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## **Exploring the medical cannabis prescribing behaviors of French general practitioners**

**Running title:** French general practitioners and cannabis

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**Authors' contributions:**

TB, HV, PC and ALPA designed the study. TB wrote the original manuscript. VDB performed the statistical analyzes. TB, VDB, HV, PC and ALPA reviewed and amended the manuscript.

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Dear Editors,

We read with great interest Manoharan et al.'s qualitative study on the medical cannabis prescribing behaviors of physicians in New Zealand (1). Whilst  $\Delta$ 9-tetrahydrocannabinol (THC)-containing products can be prescribed in New-Zealand since mid-2020, the study reported several barriers to the prescription of medical cannabis, including concerns about the lack of clinical evidence supporting adverse side effects, poor trust in patients, the complexity of the prescription process and the risk to physicians' reputation.

Cannabis use in all its forms, including for therapeutic purposes, is criminalized in France. Users may be sentenced to up to one year in prison and fined 3750€ (2). The only exception for legal therapeutic use of cannabis is through the ongoing two-year long (March 2021 – March 2023) nationwide experiment that aims to assess the feasibility of allowing the prescription of medical cannabis (3). In March 2022, 1500 patients had already been enrolled (3000 participants expected by 2023) (4). The prescription of medical cannabis is limited to the following conditions: resistant neuropathic pain, certain forms of resistant epilepsy, certain resistant symptoms in oncology, palliative treatment, and resistant painful spasticity (3). The inclusions, first medical visits, and the first prescriptions of cannabis-based products in the experiment are conducted in predetermined reference centers and patients then return to these centers for compulsory follow-up visits. However, in between those visits, they can be followed-up by a physician in a hospital or a private practice (such as a general practitioner (GP)) who has completed the compulsory training for the prescription of cannabis-based products.

In France, GPs (or 'family physicians') are the first entry point into healthcare, and refer patients to specialized physicians when needed. People generally choose a GP as their attending medical practitioner to provide a first level of care and coordinate their medical follow-up. If access to medical cannabis is legalized following the experiment, GPs will play a central role in its prescription and/or the medical follow-up of patients receiving medical cannabis. In this context, we aimed to identify the barriers reported by GPs in France with regards to the prescription of medical cannabis and to compare them to those reported by physicians in New Zealand.

An online survey targeting GPs in Southern France (Région SUD) was conducted between June 14<sup>th</sup> and July 18<sup>th</sup> 2022. Participants were reached through personal networks, health territorial professional communities, social media and young GPs federation. Participants were informed that, in the context of a medical thesis, the survey intended to explore GPs' motivations, barriers and suggestions regarding medical cannabis prescription

as implemented within the experiment. Written informed consent was obtained from each participant before accessing the questionnaire. The primary outcome of our analyses was answering 'Yes' to the question 'Are you willing to become a medical cannabis prescriber, in the context of the experiment / if GPs are authorized to prescribe it after the experiment?'. We used logistic regression models to identify the factors associated with the outcome. The explanatory variables included in a first model (model 1) were sex, age, working conditions, knowledge and experiences about medical cannabis. In the second model (model 2), beliefs and *a priori* barriers to medical cannabis prescription were added as explanatory variables. Variables with a p-value <0.20 in the univariable analyses were considered eligible for the multivariable models. Backward stepwise selection was used to determine variables in the final multivariable model with a p-value threshold set at 0.05 (Wald test). All analyses were performed using Stata software version 17.0 for Windows (StataCorp LP, College Station, TX).

Our study sample was comprised of 134 GPs (39.6% were men), of whom 77.6% were willing to prescribe medical cannabis. Study sample characteristics and results of regression models are presented in **Table 1**. The factors associated with willingness to prescribe medical cannabis in model 1 were working far from a reference center, being part of a health territorial professional community and having a good (self-reported) knowledge of THC and CBD's effects (adjusted odds ratio 4.30 [95% confidence interval] [1.17-15.75],  $p=0.028$ ). In model 2, following patients with at least one of the conditions required for the prescription of medical cannabis in the experiment (resistant neuropathic pain, etc.) was associated with willingness to prescribe medical cannabis. In contrast, believing that the prescription of medical cannabis would have an impact on GPs' security (0.10 [0.03-0.30],  $p<0.001$ ) and that the approval of medical cannabis would lead to the legalization of non-medical cannabis (0.32 [0.11-0.90],  $p=0.030$ ) were barriers to prescription (**Table 1**).

The findings of our survey echo the results of Manoharan et al.'s study.; "the way physicians regard prescribing medical cannabis is based on their personal beliefs" (1). Based on our results, these beliefs seem to be stronger predictors of GPs' willingness to prescribe medical cannabis than knowledge about cannabinoids. While we did not explore the effect of medical cannabis prescription on the risk to GPs' reputation, we found that fears related to GPs' security had the highest negative impact (odds ratio) on the likelihood of prescribing medical cannabis. We hope that the results of the nationwide experiment will reassure GPs on this point, as well as on the adverse effects and the safety of medical cannabis-based products. The role of fears related to non-medical cannabis depenalization is of high interest in France. While partly justified (5), those fears may be enhanced by prejudices and/or misconceptions about the public health impacts of legalizing cannabis (5–8). As it has been

shown previously that stigma towards medicinal cannabis users may impact the willingness to recommend it (9), this issue of prejudices should be further explored in France.

As compared to national data (mean GP age of 51 years, 50% women (10)), our study sample seemed younger and overrepresenting women. Moreover, the survey was circumscribed to a unique region. Therefore, our results cannot be unquestioningly generalized to French GPs. Another limitation was our sample size that limited the statistical power of our analyses.

To conclude, we agree with Manoharan et al.'s recommendation to provide clear and concise guidelines to physicians to reduce barriers to prescription. Moreover, providing reliable data on the consequences of cannabis legalization and on experiences of its legalization in other contexts, as well as implementing initiatives targeting substance-related stigma may help reduce misconceptions and enable patients to have access to prescribed cannabis-based products in France.

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**Table 1. Study sample characteristics and factors associated with willingness to prescribe medical cannabis among general practitioners (n=134)**

	<b>N=134 (%)</b>	<b>Univariable analyses OR [95% CI]</b>	<b>Multivariable analysis (model 1) aOR [95% CI]</b>	<b>Multivariable analysis (model 2) aOR [95% CI]</b>
<b>Sex</b>				
Men	39.6	1		
Women	60.4	1.0 [0.5-2.4]		
<b>Age (years)</b>				
< 30	12.7	1		
30 - 39	48.5	3.1 [1.0-9.8]		
40 - 49	19.4	2.3 [0.6-8.8]		
50 - 59	10.4	2.6 [0.5-12.7]		
≥ 60	9.0	3.5 [0.6-21.2]		
<b>City size</b>				
< 30 000 inhabitants	36.8	1		
≥ 30 000 inhabitants	64.2	0.4 [0.1-1.0]		
<b>Working more than 30 km away from a reference center<sup>1</sup></b>				
No	28.4	1	réf	
Yes	71.6	4.6 [1.3-16.7]	4.6 [1.2-16.7]	
<b>Being part of a health territorial professional community<sup>2</sup></b>				
No	73.1	1	1	
Yes	26.9	4.2 [1.2-14.8]	4.5 [1.2-16.4]	
<b>Having achieved complementary training<sup>3</sup></b>				
No	67.9	1		
Yes	32.1	2.2 [0.8-5.9]		
<b>Being aware that some of his/her patients are using cannabis for therapeutic purposes</b>				
No	32.1	1		
Yes	67.9	2.3 [1.0-5.2]		
<b>Considering having a good knowledge of THC and CBD's effects</b>				
No	72.4	1	1	
Yes	27.6	4.4 [1.2-15.4]	4.30 [1.2-15.8]	
<b>Being aware of the experiment led by the ANSM from March 2021 to March 2023</b>				

No	71.6	1	
Yes	28.4	1.8 [0.7-4.8]	
<b>Having patients fulfilling at least one of the five conditions to be included in the experimental test<sup>4</sup></b>			
No	21.6	1	1
Yes	78.4	5.2 [2.1-12.8]	4.8 [1.6-14.8]
<b>Would refuse to prescribe medical cannabis because of regulatory obligations<sup>5</sup></b>			
No	75.8	1	
Yes	24.2	0.3 [0.1-0.7]	
<b>Considering risks of diversion or misuse as barriers to prescribing medical cannabis</b>			
No	24.6	1	
Yes	75.4	0.1 [0.0-0.6]	
<b>Considering risks of cardiac adverse effects as barriers to prescribing medical cannabis</b>			
No	74.6	1	
Yes	25.4	0.7 [0.3-1.8]	
<b>Considering risks of psychic adverse effects as barriers to prescribing medical cannabis</b>			
No	47.8	1	
Yes	52.2	1.3 [0.6-3.0]	
<b>Considering potential risks to his/her own security as a barrier to prescribe medical cannabis<sup>6</sup></b>			
No or a little	62.4	1	1
Moderately to strongly	37.6	0.1 [0.0-0.2]	0.1 [0.0-0.3]
<b>Considering that approval of supervised medical cannabis would initiate a legal evolution leading to depenalization of non-medical cannabis<sup>7</sup></b>			
Not at all to moderate	67.1	1	1
Likely or certain	32.9	0.2 [0.1-0.4]	0.3 [0.1-0.9]

<sup>1</sup> Reference centers are hospital services entitled to include patients for the experiment and initiate medical cannabis prescription.



<sup>2</sup> A health territorial professional community is a group of health professionals that organize themselves around a common territory-based health strategy. Such organizations are supposed to ease professional relationships and patients' health path.

<sup>3</sup> Complementary trainings are diverse (e.g. gerontology). They do not give access to a specialist status.

<sup>4</sup> The five conditions are: resistant neuropathic pain, certain forms of resistant epilepsy, certain resistant symptoms in oncology, palliative treatment, resistant painful spasticity.

<sup>5</sup> The full question was: 'Would you refuse to prescribe medical cannabis because of regulatory obligations: compulsory half-a-day remote training and obligation to keep a record?'

<sup>6</sup> Participants rated their answer from 0 (no risk) to 3 (strong risk). We dichotomized those answers into 'No or a little' (0/1) and 'Moderately to strongly' (2/3).

<sup>7</sup> Participants rated their answer from 1 (not at all) to 5 (it is certain). We dichotomized those answers into 'Not at all or moderately' (1/2/3) and 'Likely or certain' (4/5).

ANSM, Agence nationale de sécurité du médicament et des produits de santé (French National Agency of Medicine and Health Products Safety); aOR, adjusted odds ratio ; CBD, cannabidiol; CI, confidence interval ; THC,  $\Delta$ 9-tetrahydrocannabinol.