



UMC Utrecht

Radboudumc

Therapeutisch gebruik van recreatieve middelen



DR. PIM B. VAN DER MEER

AIOS PSYCHIATRIE EN KLINISCHE FARMACOLOGIE, NEUROPSYCHOLOOG

AFDELING PSYCHIATRIE, UMC UTRECHT

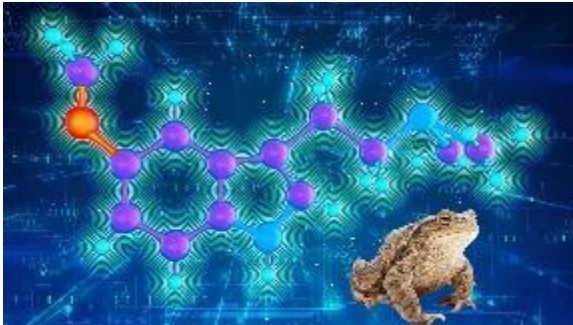
PROF. DR. KEES KRAMERS

KLINISCH FARMACOLOOG, INTERNIST

AFDELING APOTHEEK EN INTERNE GENEESKUNDE, RADBOUDUMC NIJMEGEN

Inhoud

- Vele recreationele middelen voor therapeutisch gebruik (in onderzoeksverband)
- Vandaag focus op recent geregistreerde (atypische) psychedelica evenals die het meest veelbelovend zijn



Inhoud

Komende half uur:

Pim van der Meer

- MDMA trials bij posttraumatische stressstoornis
- Esketamine trials bij therapieresistente depressie
- Psilocybine trials bij therapieresistente depressie

Kees Kramers

- MDMA: overlijden, hyponatriaemie, hyperthermie, cognitieve effecten
- Esketamine: cystitis en cholangitis
- Psilocybine: hoofdpijn, misselijk, angst, paranoia, HPPD

MDMA

- 2 trials in totaal meegenomen bij beoordeling registratie FDA
- Vergelijkbare methodologie en resultaten



Mitchell et al. (2021) Nature Medicine

Methode

- Populatie: PTSD >6 maanden en CAPS-5 ernst ≥ 35
- Interventie: 3xMDMA sessie (maand ertussen) a 120mg; 180mg; 180mg + niet directieve therapie + 3x voorbereiding/integratie sessie
- Controlegroep: Placebo + alles vergelijkbaar als interventie
- Random./ blinding: Ja/ja
- Follow-up: 18 weken
- Primaire uitkomst: Verandering in CAPS-5 score (range 0-80) baseline – 18 weken
- Statistiek: Mixed model for repeated measurements

Patiënt karakteristieken

- Aantal patiënten:
- CAPS baseline gem. (SD)

MDMA

46
44 (6)

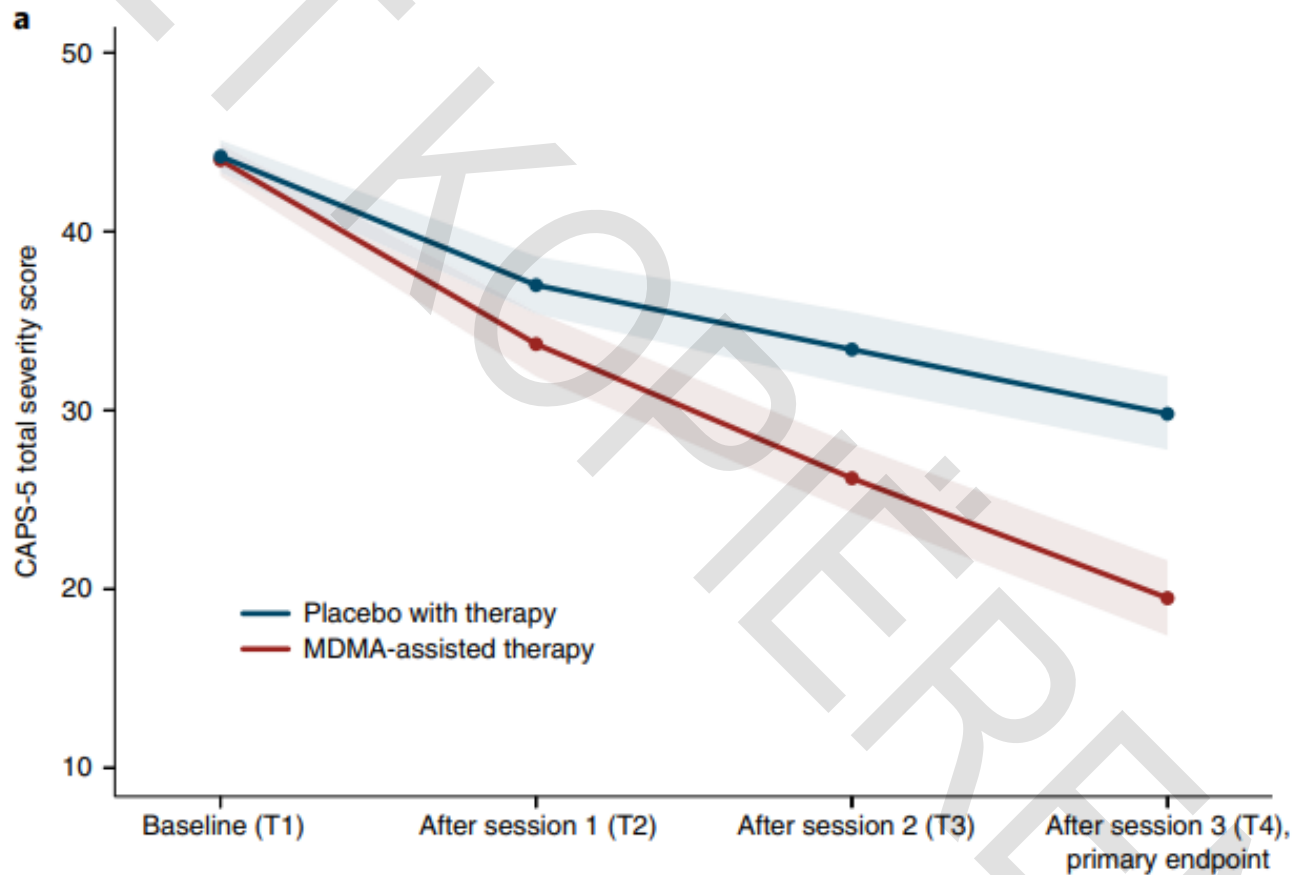
Placebo

44
44 (6)

Resultaten

- Verandering baseline – 18w: -24 (12) -14 (12)
- Least squares gem. verschil(95%BI): -11.9 (-17.4 tot -6.3)
- P-waarde: <0.001

Mitchell et al. (2021) Nature Medicine



MDMA – FDA afkeuring

- FDA adviescommissie in juni 2024:
 - 9 vs 2 tegen data voldoende effectiviteit
 - 10 vs 1 tegen MDMA voordelen opwegen tegen de risico's
- Afkeuring door de FDA in augustus 2024



De zorgen van de FDA

- Ontblinden verklaart (grotendeels) het verschil tussen MDMA en placebo
 - Advies was lage dosis of ander psychoactief middel (e.g., midazolam)
- 40% van patiënten had ervaring MDMA → verwachtingseffect
- Misbruik gerelateerde bijwerkingen (e.g., euforie) niet gerapporteerd
- FDA keurt farmacotherapie, geen psychotherapie
- Psychotherapie niet gestandaardiseerd (70% 'anders')
- Beschuldiging van wangedrag door therapeut middels misbruik bij n=1

MDMA: temperatuur

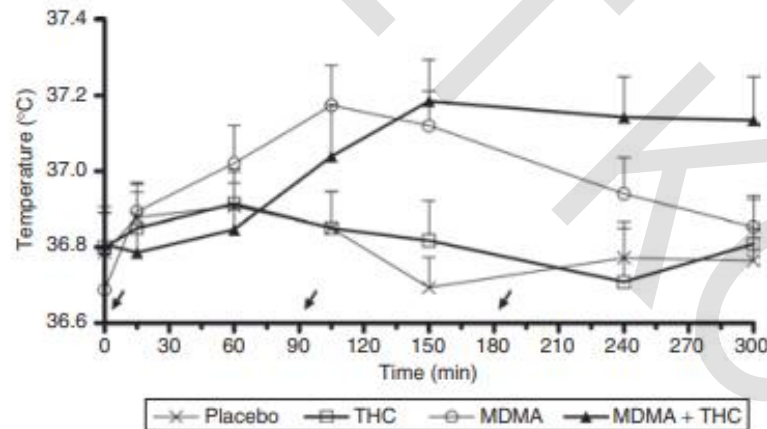
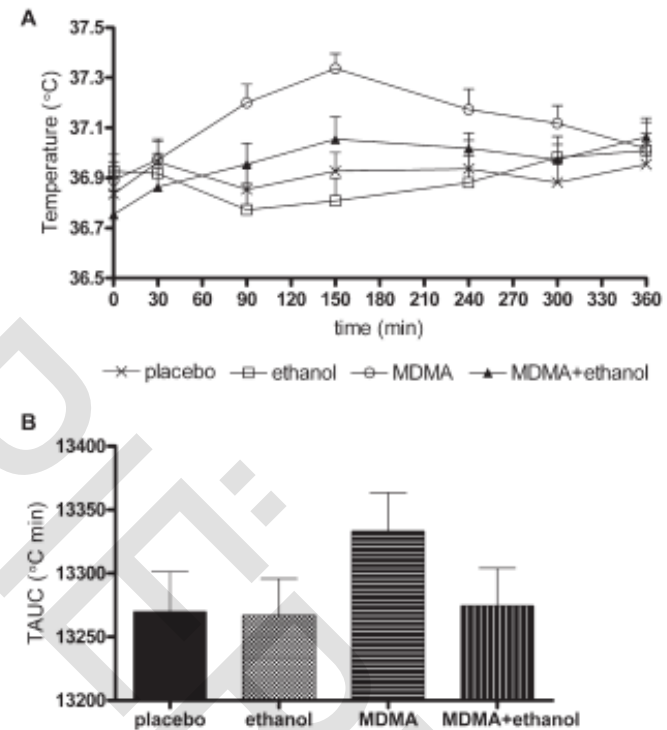
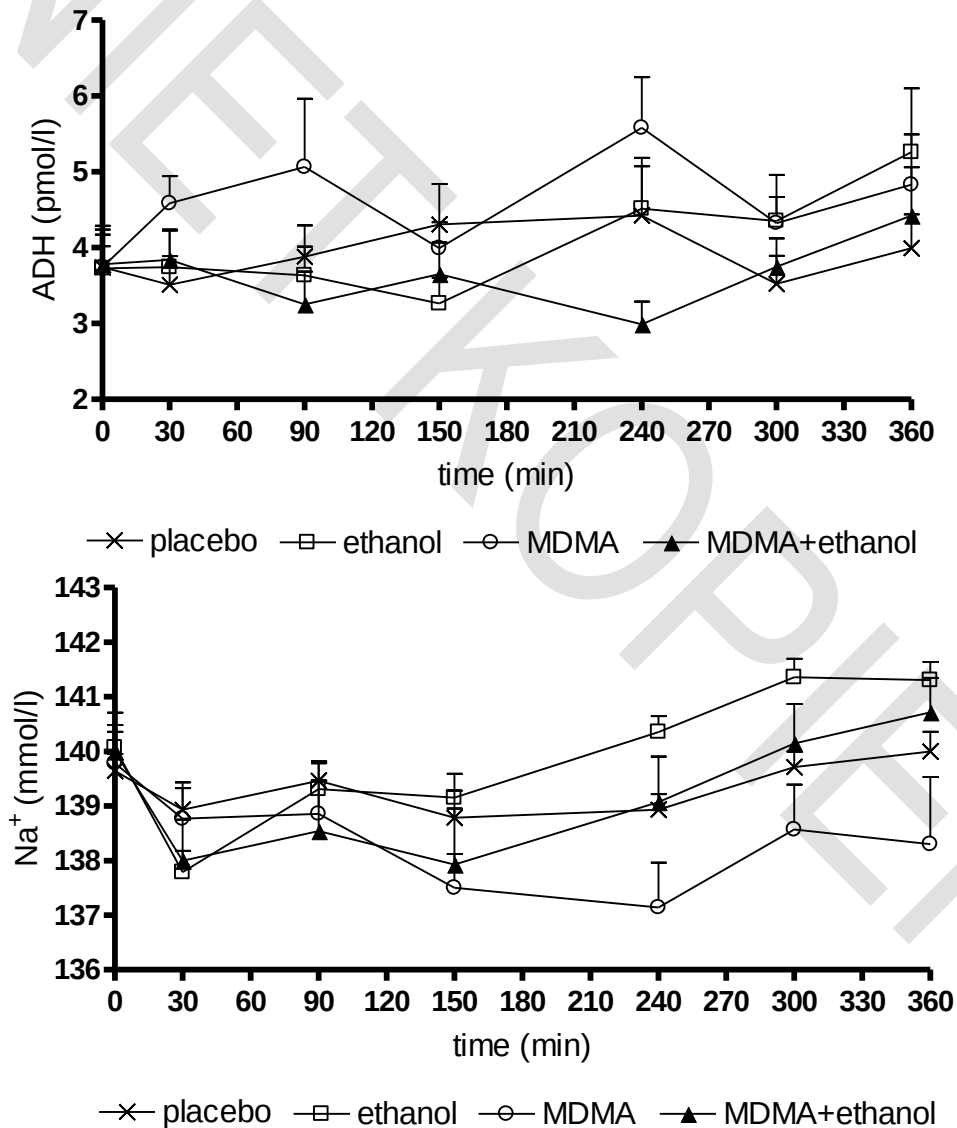


Figure 3 Temperature per drug condition (mean, SEM). Arrows indicate tetrahydrocannabinol (THC) administration at $t = 0$ min (4 mg), $t = 90$ min (6 mg), and $t = 180$ min (6 mg). MDMA, 3,4-methylenedioxymethamphetamine.



MDMA: hyponatraemia



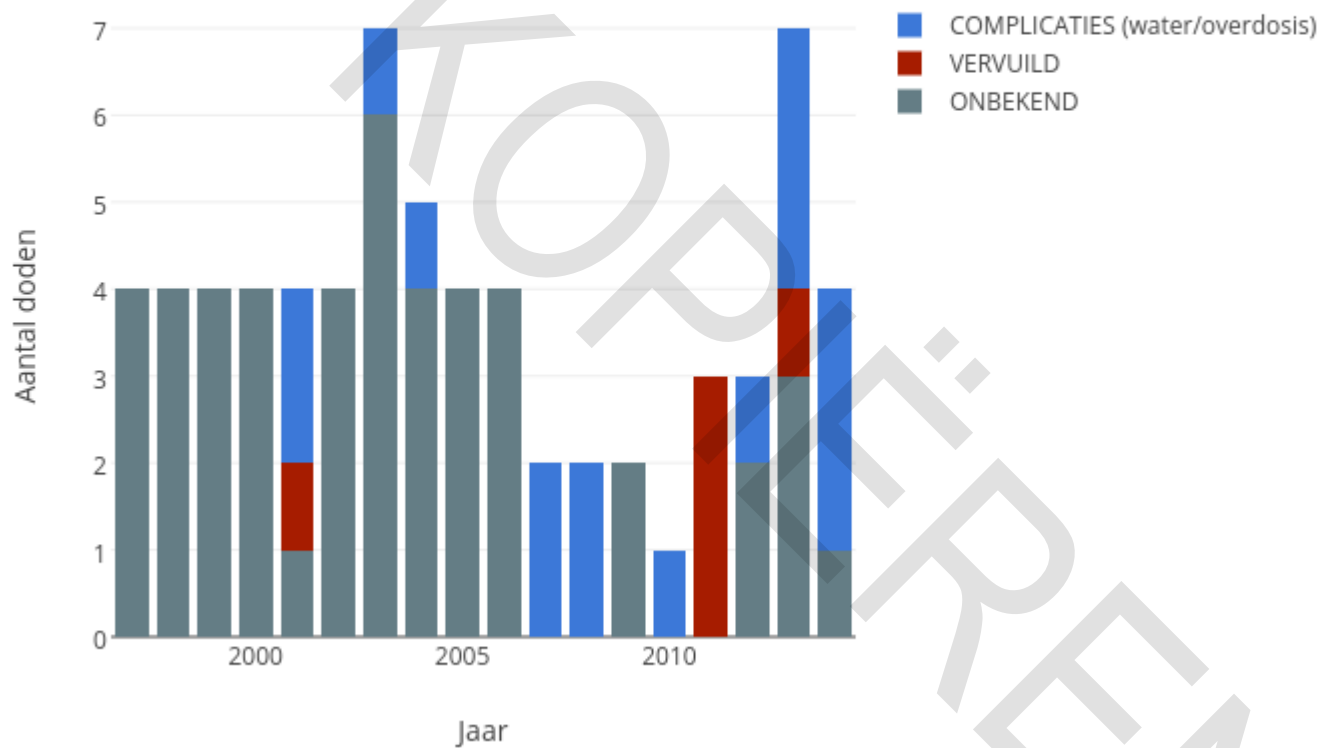
MDMA: overlijden

Table 4. Risk estimation based on the annual number of 3,4-methylenedioxymethamphetamine (MDMA)-related deaths (MRDs) in England and Wales and Scotland (56 and 27, respectively), and the number of last-year ecstasy users (550,000 and 45,000, respectively) in these countries.

	Risk of a fatal incident	
	%	Per user or per dose unit
MRDs		
England and Wales	0.010	1 in 10,000 users
England and Wales ^a	0.005	1 in 20,000 pills
England and Wales; solely MDMA ^b	0.003	1 in 33,000 pills
Scotland	0.060	1 in 1660 users
Scotland ^a	0.030	1 in 3300 pills
Scotland; solely MDMA ^b	0.003	1 in 33,000 pills
Other substances^c		
Opiates (heroin and morphine)	0.35	1 in 290 users
Cocaine	0.05	1 in 2000 users
Amphetamine	0.005	1 in 20,000 users
Alcohol-specific deaths^d		
England	0.011	1 in 9000 drinkers
Wales	0.014	1 in 7400 drinkers
Scotland	0.021	1 in 4900 drinkers
UK ^e	0.030	1 in 8200 drinkers
UK ^f	0.300	1 in 820 heavy drinkers
Other causes		
UK fatal road accidents ^g	0.0036	1 in 28,000 drivers

MDMA: overlijden

XTC Doden in Nederland sinds 1996



Cognition in Novice Ecstasy Users With Minimal Exposure to Other Drugs

A Prospective Cohort Study

Thelma Schilt, MSc; Maartje M. L. de Win, MD, PhD; Maarten Koeter, PhD; Gerry Jager, PhD; Dirk J. Korf, PhD; Wim van den Brink, MD, PhD; Ben Schmand, PhD

Context: Ecstasy (street name for [$\pm$]-3,4-methylenedioxymethamphetamine [MDMA]) use has been associated with cognitive deficits, especially in verbal memory. However, owing to the cross-sectional and retrospective nature of currently available studies, questions remain regarding the causal direction and clinical relevance of these findings.

Objective: To examine the relationship between Ecstasy use and subsequent cognitive performance.

Design: A prospective cohort study in Ecstasy-naïve subjects with a high risk for future first Ecstasy use, as part of the Netherlands XTC Toxicity study. The initial examination took place between April 10, 2002, and April 28, 2004; follow-up was within 3 years after the initial examination.

Setting and Participants: One hundred eighty-eight healthy Ecstasy-naïve volunteers (mean age, 22 years) were recruited. Of these, 58 subjects started using Ecstasy (mean cumulative dose, 3.2 tablets; median cumulative dose, 1.5 tablets). They were compared with 60 persistent Ecstasy-naïve subjects matched on age, sex, intelligence, and use of substances other than Ecstasy. Differences in cognition between Ecstasy users and Ecstasy-naïve subjects were adjusted for differences in cannabis and other recreational drug use.

Main Outcome Measures: Change scores between the initial examination and follow-up on neurocognitive tests measuring attention, working memory, verbal and visual memory, and visuospatial ability.

Results: At the initial examination, there were no statistically significant differences in any of the neuropsychological test scores between persistent Ecstasy-naïve subjects and future Ecstasy users. However, at follow-up, change scores on immediate and delayed verbal recall and verbal recognition were significantly lower in the group of incident Ecstasy users compared with persistent Ecstasy-naïve subjects. There were no significant differences on other test scores.

Conclusions: Our findings suggest that even a first low cumulative dose of Ecstasy is associated with decline in verbal memory. Although the performance of the group of incident Ecstasy users is still within the normal range and the immediate clinical relevance of the observed deficits is limited, long-term negative consequences cannot be excluded.

Arch Gen Psychiatry. 2007;64:728-736

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Table 1. Characteristics of Use of Ecstasy and Other Substances

Characteristic	Ecstasy Users (n = 58)		Ecstasy-Naive Subjects (n = 60)	
	Initial Examination	Follow-up	Initial Examination	Follow-up
Sex, male/female, No.	25/33	NA	25/35	NA
Age, mean $\pm$ SD (median; range), y	21.8 $\pm$ 3.1 (21.1; 18-29)*	22.7 $\pm$ 3.2 (21.9; 19-30)*	21.5 $\pm$ 2.1 (21.3; 18-29)†	23.0 $\pm$ 2.1 (22.9; 19-30)†
DART-IQ, mean $\pm$ SD (median; range)	103.4 $\pm$ 9.0 (101.5; 85-126)	NA	105.5 $\pm$ 10.2 (104.5; 85-126)	NA
Subjects at education level, No.‡				
Prevocation	1	1	0	0
Junior general secondary or vocation	9	7	3	1
Senior general secondary education, vocation colleges	45	46	55	55
Universities	3	4	2	4
Ecstasy, mean $\pm$ SD (median; range)				
Cumulative dose, tablets	NA	3.2 $\pm$ 5.2 (1.5; 0.5-30)	NA	NA
Time since using first tablet, wk	NA	18.6 $\pm$ 17.6 (11.1; 2-70)	NA	NA
Time since using last tablet, wk§	NA	11.8 $\pm$ 12.0 (7.9; 2-59)	NA	NA
Duration of Ecstasy use, wk	NA	6.8 $\pm$ 12.5 (0.0; 0-12)	NA	NA
Other substances used in last year, mean $\pm$ SD (median; range)				
Alcohol, units/wk	8.6 $\pm$ 7.8 (6.1; 0-31)	8.9 $\pm$ 7.8 (7.3; 1-36)	9.8 $\pm$ 9.0 (7.9; 0-55)	8.2 $\pm$ 7.9 (6.6; 0-54)
Tobacco, cigarettes/wk	33.9 $\pm$ 47.8 (1.0; 0-160)	33.6 $\pm$ 61.8 (5.0; 0-350)	26.4 $\pm$ 54.9 (0.0; 0-280)	24.4 $\pm$ 46.2 (0.0; 0-200)
Cannabis, joints in last year	48.8 $\pm$ 100.4 (15.8; 0-635)	53.6 $\pm$ 120.8 (18.5; 0-830)#	17.2 $\pm$ 25.1 (15.5; 0-133)	20.5 $\pm$ 50.3 (2.3; 0-315)#
Amphetamine, No. of times used last year	0.1 $\pm$ 0.8 (0.0; 0-6)	2.9 $\pm$ 20.5 (0.0; 0-156)	0.0 $\pm$ 0.0 (0.0; 0-0)	0.0 $\pm$ 0.0 (0.0; 0-0)
Cocaine, No. of times used last year	0.8 $\pm$ 2.1 (0.0; 0-6)	1.4 $\pm$ 2.8 (0.0; 0-12)#	0.3 $\pm$ 1.3 (0.0; 0-6)	0.3 $\pm$ 1.3 (0.0; 0-6)#

Esketamine



Esketamine trials - Spravato

Stap 1 Voorbereiding

Alleen voor het eerste pompje:



Instrueer de patiënt **alleen voor het eerste pompje** de neus te snuiten.



Bevestig het aantal benodigde pompjes.

Stap 3 Bereid de patiënt voor



Instrueer de patiënt als volgt:

- Houd het pompje vast zoals afgebeeld, met de duim zachtjes onderaan op de zuiger.
- Druk de zuiger niet in.



Instrueer de patiënt als volgt:

- Houd tijdens de toediening het hoofd ongeveer 45 graden schuin achterover. Zo blijft de medicatie in de neus.

Stap 2 Maak het pompje klaar voor gebruik



- Controleer de vervaldatum ('EXP'). Neem een nieuw pompje als de vervaldatum is verstreken.
- Verwijder de blisterfolie en haal het pompje uit de verpakking.



- **Test het pompje niet.** Dit leidt tot verlies van medicatie.
- Controleer of de indicator 2 groene stippen laat zien. Zo niet, gooi het pompje weg en neem een nieuw pompje.
- Geef het pompje aan de patiënt.

Stap 4 Patiënt verstuift één keer in elk neusgat



Volgend pompje (indien nodig)

28 mg	
56 mg	
84 mg	

Esketamine trials

- 4 trials in totaal meegenomen bij beoordeling tot registratie FDA/EMA
 - 3 effectiviteitstrials met vergelijkbare methodologie
 - 1 terugval preventie trial onder patiënten met respons op esketamine
- 2 trials negatief, 2 positieve resultaten



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Fedgchin et al. (2019) TRANSFORM-1

Methode

- Populatie: Therapieresistente depressie, ≥ 2 antidepressiva geprobeerd
- Interventie: Esketamine neusspray 56 of 84mg (2x per week) + SSRI/SNRI
- Controlegroep: Placebo (2x per week) + SSRI/SNRI
- Random./ blinding: Ja/ja
- Follow-up: 4 weken
- Primaire uitkomst: Verandering in MADRS score (range 0-60) baseline – 28 dagen
- Statistiek: Mixed model for repeated measurements

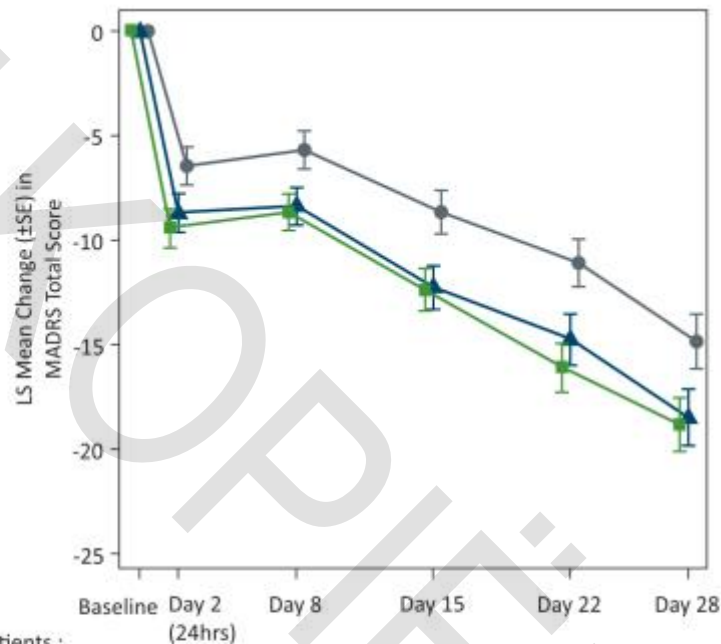
Patiënt karakteristieken

	56mg	84mg	Placebo
• Aantal patiënten:	115	114	113
• Baseline MADRS, gem. (SD):	37 (5)	38 (6)	38 (6)

Resultaten

• Verandering baseline – 28d:	-19 (14)	-19 (14)	-15 (15)
• Least squares gem. verschil(95%CI):	-4.1 (-7.7 tot -0.5)	-3.2 (-6.7 tot 0.5)	
• P-waarde	0.027	0.088	

Fedgchin et al. (2019) TRANSFORM-1



No. of Patients :	Baseline	Day 2 (24hrs)	Day 8	Day 15	Day 22	Day 28
Esketamine 56 mg/Oral Antidepressant	115	105	114	110	107	111
Esketamine 84 mg/Oral Antidepressant	114	104	107	99	96	98
Oral Antidepressant/Placebo	113	101	111	106	105	108
LS mean (SE) treatment difference vs. placebo:						
Esketamine 84 mg		-2.2 (1.29)	-2.7 (1.26)	-3.6 (1.48)	-3.7 (1.65)	-3.6 (1.86)
Esketamine 56 mg		-3.0 (1.29)	-3.0 (1.24)	-3.8 (1.45)	-5.0 (1.61)	-4.0 (1.81)

■ Esketamine 56 mg/Oral Antidepressant
 ▲ Esketamine 84 mg/Oral Antidepressant
 ● Oral Antidepressant/Placebo

Daly et al. (2019) SUSTAIN-1

Methode

- Populatie: Met respons trial TRANSFORM-1/2, allen esketamine
- Interventie: Continuëren esketamine
 - Duur: 4 + 16 weken optimalisatie, daarna onderhoud (mediaan 18 weken)
- Controlegroep: Switch naar placebo
 - Duur: 4 + 16 weken optimalisatie, daarna onderhoud (mediaan 10 weken)
- Random./ blinding: Ja/ja
- Follow-up: 92 weken
- Primaire uitkomst: Tijd tot terugval (MADRS totale score ≥ 22)
- Statistiek: Kaplan-Meier (log-rank test), Cox proportional hazards model

Patiënt karakteristieken	Remissie		Respons	
	Esketamine	Placebo	Esketamine	Placebo
• Aantal patiënten:	90	86	62	59

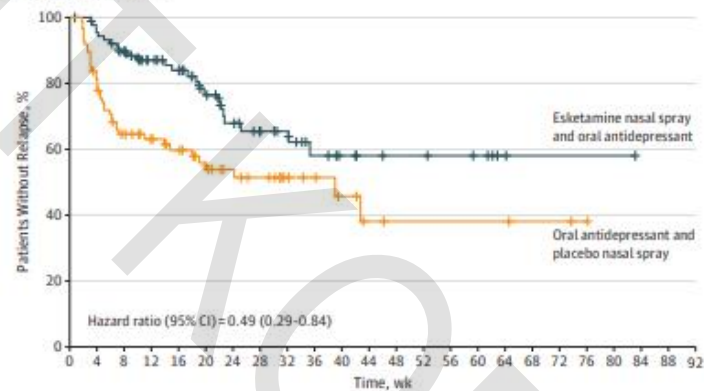
Resultaten

- Remissiegroep esketamine (ref.) vs placebo: HR (95%BI) = 0.49 (0.29 tot 0.84), $p=0.003$
- Responsgroep esketamine (ref.) vs placebo: HR (95%BI) = 0.30 (0.16 tot 0.55), $p<0.001$

Daly et al. (2019) SUSTAIN-1

Figure 2. Kaplan-Meier Estimates of Time to Relapse

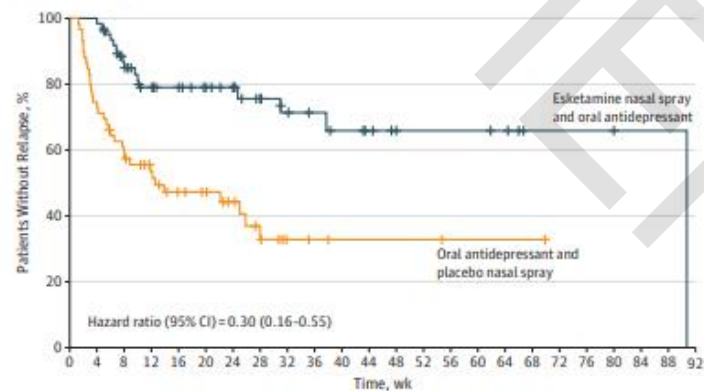
A Patients who achieved stable remission



No. at risk

Esketamine nasal spray and oral antidepressant	90	84	74	58	53	39	31	25	20	14	10	8	7	7	6	5	2	1	1	1	0	
Oral antidepressant and placebo nasal spray	86	69	52	41	34	28	22	19	12	10	7	4	3	3	3	3	3	2	2	1	0	0

B Patients who achieved stable response



No. at risk

Esketamine nasal spray and oral antidepressant	62	62	49	38	35	31	26	20	15	13	11	9	7	6	6	5	2	2	2	2	1	1	0
Oral antidepressant and placebo nasal spray	59	44	35	26	19	17	13	9	4	3	2	2	2	2	1	1	1	1	0	0	0	0	0

One patient who achieved stable response was incorrectly randomized as a patient who achieved stable remission at the end of the optimization phase. One patient did not meet stable remission or stable response criteria and was incorrectly randomized as a patient with stable response. The most common cause of censoring participants was based on being relapse free at study end (see Table 2 legend). Vertical lines indicate censored observations.

Toxicologie ketamine acuut

Meest voorkomend o.a.

- Misselijkheid en braken
- Dissociatie en verwardheid
- Verhoging tensie en hartslag
- Na staken ook weer snel voorbij
- CAVE laryngospasme (wel zeldzaam)
- K-hole
- Overlijden komt nauwelijks voor

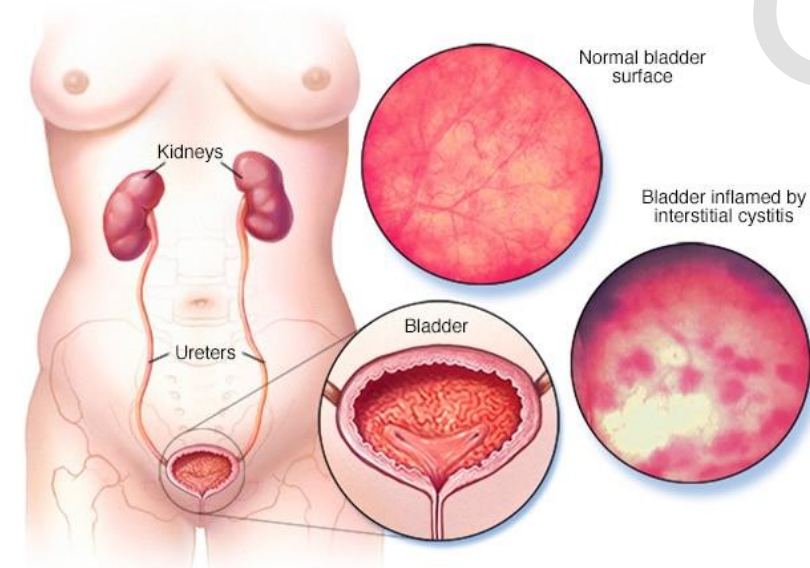
Table 3. Features following acute toxic exposure to ketamine.

System	Signs and symptoms
Neurological	Numbness Tonic-clonic movements may resemble seizures Psychological manifestations Mild/pleasant dream-like states Out-of-body experiences Vivid imagery Hallucinations Sensation of immobilization or difficulty moving Sedation Slurred speech Altered mental state Memory loss Anxiety Ataxia Confusion Dizziness Agitation/aggression Impaired consciousness Dystonia Prolonged coma Seizure
Cardiac	Chest pain Tachycardia Hypertension Palpitations
Respiratory	Dyspnoea Respiratory depression Oxygen desaturation
Gastrointestinal	Nausea Vomiting Abdominal pain
Ophthalmic	Mydriasis Blurred vision Nystagmus
Musculoskeletal	Rhabdomyolysis Muscle cramp Elevated creatine kinase activity
Haematology	Leukocytosis Thrombocytosis Thrombocytopenia Anaemia
Hepatic	Elevated alkaline phosphatase activity Elevated alanine aminotransferase activity
Renal	Elevated creatinine concentration

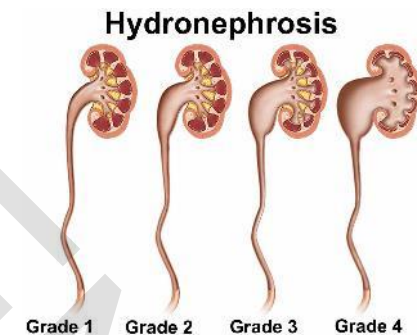
Toxicologie ketamine chronisch

Cystitis

- Ketamine geïnduceerde ulceratieve cystitis
- Tot wel 1/3^e chronische gebruikers blaasklachten
- Hydronefrose op beeldvorming
- Dilatatie, verdikking, ulceratie en verlittekening, soms obstructie ureter
- Cystoscopie: chronische inflammatie kenmerken (mucosa ulceratie, erytheem, fibrose)



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Toxicologie ketamine chronisch

Behandeling?

- Abstinentie ketamine (50% verbetering in symptomen)
- 1) Medicamenteus (NSAIDs en paracetamol);
- 2) Steroiden (e.g., hydrocortison);
- 3) Combinatie met anticholinerge middelen (e.g., oxybutinine)
- Andere middelen ook wel geprobeerd (e.g., hyaluronzuur)
- Geen respons medicatie, chirurgische interventie

Toxicologie ketamine chronisch

- Augmentatie van de blaas
- Verwijderen stuk dunne darm, daarmee vergroot blaas



Jhang et al. (2017) Neurourology and urodynamics

Methode

- Populatie: Ketamineverslaafden met ontstoken blaas en blaaspijn, niet reagerend op o.a. NSAIDs
- Interventie: Operatieve blaasaugmentatie
- Controlegroep: Conservatieve behandeling
- Random./ blinding: nee/nee
- Follow-up: 6 maanden
- Primaire uitkomst: Tevredenheid met behandeling obv pijn en urinefreq.

Patiënt karakteristieken

- | | | | |
|----------------------------|-------|----------------|-------------------|
| • Aantal patiënten: | n=53; | n=28 operatie; | n=25 conservatief |
| • Leeftijd gem.: | | 29 | 27 |
| • Man (%): | | 11 (39) | 14 (56) |
| • Verslaafd ketamine gem.: | | 4.5 jaar | 4.6 jaar |

Resultaten

Outcome			
Good	8 (32%)	24 (85.7%)	<0.0001
Fair	13 (52%)	3 (10.7%)	
Poor	4 (16%)	1 (3.6%)	

FBC, functional bladder capacity; MBC, maximal bladder capacity; VUR, vesicoureteral reflux.

TABLE IV. The Changes of Bladder Parameters in 28 Patients After AE

	Baseline	Post-AE	P-value
Bladder capacity (ml)	52.7 ± 29.7	327.0 ± 69.4	<0.0001
Voided volume (ml)	44.2 ± 28.3	250.7 ± 133.4	<0.0001
Qmax (ml/sec)	6.94 ± 4.32	13.7 ± 4.96	<0.0001
PVR (ml)	8.08 ± 19.2	82.6 ± 91.5	<0.0001
Compliance (ml/cmH ₂ O)	11.2 ± 11.9	54.0 ± 43.0	<0.0001

Jhang et al. (2017) Neurourology and urodynamics

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Toxicologie ketamine chronisch

Neurologisch

- Cognitieve problemen (verbale fluency, geheugen, executief functioneren)
- Corticale atrofie hersenen patiënten 2-4 jaar gem. 1gram/dag

Galwegen/lever

- Cholangiopathie door o.a. verwijding ductus choledochus (>7mm)
- Leverfibrose
- Scleroserende cholangiti (i.e., ontsteking galwegen)
- Inflammatie en fibrose v. porta hepatis
- ~10% van ketamine verslaafde populatie schade galwegen/lever
- Onafhankelijke risicofactoren: vrouw, CRP level, huidig ketamine gebruik

Behandeling?

- Abstinentie ketamine
- Stent indien obstructie
- Bij hepatotoxiciteit levensbedreigend, levertransplantatie

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- Onafhankelijke risicofactoren: vrouw, CRP level, huidig ketamine gebruik

Behandeling?

- Abstinentie ketamine
- Stent indien obstructie
- Bij hepatotoxiciteit levensbedreigend, levertransplantatie

Psilocybine



Goodwin et al. (2022) New England Journal of Med

Methode

- Populatie: Therapieresistente depressie, ≥ 2 antidepressiva geprobeerd
- Interventie: Psilocybine 25mg of psilocybine 10mg
- Controlegroep: Psilocybine 1mg
- Random./ blinding: Ja/ja
- Follow-up: 12 weken
- Primaire uitkomst: Verandering in MADRS score baseline – 21 dagen
- Statistiek: Mixed model for repeated measurements

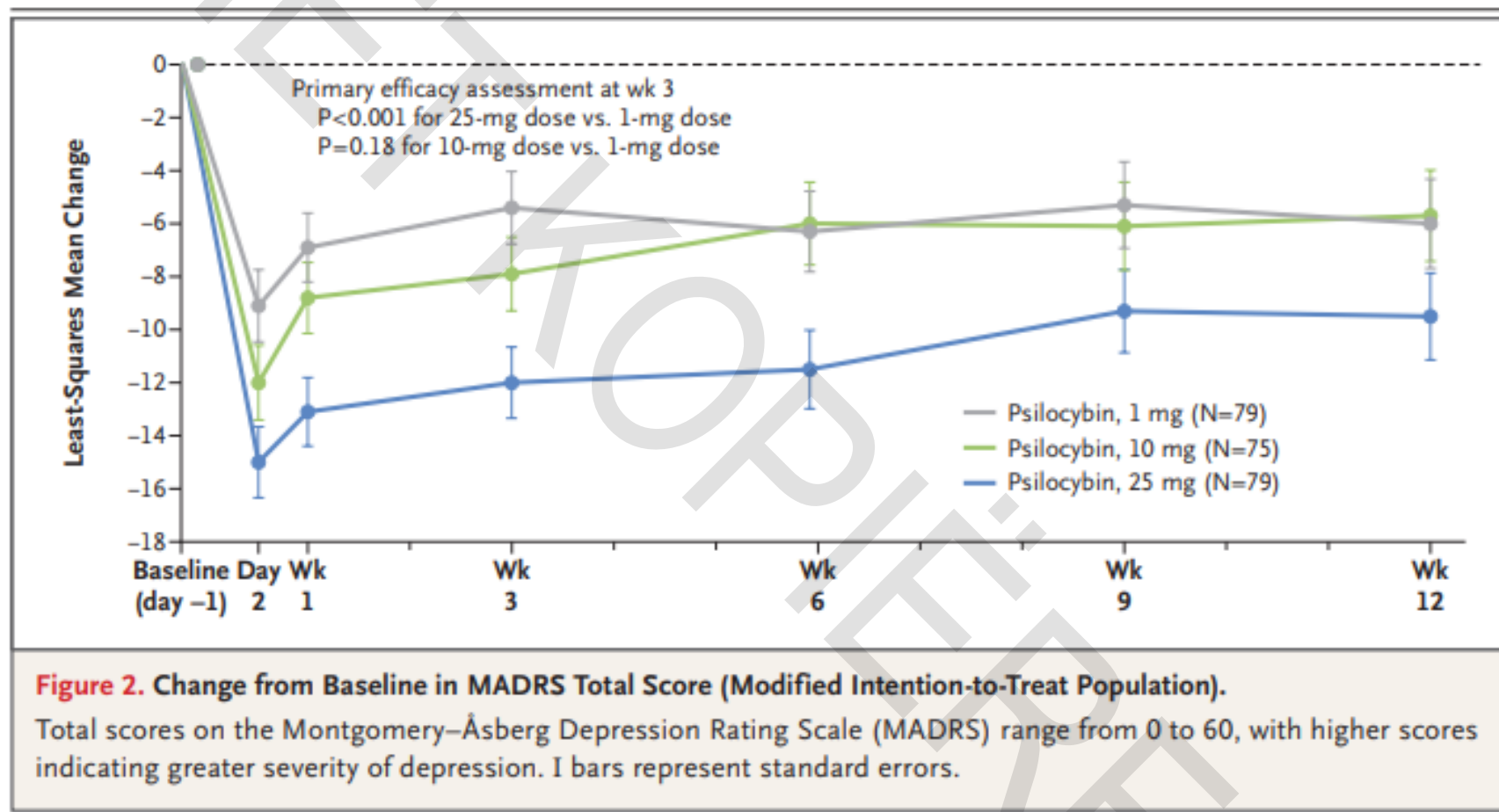
Patiënt karakteristieken

	25mg	10mg	1mg
• Aantal patiënten:	79	75	79
• Baseline MADRS, gem. (SD):	32 (5)	33 (6)	33 (6)

Resultaten

• Least squares means (95%CI):	-12 (-15 tot -9)	-8 (-11 tot -5)	-5 (-8 tot -3)
• Least squares mean diff.:	-6.6 (-10.2 tot -2.9)	-2.5 (-6.2 tot 1.2)	
• P-waarde:	<0.001	0.18	

Goodwin et al. (2022) New England Journal of Med



Psilocybine (single dose)

Table. Summary of Included Studies

Source	No. of participants	Mean age, y	Gender	Psilocybin dosing	Comparator	Disease state	Notable psilocybin adverse effects
Goodwin et al, ¹¹ 2022	79 (high dose), 75 (moderate dose), 79 (low dose)	39.8	52% Female	10 mg, 25 mg	Low dose psilocybin (1 mg)	Treatment-resistant depression	Headache with high (24%) vs moderate (15%) vs low (16%) dose, nausea with high (22%) vs moderate (7%) vs low (1%) dose, anxiety with high (4%), moderate (8%), and low (0%) dose; dizziness with high dose (6%), fatigue with high dose (6%), euphoric mood with high (5%), altered mood with high (5%)
Raison et al, ¹⁵ 2023	104	41.1	47% Female	25 mg	Niacin	Major depressive disorder (24% had treatment-resistant depression)	Headache (66%), nausea (48%), visual perceptual effects (44%)
Griffiths et al, ¹⁶ 2016	51 ^a	56.3	49% Female	22 mg	Low dose psilocybin (1 mg)	Depression and/or anxiety in cancer	Elevated systolic BP with high (34%) vs low (17%) dose, elevated diastolic BP with high (13%) vs low (2%) dose, headache with high (2%) vs low (0%) dose, nausea/vomiting with high (15%) vs low (0%) dose, physical discomfort with high (21%) vs low (8%) dose, anxiety with high (26%) vs low (15%) dose
Ross et al, ¹⁷ 2016	29 ^b	56.3	62% Female	21 mg	Niacin	Depression and/or anxiety in cancer	Nonclinically significant elevated BP and heart rate (76%), headache (28%), nausea (14%), transient anxiety (17%), transient psychoticlike symptoms (7%)
Carhart-Harris et al, ¹⁸ 2021	59	41.2	32% Female	25 mg	Escitalopram plus low-dose psilocybin (1 mg)	Major depressive disorder	Headache with high dose (43%) vs low dose plus escitalopram (17%), nausea with high dose (13%) vs low dose plus escitalopram (0%)
von Rotz et al, ¹⁹ 2022	52	36.8	63.5% Female	0.215 mg/kg body weight (estimated 15-16 mg)	Placebo	Major depressive disorder	Headache (15%), dizziness (8%), nausea (4%)

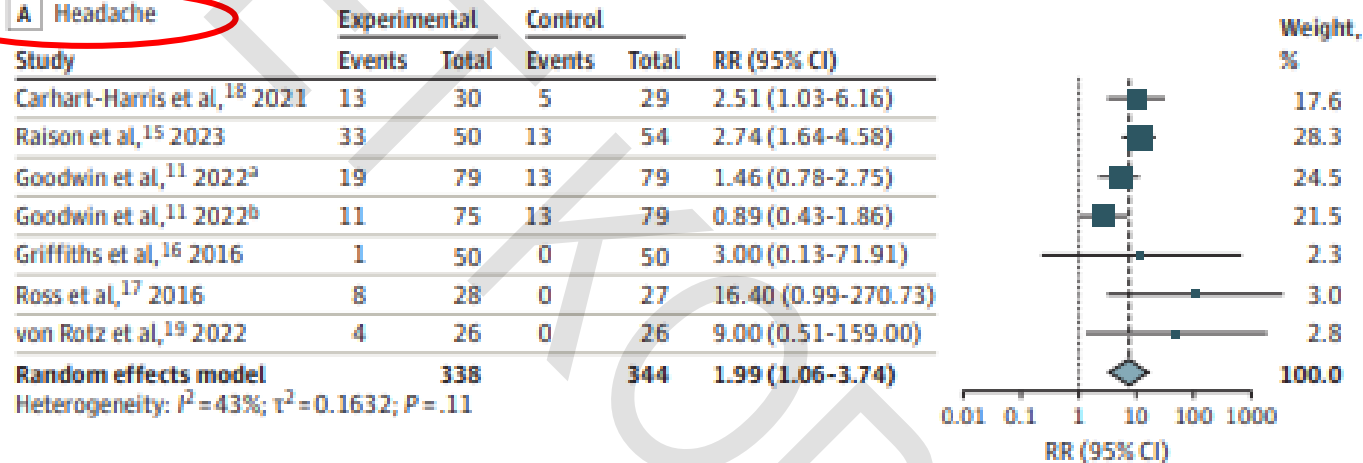
Abbreviation: BP, blood pressure.

^a Study states overall sample size of 51 for completing session 1; however, a sample size of 50 per group was used in meta-analysis per data presented in Figure 1 for data obtained.

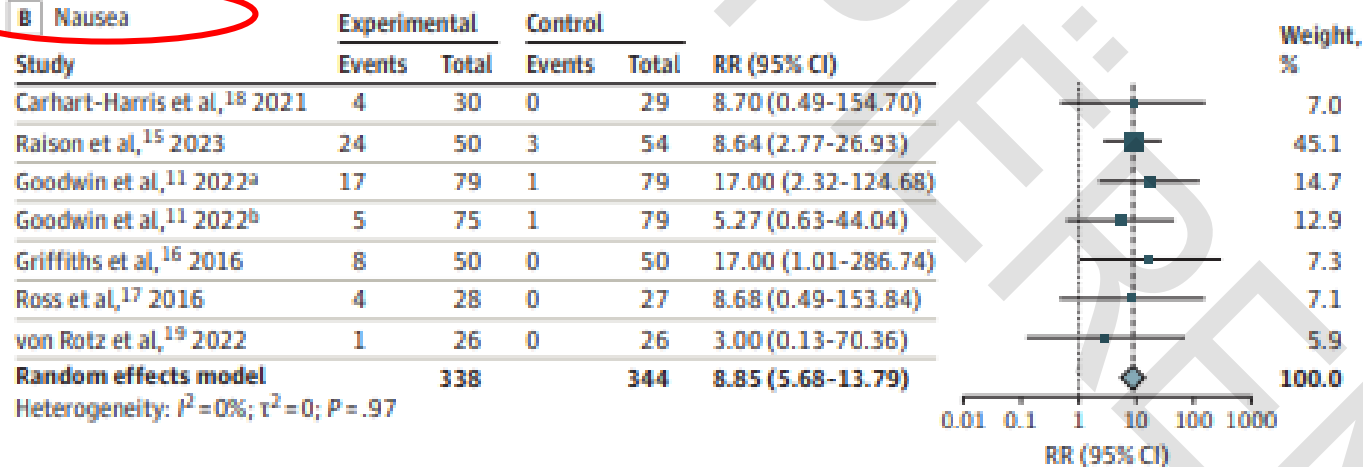
^b Study states overall sample size of 29 completing; however, a sample size of 28 (experimental) and 27 (control) was used in meta-analysis per data presented in Figure 1 for data obtained.

Figure 2. Association of Psilocybin With Headache, Nausea, and Anxiety

A Headache

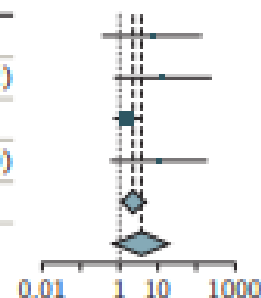


B Nausea



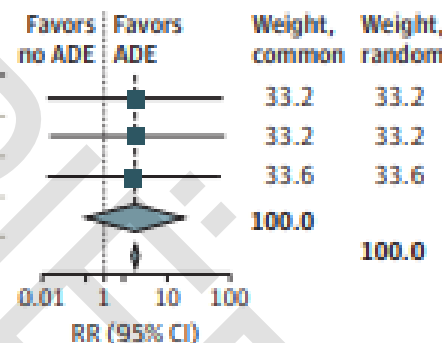
C Anxiety

Study	Experimental		Control		RR (95% CI)	Weight, common	Weight, random
	Events	Total	Events	Total			
Goodwin et al, ¹¹ 2022 ^a	3	79	0	79	7.00 (0.37-133.32)	5.8	15.0
Goodwin et al, ¹¹ 2022 ^b	6	75	0	79	13.69 (0.78-238.82)	6.2	15.7
Griffiths et al, ¹⁶ 2016	13	50	8	50	1.62 (0.74-3.58)	81.7	53.4
Ross et al, ¹⁷ 2016	5	28	0	27	10.61 (0.62-182.99)	6.3	15.8
Common effects model		232		235	2.27 (1.11-4.64)	100.0	
Random effects model					3.81 (0.69-21.09)		100.0
Heterogeneity: $I^2 = 23\%$; $\tau^2 = 0.6611$; $P = .27$							



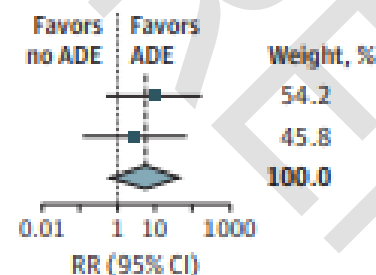
C Paranoia

Study	Experimental		Control		RR (95% CI)	Weight, common	Weight, random
	Events	Total	Events	Total			
Griffiths et al, ¹⁶ 2016	1	50	0	50	3.00 (0.13-71.91)	33.2	33.2
Raison et al, ¹⁵ 2023	1	50	0	54	3.24 (0.13-77.67)	33.2	33.2
Ross et al, ¹⁷ 2016	1	28	0	27	2.89 (0.12-68.06)	33.6	33.6
Common effect model		128		131	3.04 (0.49-18.96)	100.0	
Random effects model					3.04 (2.64-3.50)		100.0
Heterogeneity: $I^2 = 0\%$; $\tau^2 = 0$; $P = 1.00$							



D Transient thought disorder

Study	Experimental		Control		RR (95% CI)
	Events	Total	Events	Total	
Goodwin et al, ¹¹ 2022 ^b	4	75	0	79	9.48 (0.52-173.05)
Ross et al, ¹⁷ 2016	1	28	0	27	2.89 (0.12-68.06)
Common effect model		103		106	5.50 (0.65-46.66)
Heterogeneity: $I^2 = 0\%$; $\tau^2 = 0$; $P = .59$					





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Case report

Hallucinogen persisting perception disorder after psilocybin consumption: a case study

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Conclusie

- MDMA 2 positieve fase 3 trials
- Esketamine 2 positieve en 2 negatieve fase 3 trials
- Psilocybine 2 positieve fase 2 trials

Posttraumatische stressstoornis

Depressie

Depressie

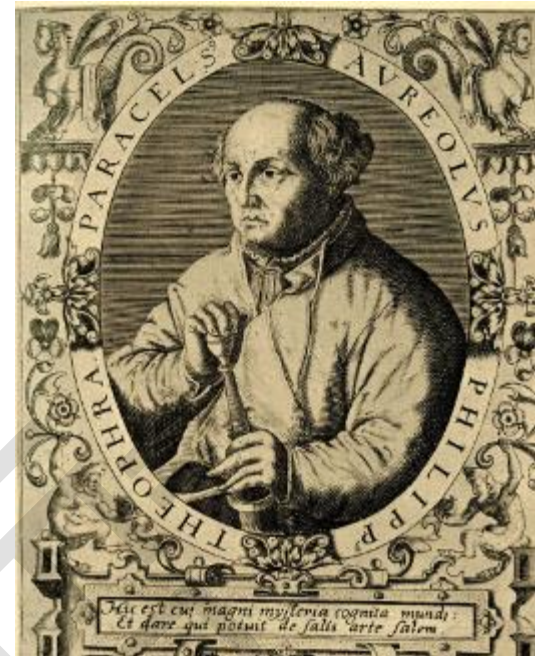


Conclusie

Veelbelovend ! (?)

Alles wat werkt heeft bijwerkingen

De dosis maakt het vergif





UMC Utrecht

Dank voor jullie aandacht, zijn er nog vragen?

Radboudumc