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Cannabis thérapeutique, cannabinoïdes, CBD... Quels usages ? Quelle efficacité ?



Dr Julie Dupouy

Médecin généraliste, MSPU de Pins Justaret (31)

MCU, Département Universitaire de Médecine Générale, Toulouse

UMR 1295 Inserm – Université Paul Sabatier CERPOP équipe Equity, Toulouse

CNGE CA secteur recherche, conseil scientifique

julie.dupouy@dumg-toulouse.fr



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Déclaration de liens d'intérêt – art. L.4113-13 CSP

Pour cette intervention, je déclare les liens d'intérêt suivants avec des organismes produisant ou exploitant des produits de santé ou avec des organismes de conseil intervenant sur ces produits :

Nom de l'organisme	Nature du lien	Année

X Pour cette intervention, je déclare n'avoir aucun lien d'intérêt avec des organismes produisant ou exploitant des produits de santé ou avec des organismes de conseil intervenant sur ces produits.

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De quoi parle t'on ?

Chanvre (*cannabis sativa*) :
propriétés antiémétiques, anticonvulsivantes, antispasmodiques
(500 constituants)

- THC : effet psychotrope
- CBD : pas psychotrope
- CBC
- CBN, CBGM, CBL, CBV, THCV...

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Différents produits

- Cannabis récréatif (THC + CBD)
 - Sous forme d'herbe ou de résine (haschich)
- Cannabis médical (THC + CBD)
 - Dont médicaments à base de cannabis
 - Cannabidiol Epidyolex[°] épilepsie résistance de l'enfant (grands essais) ASMR IV
 - Cannabis en spray Sativex[°] : spasticité SEP / ASMR V
 - Dronabinol Marinol[°] : douleurs neuropathiques réfractaires / ATU
- Cannabis bien être : CBD (traces de THC) :
 - produits variés en forme et en composition

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Pharmacologie

THC

- Interactions in vitro avec CYP 450
- EI : syndrome amotivationnel, décrochage scolaire, troubles cardiovasculaires, psychose

CBD

- EI : somnolence, baisse de l'appétit, troubles digestifs, fièvre, fatigue, vomissements
- Positivité THC lors contrôles routiers

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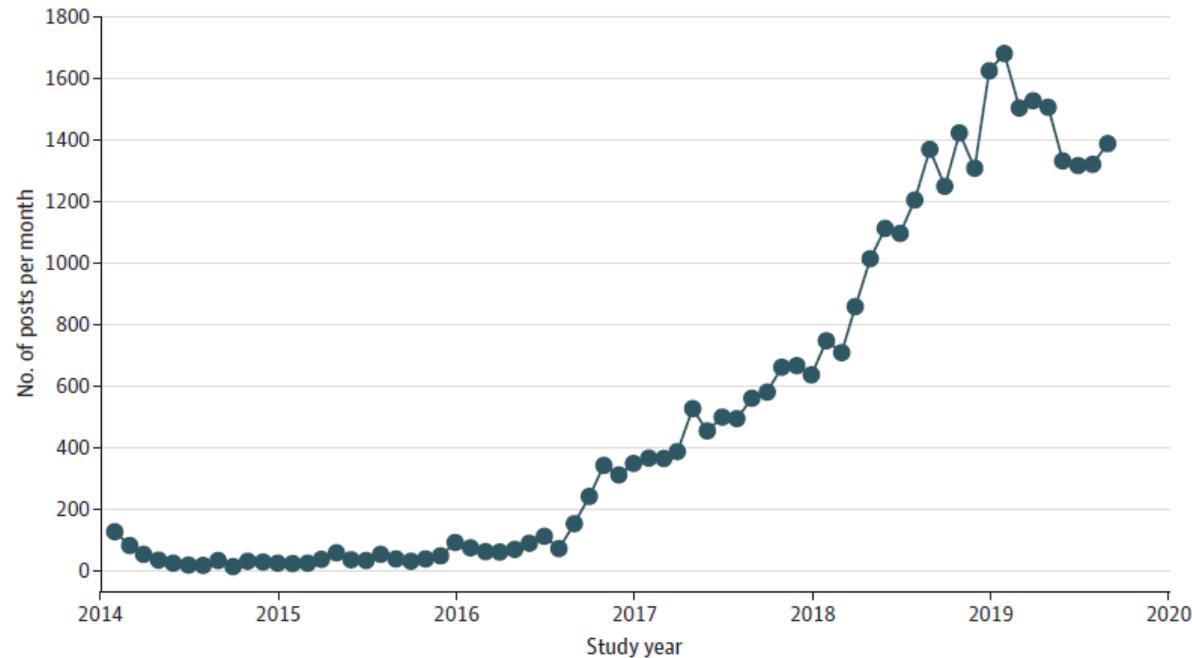
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Enquête US : 376 posts réseaux sociaux

Figure. Posting Behavior on Reddit Cannabidiol Forum (r/CBD)



JAMA
Network | **Open.**

Original Investigation | Public Health

Self-reported Cannabidiol (CBD) Use for Conditions With Proven Therapies

- Augmentation dans contexte crise des opioïdes aux USA

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Motifs

- 63 % : symptômes liés à l'anxiété, la dépression ou des TSA
- 26% : douleurs orthopédiques
- 15% : troubles du sommeil

Table 2. Treatment Testimonials for CBD as Reported by CBD Users on Reddit

Treated condition ^a	Subcategories ^a	Relevant content from example posts ^b	Category prevalence, % (95% CI)
Diagnosable condition			
Psychiatric conditions	Attention deficit disorder, anxiety disorder, autism spectrum disorder, mood disorders (manic or depressive), borderline personality disorder, dissociation disorder, depersonalization disorder, hallucinogen persisting perception disorder, obsessive compulsive disorder, panic disorder, symptoms of psychosis, posttraumatic stress disorder, schizotypal personality disorder	"After using CBD for 2 mo, my autism symptoms have improved. My family has noticed great improvements and I have finally been able to attend important social events."	63.9 (59.0-69.1)
Orthopedic conditions	Arthritis, ganglion cyst reduction, herniated disc, inflammation, muscle tension, muscle cramps, musculoskeletal pain, piriformis syndrome, sciatica	"I have spinal arthritis and back pain from sitting at a desk for 30 y. I like to hike but can't do it without pain. Yesterday after taking CBD I went for a hike, it just wasn't there at all."	26.4 (21.8-31.1)
Sleep conditions	Insomnia, nightmares	"A life-long sufferer of insomnia, after trying CBD I finally am sleeping at night and waking up the next day feeling refreshed."	14.6 (11.3-18.5)
Neurological conditions	Dizziness, epilepsy, headaches, Ménière disease, migraines, neurological pain, motor tics or tremors, speech disorders, vagal neuropathy	"I have been struggling with a chronic neurological illness for years that cause tremors. After trying CBD isolate, I began to feel immediate relief."	6.9 (4.4-9.6)
Gastroenterological conditions	Appetite increase, acid reflux, gastroparesis, gastrointestinal pain, diarrhea, irritable bowel syndrome, nausea, ulcerative colitis	"I tried CBD for gastroparesis and my stomach started to get much better...after 20 y I finally feel normal."	3.9 (1.9-6.1)
Addiction conditions	Cravings or withdrawal symptoms [including alcohol, kratom, opioids, risperidone, Δ ⁹ -tetrahydrocannabinol], anxiety induced by Δ ⁹ -tetrahydrocannabinol	"I developed an opioid addiction in the past few years, so I gave CBD a try. It's helped me control my cravings and withdrawal symptoms as I've tried to get off opioids."	1.9 (0.8-3.3)
Sexual health conditions	Erectile dysfunction, libido, menstrual disorders	"I used to suffer from erectile dysfunction, but after using CBD I can now perform."	1.1 (0.3-2.2)
Cardiological conditions	Heart palpitations	"Other medications I used for heart palpitations gave me side effects, CBD has been much better and has helped to stop my heart palpitations."	0.6 (0.0-1.4)
Dermatological conditions	Acne, psoriasis	"After trying CBD over a year ago, my psoriasis is much better."	0.6 (0.0-1.4)
Oral health conditions	Aphthous ulcers, mouth sore-related pain	"I have been suffering from canker sores for many years, they historically lasted at least 10 d. After using CBD as an oral rinse, they now are only lasting 3 d."	0.6 (0.0-1.4)
Ophthalmological conditions	Color vision deficiency	"After taking CBD I am seeing colors more vividly than I was before."	0.3 (0.0-0.8)
Wellness			
Mental wellness	Mood control, mental acuity, stress control	"CBD has helped me to quiet my racing thoughts and mentally process things that normally overwhelmed me."	29.5 (24.8-34.2)
Physical wellness	Enhanced energy, exercise, dietary supplement	"CBD has given me more energy for daily functions."	1.4 (0.3-2.8)

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Royaume Uni : N= 387 usagers actuels ou passés de CBD

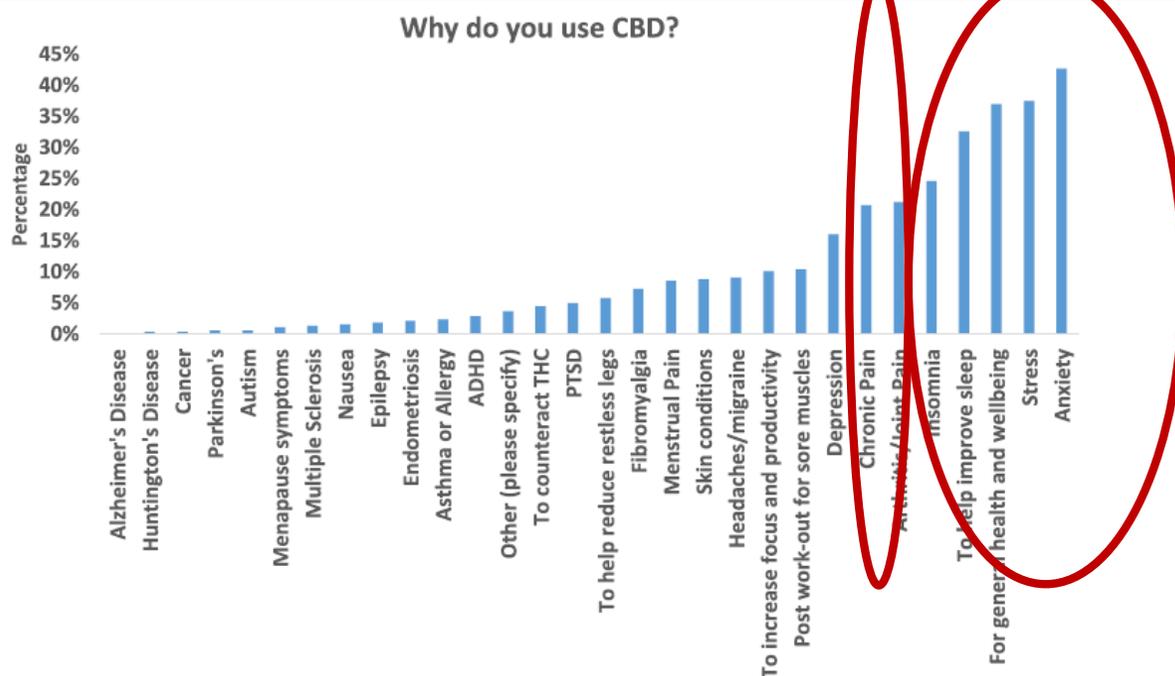


Fig. 1 Reasons for cannabidiol use amongst 397 adult cannabidiol users who were allowed to respond to more than one option leading to a total of 1622 responses. Y-axis represents percentage based on total responses

Moliki and Hindocha *Journal of Cannabis Research*
<https://doi.org/10.1186/s42238-021-00061-5>

(2021) 3:5

Journal of Cannabis
Research

ORIGINAL RESEARCH

Open Access

Reasons for cannabidiol use: a cross-sectional study of CBD users, focusing on self-perceived stress, anxiety, and sleep problems



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Douleur chronique

Medical cannabis or cannabinoids for chronic non-cancer and cancer related pain: a systematic review and meta-analysis of randomised clinical trials

[thebmj](#) | *BMJ* 2021;373:n1034 | doi: 10.1136/bmj.n1034

- 28 essais inclus DCNC
- 4 essais DCC
- Cannabis médical
 - THC / CBD / les deux
 - Aucun essai avec cannabis inhalé n'a été éligible

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- 27 ECR, 3939 patients
- légère augmentation de la proportion de patients présentant au moins la différence minimale importante (DMI) de 1 cm EVA en matière de soulagement de la douleur
 - différence de risque modélisée (RD) de 10% (IC95% : 5% à 15%)

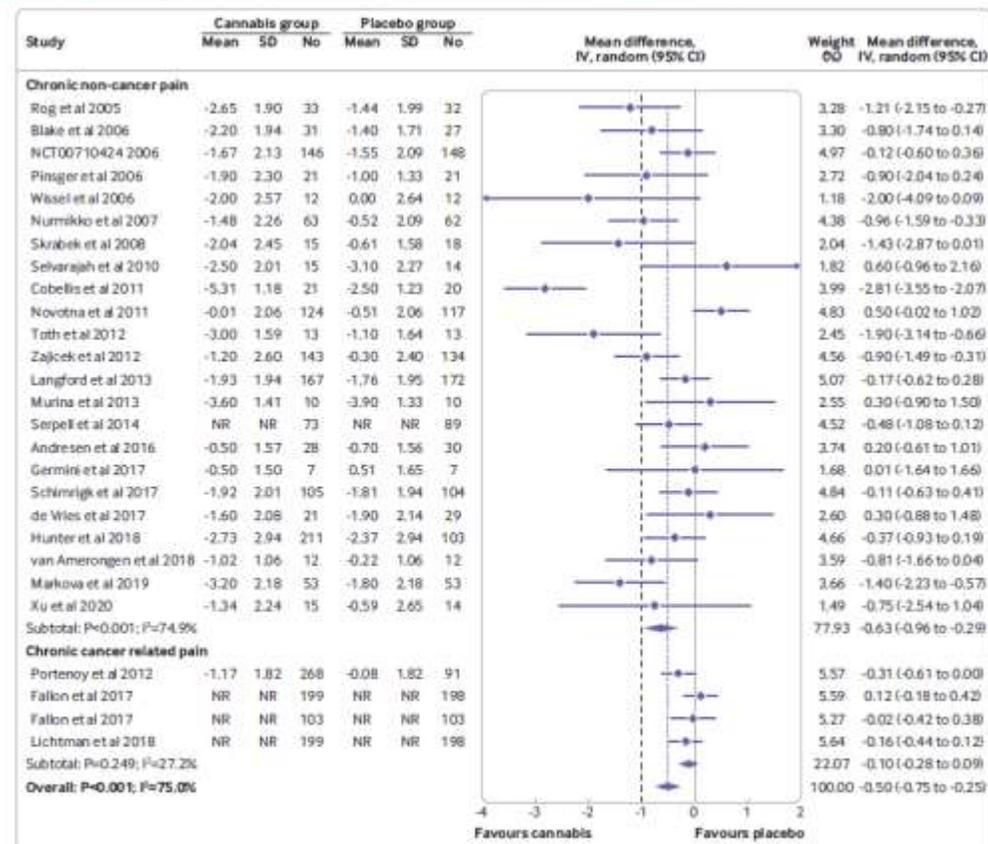


Fig 2 | Pain relief on a 10 cm visual analogue scale (VAS) among people living with chronic pain who received non-inhaled medical cannabis or cannabinoids versus placebo. Test of interaction P=0.16 for chronic non-cancer pain versus chronic cancer related pain. Black dashed vertical line represents the minimally important difference of 1 cm for the 10 cm VAS for pain. Purple dashed vertical line represents the overall pooled measure of effect.

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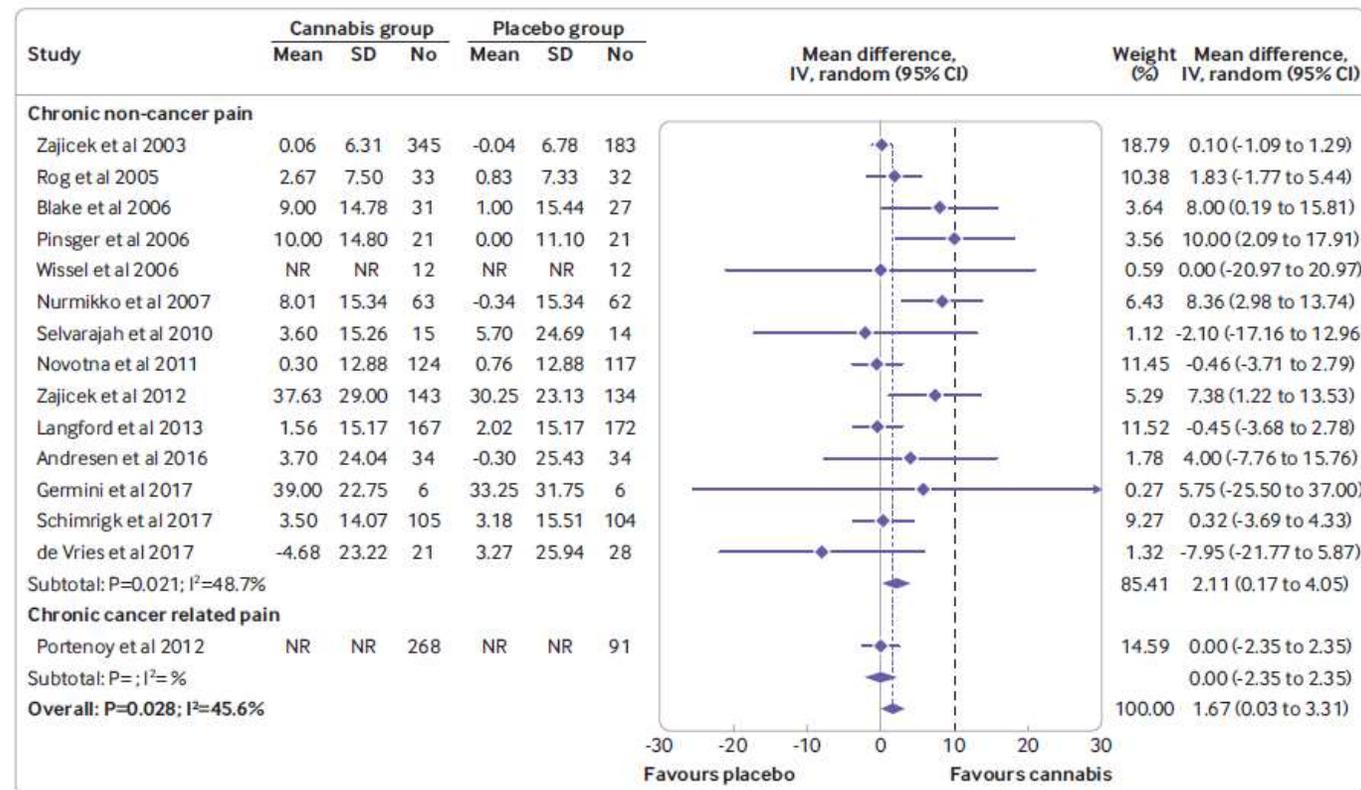
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- 15 ECR, 2425 patients
- très faible amélioration du fonctionnement physique
 - 4% modélisé (0,1 % à 8 %) pour l'obtention d'au moins la valeur MID de 10 points sur le score de 100 points du SF-36 relatif au fonctionnement physique



IV = inverse variance; random = random-effects model; NR = arm-level data not reported

Fig 3 | Physical functioning assessed by the 100-point SF-36 physical functioning scale among people living with chronic pain who received non-inhaled medical cannabis or cannabinoids versus placebo. Black dashed vertical line represents the minimally important difference of 10 points for the 100-point SF-36 physical functioning scale. Purple dashed vertical line represents the overall pooled measure of effect.

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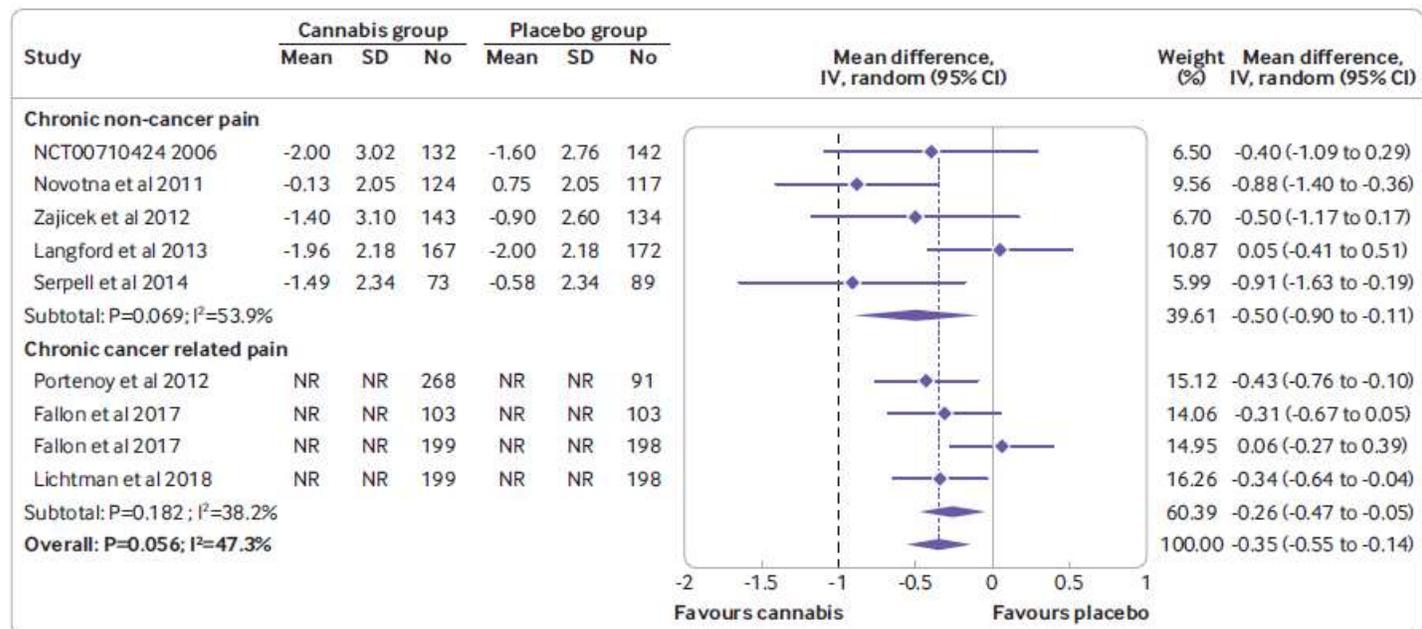
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- 16 ECR, 3124 patients
- légère amélioration de la qualité du sommeil
 - RD modélisé de 6% (2% à 9%) pour l'atteinte d'au moins de 1 cm sur une EVA de 10 cm



IV = inverse variance; random = random-effects model; NR = arm-level data not reported

Fig 4 | Sleep quality on a 10 cm visual analogue scale (VAS) among people living with chronic pain who received non-inhaled medical cannabis or cannabinoids versus placebo Test of interaction P=0.32 for chronic non-cancer pain versus chronic cancer related pain when analysis was restricted to larger trials (standard error of the WMD \leq 0.4) due to small study effects. Black dashed vertical line represents the minimally important difference of 1 cm for the 10 cm VAS for sleep quality. Purple dashed vertical line represents the overall pooled measure of effect.

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Pas d'effet sur :

- Fonctionnement émotionnel
- Fonctionnement rôle physique
- Fonctionnement rôle social
- Troubles cognitifs

Table 1 | GRADE evidence profile of non-inhaled medical cannabis versus placebo for people living with chronic pain

No of trials (No of patients)	Follow-up period (months)	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Treatment association (95% CI)		Overall quality of evidence
							Placebo	Cannabis/ cannabinoids	
Pain: 10 cm VAS for pain; lower is better; MID=1 cm									
27 (3939)	1 to 4	No serious risk of bias*	Serious inconsistency I ² =75%	No serious indirectness	No serious imprecision	Undetected, Symmetric funnel plot; Begg's test P=0.55	952 (52%) achieved at or above MID	1309 (62%) achieved at or above MID	Moderate
							Modelled RD 10% (5% to 15%)		
							WMD -0.50 cm (-0.75 to -0.25)		
Pain: ≥30% pain reduction from baseline									
10 (1691)	1.25 to 3.5	No serious risk of bias*	No serious inconsistency I ² =38%	No serious indirectness	Serious imprecision†	Undetected, Symmetric funnel plot; Harbord's test P=0.77	238 (33%) achieved at or above MID	718 (40%) achieved at or above MID	Moderate
							RD 7% (0.1% to 16%)		
							RR 1.21 (1.004 to 1.47)		
Physical functioning: 0-100 point SF-36 physical functioning scale; higher is better; MID=10 points									
15 (2425)	1 to 4	No serious risk of bias*	No serious inconsistency I ² =46%	No serious indirectness	No serious imprecision	Undetected, Symmetric funnel plot; Begg's test P=0.10	289 (28%) achieved at or above MID	440 (32%) achieved at or above MID	High
							Modelled RD 4% (0.1% to 8%)		
							WMD 1.67 points (0.03 to 3.33)		
Sleep quality: 0-10 sleep quality scale; higher is worse; MID=1									
9 [‡] (2652)	1.25 to 3.5	No serious risk of bias*	No serious inconsistency I ² =47%	No serious indirectness	No serious imprecision	Undetected, Symmetric funnel plot; Begg's test P=0.24	601 (48%) achieved at or above MID	765 (54%) achieved at or above MID	High
							Modelled RD 6% (2% to 9%)		
							WMD -0.35 cm (-0.55 to -0.14)		
Emotional functioning: 0-100 point SF-36 mental component summary scale; higher is better; MID=10 points									
10 (2115)	1 to 4	No serious risk of bias*	No serious inconsistency I ² =0%	No serious indirectness	No serious imprecision [§]	Undetected, Symmetric funnel plot; Begg's test P=0.64	276 (31%) achieved at or above MID	403 (33%) achieved at or above MID	High
							Modelled RD 2% (-2% to 4%)		
							WMD 0.33 points (-0.67 to 1.73)		
Role functioning: 0-100 point SF-36 physical role functioning scale; higher is better; MID=10 points									
7 (1128)	1 to 3.5	No serious risk of bias*	No serious inconsistency I ² =21%	No serious indirectness	No serious imprecision [§]	Undetected	195 (41%) achieved at or above MID	267 (41%) achieved at or above MID	High
							Modelled RD 0% (-4% to 5%)		
							WMD 0.20 points (-3.02 to 3.42)		
Social functioning: 0-100 point SF-36 social role functioning scale; higher is better; MID=10 points									
8 (1405)	1 to 3.5	No serious risk of bias*	No serious inconsistency I ² =0%	No serious indirectness	No serious imprecision [§]	Undetected	239 (39%) achieved at or above MID	301 (38%) achieved at or above MID	High
							Modelled RD -1% (-4% to 2%)		
							WMD -0.63 points (-2.27 to 1.02)		
Cognitive impairment									
5 for oral cannabis (1033)	1.25 to 3.5	No serious risk of bias	No serious inconsistency I ² =0%	No serious indirectness	Serious imprecision [†]	Undetected	7 (1%) experienced cognitive impairment	21 (3%) experienced cognitive impairment	Moderate
							RD 2% (0.1% to 6%)		
							RR 2.39 (1.06 to 5.38)		

95%CI=95% confidence interval; VAS=visual analogue scale; MID=minimally important difference; RD=risk difference; WMD=weighted mean difference; RR=relative risk; SF=standard error.

*We did not rate down for risk of bias as subgroup analysis showed no significant difference in trials at low versus high risk of bias on a component-by-component basis.

†Although the estimate of precision excluded no effect, we rated down for imprecision because the guideline panel determined the lower and upper limits of 95%CI associated with the risk difference included both patient-important and unimportant effects, and/or there were less than 300 observations or events to inform the pooled effect estimate.

‡We found evidence of small study effects for sleep quality among 16 eligible studies (Egger's P=0.02). We therefore removed small studies (sample size < 130 patients and SE > 0.4) from our pooled estimate of effect.

§Although the estimate of precision included no effect, we did not rate down for imprecision because the guideline panel determined that the 95%CI did not include patient-important effects.

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Douleur neuropathique



[Intervention Review]

Cannabis-based medicines for chronic neuropathic pain in adults

- NNT 20
- NNH 25
- Rapport bénéfique
risque peut être
défavorable

Outcomes	Probable outcome with intervention 95% CI	Probable out- come with placebo	Relative effect Risk difference (95% CI)	No. of partici- pants (studies)	Quality of the evidence (GRADE)	Comments
Participant-reported pain relief of 50% or greater	209 per 1000 (196 to 222)	173 per 1000	0.05 (0.00 to 0.09)	1001 (8 studies)	⊕⊕⊕⊕ low 1,2	NNTB 20 (11 to 100)
Patient Global Impression of Change much or very much improved	261 per 1000 (246 to 276)	211 per 1000	0.09 (0.01 to 0.17)	1092 (6 studies)	⊕⊕⊕⊕ very low 1,3,4	NNTB 11 (6 to 100)
Withdrawals due to adverse events	104 per 1000 (99 to 107)	47 per 1000	0.04 (0.02 to 0.07)	1848 (13 studies)	⊕⊕⊕⊕ moderate 1	NNTH 25 (16 to 50)
Serious adverse events	66 per 1000 (63 to 69)	52 per 1000	0.01 (-0.01 to 0.03)	1876 (13 studies)	⊕⊕⊕⊕ low 1,2	NNTH not calculated
Participant-reported pain relief of 30% or greater	377 per 1000 (358 to 396)	304 per 1000	0.09 (0.03 to 0.15)	1586 (10 studies)	⊕⊕⊕⊕ moderate 1	NNTB 11 (7 to 33)
Specific adverse events: nervous system disorder	611 per 1000 (576 to 644)	287 per 1000	0.38 (0.18 to 0.58)	1304 (9 studies)	⊕⊕⊕⊕ low 1,3	NNTH 3 (2 to 6)
Specific adverse events: psychiatric disorders	165 per 1000 (156 to 174)	49 per 1000	0.10 (0.06 to 0.15)	1314 (9 studies)	⊕⊕⊕⊕ low 1,3	NNTH 10 (7 to 16)

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Pathologies psychiatriques

- THC-CBD pharmaceutique : réduit anxiété
 - Chez population de patients ayant co morbidité
 - 2 essais
 - GRADE faible
- Mais pas valable pour CBD seul
- Pas d'effet clair dans autres pathologies
- Augmentation EI OR=1.99 [1.20:3.29]
- Pas d'ECR avec cannabis médical ou CBD pharmaceutique

Lancet Psychiatry. 2019 December ; 6(12): 995–1010. doi:10.1016/S2215-0366(19)30401-8.

Cannabinoids for the treatment of mental disorders and symptoms of mental disorders: A systematic review and meta-analysis

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Méta analyses

Journal of Psychiatric Research 140 (2021) 267–281



Contents lists available at ScienceDirect

Journal of Psychiatric Research

journal homepage: www.elsevier.com/locate/jpsychires



Potential therapeutic benefits of cannabinoid products in adult psychiatric disorders: A systematic review and meta-analysis of randomised controlled trials



- Données au mieux de qualité faible à modérée
- Pas d'efficacité claire
- Essais de plus grande ampleur nécessaires (la plupart ≤ 40)

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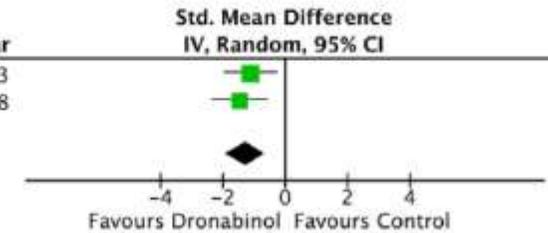
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TU cannabis

- 10 essais
- Diminution des symptômes de sevrage mais pas d'effet sur le pourcentage de sujets abstinents à 3 mois

Study or Subgroup	Dronabinol			Control			Weight	Std. Mean Difference IV, Random, 95% CI	Year
	Mean	SD	Total	Mean	SD	Total			
Vandrey 2013	1.7	1.44	13	4.6	3.25	13	52.6%	-1.12 [-1.95, -0.28]	2013
Schlienz 2018	0.91	1.37	13	2.44	0.43	13	47.4%	-1.46 [-2.34, -0.58]	2018
Total (95% CI)			26			26	100.0%	-1.28 [-1.89, -0.67]	

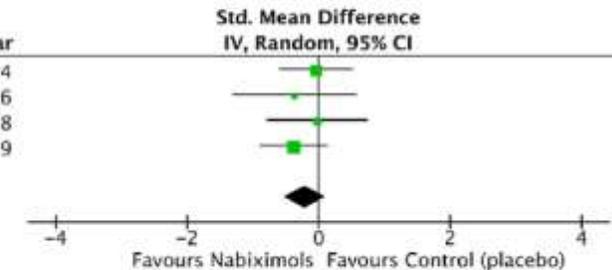
Heterogeneity: Tau² = 0.00; Chi² = 0.30, df = 1 (P = 0.58); I² = 0%
Test for overall effect: Z = 4.13 (P < 0.0001)



(b)

Study or Subgroup	Nabiximols			Control			Weight	Std. Mean Difference IV, Random, 95% CI	Year
	Mean	SD	Total	Mean	SD	Total			
Allsop 2014	1.88	8.52	27	2.22	7.94	24	32.9%	-0.04 [-0.59, 0.51]	2014
Trigo 2016	4	4.2	9	5.9	5.5	9	11.4%	-0.37 [-1.30, 0.56]	2016
Trigo 2018	5	4.7	13	5.1	3.9	14	17.5%	-0.02 [-0.78, 0.73]	2018
Lintzeris 2019	30.7	28.9	30	43.6	37.3	30	38.2%	-0.38 [-0.89, 0.13]	2019
Total (95% CI)			79			77	100.0%	-0.21 [-0.52, 0.11]	

Heterogeneity: Tau² = 0.00; Chi² = 1.15, df = 3 (P = 0.77); I² = 0%
Test for overall effect: Z = 1.27 (P = 0.20)



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Conclusion

- Données sur douleur chronique : effet faible / NNH quasi = NNT
- Données non convaincantes dans pathologies psychiatriques
- Déterminer ratio THC/CBD utiles dans chaque indication
- CBD : multiplicité des produits et pureté en question

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