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► To cite this version:

Tangui Barré, Clémence Ramier, Camelia Protopopescu, Patrizia Carrieri, Lise Radoszycki. Symptom improvements following therapeutic use of cannabis-based products in French people with multiple sclerosis. *Multiple Sclerosis and Related Disorders*, 2022, 67, pp.104093. 10.1016/j.msard.2022.104093 . hal-03817248

HAL Id: hal-03817248

<https://hal.science/hal-03817248v1>

Submitted on 17 Oct 2022

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Symptom improvements following therapeutic use of cannabis-based products in French people with multiple sclerosis

Tangui Barré¹, Clémence Ramier¹, Camelia Protopopescu¹, Patrizia Carrieri¹, Lise Radoszycki²

¹ Aix Marseille Univ, Inserm, IRD, SESSTIM, Sciences Economiques & Sociales de la Santé & Traitement de l'Information Médicale, ISSPAM, Marseille, France

² Carenity, Paris, France

Correspondence to Clémence Ramier, clemence.ramier@inserm.fr; SESSTIM, Faculté de Médecine 27 Bd Jean Moulin 13385 Marseille.

Keywords: cannabis; multiple sclerosis; neurologic manifestations; pain; muscle spasticity.

Declarations of interest: none

Authors' contributions

TB, CR, CP, PC, LR: Conceptualization

CP: Data curation

CR: Formal analysis

TB: Writing - original draft

TB, CR, CP, PC, LR Writing - review & editing

Financial support: there was no financial support related to this work.

Dear Editors,

We read with great interest the recent article by Santarossa et al. who explored the extent of medical cannabis use in people with multiple sclerosis in Canada, the symptoms for which it is used, and perceived effectiveness (1). Sleep problems, pain and spasticity were the most quoted symptoms, and substantial effectiveness was reported for eight symptoms including the three just mentioned. Drowsiness was the most reported adverse effect, but overall, experience of adverse effects was limited.

Santarossa et al.'s results come from a country where recreational cannabis has been legal since 2018, and medical cannabis since 2001. The experience of cannabis use for medical purposes and controlled channels of cannabis supply are therefore relatively well established. This is not the case in other countries where cannabis use is still prohibited.

In France, cannabis use in all its forms, including for therapeutic purposes, is criminalized. The only exception is an experimental therapeutic program which started in 2019. Users may be punished by up to one year in prison and a fine of 3750 € (2).

Tetrahydrocannabinol (THC)-containing cannabis is illegal in France and can only be bought on the black market. Its composition is therefore uncontrolled and may in certain cases be adulterated (4,5). Furthermore, data highlight that its potency (i.e., THC concentration) is increasing (6).

On the contrary, cannabidiol (CBD)-based products with 'zero' THC content are freely sold in France. Recently the French government unsuccessfully tried to ban CBD-rich (Δ^9 -THC-deprived) cannabis flowers (3). However, France's, and more generally Europe's vague regulatory context (7) indirectly encourages the adulteration and mislabeling of CBD-products (8,9) and misinformation (10), thereby increasing the risk of CBD-related harms.

Despite Nabiximols - an oro-mucosal spray with a balanced mixture of THC and CBD - being the only legal cannabinoid-based medical drug in the France (approved for MS-related spasticity), it is unavailable because of failures in price negotiations between its producer and French health authorities. There is therefore a need to explore the therapeutic use of cannabis-based products (CBP) by people living with MS in the country.

We conducted an online survey of people living with multiple sclerosis (MS) in France. People using CBP for therapeutic motives were recruited on Carenity, a social network for people living with chronic conditions. Participants completed a self-administered online questionnaire that collected data on socio-demographic characteristics, type of CBP (including herb, resin, CBD extract etc.), route of administration, self-reported motives to use CBP, and perceived effectiveness. The study was conducted in accordance with the Declaration of Helsinki. According to French law and anonymity of data, no approval from

ethics committee was needed. Informed written consent was obtained from all individual participants included in the study.

Our study sample (n=104) mainly comprised females (64.4%), had a median [interquartile range (IQR)] age of 48 years [41.0 – 58.5], and a median [IQR] time since MS diagnosis of 11.5 years [7 – 19]. Half of the participants (50.0%) had experienced relapsing-remitting MS, 18.3% primary progressive MS, 27.9% secondary progressive MS, and 3.9% did not know their form of MS. With regard to CBP route of administration, 31.7% used inhalation only (i.e., cannabis herb/resin or vaping products), 45.2% used non-inhalation (i.e., all other) routes, while 23.1% used both. In terms of frequency of use, 69.2% consumed CBP once daily or more often.

Among the twelve explored MS symptoms for which CBP were used, the most cited were pain (70.2%), spasticity (61.5%), sleep disorders (51.0%), sensitivity disorders (38.0%) and fatigue (26.9%). The self-reported effects of CBP on MS-related symptoms are given in **Figure 1**. Of the negative effects, 8.1% were ‘strongly negative’, 16.2% were ‘negative’ and 75.7% were ‘moderately negative’.

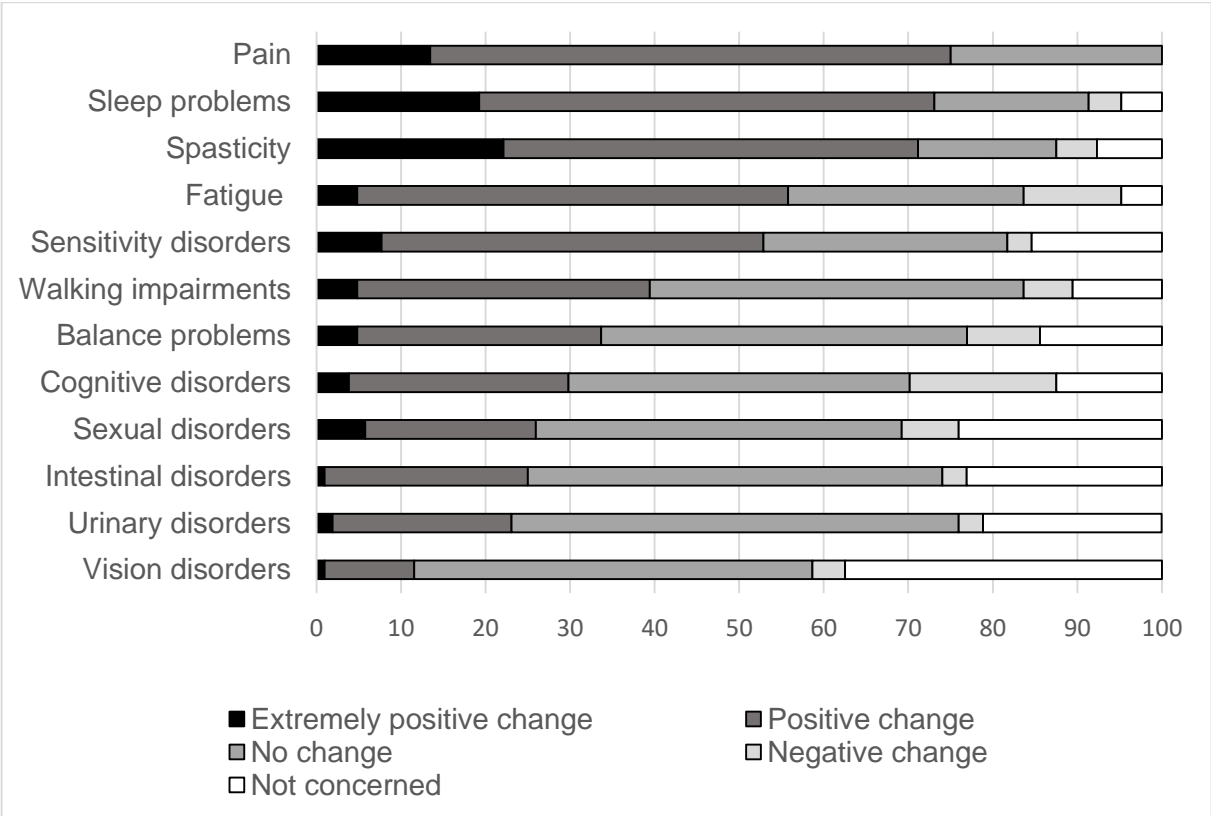


Figure 1. Self-reported effects of cannabis-based products on 12 symptoms of multiple sclerosis in patients living in France (Carenity social network, n=104)

The most important benefits among participants concerned were observed for spasticity (77.1% positive rating), sleep disorders (76.7%), and pain (75.0%). The least

improved were vision disorders (18.5% positive rating), urinary disorders (29.3%), and intestinal disorders (32.5%).

Among the ten reported adverse effects explored, the most cited were increased appetite and fatigue, while 27.9% of participants experienced no adverse effect (**Table 1**).

Table 1. Reported adverse effects of using cannabis-based products in people living with multiple sclerosis in France (Carenity social network, n=104)

| Adverse effects | N (%) |
|------------------------|--------------|
| Feeling of hunger | 41 (39.4) |
| Fatigue | 27 (26.0) |
| Concentration problems | 9 (8.7) |
| Memory problems | 9 (8.7) |
| Balance problems | 4 (3.8) |
| Paranoia / anxiety | 2 (1.9) |
| Hallucinations | 1 (1.0) |
| Nausea | 1 (1.0) |
| Schizophrenia | 0 (0.0) |
| Other adverse effects | 1 (1.0) |
| No adverse effect | 29 (27.9) |

Cannabis dependence may occur using THC-containing products. Only two of the 60 participants who tried to reduce their CBP use did not succeed. Less than 20% (17.3%) of users declared increased use of CBP. Finally, on a visual analog scale ranging from zero (no CBP dependence) to 10 (very strong CBP dependence), the median [IQR] self-reported dependence score was zero [0-2].

The main patient-reported MS symptoms motivating CBP use in our study sample were similar to those in Santarossa et al.'s sample in Canada, despite the very different legal contexts. Furthermore, just as in their study (1), our participants reported high levels of effectiveness for several symptoms including the main ones. Our data suggest that people in France living with MS find relieve from CBP, despite barriers to accessing CBP and a lack of quality control. Although our study has limitations, including the non-representativeness of our study sample and the unknown cannabinoid content of CBP consumed, we agree wholeheartedly with Santarossa et al.'s conclusions that more clinical research is needed, and that the benefits and risks of therapeutic cannabis use should be highlighted to reduce social stigma. There is also a need to promote a long-term (medical) cannabis policy that maximizes health and minimizes harm by ensuring safe content of CBP in France, while increasing the quality of life of patients with MS.

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