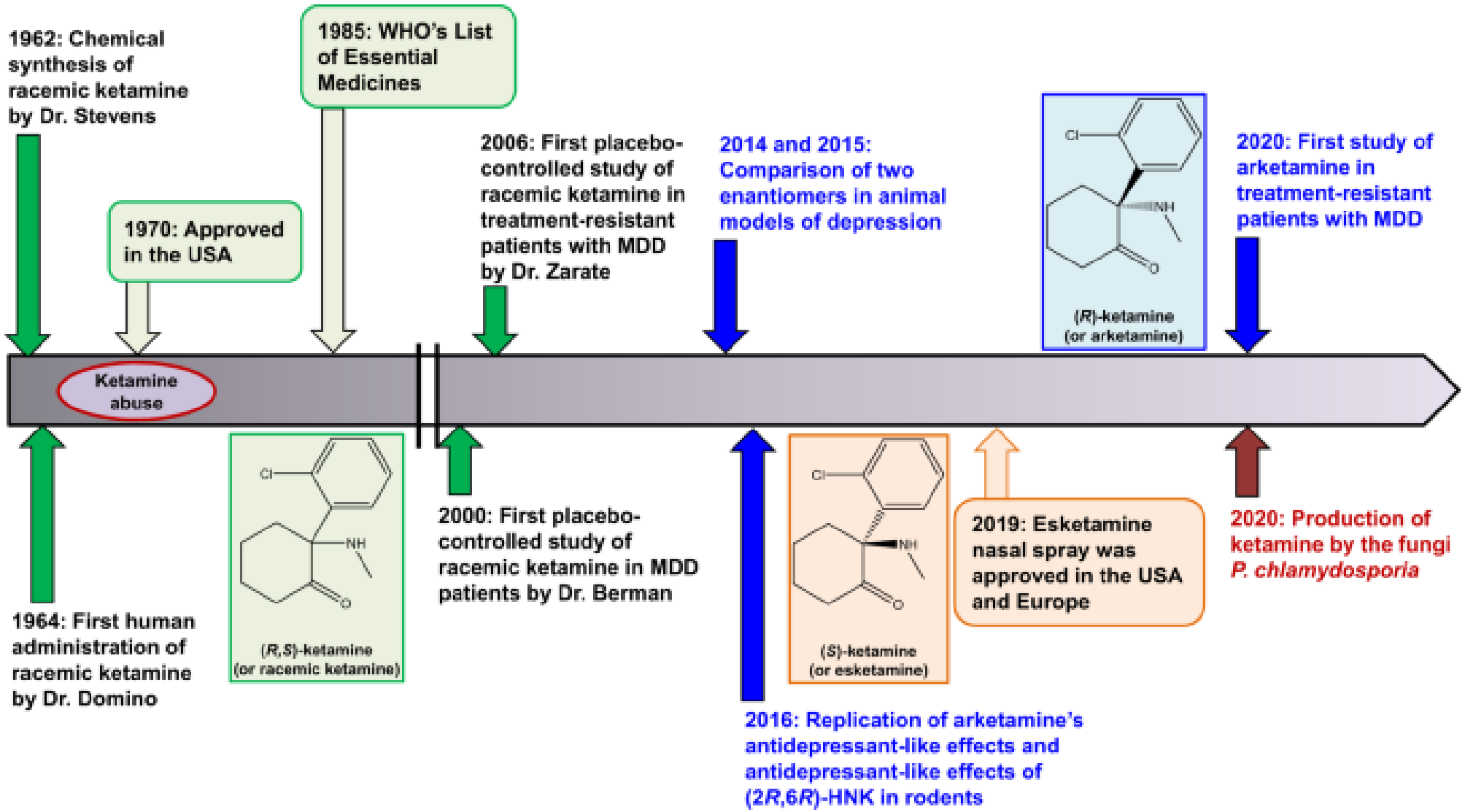
In addition to providing relief of withdrawal and craving, psychostimulants medications may have mildly positive effects which will be an incentive for patients to come to the clinic for prescription or to have medication administered on-site. That way patients may be motivated and willing to accept additional behavioral and supportive interventions, participate in recovery-oriented activities, and seek additional medical and psychiatric care. This model is similar to clinic-based, long-term treatment with methadone or buprenorphine which includes supervised doses of the medication, with small number of take-home doses, in addition to all other medical and recovery services available on-site.

Psychostimulant medications have a pharmacological effect that is similar to the effect of drugs that the patient may be addicted to. The main difference is that psychostimulant medications are taken orally, on daily basis, providing consistent dopaminergic stimulation. Prescription psychostimulants produce minimal or no psychoactive effects as the medication is constantly present in the brain and patients usually develop tolerance to stimulant psychological and physical effects. This is very different from the effects of injected or smoked cocaine or methamphetamine, or irregularly swallowed or snorted high doses of oral stimulants, with large doses rapidly entering the brain causing the individual to experience extreme stimulation and euphoric effects. When

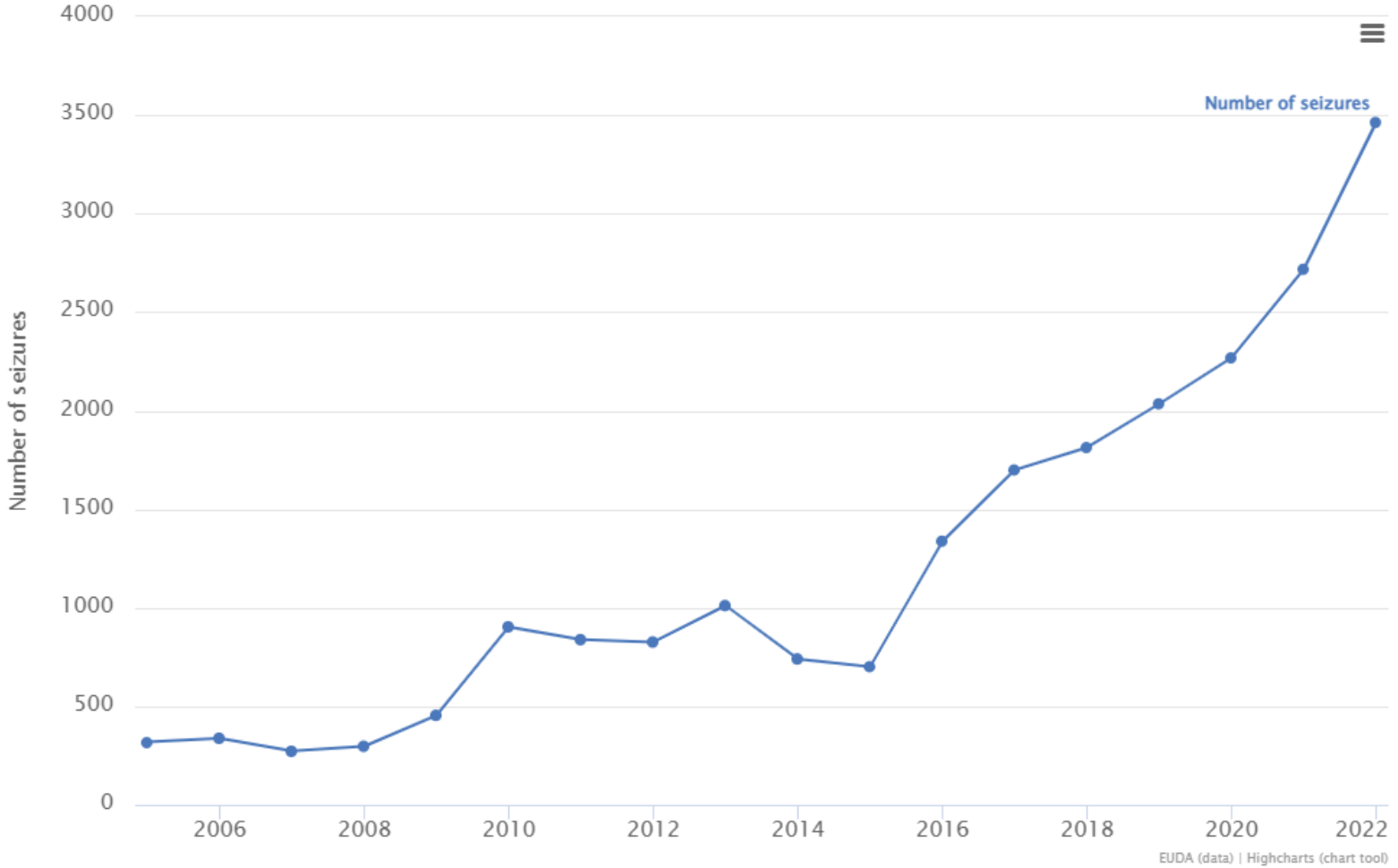
https://www.unodc.org/documents/drug-prevention-and-treatment/Treatment_of_PSUD_for_website_24.05.19.pdf



KETAMINE: KOPZORGEN OVER DE BLAAS


1962: Chemical synthesis of racemic ketamine by Dr. Stevens
1985: WHO's List of Essential Medicines
1970: Approved in the USA
2006: First placebo-controlled study of racemic ketamine in treatment-resistant patients with MDD by Dr. Zarate
2014 and 2015: Comparison of two enantiomers in animal models of depression
2020: First study of arketamine in treatment-resistant patients with MDD
(R)-ketamine (or arketamine)
Ketamine abuse
(R,S)-ketamine (or racemic ketamine)
1964: First human administration of racemic ketamine by Dr. Domino
2000: First placebo-controlled study of racemic ketamine in MDD patients by Dr. Berman
(S)-ketamine (or esketamine)
2019: Esketamine nasal spray was approved in the USA and Europe
2020: Production of ketamine by the fungi P. chlamydosporia
2016: Replication of arketamine's antidepressant-like effects and antidepressant-like effects of (2R,6R)-HNK in rodents

Seizures of ketamine reported to the EU Early Warning System: trends in numbers of seizures, European Union, 2005-2022



In Europe, evidence of illicit production of ketamine is limited to a small number of seizures of precursors and a few dismantled production sites in the Netherlands and Belgium. At least four ketamine production sites were dismantled between 2017 and 2021 (excluding storage sites). All findings occurred in the Netherlands, with the exception of one production site, which was discovered in Belgium in 2020. In these facilities, manufacturing processes included extraction of medicinal products (evaporation of commercial pharmaceutical solutions of ketamine) and crystallisation of ketamine (as ketamine 'needles', or small crystals, are a highly valued product in the illicit market) (National Police of the Netherlands, 2022). In one of the dismantled facilities, approximately 500 kilograms of ketamine hydrochloride was recovered.

Price of ketamine in the Netherlands, 2022

Product	Location in the supply chain	Price
Ketamine powder/sugar/needles	Retail trade	EUR 2 373 per kilogram
Ketamine chunks/lumps	Retail trade	EUR 3 900 per kilogram
Ketamine	Consumer price (street-level)	EUR 21.80 per gram

Source: Central Criminal Investigations Division, Dutch Police, Netherlands.

KETAMINE GEÏNDUCEERDE BLAASONTSTEKING: BEHANDELOPTIES

Health Psychol Res. 2022; 10(3): 38247.
Published online 2022 Sep 15. doi: 10.52965/001c.38247

PMCID: PMC9476224
PMID: 36118982

Ketamine-Induced Cystitis: A Comprehensive Review of the Urologic Effects of This Psychoactive Drug

Danyon J. Anderson,[1] Jessica Zhou,[1] David Cao,[1] Matthew McDonald,[2] Maya Guenther,[1] Jamal Hasoon,[3] Omar Viswanath,[4] Alan D. Kaye,[5] and Ivan Urits[6]

Neurourology and Urodynamics

SUFU Society of Urodynamics, Female Pelvic Medicine & Urogenital Reconstruction

REVIEW | Open Access

Current approaches for the treatment of ketamine-induced cystitis

Juan Zhou, Cassidy Scott, Ziba Rovei Miab, Christian Lehmann

First published: 13 February 2023 | https://doi.org/10.1002/nau.25148

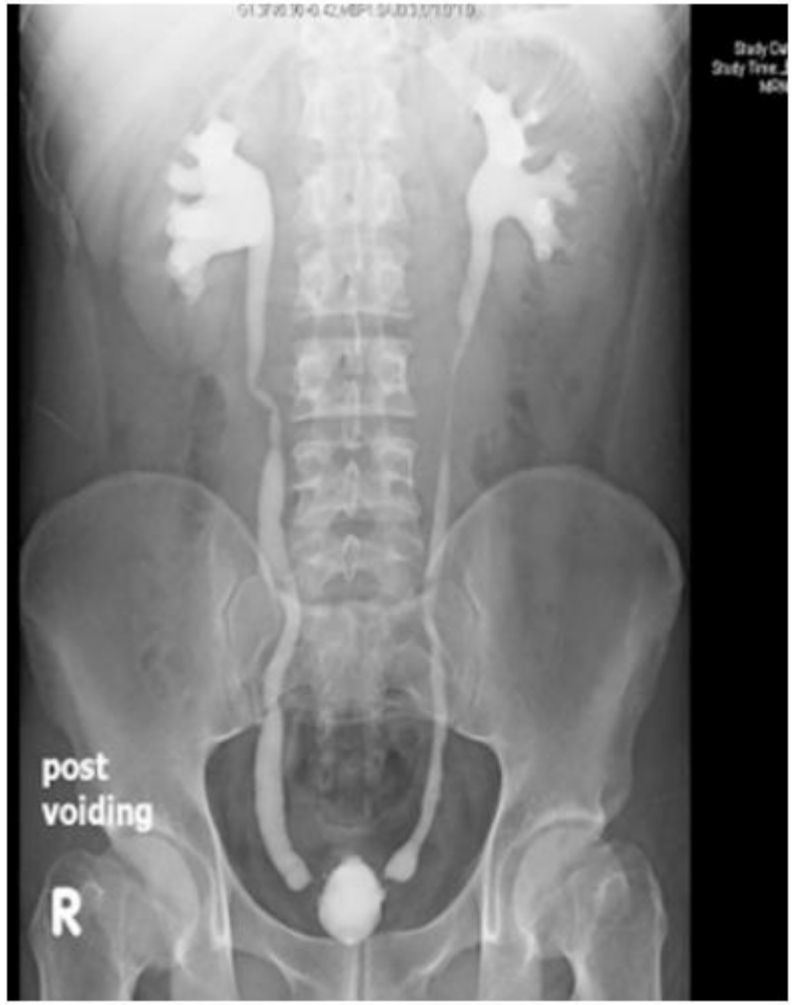
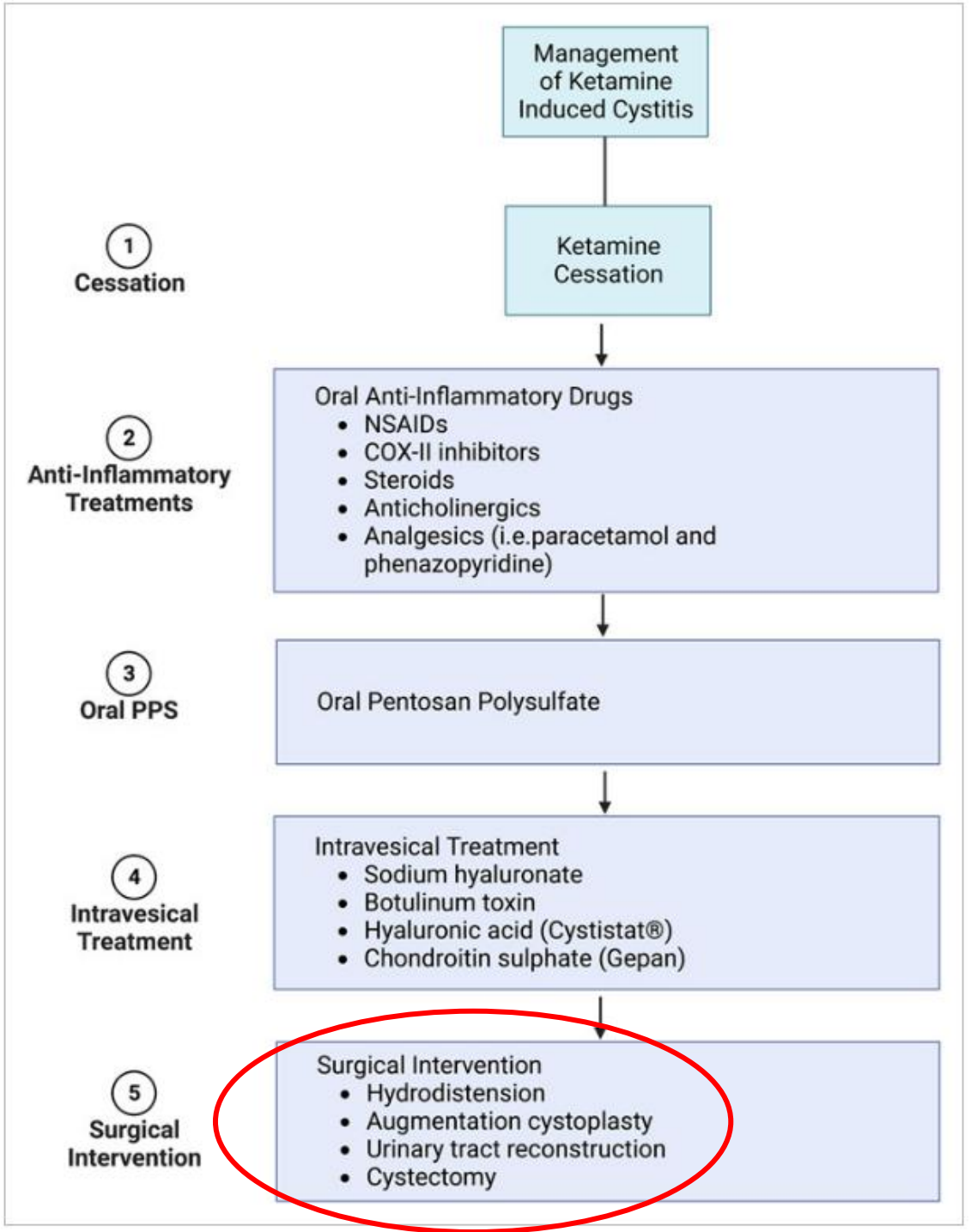


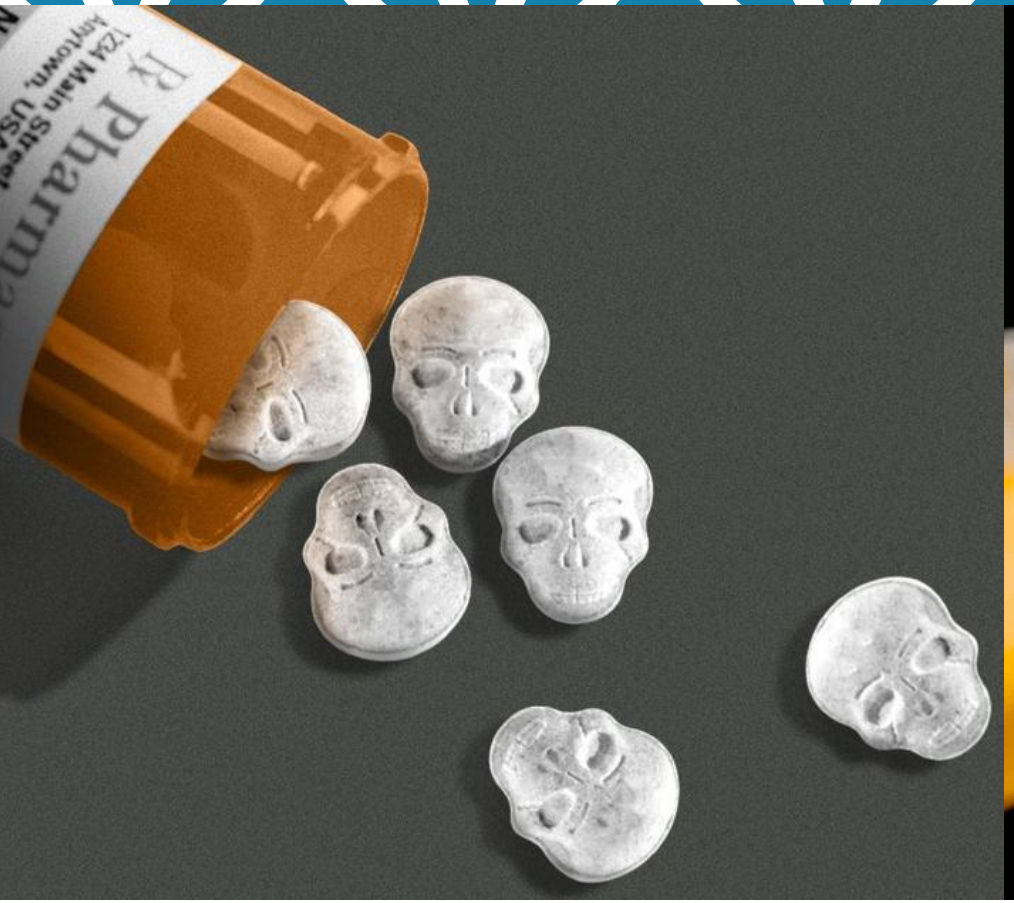
Fig. 1. Intravenous pyelography in a man with ketamine cystitis reveals bilateral hydronephroureters and contracted urinary bladder.



3.3.1 Oral treatment for pain and inflammation

Pain is the primary symptom of KIC, therefore oral nonsteroidal anti-inflammatory drugs (NSAIDs) are often used as the first line medication. If patients cannot tolerate NSAIDS, other anti-inflammatory drug such as COX-II inhibitors, steroids, anticholinergics to block neurotransmitters action, and/or simple analgesics such as paracetamol and phenazopyridine are used for relieving bladder pain.[35] In a Youth Urological Treatment Center in Hong Kong, 290 patients with KIC received first-line treatment. Among them, 202 patients (69.7%) had significant improvement in pelvic pain, urgency scores and functional bladder capacity. When the first line treatment was insufficient for symptom relief, opioid and pregabalin were suggested as a second line treatment. Forty-two of 62 patients (67.7%) reported symptoms improvement after receiving the second-line treatment.[32] However, opioid therapy for the treatment of chronic pain remains controversial. Opioid therapy can

Fenazopyridine wordt, zonder argumenten, voorgesteld voor verschillende symptomen ter hoogte van de urinaire tractus; bij bewezen infectie of bij sterk vermoeden ervan, dient gekozen te worden voor een antibacterieel middel. Het is niet langer beschikbaar sinds juni 2021.



NPS OPIOÏDEN: MOLECULES MACABRES

EUDA
EUROPEAN UNION DRUGS AGENCY

EUROPOL

Background

New opioids are sold as substances in their own right and as replacements for controlled opioids. They are also mis-sold as or used to adulterate heroin and other controlled opioids for unsuspecting consumers. In some cases, they are used to make fake tablets of opioid analgesic medicines, such as oxycodone. Recent signs of the emergence in Europe of mixtures of benzodiazepines and xylazine with new opioids – seemingly copied from North America – also raise concerns. Occasionally, new opioids are found in non-opioid controlled drugs, such as cocaine.

New opioids are typically found as powders and, to a lesser degree, tablets and capsules. Other physical forms, such as liquids, are also reported but are far less common.

This resource is part of EU Drug Market: New psychoactive substances — In-depth analysis by the EMCDDA and Europol.

Table of contents/Search

Last update: *27 June 2024*

GLOBAL COMMISSION ON DRUG POLICY

POSITION PAPER

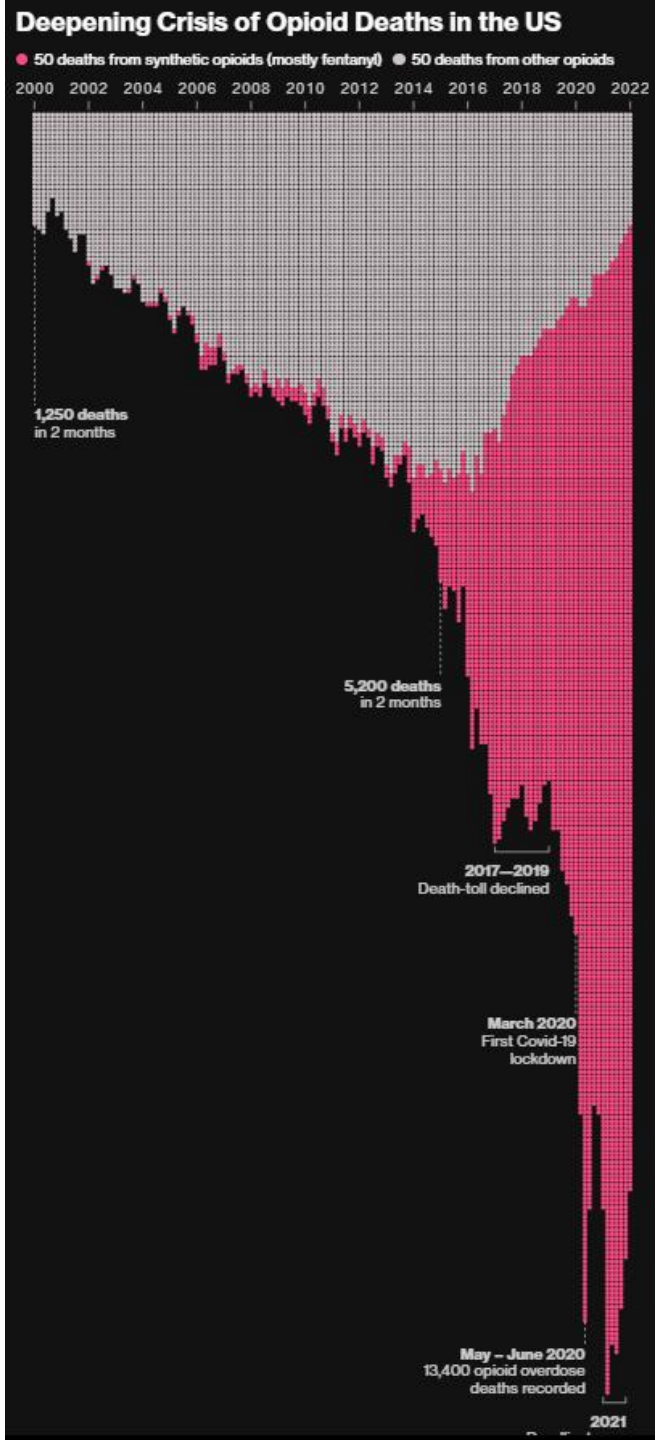
THE OPIOID CRISIS IN NORTH AMERICA

October 2017

The opioid epidemic has occurred in three waves. The podcast episode, "Introduction to the Opioid Epidemic" explains these waves in greater detail. The first wave began in 1991 when deaths involving opioids began to rise following a sharp increase in the prescribing of opioid and opioid-combination medications for the treatment of pain. The increase in opioid prescriptions was influenced by reassurances given to prescribers by pharmaceutical companies and medical societies claiming that the risk of addiction to prescription opioids was very low. During this time, pharmaceutical companies also began to promote the use of opioids in patients with non-cancer related pain even though there was a lack of data regarding the risks and benefits in these patients. By 1999, 86% of patients using opioids were using them for non-cancer pain. Communities where opioids were readily available and prescribed liberally were the first places to experience increased opioid abuse and **diversion** (the transfer of opioids from the individual for whom they were prescribed, to others, which is illegal).

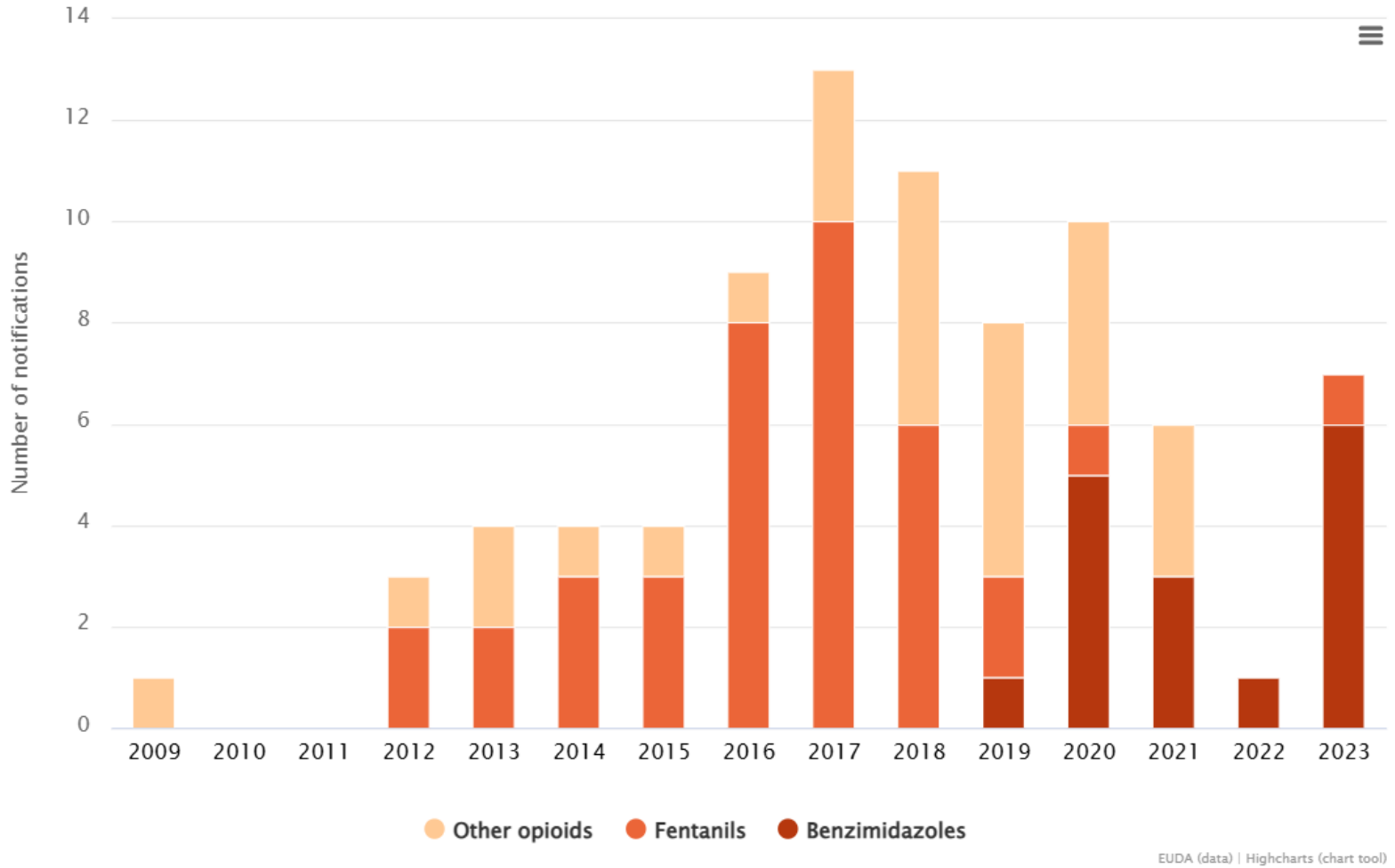
The second wave of the opioid epidemic started around 2010 with a rapid increase in deaths from heroin abuse. As early efforts to decrease opioid prescribing began to take effect, making prescription opioids harder to obtain, the focus turned to heroin, a cheap, widely available, and potent illegal opioid. The use of heroin increased in both sexes, the majority of age brackets, and all socioeconomic groups. Deaths due to heroin-related overdose increased by 286% from 2002 to 2013, and approximately 80% of heroin users admitted to misusing prescription opioids before turning to heroin. Heroin is commonly injected, which puts users at risk for injection-related diseases like HIV/AIDS, hepatitis B and C, skin infections, bloodstream infections, and infections of the heart.

The third wave of the epidemic began in 2013 as an increase in deaths related to synthetic opioids like fentanyl. The sharpest rise in drug-related deaths occurred in 2016 with over 20,000 deaths from fentanyl and related drugs. The increase in fentanyl deaths has been linked to illicitly manufactured fentanyl (not diverted medical fentanyl) used to replace or adulterate other drugs of abuse.



https://www.bloomberg.com/graphics/2022-us-fentanyl-opioid-deaths/

Number and types of new opioids notified to the EU Early Warning System for the first time, 2005-2023



Seizures of new opioids reported to the EU Early Warning System: quantities seized for all forms reported in weight, by type of opioid, European Union, 2005-2022

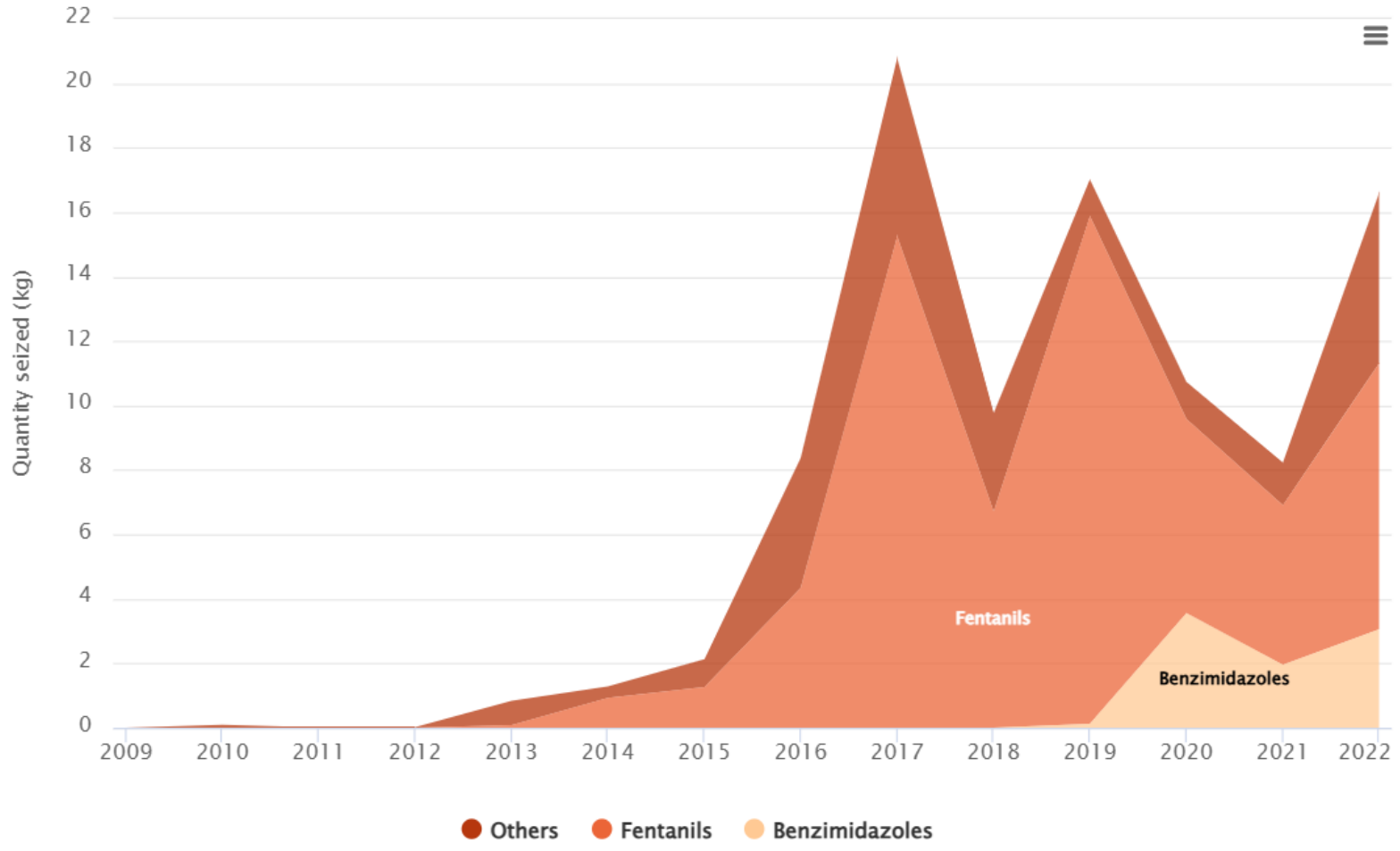
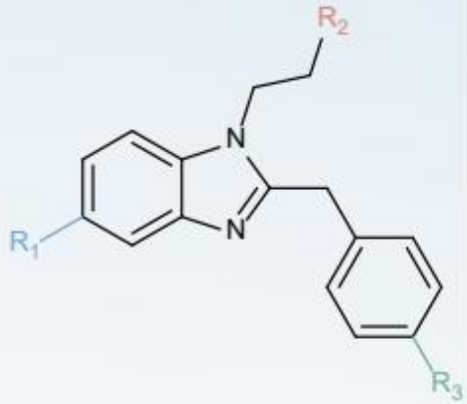
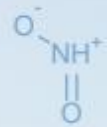
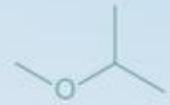
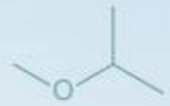
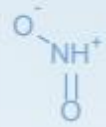
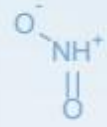
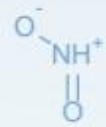
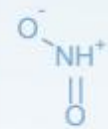
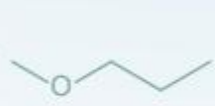
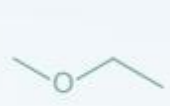
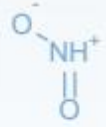


Figure 7. Nitazene opioids that have been reported to the UNODC Early Warning Advisory

Core structure	R1	R2	R3	Name
				Isotonitazene
	NH_2			5-Aminoisotonitazene
				*N*-Pyrrolidino-etonitazene
				Butonitazene
				Metonitazene
				Protonitazene
	H			Etodesnitazene
				Fluonitazene
	H			Metodesnitazene

LEGISLATIVE ANALYSIS AND PUBLIC POLICY ASSOCIATION

NOVEL PSYCHOACTIVE SUBSTANCES: "PYRO"

AUGUST 2022

The Legislative Analysis and Public Policy Association (LAPPA) is monitoring the emergence of novel psychoactive substances (NPS) appearing on the streets of the United States. This fact sheet, which focuses on ***N*-pyrrolidino etonitazene**, is the first in a series that highlights these dangerous drugs.

N-pyrrolidino etonitazene, also known as etonitazepyne and by the street name "Pyro," is a relatively new high potency synthetic opioid increasing in prevalence in the U.S. Pyro belongs to an opioid subclass of NPS called 2-benezylbenzimidazoles, or nitazenes, and is structurally similar to etonitazene, a synthetic opioid that is nationally and internationally controlled. The nitazene subclass also includes isotonitazene, also known as "Iso," which the U.S. Drug Enforcement Administration (DEA) temporarily listed as a Schedule I controlled substance on August 20, 2020 and permanently scheduled on December 6, 2021.[1] Unlike other nitazenes identified thus far, *N*-pyrrolidino etonitazene is not described or mentioned in any medical literature or patents, meaning that it is a truly "novel" NPS and likely developed independently from the pharmaceutical industry. Researchers believe that N-pyrrolidino etonitazene is coming to the U.S. via purchases on the dark web and is likely being produced in China. *N*-pyrrolidino etonitazene can be found in powder form or pressed into pills to resemble other substances. Studies estimate that *N*-pyrrolidino etonitazene is over 800 times more potent than morphine and 20-40 times more potent than fentanyl. Like other opioids, *N*-pyrrolidino etonitazene use can potentially cause fatal respiratory depression in the person ingesting the drug. However, because *N*-pyrrolidino etonitazene is an opioid, naloxone can be used to reverse an overdose.

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Xylazine in the Opioid Epidemic: A Systematic Review of Case Reports and Clinical Implications

Monitoring Editor: Alexander Muacevic and John R Adler

Shahana Ayub,[1] Shanli Parnia,[2] Karuna Poddar,[3] Anil K Bachu,[4] Amanda Sullivan,[5] Ali M Khan,[6] Saeed Ahmed,[7,8,9] and Lakshit Jain[10]

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Results: Intravenous (IV) administration was a common route for Xylazine use among various methods, including subcutaneous (SC), intramuscular (IM), and inhalation, with overall doses ranging from 40 mg to 4300 mg. The average dose in fatal cases was 1,200 mg, compared to 525 mg in non-fatal cases. Concurrent administration of other drugs, primarily opioids, occurred in 28 cases (47.5%). Intoxication was identified as a notable concern in 32 out of 34 studies, and treatments varied, with the majority experiencing positive outcomes. Withdrawal symptoms were documented in one case study, but the low number of cases with withdrawal symptoms may be attributed to factors such as a limited number of cases or individual variation. Naloxone was administered in eight cases (13.6%), and all patients recovered, although it should not be misconstrued as an antidote for Xylazine intoxication. Of the 59 cases, 21 (35.6%) resulted in fatal outcomes, with 17 involving Xylazine use in conjunction with other drugs. The IV route was a common factor in six out of the 21 fatal cases (28.6%).

Drug Checking — Quarterly Report

PHILADELPHIA, PENNSYLVANIA | DRUG CHECKING | Q1 & Q2 2023

PURPOSE: This report provides up-to-date information regarding the drug supply in Philadelphia, Pennsylvania, United States of America, including quantitative data on the purity of fentanyl, xylazine, cocaine, methamphetamine, and more in various sample types analyzed.

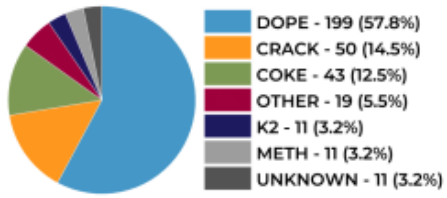
OVERVIEW: Traditional drugs (e.g., heroin, fentanyl, cocaine, methamphetamine) are commonly identified among drug samples in cities across the United States, albeit at varying purities and combinations. Novel psychoactive substances (NPS) continue to appear within the drug supply, masked as traditional drugs or added to traditional drug preparations. Nationally, the drug supply remains a dynamic and evolving environment, with respect to the active drug components, cutting agents, and/or adulterants added to drug preparations. The drug supply and drug use trends can be different from city to city or even within a given community, requiring specific regional or local assessments. Accurate understanding of drug materials and the drug supply in real-time is imperative for effective public health and safety preparedness and response.

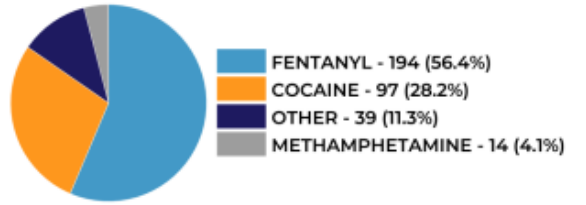
OBJECTIVE: A partnership between the Center for Forensic Science Research and Education (CFSRE) and the Philadelphia Department of Public Health (PDPH) has been established to accurately assess the drug supply in Philadelphia, Pennsylvania. Samples were provided to PDPH staff conducting field-based harm reduction supply distribution and forwarded to the CFSRE for analysis. The CFSRE laboratory utilizes novel approaches for the analysis of drugs using comprehensive non-targeted data acquisition by gas chromatography mass spectrometry (GC-MS) and liquid chromatography quadrupole time-of-flight mass spectrometry (LC-QTOF-MS). The scope of analysis for testing contains more than 1,100 drugs, including a vast majority of NPS and relevant substances. This initiative was established as a comprehensive effort examining various drug materials and drug forms. All drug testing results are summarized in this report, with notable results selected for emphasis. Note: The results reported herein represent a subset of the drug supply and do not represent the drug supply in its entirety.

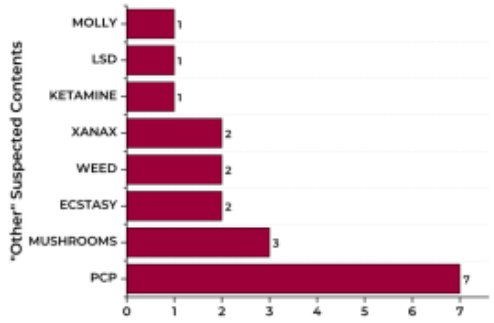
SUMMARY & RECENT NOTABLE FINDINGS

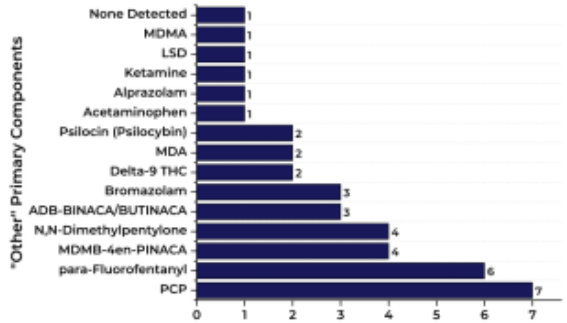
- 344 samples were analyzed between January 1, 2023, and June 30, 2023.
- ***N*-Desethyl Isotonitazene** (n=3) was detected in dope samples alongside fentanyl, xylazine, bromazolam, flubromazepam, and caffeine.
- **Bromazolam** (n=2) was detected without opioids in purported dope samples.
- Coke (n=6) & crack (n=4) samples contained fentanyl. One methamphetamine sample contained fentanyl; however, it was noted as known contamination.
- Nearly all dope samples (99%) contained fentanyl and/or *para*-fluorofentanyl.
- Over the last 12 months, the average amount of fentanyl in dope samples remained mostly consistent while the average amount of xylazine increased 34%.

SUSPECTED CONTENTS vs. PRIMARY COMPONENT









Note: "Suspected contents" (left) refers to the purported sample identity, not necessarily the "sold as" designation. "Primary component" (right) reflects the largest substance, by peak area, detectable during GC-MS analysis. (See Disclaimer on Page 3.)

Table 1: Descriptive Statistics for Drug Amount* Based on Suspected Contents

Drug	Suspected	N	Mean	Median	Min.	Max.
Cocaine	Coke	42	37.0%	32.9%	6.4%	85.2%
Lidocaine	Coke	31	24.6%	16.8%	1.1%	55.0%
Xylazine	Coke	8	14.4%	4.8%	0.9%	44.8%
Fentanyl	Coke	6	3.8%	2.2%	1.0%	9.0%
4-ANPP	Coke	5	0.7%	0.5%	0.3%	1.4%
Caffeine	Coke	1	--	--	2.2%	--
Cocaine	Crack	49	69.8%	72.0%	16.7%	99.0%
Fentanyl	Crack	4	0.6%	0.7%	0.1%	1.0%
Xylazine	Crack	4	6.4%	3.9%	1.3%	16.3%
4-ANPP	Crack	2	--	--	0.2%	0.3%
para-Fluorofentanyl	Crack	1	--	--	0.5%	--
Lidocaine	Crack	1	--	--	11.9%	--
Caffeine	Crack	1	--	--	0.5%	--
Fentanyl	Dope	177	14.0%	12.4%	0.2%	40.0%
Xylazine	Dope	177	44.2%	45.1%	0.9%	71.8%
4-ANPP	Dope	172	2.4%	2.0%	0.1%	10.1%
para-Fluorofentanyl	Dope	53	2.7%	1.0%	0.2%	39.3%
Caffeine	Dope	39	4.2%	1.1%	0.1%	23.5%
Heroin	Dope	20	2.0%	1.8%	0.1%	4.7%
Lidocaine	Dope	17	2.8%	0.8%	0.2%	19.0%
Cocaine	Dope	6	6.7%	5.4%	0.4%	16.8%
Methamphetamine	Meth	13	62.6%	52.9%	50.3%	85.7%
Cocaine	Meth	2	--	--	0.4%	0.5%
Fentanyl	Meth	1	--	--	1.2%	--
Xylazine	Meth	1	--	--	3.2%	--
para-Fluorofentanyl	Meth	1	--	--	0.6%	--

Note: Drug amount (as referred to as "purity" or "concentration") is the proportion or percent of the sample that consists of a single detected drug or substance.

cfsre | NPS DISCOVERY

Department of Public Health CITY OF PHILADELPHIA

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Summary and Key Findings:

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THE DRUG SITUATION IN BELGIUM IN 2022

- Based on the NEP in the Flemish Community and the treatment data, heroin seems to remain the opioid of preference among people who inject drugs (PWID) and is also the substance most commonly used intravenously.
- The presence of other synthetic opioids without prescription such as fentanyl remains relatively limited. This has also been observed by a study on retail drug quality on heroin where no samples including fentanyl have been found.

‘Fentanyl zal overwaaien naar Europa, daar ben ik van overtuigd. We moeten onze politiemensen nu al opleiden om ermee om te gaan’

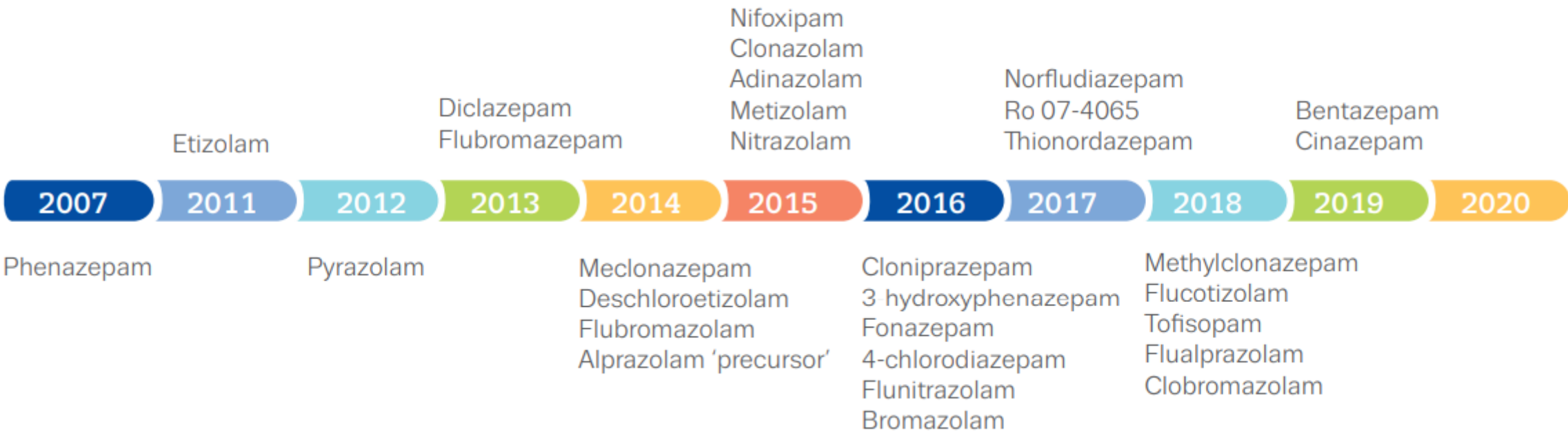
Ine Van Wymersch: ‘Ik kijk op feestjes altijd eens rond: zou die of die gebruiken? Maar ik zie het niet in mijn omgeving. Misschien denken ze: ‘De drugscommissaris is daar, bukken!’’ Beeld Marco Mertens

De Morgen, 27/2/24

NPS BENZODIAZEPINES: VALIUM VS GOLIATH

FIGURE 2

Timeline of benzodiazepines formally notified to the EU Early Warning System for the first time, 2007–2020



EU Drug Market: New psychoactive substances — Distribution and supply in Europe: Benzodiazepines

Many new benzodiazepines are potent substances (EMCDDA, 2021b; El Balkhi, 2020). The dose used in fake medicines can also be significantly higher than those used in legitimate licensed medicines. Increasingly, new benzodiazepines are involved in acute poisonings and deaths, particularly in parts of northern Europe (Essink et al., 2022; Kriikku et al., 2020; Rice et al., 2021), where many of the deaths linked to new benzodiazepines involve high-risk drug users who also use opioids and other central nervous system depressants (Kriikku et al., 2020; Rice et al., 2021; McAuley, 2022). Of note, the imposition of restrictions on prescribing benzodiazepine medicines over concerns of their abuse has been associated with an increase in the availability and use of new benzodiazepines in some places, including Scotland (the United Kingdom) and the United States (McAuley, 2022).

FIGURE 8

Fake diazepam tablets packaged in blister packs resembling those of the legitimate products. The tablets were purchased as 'Diazepam Activis' but were found to contain flubromazolam and diazepam on analysis by Wedinos in May 2020

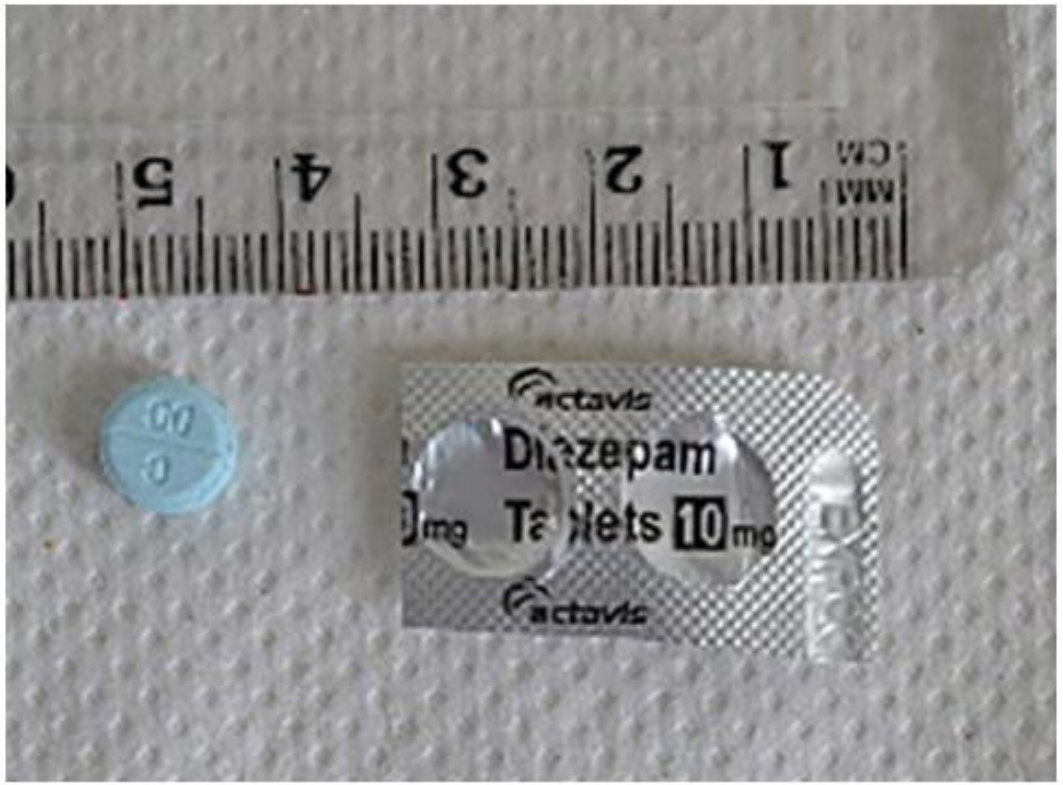
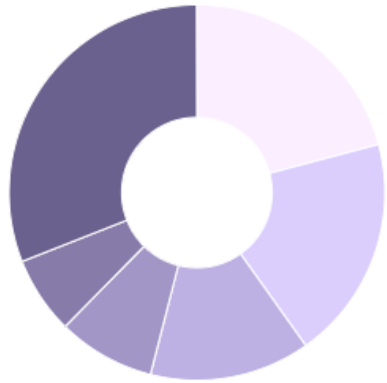


Photo: Wedinos.

opioids. Of particular concern is the growing use of new benzodiazepines to make falsified (fake) tablets of commonly prescribed benzodiazepine medicines, such as diazepam (Valium) and alprazolam (Xanax), and the involvement of criminal groups in producing such tablets. In some cases, the fake tablets are packaged in blister packs resembling legitimate products, which makes it more difficult for consumers to spot the fakes. Serious adverse events, such as severe poisonings, involving such fake medicines have been reported in Europe. Other risks

Seizures of new benzodiazepines reported to the EU Early Warning System: number of seizures, European Union, 2022

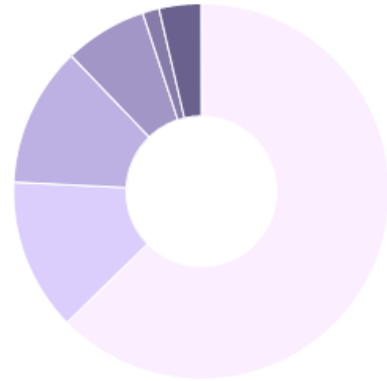


Bromazolam
Etizolam
Flualprazolam
Flunitrazolam
Flubromazepam
Other

EUDA (data) | Highcharts (chart tool)

Show data table

Seizures of new benzodiazepines reported to the EU Early Warning System: quantity seized for all forms reported in weight, European Union, 2022

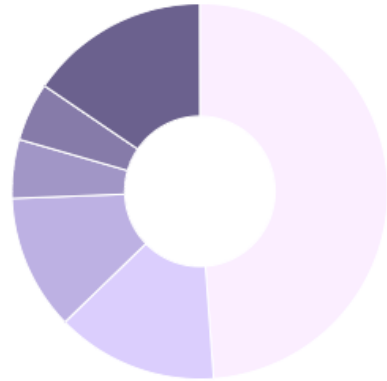


Etizolam
Flualprazolam
Deschloroetizolam
Bromazolam
Clonazolam
Other

EUDA (data) | Highcharts (chart tool)

Show data table

Seizures of new benzodiazepines reported to the EU Early Warning System: quantity of tablets and capsules, European Union, 2022



Flubromazolam
Clonazolam
Flualprazolam
Flubromazepam
Etizolam
Other

EUDA (data) | Highcharts (chart tool)

Show data table

UNODC

United Nations Office on Drugs and Crime

Current NPS Threats

Volume VI

August 2023

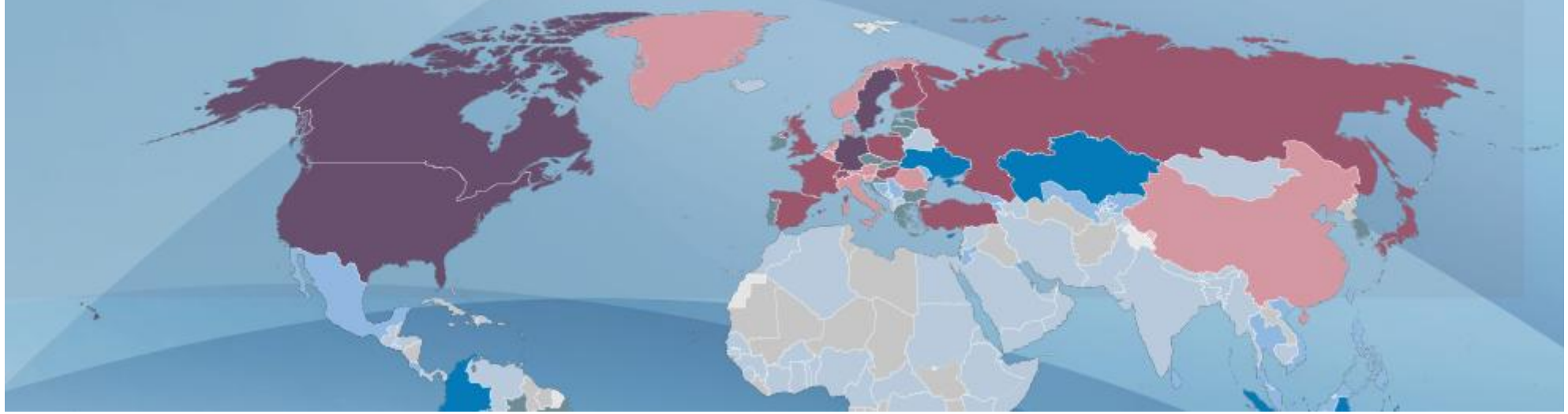
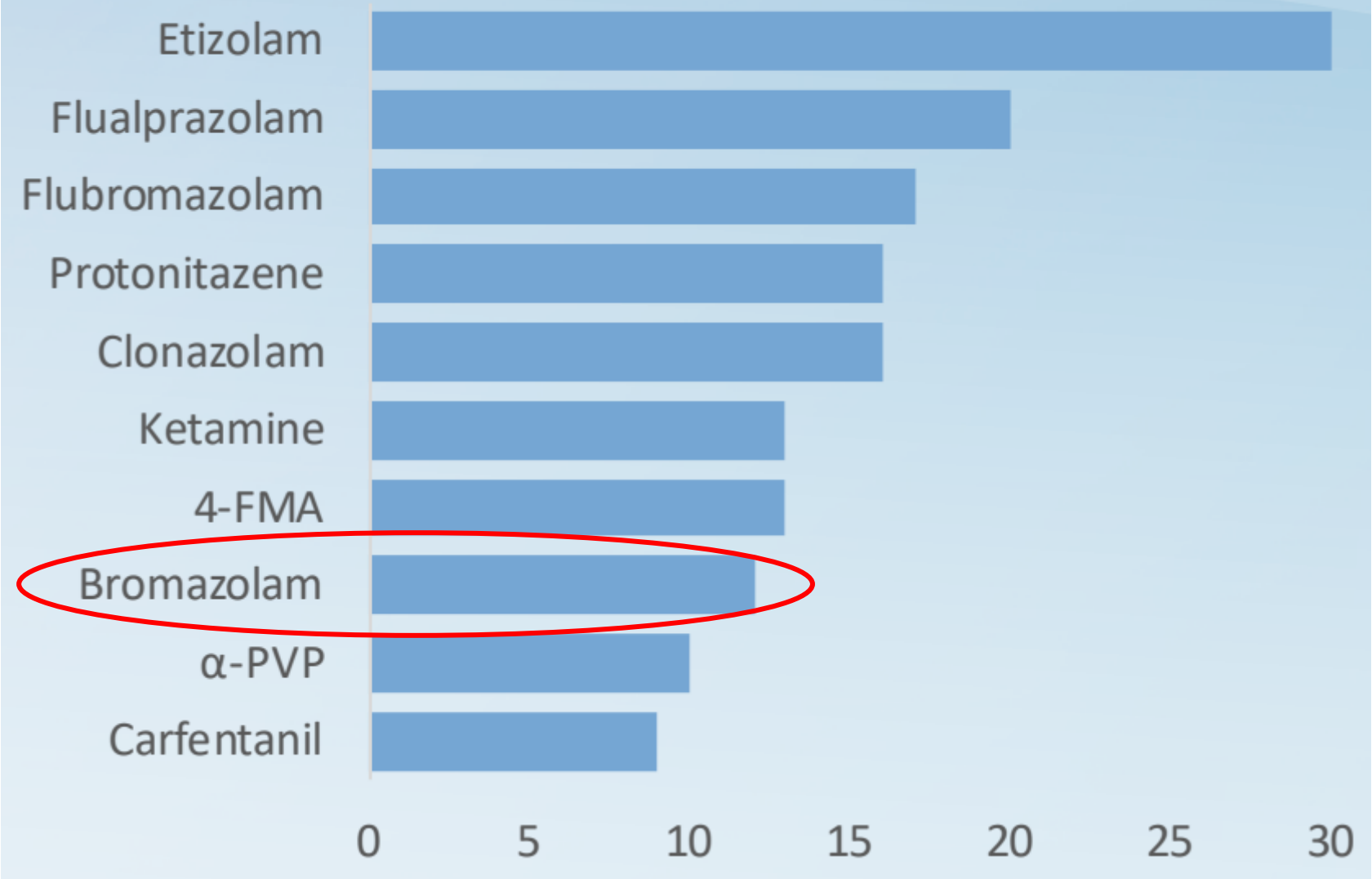


Figure 6: Substances most often reported in post-mortem (PM) cases



UNODC

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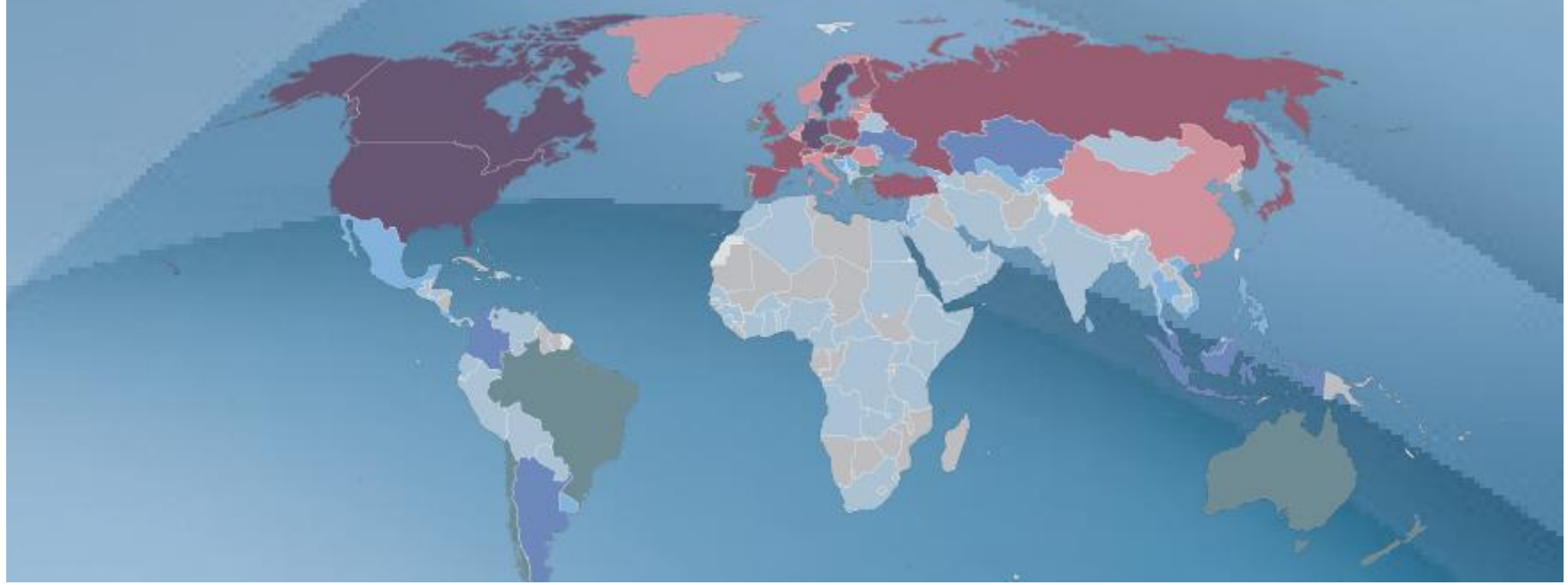
Current NPS Threats

Volume VII

July 2024



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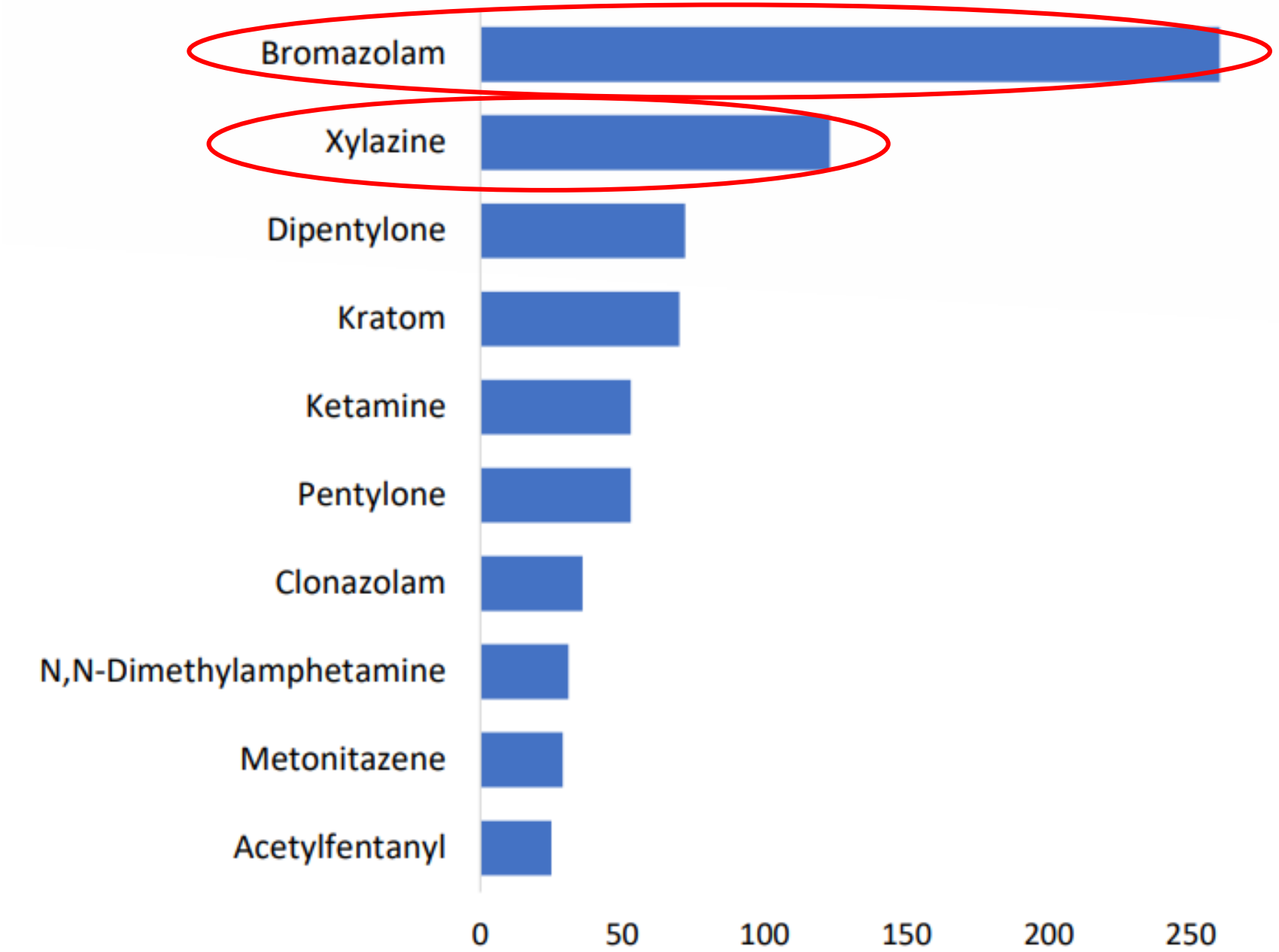

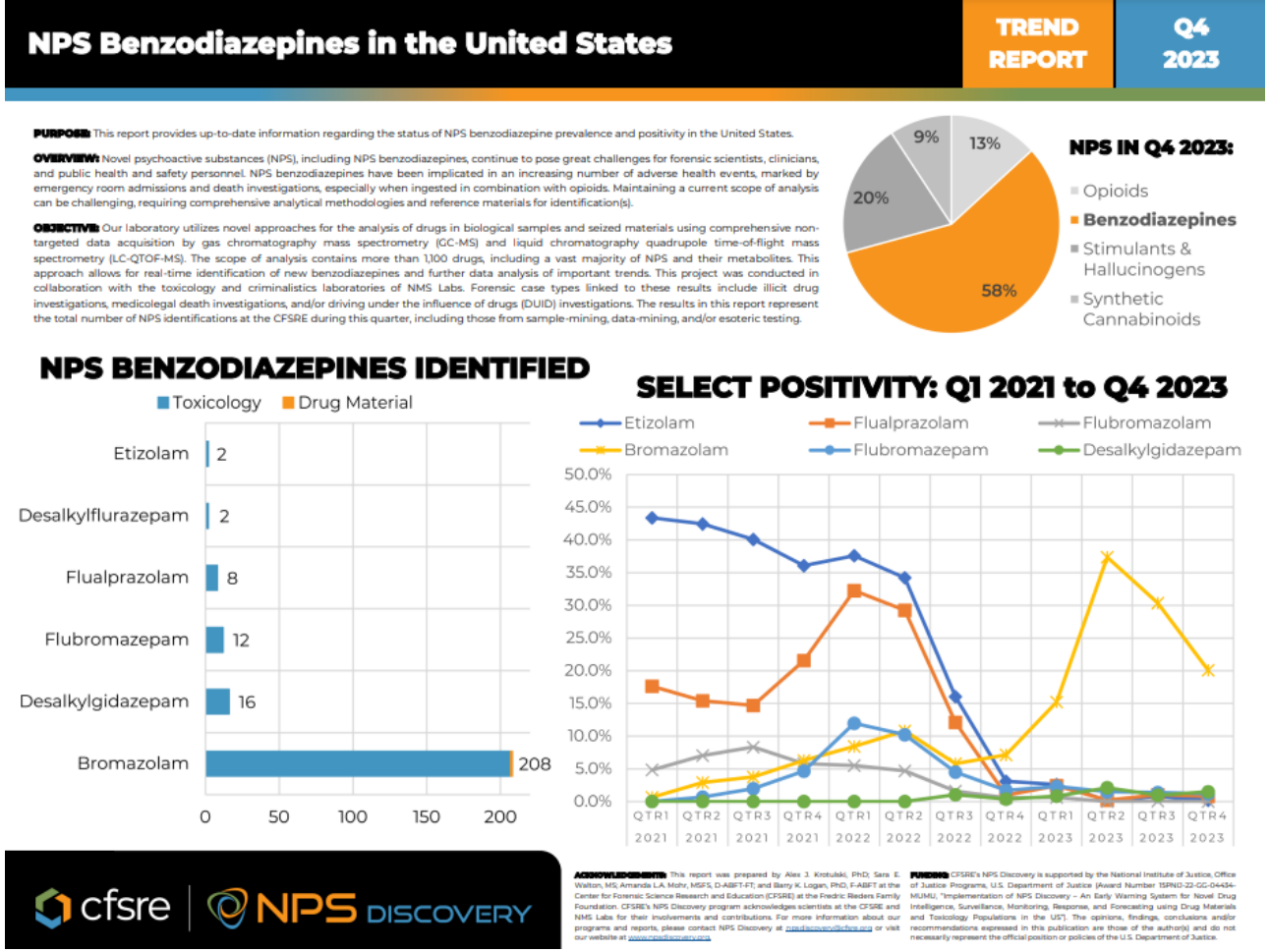

Following the international control of etizolam and flualprazolam, which came into force in November 2020 (CND, 2020a, b), producers and distributors appeared to switch to other new benzodiazepines, such as flubromazolam, clonazolam and bromazolam. Subsequently, flubromazolam and clonazolam were internationally controlled in 2021 (CND, 2021b, c). As a result, it is likely that these substances will be replaced by others, such as bromazolam, as countries, particularly producer countries, implement control measures. In 2023, there were signs in both Europe and the United States of an increase in detections of bromazolam (CFSRE, 2022; Drug Enforcement Administration, 2022).

3-MMC/3-CMC KOPEN?!

WEEK ACTIEPRODUCTEN

POPULAIRE CHEMICALS

NIEUWE CHEMICALS

GEFLUOREERDE CHEMICALS

CATHINONE CHEMICALS

ARYLCYCLOHEXYLAMINE CHEMICALS

LYSERGAMIDE CHEMICALS

BENZODIAZEPINE CHEMICALS

Flubromazolam Pellets (25×0,5mg)

Vanaf €0,64 tot €0,31 per pellet

Dit product is helaas niet meer verkrijgbaar. Gelukkig is er ruim voldoende keuze voor geschikte alternatieve producten binnen ons assortiment.

Best beoordeelde alternatieve producten:

Metizolam Pellets

Vanaf €1,20 per pellet

Flubrotizolam Pellets

Van €0,98 tot €2,00 per pellet

Flunitrazolam Pellets

Van €0,28 tot €0,64 per pellet

Flunitrazolam

Fatal overdose may occur when benzodiazepines are combined with other depressants such as opiates, barbiturates, gabapentinoids, thienodiazepines, alcohol or other GABAergic substances.[1]

It is strongly discouraged to combine these substances, particularly in common to heavy doses.

Summary sheet: Flunitrazolam

Flunitrazolam is a novel lesser-known depressant substance of the benzodiazepine class. It has been noted for its unusual potency for a benzodiazepine compound, being active in the low microgram range. This trait is also shared by compounds such as flubromazolam and clonazolam. Similar to flubromazolam, this is an ultra potent benzodiazepine. A dose of about 0.1 mg (100 µg) is equivalent to 10 mg diazepam or 0.25 mg alprazolam.[2]

Flunitrazolam first appeared on the online research chemical market in 2016.[3] It appeared in the form of pressed pellets and was offered alongside other novel benzodiazepines such as clonazolam and flubromazolam. Of these, it appears to be entirely novel and has no precedent in the scientific literature before being made available for sale on online.

Information regarding dosage, effects, and toxicity should be regarded with caution. Any comments regarding its pharmacology are purely speculation based upon the subjective effects it induces and its structural similarity to funitrazolam and other benzodiazepines, with very little research done for far with this particular compound.

Subjective effects include sedation, anxiety suppression, muscle relaxation, disinhibition, and memory suppression. Some users have reported seizures on high doses of this compound, without any contributing cause or withdrawal that might have triggered this. Only r05-4864 has this property, although to a greater extent.

Very little data exists about the pharmacological properties, metabolism, and toxicity of flunitrazolam in humans. Preliminary reports suggest it has high abuse potential similar to that of other potent benzodiazepines. It likely produces physical dependence with chronic use. Additionally, dosing is a concern, as potent benzodiazepines can cause long-lasting blackouts with minor dosing miscalculations.

It is worth noting that the sudden discontinuation of benzodiazepines can be potentially dangerous or life-threatening for individuals using regularly for extended periods of time, sometimes resulting in seizures or death.[4] It is highly recommended to taper one's dose by gradually lowering the amount taken each day for a prolonged period of time instead of stopping usage abruptly.[5]

It is highly advised to use harm reduction practices if using this substance.

BENZODIAZEPINE CHEMICALS

Meclonazepam pellets (15x1mg)
Desmethylflunitrazepam pellets (15x1mg)
Difludiazepam pellets (15×2,5mg)
Bromonordiazepam Pelletstrips (10×2,5mg)
Bromonordiazepam Pellets (35×2,5mg)
Bromonordiazepam Poeder (125mg)
Bromazolam Pellets (10×2,5mg)
Bromazolam Pellets (25x3mg)
Deschloroetizolam Pelletstrips (10x5mg)
Deschloroetizolam Pellets (22x5mg)
Flubromazepam Pelletstrips (10x5mg)
Flubromazepam Pelletstrips (10x10mg)
Flubromazepam Pellets (25x8mg)
Flubrotizolam Pellets (8×0,5mg)
Fluetizolam Poeder (30mg)
Flunitrazolam Pellets (25×0,25mg)
Gidazepam Pellets (21x3mg)
Metizolam (15x2mg)
Metizolam (10x5mg)
Norflurazepam Pellets (10x5mg)
Norflurazepam Pellets (10x10mg)
Norflurazepam Pellets (25x5mg)
Pyrazolam Pellets (25x3mg)
Pagoclone Pelletstrips (10x10mg)
Pagoclone Pellets (15x10mg)

Flunitrazolam Pellets (25×0,25mg)

Vanaf €1,59 per pellet

Maximaal 10 units per klant.

Supersnelle en discrete levering van de beste Flunitrazolam Pellets (25×0,25mg).

Op werkdagen voor 19.30 besteld is dezelfde dag verzonden!*

Waarschuwing: We verkopen niet aan personen onder de 21 jaar.
Het product Flunitrazolam Pellets (25×0,25mg) kan schadelijk zijn voor uw gezondheid en is niet geschikt voor consumptie. Wees u er van bewust dat het niet naleven van onze veiligheidsvoorschriften mogelijk ernstige gezondheidsrisico's met zich mee kan brengen. Houd u zich daarom aan onze veiligheidsvoorschriften.

1 unit bestaat uit **25 x0,25mg Pellets**

Aantal	Prijs per unit	Totaalprijs	Prijs per Pellet
1 Unit	€39,950	€39,95	€1,598
2 Units	€39,950	€79,90	€1,598
3 - 4 Units	€39,920	€119,76	€1,597
5 - 9 Units	€39,900	€199,50	€1,596
10 Units	€39,750	€397,50	€1,590

*** Vanaf 3 units gratis brievenbus verzending!**

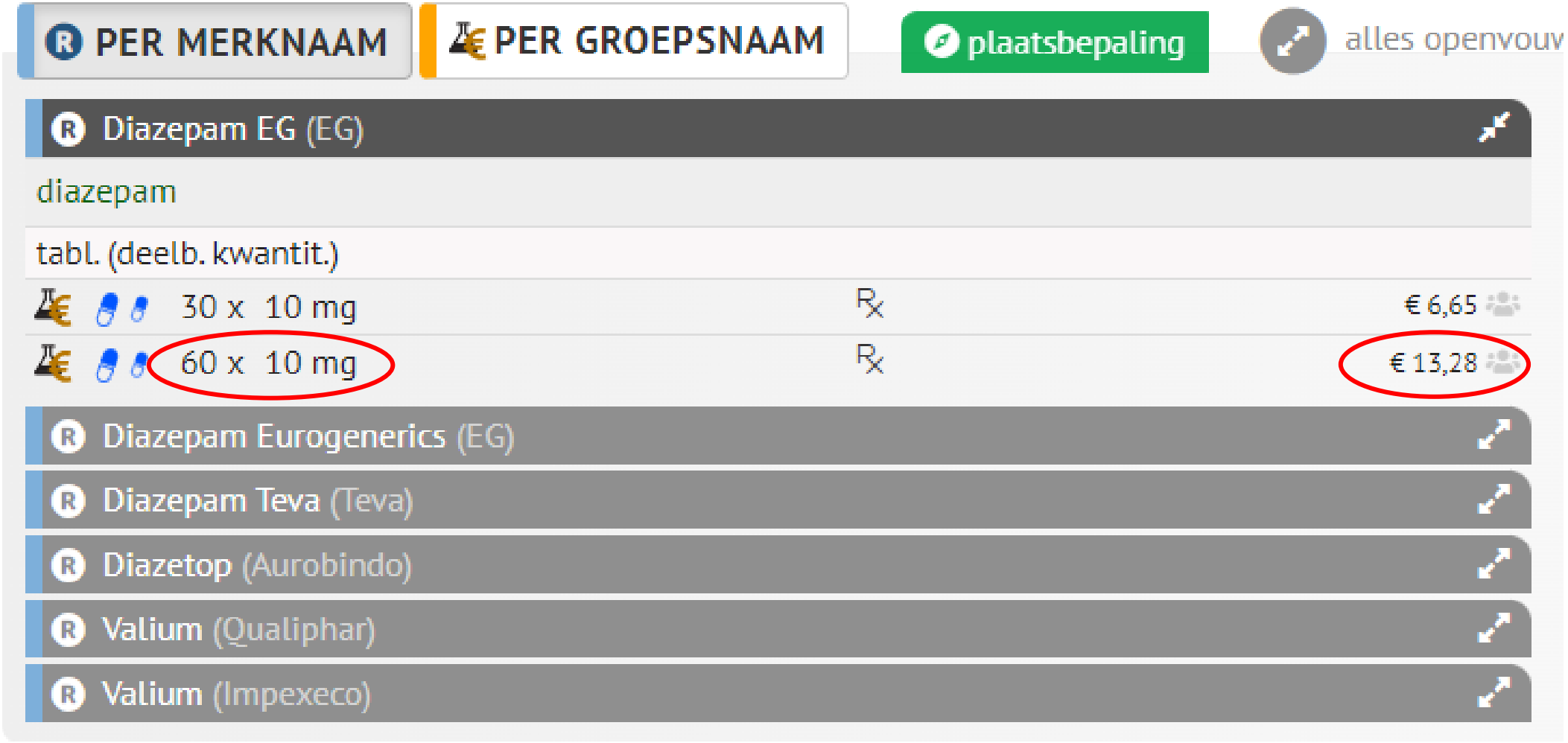
PER MERKNAAM
PER GROEPSNAAM
plaatsbepaling
alles openvouv
Diazepam EG (EG)
diazepam
tabl. (deelb. kwantit.)
30 x 10 mg
€ 6,65
60 x 10 mg
€ 13,28
Diazepam Eurogenerics (EG)
Diazepam Teva (Teva)
Diazetop (Aurobindo)
Valium (Qualiphar)
Valium (Impexeco)

TABLE 2

Binding values to the $GABA_A$ receptor and dosages of new benzodiazepines

Compound	Predicted binding value (log 1/c)	Common dose (mg) (*)
Flunitrazolam	8.88	0.08–0.15
Clonazolam	8.86	0.2–0.4
Flubromazolam	8.77	0.2–0.4
Etizolam	8.64	1–2
Nifoxipam	8.63	0.5–1
Meclonazepam	8.52	3–6
Fonazepam (desmethyl-flunitrazepam)	8.46	1–2
N-Desalkylflurazepam (norflurazepam)	8.44	5–10
3-Hydroxy-phenazepam	8.42	1–2
Diclazepam (Ro5-3448)	8.39	1–2
Flubromazepam	8.37	4–8
Metizolam (desmethyl-etizolam)	8.34	2–4
Nitrazolam	8.34	1–2
Bromazolam	8.25	1–3
Phenazepam	8.12	1–2
Deschloroetizolam	7.96	4–6
4'-Chlorodiazepam (Ro5-4864)	7.88	n.g.
Cloniprazepam	7.83	1–2
Pyrazolam	7.79	2–3
Adinazolam	7.18	15–30
Flutazolam	6.83	5–10
Ro7-4065 (difludiazepam)	n.t.	n.g.
Flualprazolam	n.t.	0.25–0.5
Fluclotizolam	n.t.	0.25–0.5
Thionordazepam	n.t.	n.g.

(*) Data from https://tripsit.me/ (October 2019).

CONVERSIE NPS BENZO'S NAAR DIAZEPAM

- 1mg etizolam = 5mg diazepam
- 1mg bromazolam = 5mg diazepam
- 1mg flualprazolam = 20mg diazepam
- **1mg flubromazolam = 50mg diazepam (+ zeer lange werkingsduur)**
- **1mg flunitrazolam = 100mg diazepam**

Louter indicatief, CAVE persoonsgebonden verschillen!

Neuropsychiatric Disease and Treatment

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REVIEW

Bridging the gap between education and appropriate use of benzodiazepines in psychiatric clinical practice

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Abstract: More than half a century after their discovery, benzodiazepines (BDZs) still represent one of the largest and most widely prescribed groups of psychotropic compounds, not only in clinical psychiatry but also in the entire medical field. Over the last two decades, however, there has been an increased focus on the development of antidepressants and antipsychotics on the part of the pharmaceutical industry, clinicians, and researchers, with a reduced interest in BDZs, in spite of their widespread clinical use. As a consequence, many psychiatric residents, medical students, nurses, and other mental health professionals might receive poor academic teaching and training regarding these agents, and have the false impression that BDZs represent

the alternatives.[9] Practical advice includes remembering that dependence is neither a valid reason to continue prescribing, nor a sufficient reason, on its own, to refuse to prescribe BDZs. Active consent and cooperation from the patient is required before attempting to reduce, gradually withdraw, or terminate a dependent patient's use of BDZs; and a blanket refusal to prescribe BDZs without adequate assessment can be as problematic as prescribing them.[247]

'Purple Haze' product consisting of low-T

NPS CANNABINOÏDEN

Synthetische cannabinoïden vormen de grootste en meest diverse groep NPS. Ze kunnen meer ernstige bijwerkingen veroorzaken dan cannabis en hun effecten kunnen onvoorspelbaar zijn. Synthetische cannabinoïden leiden vaak tot vergiftigingen, waaronder fatale vergiftigingen [1]. Bovendien kunnen de producten waarin de synthetische cannabinoïden worden aangeboden ook nog eens versnijdingsproducten bevatten [2].

- Intoxicatie met synthetische cannabinoïden kan leiden tot cardiovasculaire problemen, lever- en nierschade, epileptische aanvallen, psychische problemen en cognitieve stoornissen, als ook hartinfarcten, herseninfarcten en orgaanfalen [1].
- In vergelijking met cannabis veroorzaakt het gebruik van synthetische cannabinoïden sterkere symptomen zoals meer psychose-achtige symptomen, angst, hoge bloeddruk, misselijkheid, verwardheid, duizeligheid, en pijn op de borst [2–4].

- Er is een wetenschappelijke verklaring voor waarom synthetische cannabinoïden sterkere effecten hebben dan cannabis. THC is een agonist van CB1R, een cannabinoïde receptor in het menselijk lichaam. Activering van CB1R faciliteert de ontwikkeling van cardiometabolische ziekten, zoals hart- en vaatziekten, diabetes en nierfunctiestoornissen. Synthetische cannabinoïden zijn tot 200 keer sterker dan THC bij het activeren van CB1R, en synthetische cannabinoïden zijn volledige agonisten van CB1R terwijl THC slechts een gedeeltelijke agonist is. Daardoor veroorzaken synthetische cannabinoïden veel sterkere effecten en ernstigere bijwerkingen dan cannabis [5].

- Stoppen met dagelijks gebruik van synthetische cannabinoïden kan leiden tot ernstige onttrekkingsverschijnselen zoals epileptische aanvallen, hartkloppingen en ademhalingsproblemen. Mildere symptomen zijn cravings, angst, slapeloosheid, misselijkheid, braken, geen eetlust, en zweten [6].
- Synthetische cannabinoïden leiden vaker tot ziekenhuisopnames dan andere NPS, behalve synthetische cathinonen [7].
- In Nederland lijkt het gebruik van synthetische cannabis beperkt. Verondersteld wordt dat dit komt vanwege de goede kwaliteit en ruime beschikbaarheid van cannabis, en vanwege het gedogen van cannabisgebruik [3].

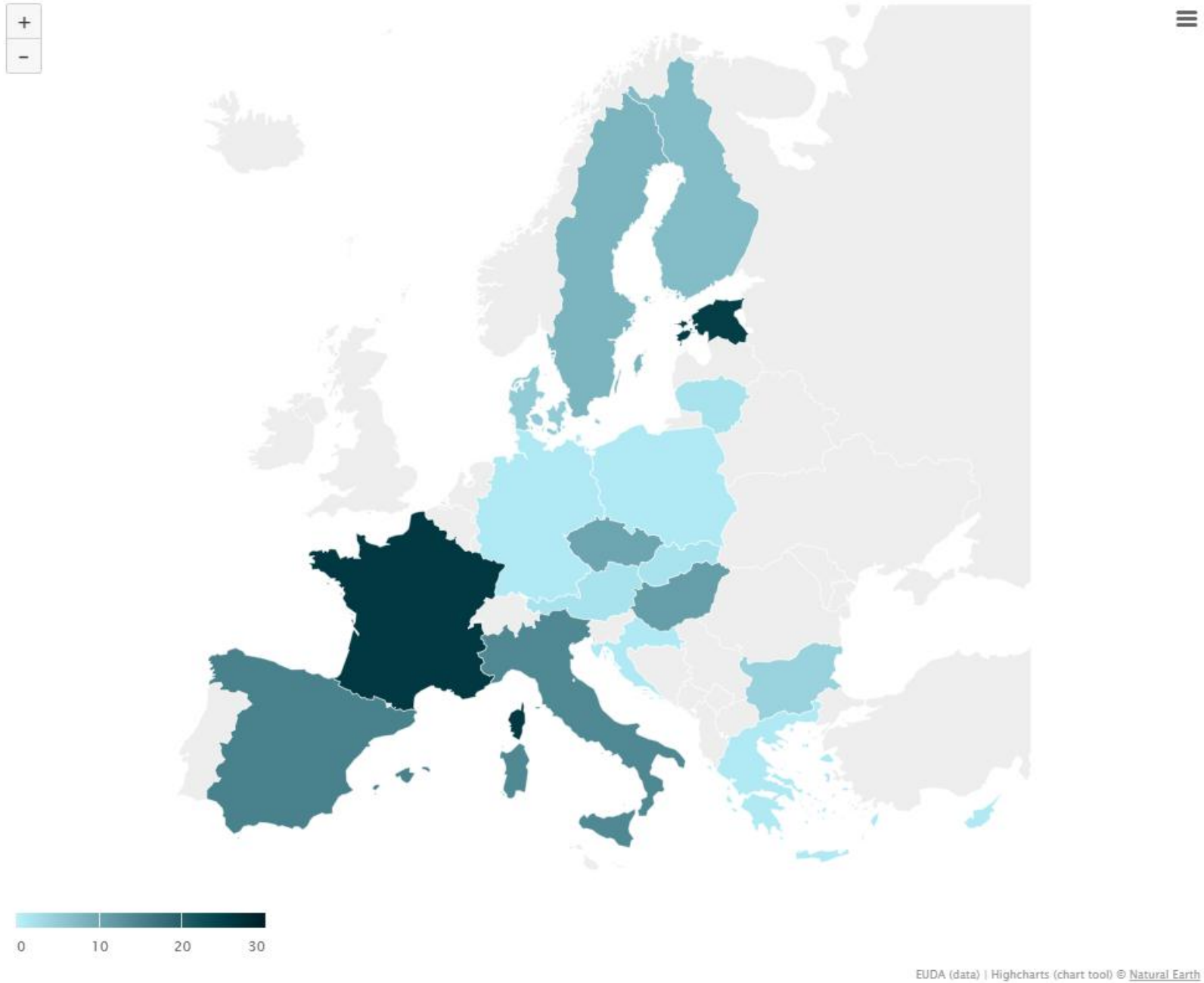
- In 2018 publiceerde het EMCDDA diverse risicoschattingen voor synthetische cannabinoïden (5F-MDMB-PINACA; AB-CHMINACA; ADB-CHMINACA, CUMYL-4CN-BINACA). Voor deze middelen zijn tal van fatale en niet-fatale intoxicaties gerapporteerd, in diverse Europese landen, waaronder het Verenigd Koninkrijk, Duitsland en Zweden, maar ook in de Verenigde Staten en Japan [8–12].
- MDMB-CHMICA wordt in verband gebracht met een hoog risico op ernstige intoxicatie en heeft minstens 29 doden veroorzaakt in 6 landen in Europa [13]. Ook is er een aantal sterfgevallen gemeld als gevolg van het gebruik van 5F-AMB, ADB-FUBINACA, XLR-11, en 5F-Cumyl-PEGACLONE [14–18]. In Australië hebben synthetische cannabinoïden tussen 2000 en 2017 mogelijk bijgedragen aan de dood van 55 personen [19].

The EMCDDA currently monitors six semi-synthetic cannabinoids. This includes four that were reported for the first time in 2023 (see Table Number of countries reporting detections of semi-synthetic cannabinoids, as notified to the EU Early Warning System, 2022-2023).

Number of countries reporting detections of semi-synthetic cannabinoids, as notified to the EU Early Warning System, 2022-2023

Substance	Date first identified	Number of countries reporting identifications
HHC	May 2022	24
HHC-O	August 2022	10
HHC-P	November 2022	8
H4-CBD	December 2022	9
THC-P	March 2023	5
HHCH	June 2023	1

Number of seizures of HHC (all forms) reported to the EU Early Warning System, European Union, 2022



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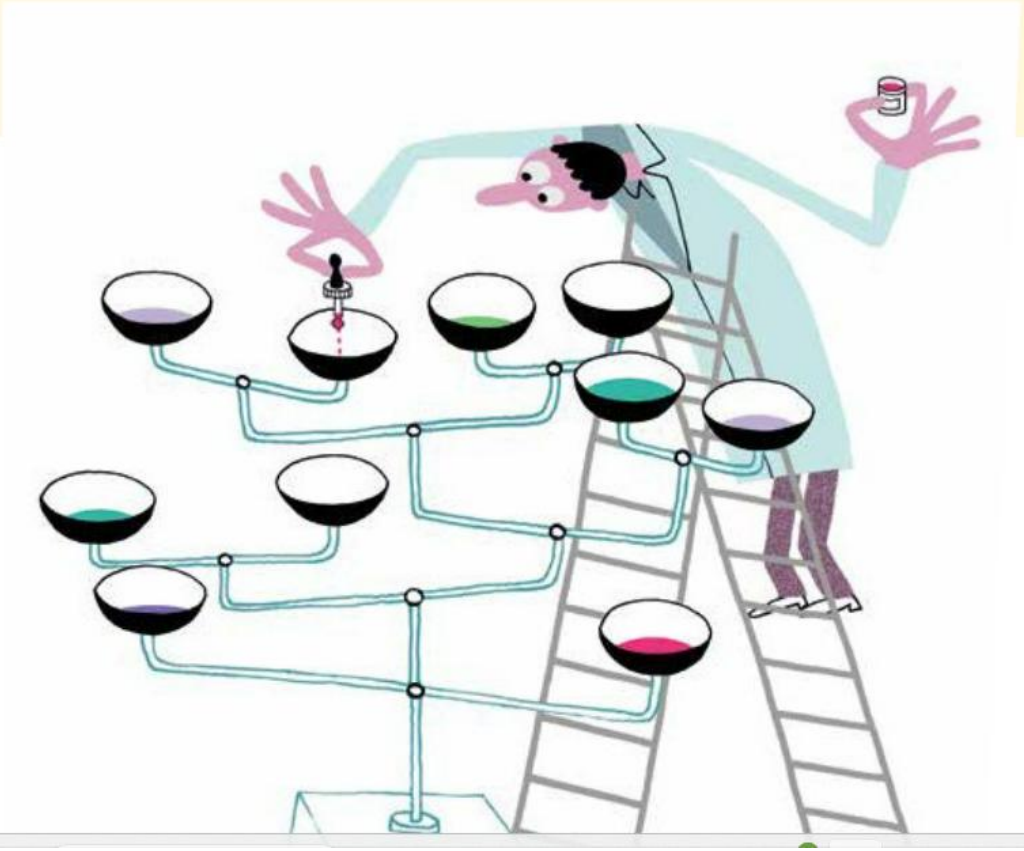
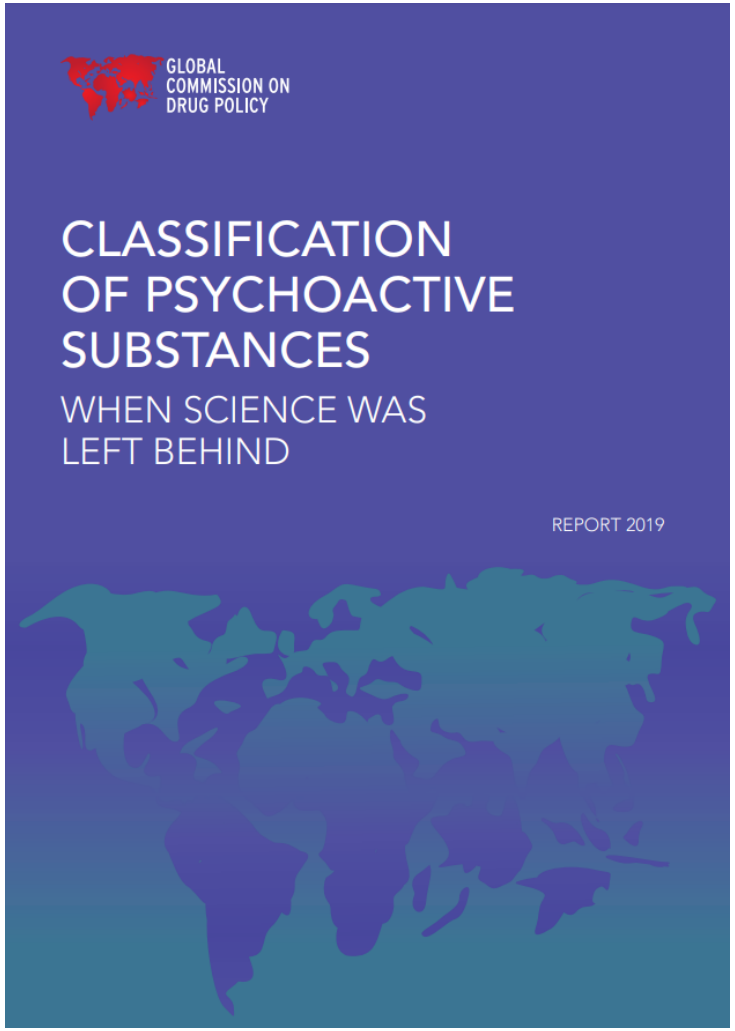


https://maguza.be/technologie/artikel/designer-drugs-op-de-weegschaal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VLAAMS EXPERTISECENTRUM
ALCOHOL EN ANDERE DRUGS

Cannabisbeleid

december 2020

Figuur 1: Mogelijke beleidsopties (Rolles & Murkin, 2013)

DANK VOOR JULLIE AANDACHT EN SUCCES IN DE PRAKTIJK! CASUS OVERLEGGEN OF SPECIFIEKE VRAAG?

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[DeSleutel]

MENSEN KANSEN GROEIEN