



<sup>1</sup> Centre d'excellence sur le vieillissement de Québec, CIUSSS CN Hôpital St-Sacrement, Québec, QC G1S 4L8, Canada

<sup>2</sup> Department of social and preventive medicine, Faculty of Medicine, Université Laval, Pavillon Ferdinand-Vandry, Québec, QC G1V 0A6, Canada

Corresponding author: E Kröger edeltraut.kröger.ciusscn@sss.gouv.qc.ca

Cite this as: *BMJ* 2021;374:n1942 <http://dx.doi.org/10.1136/bmj.n1942>

Published: 09 September 2021

## Medical cannabis for chronic pain

### Patient centred guidance recommends a trial of treatment

Edeltraut Kröger,<sup>1</sup> Clermont E Dionne<sup>2</sup>

Patients with persistent pain continue to search for new therapeutic options and often perceive cannabis as a worthwhile alternative.<sup>1</sup> Clinicians need guidance on this option to inform shared decision-making with patients.<sup>2</sup> The linked clinical guidance by Busse and colleagues was developed for this purpose and comes from an international panel combining several disciplines, specialties, and patient groups.<sup>3</sup> The new guidance is based on a systematic review of the effectiveness of medical cannabis for chronic pain,<sup>4</sup> offers an online tool, and has the potential to fill a critical gap in information for decision making, enabling more inclusive management of chronic pain.

The guidance offers a weak recommendation for a trial of non-inhaled medical cannabis for the treatment of chronic pain. Its summary indicates moderate evidence of a clinically important decrease in pain for a small to very small proportion of patients. The recommendation for a trial of treatment is based on two meta-analyses of randomised trials within the systematic review<sup>4</sup>: first, a meta-analysis of 27 randomised controlled trials finding an increase in the proportion of patients reporting an improvement in pain of at least 1 cm on a 10 cm visual analogue scale (although a minimum reduction of 1.5 cm is considered clinically relevant<sup>5</sup>); second, a meta-analysis of 10 placebo controlled trials reporting a 7% increase in the proportion of people reporting at least a 30% reduction in pain in favour of cannabis compared with placebo.<sup>4</sup>

Methodological and ethical problems in these trials limited the level of certainty in the evidence underpinning Busse and colleagues' recommendations. They include follow-up periods of less than six months (very short for chronic conditions<sup>6</sup>), small sample sizes, funding by industry, and use of different outcome measures that complicate comparisons.

The new guidance adds to previous guidance<sup>7</sup> by combining evidence from trials of medical cannabis and cannabinoids in patients with all types of chronic pain. This is important, since only a minority of included studies evaluated these agents in the management of chronic musculoskeletal pain, which is common, difficult to treat, increases with age, and has given rise to problematic prescribing of opiates.<sup>8</sup> Evidence on the effectiveness of medical cannabis against chronic musculoskeletal pain is rare,<sup>9</sup> and several previous guidelines did not recommend cannabis for this indication.<sup>7</sup> However, in its most recent edition (11th) the *International Classification of Diseases* defines three major types of chronic pain: neuropathic, nociplastic, and nociceptive pain.<sup>10</sup> Busse and colleagues found no significant differences in the effects of medical cannabis on neuropathic

pain and the other two subtypes, and thus recommended non inhaled medical cannabis for all chronic pain, regardless of origin.

It may be time for more inclusive recommendations. However, given the high prevalence of chronic musculoskeletal pain and the frequent use of self medication by patients,<sup>11</sup> some caution may be warranted.

First, self medication might lead to increased use of cannabis products with a worse risk-benefit profile (higher doses or a higher concentration of tetrahydrocannabinol, for example) than the products recommended by Busse and colleagues.<sup>3</sup> Also, since inhalation leads to a faster and more powerful pharmacological effect than other routes of administration, patients may prefer inhaled cannabis products<sup>12</sup> despite their potential for harm. Access to optimal pain treatment is often limited, which could lead to a widespread and problematic use of cannabis. In many countries, nabilone and nabiximols are the only regulated cannabis medications. Other products available for self medication have uncertain compositions that may often vary between batches, making accurate dosing challenging.

The frontier between recreational and medical use of cannabis and cannabinoids is not always clearly drawn.<sup>13</sup> Teenagers and younger adults particularly, may self medicate with recreational cannabis or consider a "medically recommended" substance as safe, potentially putting them at increased risk of neurological or psychiatric adverse events. Although the review underpinning Busse and colleagues' guidance found no evidence linking psychosis to the use of medical cannabis,<sup>4</sup> knowledge of the effects of cannabis products on the young brain is just emerging. Researchers have observed, for example, that simultaneous use of recreational cannabis and alcohol increases the potential for addiction.<sup>14</sup> More widespread use of cannabis products for chronic pain could mean that "vulnerable populations...may experience novel toxic effects."<sup>15</sup> Finally, long term harms of new treatments often take years to emerge, including the dependency associated with use of opiates for chronic pain.<sup>16</sup>

This new patient centred guidance can improve shared decision making: clinicians should emphasise the harms associated with vaping or smoking cannabis and, as recommended by other guidelines,<sup>17</sup> suggest products with known compositions such as nabilone or nabiximols, discourage self medication, and pay particular attention to vulnerable populations. Increased pharmacovigilance of all cannabis use<sup>18</sup> remains a priority, along with an ambitious programme of rigorous research on the

## short and long term effectiveness and safety of individual cannabis products for specific types of chronic pain.

Competing interests: *The BMJ* has judged that there are no disqualifying financial ties to commercial companies. The authors have no other interests to declare. *The BMJ* policy on financial interests is here: <https://www.bmj.com/sites/default/files/attachments/resources/2016/03/16-current-bmj-education-coi-form.pdf>.

Provenance and peer review: Commissioned; not externally peer reviewed.

We thank our patient partner, Mr David Bouchard, Quebec City, for reviewing and advising on this text.

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