JWH-2020-8668-ver9-Armour\_1P Type: research-article

# **Original Article**

JOURNAL OF WOMEN'S HEALTH Volume 00, Number 00, 2020 © Mary Ann Liebert, Inc. DOI: 10.1089/jwh.2020.8668

# Illicit Cannabis Usage as a Management Strategy in New Zealand Women with Endometriosis: An Online Survey

AU3 ► AU2 ►

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#### **Abstract**

**Background:** Endometriosis affects around 10% of women worldwide. Many women with endometriosis struggle with finding adequate pain management, and data from other countries suggest that women use cannabis, either legal or illicit, to help manage their endometriosis symptoms. The aim of this study was to determine use of cannabis where endometriosis was self-identified as a condition that was being treated with cannabis, as well as the impact of cannabis use on the usage on other pharmaceuticals.

*Materials and Methods:* A cross-sectional online survey of those using cannabis for health-related conditions run between May and July 2019. This article reports on the subset of this larger data set for those reporting they had a diagnosis of endometriosis and/or polycystic ovary syndrome. Data were collected on demographics, modes of cannabis administration, symptoms treated, changes in pharmaceutical usage, and adverse events.

**Results:** Two hundred thirteen valid responses were analyzed. Mean age of respondents was 32 years and 79.8% were current cannabis users. The most common outcomes that cannabis was used for were to improve pain relief (95.5%) and to improve sleep (95.5%). Respondents reported that their symptom was "much better" for pain (81%), sleep (79%), and nausea or vomiting (61%). Over three-quarters (81.4%) indicated cannabis had reduced their normal medication usage. Over half (59%) were able to completely stop a medication, most commonly (66%) analgesics. Opioids (40%) were the most common class of analgesic stopped.

**Conclusions:** Cannabis is reported as an effective intervention for pain and other endometriosis symptoms with potential substitution effects on opioid usage.

AU6 Keywords: cannabis, endometriosis, pelvic pain, New Zealand

# Introduction

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Endometriosis is an estrogen-dependent, chronic, inflammatory disease characterized by the presence of lesions containing endometrial-like tissue outside the uterus. The estimates of prevalence worldwide suggest endometriosis occurs in 5%–10% of reproductive-age females. 3,4

In recent Australian data, one in nine women were diagnosed with endometriosis by the age of 40–44 (prevalence rate of 11%).<sup>5</sup>

Symptom presentation in endometriosis is heterogenous, but most commonly includes severe dysmenorrhea (period pain), noncyclic pelvic pain, and infertility. Other symptoms include bloating, dyspareunia (painful sex), dyschezia (pain



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on defecation), dysuria (painful urination), fatigue, and gastrointestinal issues often similar to irritable bowel syndrome (IBS).9 Alongside the reduction in overall quality of life,10 endometriosis impacts women's well-being and health, including mental and emotional health, 11 sexual/intimate relationships, 12 and social activities. 10

Both surgical and pharmaceutical treatments are commonly used for endometriosis, with surgery showing benefits for pain, at least in the short to medium term. 13 Current pharmaceutical treatments for endometriosis include the use of the oral contraceptives or progestogens and nonsteroidal anti-inflammatory drugs (NSAIDs). Effectiveness for pain control is variable among individuals and for some interventions (such as NSAIDs) is inconclusive. 14 In addition, for some treatments that are effective for pain, such as gonadotropin-releasing hormone (GnRH) analogues, the side effects are problematic for many women, and discontinuation rates are high. 15 While we do not have New Zealand data, in the United States, opioids are commonly prescribed for women with endometriosis<sup>16</sup>; in Australia, common opioids such as oxycodone and codeine carry an increased risk of dependency and overdose. 17 These factors are likely, at least in part, to explain why 76% of Australian women report selfmanagement of endometriosis symptoms. 18 Australian data suggest that around 1 in 10 of the women who used selfmanagement strategies had tried cannabis, most likely from illicit sources, to manage their pain and other symptoms; 56% of these women report a subsequent significant reduction in pharmaceutical medication use related to endometriosis.<sup>19</sup>

Recreational cannabis use was illegal in New Zealand at the time of the survey and access to cannabis for therapeutic purposes was limited. A small number of cannabis-based pharmaceutical medicines were available by prescription, including Sativex, as well as a limited number of cannabidiol products containing <2% THC. Despite the illegality, we hypothesized that, similar to Australia, 19 cannabis use would not be uncommon in endometriosis patients in New Zealand and that their use of cannabis would impact on their use of prescribed pain and other medications.

The aim of this survey was to explore New Zealanders' use of cannabis where endometriosis was self-identified as a condition that was being treated with cannabis, as well as the impact of cannabis use on the usage on other pharmaceuticals.

#### AU9 Materials and Methods

# Study population

We surveyed a convenience sample of people in New Zealand self-reporting therapeutic use of cannabis or a cannabis-based medicine through the administration of a cross-sectional online survey. A cannabis-based medicine may have been formally prescribed as a pharmaceutical product or "natural" or "raw" cannabis may have been used in any form (e.g., flowers, edible, oil, tincture). Eligibility criteria included participants being 18+ years, having used or currently using cannabis therapeutically, and being able to provide informed consent. This article only reports on people who indicated they had a diagnosis of endometriosis and/or polycystic ovary syndrome (PCOS). Proof of a formal diagnosis (e.g., laparoscopy or ultrasound scan) was not required.

Survey design and hosting

Accessing the survey required prospective participants to acknowledge reading and understanding the participant information sheet and then consenting via a link. The survey was run for 3 months (May to July 2019), linked to a medicinal cannabis patient advocacy Facebook group, and subsequently promoted through online cannabis and patient fora, consumer groups, and patient-specific and professional networks. Data were collected and managed through SurveyMonkey, a secure web-based platform compliant with the US HIPAA standard for medical systems. No personal data were logged and only the researchers had access to the raw data via two-factor authentication.

The survey questionnaire drew on a previously published Australian online survey<sup>20</sup> and was adapted to reflect New Zealand conditions. The views of consumer advisors, focus groups, clinicians, and researchers were sought to refine the questionnaire, with the following areas of interest identified:

- Participant demographics;
- cannabis use in relation to current treatment, including discussion with health professionals;
- use patterns, including current and lifetime; dosage, frequency, and time of use; form of cannabis and route of administration; changes in use over time;
- efficacy, including negative effects and comparisons with other medicines, incorporating items from the Patient Global Impression of Change.<sup>21</sup>

This article reports on demographics, use, efficacy, and side effects of cannabis, and comparison with, and where relevant, any substitution of current medications taken.

#### Analyses

Data were analyzed using SPSS v26 (IBM Corporation, Chicago, IL). Descriptive statistics were presented as means and standard deviations (for normally distributed data), medians and interquartile ranges (for non-normally distributed data), or numbers and percentages (for categorical data). Missing data were reported and not replaced. Individual medications were classified into categories (e.g., NSAIDs) by a medical doctor (E.H.).

### Results

The data reported here are a subset of a larger data set examining the therapeutic use of cannabis and cannabisbased medicines in New Zealanders across multiple selfidentified conditions. Eligible responses were received from 213 participants, this being 10% of the total respondent sample (n=2125). The mean age of respondents with endometriosis and/or PCOS was 32 (±9) years, with the Auckland (19.7%) and Canterbury (18.8%) regions having the most respondents (Table 1). Most respondents identified as NZ ◀T1 European (84.1%) and were working (55.8%); however, a substantial minority (36.6%) were unemployed. Most respondents report having endometriosis and/or PCOS symptoms for at least 5 years (73.7%).

Most respondents were current cannabis users (79.8%) for medical purposes (Table 2). All respondents with endome- ◀T2 triosis and/or PCOS had at least one comorbidity, most commonly depression and/or anxiety (80%), migraine

2.3

0.5

7.0

8.5

11.7

2.8

5

1

15

18

25

6

#### AU1 ► ILLICIT CANNABIS USAGE IN NEW ZEALAND WOMEN WITH ENDOMETRIOSIS

TABLE 1.	(CONTINUED)

n=213			TABLE 1. (CONTINUED) $n=213$
-		22.2 (0.9)	
Mean (SD)	,	32.3 (9.8)	Working part-time, receiving a supported living payment
Age	n	%	Working part-time, receiving
18–25	67	31.5	ACC earnings-related compensation
26–35	79	37.1	Working part-time, receiving
36–45	46	21.6	another benefit
46–55	17	8.0	Unemployed
56+	4	1.9	Unemployed, receiving supported
Did not answer	2	0.9	living payment
Gender			Unemployed, receiving
Female	209	98.1	ACC earnings-related compensation
Other	3	1.4	Unemployed, receiving other benefits
Transgender	1	0.5	Student
Regions of New Zealand			Retired
Northland region	10	4.7	Duration of having endometriosis and/or p
Auckland region	42	19.7	syndrome
Waikato region	22	10.3	0–6 months
Bay of Plenty region	21	9.9	6–12 months
Gisborne region	2	0.9	1–2 years
Hawke's Bay region	5	2.3	2–5 years
Taranaki region	6	2.8	5–10 years
Manawatu-Wanganui region	18	8.5	10–20 years
Wellington region	13	6.1	20+ years Missing
Tasman region	3	1.4	Wiissing
Nelson region	6	2.8	<sup>a</sup> Multiple options allowed.
Marlborough region	4	1.9	ACC; SD, standard deviation.
West Coast region	6	2.8	
Canterbury region	40	18.8	
Otago region	12	5.6	headaches (46%), persistent nausea (42%)
Southland region	3	1.4	pain (41%). The most common symptoms
Ethnicity <sup>a</sup>			used for were pain relief (95.5%), improvi
NZ European	180	84.1	increasing the ability to cope (80%), and nat
Māori	51	23.9	(78.5%). Respondents reported a median
Chinese	2	0.9	100) to the question "How does (or did) can
Indian	3 0	1.4	conditions or symptoms overall?" where 0
Samoan	0	$0.0 \\ 0.0$	100 was excellent relief. Of the most co
Tongan Niuean	0	0.0	symptoms, respondents reported that the
Other	29	13.6	"much better" for pain (81%), sleep (79%)
	2)	13.0	vomiting (61%). Very few reported their sys
Total household income Zero income	7	3.3	or much worse (Supplementary Table S1).
\$1–\$5,000	4	1.9	Respondents had tried a wide range
\$5,001-\$10,000	7	3.3	methods (Table 2) and the majority (67.8%
\$10,001-\$15,000	9	4.2	haled forms of cannabis were the most ef
\$15,001–\$20,000	11	5.2	
\$20,001–\$25,000	9	4.2	common time period for using cannabis
\$25,001-\$30,000	15	7.0	(50.4%). Most had been using cannabis for
\$30,001–\$35,000	8	3.8	(75.6%), with a substantial proportion being
\$35,001–\$40,000	12	5.6	10 years (29.6%). Most current cannabis use
\$40,001–\$50,000	18	8.5	amount of cannabis use varied depending
\$50,001–\$60,000	20	9.4	(45%), or that there had been no change in
\$60,001-\$70,000	17	8.0	they first started (17%), but around one in
\$70,001-\$100,000	27	12.7	reported they had to use more cannabis ove
\$100,001-\$150,000	15	7.0	vaporizers was low, with less than a quart
\$150,001 or more	4	1.9	(23%) reporting owning one, while 12%

13

17

73

25

6.1

8.0

34.3

11.7

(continued)

Don't know

Employment status

I would rather not say

or more a week

Working part-time

Working full-time, 30+ hours

29 er benefits 13.6 14 6.6 2 0.9 osis and/or polycystic ovarian 1.9 4 11 5.2 33 52 15.5 24.4 58 27.2 47 22.1 3.3

**■**AU16

**⋖**ST1

ausea (42%), or lower back symptoms that cannabis was %), improving sleep (95.5%), 0%), and nausea and vomiting d a median score of 90 (80s (or did) cannabis affect your 1?" where 0 was no relief and the most common individual ted that their symptom was , sleep (79%), and nausea or rted their symptom was worse Table S1).

vide range of administration ority (67.8%) reported that inthe most effective. The most ng cannabis was after 6 pm cannabis for at least 2 years ortion being users of more than cannabis users reported that the depending on their condition to change in the amount since ound one in five users (21%) cannabis over time. The use of than a quarter of respondents (23%) reporting owning one, while 12% reported they intended to purchase one. The most common reason for lack of a vaporizer was cost (26%). If a GP or a pharmacy provided a ◀AU10

Of the respondents, 176 (81.4%) indicated that cannabis had changed their normal medication usage; 128 (59%) were able to completely stop a medication, 97 (45%) were able to reduce a medication by at least half of the total dose, and 41

vaporizer, then almost all respondents (93%) would use one.

TABLE 2. CANNABIS USAGE CHARACTERISTICS

AU17▶

n = 213			
Macri (CD)		22.7 (7.6)	
Mean (SD)	n	%	
Age when first started using cannabis for medicinal Are you still using cannabis for any medical condition		es?	
Yes	170	79.8	
No—It didn't work	0	0.0	
No—I was unable to find a regular supply	9	4.2	
No—It stopped working	0	0.0	
No—I didn't like the side effects	6	2.8	
No—I could not afford it	6	2.8	
No—Because of its illegal status	9	4.2	
Other	6	2.8	
Did not answer	7	3.3	
In what forms have you tried cannabis for medicinal	reasor	ıs? <sup>a</sup>	
Eaten as a cooked recipe (biscuits, cookies, etc.)	140	65.7	
Eaten as an oil-filled capsule	55	25.8	
Consumed as a liquid (oil or tincture)	79	37.1	

Drunk as a tea 14.6 Smoked as a cigarette (ioint) 171 80.3 Smoked through a dry pipe (chillum) 63.4 135 145 Smoked through a water pipe (bong) 68.1 86 40.4 Inhaled through a vaporizer 29 Eaten as leaf/flower matter 13.6 Consumed raw blended into drinks (smoothie) 20 9.4 93 Used in a balm on the skin 43.7 13 6.1 What form of administration has helped you the most with your condition? (n=177)

Eaten as a cooked recipe (biscuits, cookies, etc.) 13.6 5 17 2.8 9.6 Eaten as an oil-filled capsule Consumed as a liquid (oil or tincture) 3 51 Drunk as a tea 1.7 Smoked as a cigarette (joint) 28.8 Smoked through a dry pipe (chillum) 17 9.6 Smoked through a water pipe (bong) 38 21.5 14 Inhaled through a vaporizer 0 0.0 Eaten as leaf/flower matter 0 Consumed raw blended into drinks (smoothie) 0.0 Used in a balm on the skin

Other	6	3.4
How frequently do you or did you use cannabis in you	ır usual	form
of cannabis? $(n=177)$		
Once a day	28	15.8
2–3 times day	56	31.6
4–5 times a day	24	13.6
Six or more times a day	16	9.0
1–2 times a week	18	10.2
3–5 times a week	19	10.7
Less than weekly	11	6.2
Very rarely	5	2.8

<sup>&</sup>lt;sup>a</sup>Multiple options allowed.

(19%) were able to reduce a medication but by less than half T3 of the total dose (Table 3). Of the medications that were completely stopped, 66% were considered to be analgesics. The most common class of medication stopped was opioids (40%), followed by NSAIDs (17%), antidepressants (16%), and benzodiazepines (15%). Similar trends were seen in medication reduction where opiates (33%) and NSAIDs (16%) were the most common classes of medication reduced by at least half. Paracetamol was the most common medication (41%) that was able to be reduced by less than half. Only two respondents reported using metformin, consistent with our assumption that most respondents were using cannabis for endometriosis rather than PCOS symptoms.

TABLE 3. CANNABIS USAGE AND MEDICATION

	n	%
If you experience any undesirable effects from		
cannabis, how does this compare with any		
undesirable effects from your usual medication?		
Much better	60	28.2
Somewhat better	25	11.7
No effect	7	3.3
Somewhat worse	5	2.3
Much worse	0	0.0
I have no undesirable effects from cannabis	74	34.7
I have no undesirable effects from my usual medication	5	2.3
I have not tried any/many other medications	2	0.9
Overall, how does (or did) cannabis compare with you medicines in giving you relief from your condition		er
Other medicines work much better than cannabis	0	0.0
Other medicines work a bit better than cannabis	8	3.8
Other medicines work about the same as cannabis	15	7.0
Cannabis works a bit better than other medicines	22	10.3
Cannabis works much better than other medicines	84	39.4
Only cannabis gives me relief from my condition	49	23.0

#### **Discussion**

This survey data demonstrate that cannabis was being used by endometriosis sufferers in New Zealand, despite illegalities at the time of the survey. Cannabis, most commonly inhaled via a pipe, joint, or bong, was considered by our respondents with endometriosis and/or PCOS to be very effective for the management of their symptoms especially in regard to pain, sleep, and gastrointestinal symptoms. The use of cannabis also allowed respondents to cease or reduce their usage of other medications, particularly opiate and NSAID analgesics.

A key strength to this study is that our respondents were fairly representative of New Zealand demographics based on recent census<sup>22</sup> and government data,<sup>23</sup> with some notable exceptions. Respondents in 14 of the 16 regions were within 5% of the estimated 2019 population of that region,<sup>24</sup> with Auckland underrepresented (19.7% in our sample and 33.4% in the wider population) and Canterbury overrepresented (18.8% in our sample and 12.8% in the wider population). Participants identifying as New Zealand European and/or Māori are overrepresented in the sample in comparison with the New Zealand population 2018 census data (84.1% vs. 70.2%, and 23.9% vs. 16.5%, in our sample, and in the wider population, respectively). While the Māori are more likely to have used cannabis medicinally than the non-Māori, their recreational use is significantly greater than therapeutic use.<sup>25</sup> The greater magnitude of recreational use for Māori is also noted in recent government data, <sup>26</sup> twice that (32% vs. 15.5%) of non-Māori, and even more pronounced when comparing Māori women with non-Māori women (OR 2.46). ◀AU11 Thus, while Māori comprise 23.9% of the present sample, this is less than what would be anticipated for recreational use. Finally, respondents had a slightly higher unemployment rate, with 56% of our respondents working compared with 63% of New Zealand women. <sup>27</sup> This may reflect the negative impact that endometriosis often has on employment. <sup>10,28</sup> This assumption is supported by the fact that our sample of medicinal users has a much lower employment rate than recreational cannabis users (67.4%) in New Zealand.<sup>25</sup>

#### AU1 ► ILLICIT CANNABIS USAGE IN NEW ZEALAND WOMEN WITH ENDOMETRIOSIS

There were important limitations. First, all data, including diagnosis, was self-reported, and therefore, it is possible that those without a confirmed diagnosis of endometriosis may be included. All benefits and harms were likewise selfreported and it is possible that those who had negative experience with cannabis may not have answered this survey, given it was promoted via a cannabis patient advocacy group. These findings thus may not be extrapolated to wider populations. Second, the survey asked participants whether they had PCOS and/or endometriosis in a single question and it was, therefore, not possible to guarantee that all individuals examined in the current study had endometriosis. However, considering pain or nausea, the two-most commonly treated symptoms are not symptoms of PCOS<sup>29</sup> but are of endometriosis<sup>6,9</sup> and that only two people indicated they were using metformin (a key medication in the management of PCOS<sup>30</sup>), suggesting that the majority of people in this sample were likely experiencing endometriosisrelated symptoms.

Substantial evidence already exists for the use of cannabis or cannabinoids in other chronic pain conditions. 31-33 Cannabis was reported to significantly improve pain, sleep, and nausea and vomiting in people with endometriosis in both New Zealand and in our previous work in Australia. 19 Similar to our previous study on Australian women with endometriosis, 19 cannabis was being used despite a lack of access to legal, medicinal cannabis. Most respondents were regular users whose use depended on their symptoms, with almost a third being long-term users of more than 10 years. Selfreported side effects, especially in comparison with their current medications, were low, with a third of users reporting no side effects at all. However, a small number of previous users indicated that undesirable side effects led to their cessation of cannabis usage. The number of comorbid symptoms in our respondents is not unusual, as depression, anxiety, chronic fatigue syndrome, IBS, and migraines are common, with around 95% of all women diagnosed with endometriosis experiencing at least one comorbidity.34 Respondents reported clear evidence of a substitution effect, where the use of cannabis reduced or replaced other pharmaceutical medications, 16 especially with respect to opioid-based analgesics, and also to other medications commonly used in the management of endometriosis-related symptoms, 16 such as antidepressants, benzodiazepines, and NSAIDs. The preferred administration route in both populations was inhalation (inclusive of smoked and vaporized forms), with 67.8% of New Zealand and 61.9% of Australian respondents utilizing this method of administration. These findings are consistent with outcomes from other studies conducted in Australia and internationally. 20,35 Whether this is due to lack of sophistication in administration methods in illicit markets, or perhaps consequent upon a more rapid onset of effect commonly observed via inhaled routes, is currently unknown.<sup>36</sup> Emerging evidence of the substitution effect of cannabis is increasing in the scientific literature <sup>37–40</sup> and reports of deprescribing trends are common, particularly for drugs of the opioid class<sup>34,41</sup> similar to the findings in the current survey. The reduction in pharmaceutical medications by our respondents, with 59% reporting being able to cease a medication and 45% being able to reduce medication by at least 50%, reflects similar trends to our previous study on cannabis usage in Australian women. In the Australian study, 19 56% of the cannabis-using cohort self-reported significant reductions (defined as 50% or more reduction) in pharmaceutical medication use. There were also similarities between the New Zealand cohort and Canadian data on patients using medicinal cannabis. <sup>41</sup> Canadian patients self-reported substituting opioids with cannabis (35%), with 59% reporting total cessation of opioid use and 18% reducing opioid use by 75% <sup>41</sup>; further substitutions of cannabis were reported for antidepressants (21%), nonopioid pain medications (10%), and benzodiazepines (4%). Similar substitution effects were also observed in an earlier survey of patients registered to purchase medicinal cannabis from a Canadian Licensed Producer, with cannabis being substituted for opioids (32%), benzodiazepines (16%), and antidepressants (12%). <sup>34</sup>

There are some differences apparent in this population compared with those previously studied. Total oral consumption of cannabis (oils, edible, *etc.*) was notably higher in the New Zealand data (27.7%) compared with Australian (11.9%). Cannabis use was more frequent in the New Zealand sample, with 70% of New Zealand respondents reporting cannabis use daily or multiple times per day compared with 43.7% of Australian respondents. In addition, a higher proportion of Australian women (25%) reported requiring cannabis less than once per week compared with those from New Zealand (6.2%).

Understanding the relative risks and/or benefits of these substitutions is complex, particularly as our data demonstrate that the type and dosage of cannabis used, and the route of application, vary widely in the community. Opioids account for over 30 unintentional overdose deaths per annum reported in New Zealand, 42 with risks exacerbated where opioids are combined with benzodiazepines.<sup>43</sup> There is no doubt that improved pain relief options are needed for endometriosis patients.<sup>44</sup> Various phytochemicals (mainly cannabinoids) from Cannabis spp. have well-described analgesic, antiinflammatory, anxiolytic, antidepressant, and antiemetic actions<sup>31,45–49</sup> and provide a plausible mechanism of action for the improvement of these symptoms via the endocannabinoid system (ECS) and other receptor types. 50 Our understanding of the mechanisms associated with endometriosis pain is still limited,<sup>51</sup> and the effectiveness of different pharmaceutical analgesics and hormonal methods of pain control is highly variable 14 with high discontinuation rates. 15 In light of these well-known risks and side effects of current analgesics, it is easy to understand why cannabis may be considered a panacea for the management of endometriosis symptoms. However, cannabis usage is not without risks. General areas of concern include early initiation of use, that is, before age 18, being associated with mental ill-health, particularly in vulnerable populations<sup>52,53</sup>; dependence,<sup>5</sup> including heightened risk with higher potency cannabis.<sup>55</sup> There are also risks associated with driving and operating machinery while impaired, described as mild to moderate, 56 although increasing with dose<sup>57</sup> and more so in combination with alcohol.<sup>58</sup> While concerns are commonly raised concerning cannabis inhalation, including pulmonary and bronchial problems, particularly associated with intensity of use, these may be reversible following cessation.<sup>59</sup> Interestingly, however, findings are more equivocal for other respiratory diseases, including lung cancer, <sup>60</sup> with confounding effects of tobacco use being problematic. <sup>61</sup> Recognizing that cannabis use, including for therapeutic purposes, is unlikely to

diminish, a recent review has proposed lower risk cannabis use guidelines and recommendations. These recommendations range from abstinence where possible to delayed initiation of use, use of lower potency products, lower intensity, and frequency of use. It is also suggested that combusted cannabis inhalation is avoided in favor of edibles and vaporizers, with evidence showing improvements in acute symptoms with their use, <sup>63</sup> although currently, evidence based on long-term studies is lacking. <sup>64</sup>

#### **Conclusions**

Cannabis, both medical and illicit, is being used in New Zealand and internationally as a self-management tool and is reported to effectively relieve symptoms of endometriosis, including pain, sleep, and nausea. Cannabis appears to be preferred by respondents in this series to other pharmaceuticals such as opioids. Self-reported community data, such as these, add to the growing body of evidence that medicinal cannabis may be a potentially effective part of a multidisciplinary toolkit to manage the symptoms of endometriosis and support reduction of other classes of medication, including opioids. However, well-designed, blinded randomized trials are needed to determine the short- and long-term safety and effectiveness of various dosages and modes of administration of legally available cannabis.

#### **Acknowledgments**

We wish to acknowledge those participating in the online survey, many of whom provided information on activities that at the time of the survey were illegal.

We acknowledge the support of Medicinal Cannabis Awareness New Zealand (MCANZ) and particularly its coordinator at the time of the survey, Mr. Shane Le Brun.

#### Availability of Data and Materials

The data sets generated and/or analyzed during the current study are available from the corresponding author on reasonable request.

#### **Authors' Contributions**

All authors contributed significantly to this work. M.A., J.S., G.N., M.L., J.G., D.B., and N.J. conceptualized the study. G.N. and M.L. designed the survey. G.N. and M.L. performed the data collection and cleaned the data. M.A., M.L., and M.A.A.-D. performed the statistical analysis. M.A., J.S., N.J., E.H., and J.G. assisted with data interpretation. M.A. and J.S. drafted the article. G.N., M.L., J.G., E.H., D.B., N.J., and M.A.A.-D. contributed to critical revisions on the articles. All authors reviewed the article and approved the final draft.

#### **Ethics Approval and Consent to Participate**

The study was approved by the New Zealand National Health and Disability Ethics Committees (HDEC; reference: 19/CEN/54). Consent was by online access only, with participants being required to acknowledge they were 18 years or older, that they had read and understood the participant information sheet, before accessing the online questionnaire itself, and that they were able to provide informed consent.

#### **Author Disclosure Statement**

G.N. received funding from Medicinal Cannabis Awareness New Zealand (MCANZ), a not-for-profit registered charitable trust and medicinal cannabis patient advocacy group. M.A., M.A.A.-D., and J.S. as a medical research institute, NICM Health Research Institute receives research grants and donations from foundations, universities, government agencies, and industry. Sponsors and donors provide untied and tied funding for work to advance the vision and mission of the institute. This study was not specifically supported by donor or sponsor funding to NICM. M.A. is a member of the clinical advisory board for Endometriosis Australia and ESIG member for Endometriosis NZ.

#### **Funding Information**

No funding was received for this article.

#### **Supplementary Material**

Supplementary Table S1

#### References

- Hickey M, Ballard K, Farquhar C. Endometriosis. BMJ 2014;348:g1752.
- Johnson NP, Hummelshoj L, Adamson GD, et al. World Endometriosis Society consensus on the classification of endometriosis. Hum Reprod 2017;32:315–324.
- Global Burden of Disease Study2013 Collaborators. Global, regional, and national incidence, prevalence, and years lived with disability for 301 acute and chronic diseases and injuries in 188 countries, 1990–2013: A systematic analysis for the Global Burden of Disease Study 2013. Lancet 2015; 386:743–800.
- Vigano P, Parazzini F, Somigliana E, Vercellini P. Endometriosis: Epidemiology and aetiological factors. Best Pract Res Clin Obstet Gynaecol 2004;18:177–200.
- Australian Institute of Health and Welfare. Endometriosis in Australia: Prevalence and hospitalisations. Canberra: 2019.
- Zondervan KT, Becker CM, Missmer SA. Endometriosis. N Engl J Med 2020;382:1244–1256.
- 7. Markham R, Luscombe GM, Manconi F, Fraser IS. A detailed profile of pain in severe endometriosis. J Endometr Pelvic Pain Disord 2019;11:85–94.
- Ramin-Wright A, Schwartz ASK, Geraedts K, et al. Fatigue—A symptom in endometriosis. Hum Reprod 2018; 33:1459–1465.
- Moore JS, Gibson PR, Perry RE, Burgell RE. Endometriosis in patients with irritable bowel syndrome: Specific symptomatic and demographic profile, and response to the low FODMAP diet. Aust N Z J Obstet Gynaecol 2017;57:201–205.
- Nnoaham KE, Hummelshoj L, Webster P, et al. Impact of endometriosis on quality of life and work productivity: A multicenter study across ten countries. Fertil Steril 2011;96: 366–373.e8.
- Sepulcri Rde P, do Amaral VF. Depressive symptoms, anxiety, and quality of life in women with pelvic endometriosis. Eur J Obstet Gynecol Reprod Biol 2009;142:53–56.
- Pluchino N, Wenger JM, Petignat P, et al. Sexual function in endometriosis patients and their partners: Effect of the disease and consequences of treatment. Hum Reprod Update 2016;22:762–774.

#### AUI > ILLICIT CANNABIS USAGE IN NEW ZEALAND WOMEN WITH ENDOMETRIOSIS

- AU12 ▶ 13. Leonardi M, Gibbons T, Armour M, et al. When to do surgery and when not to do surgery for endometriosis: A systematic review and meta-analysis. J Minim Invasive Gynecol 2020;27:390–407.e3.
  - Brown J, Farquhar C. Endometriosis: An overview of Cochrane Reviews. Cochrane Database Syst Rev 2014;2014: CD009590.
  - 15. Sinaii N, Cleary SD, Younes N, Ballweg ML, Stratton P. Treatment utilization for endometriosis symptoms: A cross-sectional survey study of lifetime experience. Fertil Steril 2007;87:1277–1286.
  - Lamvu G, Soliman AM, Manthena SR, Gordon K, Knight J, Taylor HS. Patterns of prescription opioid use in women with endometriosis: Evaluating prolonged use, daily dose, and concomitant use with benzodiazepines. Obstet Gynecol 2019;133:1120–1130.
  - Australian Institute of Health and Welfare. Opioid harm in Australia: And comparisons between Australia and Canada. Canberra: 2018.
  - Armour M, Sinclair J, Chalmers KJ, Smith CA. Selfmanagement strategies amongst Australian women with endometriosis: A national online survey. BMC Complement Altern Med 2019;19:17.
  - Sinclair J, Smith CA, Abbott J, Chalmers KJ, Pate DW, Armour M. Cannabis use, a self-management strategy among Australian women with endometriosis: Results from a national online survey. J Obstet Gynaecol Can 2020;42: 256–261.
  - Lintzeris N, Driels J, Elias N, Arnold JC, McGregor IS, Allsop DJ. Medicinal cannabis in Australia, 2016: The Cannabis as Medicine Survey (CAMS-16). Med J Aust 2018;209:211–216.
  - Dworkin RH, Turk DC, Farrar JT, et al. Core outcome measures for chronic pain clinical trials: IMMPACT recommendations. Pain 2005;113:9–19.
- AU13 ► 22. Stats NZ. Ethnicity, culture and identify: Ethnicity, 2018. Available at: https://www.stats.govt.nz/tools/2018-census-place-summaries/new-zealand?gclid=Cj0KCQjwtLT1BRD 9ARIsAMH3BtXKUnpGSv0wzD7CZ9rM4bjZHFShWOn KPUdnRVEnLvLdiWU6X5PvzOYaApBVEALw\_wcB# identity
  - Stats NZ. Household income and housing-cost statistics: Year ended June 2018, 2018. Available at: https://www.stats.govt.nz/information-releases/household-income-and-housing-cost-statistics-year-ended-june-2018
  - 24. Stats NZ. Subnational population estimates: At 30 June 2019 (provisional): Subnational population estimates: At 30 June 2019—CSV, 2019. Available at: https://www.stats.govt.nz/information-releases/subnational-population-estimates-at-30-june-2019-provisional
  - 25. Pledger M, Martin G, Cumming J. New Zealand Health Survey 2012/13: Characteristics of medicinal cannabis users. N Z Med J 2016;129:25–36.
- AU14 ▶ 26. New Zealand Ministry of Social Development. All main benefits—December 2019 quarter. 2019.
  - Stats NZ. Labour market statistics: June 2019 quarter: Employment rate. 2019.
  - Armour M, Lawson K, Wood A, Smith CA, Abbott J. The cost of illness and economic burden of endometriosis and chronic pelvic pain in Australia: A national online survey. PLoS One 2019;14:e0223316.
  - Hart R, Hickey M, Franks S. Definitions, prevalence and symptoms of polycystic ovaries and polycystic ovary syndrome. Best Pract Res Clin Obstet Gynaecol. 2004;18:671–683.

- Johnson NP. Metformin use in women with polycystic ovary syndrome. Ann Transl Med 2014;2:56.
- National Academies of Sciences, Engineering and Medicine. The health effects of cannabis and cannabinoids: The current state of evidence and recommendations for research. Washington, DC: The National Academies Press, 2017.
- 32. Martin-Sanchez E, Furukawa TA, Taylor J, Martin JL. Systematic review and meta-analysis of cannabis treatment for chronic pain. Pain Med 2009;10:1353–1368.
- Ware MA, Wang T, Shapiro S, et al. Smoked cannabis for chronic neuropathic pain: A randomized controlled trial. CMAJ 2010;182:E694–E701.
- 34. Lucas P, Walsh Z. Medical cannabis access, use, and substitution for prescription opioids and other substances: A survey of authorized medical cannabis patients. Int J Drug Policy 2017;42:30–35.
- Sexton M, Cuttler C, Finnell JS, Mischley LK. A Crosssectional survey of medical cannabis users: Patterns of use and perceived efficacy. Cannabis Cannabinoid Res 2016;1: 131–138.
- Grotenhermen F. Pharmacokinetics and pharmacodynamics of cannabinoids. Clin Pharmacokinet 2003;42:327–360.
- 37. Reiman A, Welty M, Solomon P. Cannabis as a substitute for opioid-based pain medication: Patient self-report. Cannabis Cannabinoid Res 2017;2:160–166.
- Lucas P. Cannabis as an adjunct to or substitute for opiates in the treatment of chronic pain. J Psychoact Drugs 2012; 44:125–133.
- Bachhuber MA, Saloner B, Cunningham CO, Barry CL. Medical cannabis laws and opioid analgesic overdose mortality in the United States, 1999–2010. JAMA Intern Med 2014;174:1668–1673.
- Reiman A. Cannabis as a substitute for alcohol and other drugs. Harm Reduct J 2009;6:35.
- 41. Lucas P, Baron EP, Jikomes N. Medical cannabis patterns of use and substitution for opioids & other pharmaceutical drugs, alcohol, tobacco, and illicit substances; results from a cross-sectional survey of authorized patients. Harm Reduct J 2019;16:9.
- 42. Shipton EE, Shipton AJ, Williman JA, Shipton EA. Deaths from opioid overdosing: Implications of coroners' inquest reports 2008–2012 and annual rise in opioid prescription rates: A population-based cohort study. Pain Ther 2017;6: 203–215.
- 43. Deering DEA, Adamson SJ, Sellman JD, et al. Potential risk for fatal drug overdose perceived by people using opioid drugs. Drug Alcohol Rev 2018;37(S1):S309–S313.
- 44. As-Sanie S, Black R, Giudice LC, et al. Assessing research gaps and unmet needs in endometriosis. Am J Obstet Gynecol 2019;221:86–94.
- Aggarwal SK. Cannabinergic pain medicine: A concise clinical primer and survey of randomized-controlled trial results. Clin J Pain 2013;29:162–171.
- 46. Rahn EJ, Hohmann AG. Cannabinoids as pharmacotherapies for neuropathic pain: From the bench to the bedside. Neurotherapeutics 2009;6:713–737.
- Burstein S. Cannabidiol (CBD) and its analogs: A review of their effects on inflammation. Bioorg Med Chem 2015;23: 1377–1385.
- Bolognini D, Costa B, Maione S, et al. The plant cannabinoid Delta9-tetrahydrocannabivarin can decrease signs of inflammation and inflammatory pain in mice. Br J Pharmacol 2010;160:677–687.

49. Zanelati TV, Biojone C, Moreira FA, Guimaraes FS, Joca SR. Antidepressant-like effects of cannabidiol in mice: Possible involvement of 5-HT1A receptors. Br J Pharmacol 2010;159:122–128.

- Bouaziz J, Bar On A, Seidman DS, Soriano D. The clinical significance of endocannabinoids in endometriosis pain management. Cannabis Cannabinoid Res 2017;2:72–80.
- Coxon L, Horne AW, Vincent K. Pathophysiology of endometriosis-associated pain: A review of pelvic and central nervous system mechanisms. Best Pract Res Clin Obstet Gynaecol 2018;51:53–67.
- 52. Caspi A, Moffitt TE, Cannon M, et al. Moderation of the effect of adolescent-onset cannabis use on adult psychosis by a functional polymorphism in the catechol-Omethyltransferase gene: Longitudinal evidence of a gene X environment interaction. Biol Psychiatry 2005;57:1117– 1127.
- 53. Fergusson DM, Boden JM. Cannabis use and later life outcomes. Addiction 2008;103:969–976.
- 54. Budney JA, Hughes RJ. The cannabis withdrawal syndrome. Curr Opin Psychiatry 2006;19:233–238.
- Freeman TP, Winstock AR. Examining the profile of highpotency cannabis and its association with severity of cannabis dependence. Psychol Med 2015;45:3181–3189.
- Asbridge M, Hayden J, Cartwright J. Acute cannabis consumption and motor vehicle collision risk: Systematic review of observational studies and meta-analysis. BMJ 2012;344:e536.
- 57. Asbridge M, Mann R, Cusimano M, et al. Cannabis and traffic collision risk: Findings from a case-crossover study of injured drivers presenting to emergency departments. Int J Public Health 2014;59:395–404.

- 58. Dubois S, Mullen N, Weaver B, Bédard M. The combined effects of alcohol and cannabis on driving: Impact on crash risk. Forensic Sci Int 2015;248:94–100.
- Hancox RJ, Shin HH, Gray AR, Poulton R, Sears MR. Effects of quitting cannabis on respiratory symptoms. Eur Respir J 2015;46:80–87.
- Martinasek MP, McGrogan JB, Maysonet A. A systematic review of the respiratory effects of inhalational marijuana. Respir Care 2016;61:1543.
- Zhang LR, Morgenstern H, Greenland S, et al. Cannabis smoking and lung cancer risk: Pooled analysis in the International Lung Cancer Consortium. Int J Cancer 2015; 136:894–903.
- 62. Fischer B, Russell C, Sabioni P, van den Brink W, Foll BL. Lower-risk cannabis use guidelines: A comprehensive update of evidence and recommendations (Author abstract). Am J Public Health 2017;107:e1.
- 63. Earleywine M, Van Dam NT. Case studies in cannabis vaporization. Addict Res Theory 2010;18:243–249.
- 64. Loflin M, Earleywine M. No smoke, no fire: What the initial literature suggests regarding vapourized cannabis and respiratory risk. Can J Respir Ther 2015;51:7–9.

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