

UK Medical Cannabis Registry: An Analysis of Clinical Outcomes of Medicinal Cannabis Therapy for Cancer Pain

Madhur Varadpande^{1*}, Simon Erridge^{1,2}, Arushika Aggarwal¹, Isaac Cowley¹, Lilia Evans¹, Evonne Clarke², Katy McLachlan², Ross Coomber^{2,3}, James J Rucker^{2,4,5}, Michael W Platt², Shaheen Khan^{2,6}, Mikael Sodergren^{1,2}

1. Medical Cannabis Research Group, Imperial College London, London, UK 2. Curaleaf Clinic, London, UK 3. St George’s NHS Trust, London, UK 4. Department of Psychological Medicine, Kings College London, London, UK 5. South London & Maudsley NHS Foundation Trust, London, UK 6. Guy’s & St. Thomas’ NHS Foundation Trust, London, UK *Presenting author

Introduction

Cancer pain is a prevalent condition, affecting 44.5% of cancer patients, with limited pharmacotherapeutic options^{1,2}. Pre-clinical studies have shown that cannabinoids and terpenes can affect the transmission of nociceptive signals, as well as the emotional and cognitive manifestations of pain^{3,4}. However, the efficacy of cannabis-based medicinal products (CBMPs) in cancer pain remains contentious⁵. This study aims to evaluate the change in patient-reported outcome measures (PROMs) and adverse events (AEs) associated with CBMPs prescribed for cancer pain patients.

Methods

Study Design: Case series using prospectively collected clinical data from the UK Medical Cannabis Registry. The primary outcome was the changes in PROMs from baseline to follow-up at 1, 3 and 6 months. The secondary outcome was the incidence of adverse events. Analysis included a repeated measures ANOVA, post-hoc multiple pairwise comparisons with Bonferroni correction. Logistic regression was also conducted. p<0.050 was considered statistically significant.

Results

- One hundred and sixty-eight participants were included (Image 3).
- Primary Outcome:** CBMPs were associated with improvements in all pain-specific PROMs at all follow-up periods (p<0.050) (Table 1). Improvements in GAD-7, SQS, and EQ-5D-5L index scores were also observed (p<0.050) (Table 2). Multivariable logistic regression found higher tetrahydrocannabinol (THC) doses as a predictor of achieving a clinically significant response on the BPI-Severity scale (odds ratio = 9.72; 95% confidence interval: 1.54-61.51; p=0.016). Administering CBMPs as combined oils and dry flower was associated with an increased likelihood of clinically significant change on the BPI-Interference scale only (odds ratio = 5.81; 95% confidence interval: 1.09-30.85; p=0.039).
 - Secondary outcome:** Twenty-nine AEs (17.26%) were reported by five patients (2.98%), mostly mild-to-moderate (72.41%) (Image 2).

CBMPs: Most patients administered CBMPs as oils only at baseline (n=133, 79.17%) and at 6 months (n=115, 68.45%). Median CBD dose increased from 21.00 [20.00-40.00] milligrams/day at baseline to 40.00 [20.00-40.00] milligrams/day at 1 month follow-up and remained stable thereafter. Median THC dose increased, from 4.20 [2.15-5.15] milligrams/day at baseline to 14.60 [8.20-100.90] milligrams/day at 6 months.

Discussion

Initiation of CBMPs was associated with improved pain-specific and general health-related outcomes in cancer pain patients over six months, with a favorable safety profile. However, the observational design means causality cannot be established. The observational design means causality cannot be established. Through multivariable logistic regression analysis, this study highlighted that individuals prescribed higher doses of THC and a combination of oils and flower were associated with clinically significant changes in pain severity and interference, respectively. This may inform the optimum products to study in randomized controlled trials in cancer pain, considering the heterogeneity of potential products.

Image 1 – Comparison of mean pain-specific PROMS from baseline to follow-up at 1, 3 and 6 months.

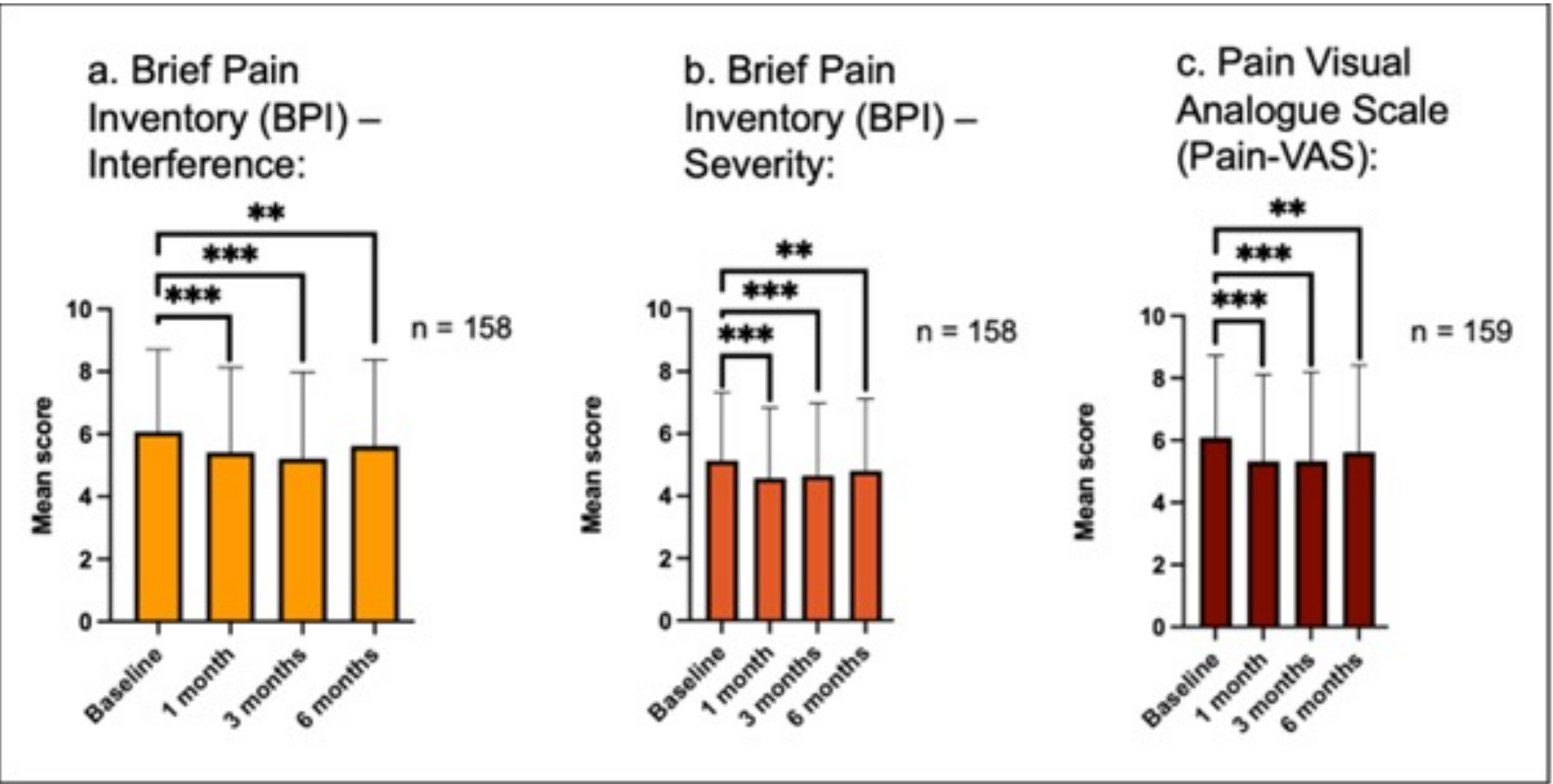
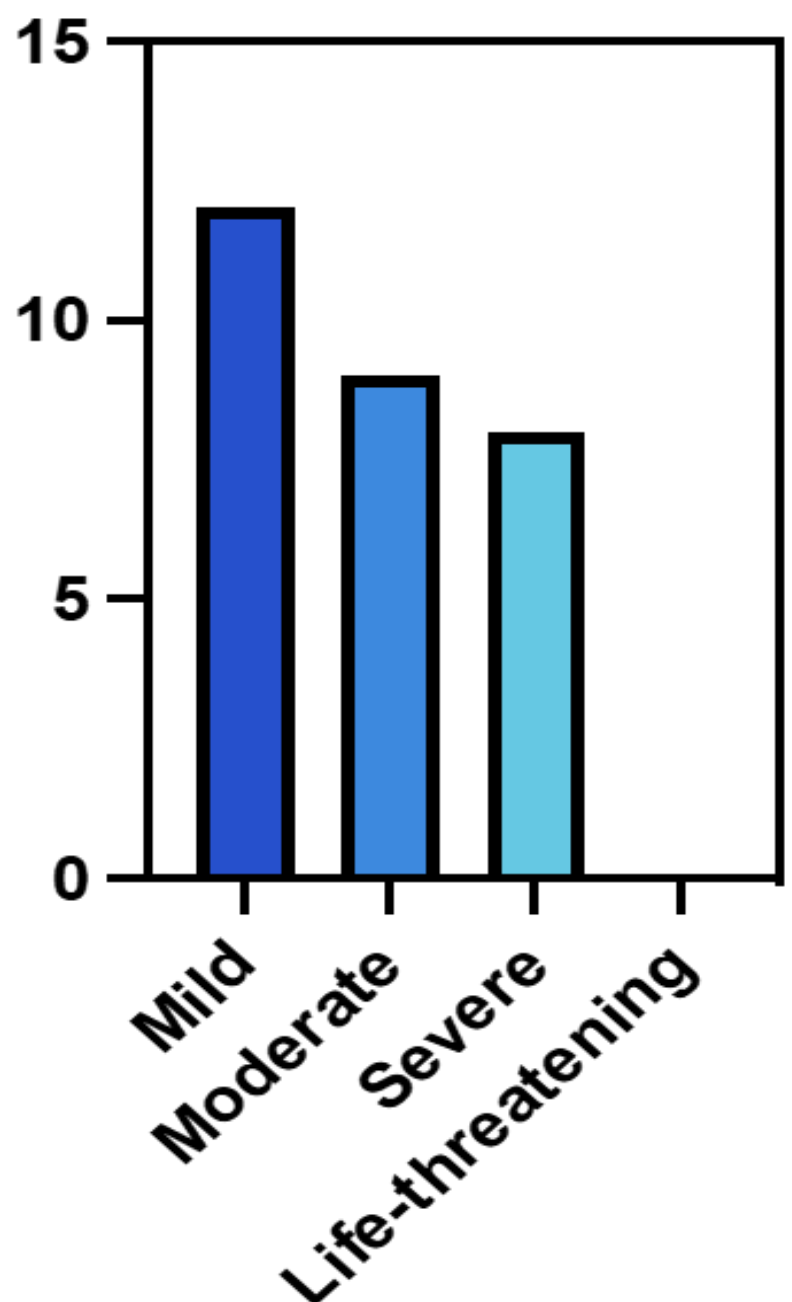


Image 2 – A bar graph illustrating the frequency of mild, moderate, severe and life-threatening adverse events reported by participants in this study.



Twelve adverse events (AEs) were classed as mild severity (41.38%), nine as moderate (31.03%), and eight as severe (16.41%), with no life-threatening events reported.

The mean duration of all AEs was 6.93 ± 5.04 days.

The most common AEs were fatigue (n=3) and lethargy (n=3). Severe AEs included insomnia (n=2), constipation (n=1), vomiting (n=1), anorexia (n=1), dyspepsia (n=1), fatigue (n=1) and nausea (n=1)

Cannabis-based medicinal products were associated with improved pain-specific and general-health related outcomes over 6 months, with a favorable safety profile.

Table 1 – Mean pain-specific PROMS at baseline and follow-up at 1,3 and 6 months

Patient-reported outcome measure	Mean baseline score ± S.D.	n	Follow-Up (months)	n	Mean difference from baseline ± S.D.	p-value
Brief Pain Inventory Interference	6.08 ± 2.62	158	1	158	-0.67 ± 0.17	< 0.001***
			3	158	-0.87 ± 0.17	< 0.001***
			6	158	-0.46 ± 0.14	0.007**
Brief Pain Inventory Severity	5.14 ± 2.18	158	1	158	-0.57 ± 0.12	< 0.001***
			3	158	-0.49 ± 0.12	< 0.001***
			6	158	-0.33 ± 0.10	0.006**
Visual Analogue Scale - Pain	6.09 ± 2.64	159	1	159	-0.77 ± 0.16	< 0.001***
			3	159	-0.76 ± 0.17	< 0.001***
			6	159	-0.48 ± 0.13	0.003**

Table 2 – Mean general health-related PROMS at baseline and follow-up at 1,3 and 6 months

Patient-reported outcome measure	Mean baseline score ± S.D.	n	Follow-Up (months)	n	Mean difference from baseline ± S.D.	p-value
EQ-5D-5L Index Values	0.34 ± 0.35	167	1	167	0.12 ± 0.02	<0.001***
			3	167	0.11 ± 0.02	<0.001***
			6	167	0.06 ± 0.02	<0.001***
Generalized Anxiety Disorder scale	10.09 ± 6.76	168	1	168	-2.67 ± 0.42	< 0.001***
			3	168	-1.95 ± 0.35	< 0.001***
			6	168	-1.27 ± 0.29	< 0.001***
Single-Item Sleep Quality Scale	3.90 ± 2.38	166	1	166	1.31 ± 0.19	< 0.001***
			3	166	0.98 ± 0.17	< 0.001***
			6	166	0.73 ± 0.14	< 0.001***

Image 3 – Flowchart summarising study inclusion and exclusion criteria.

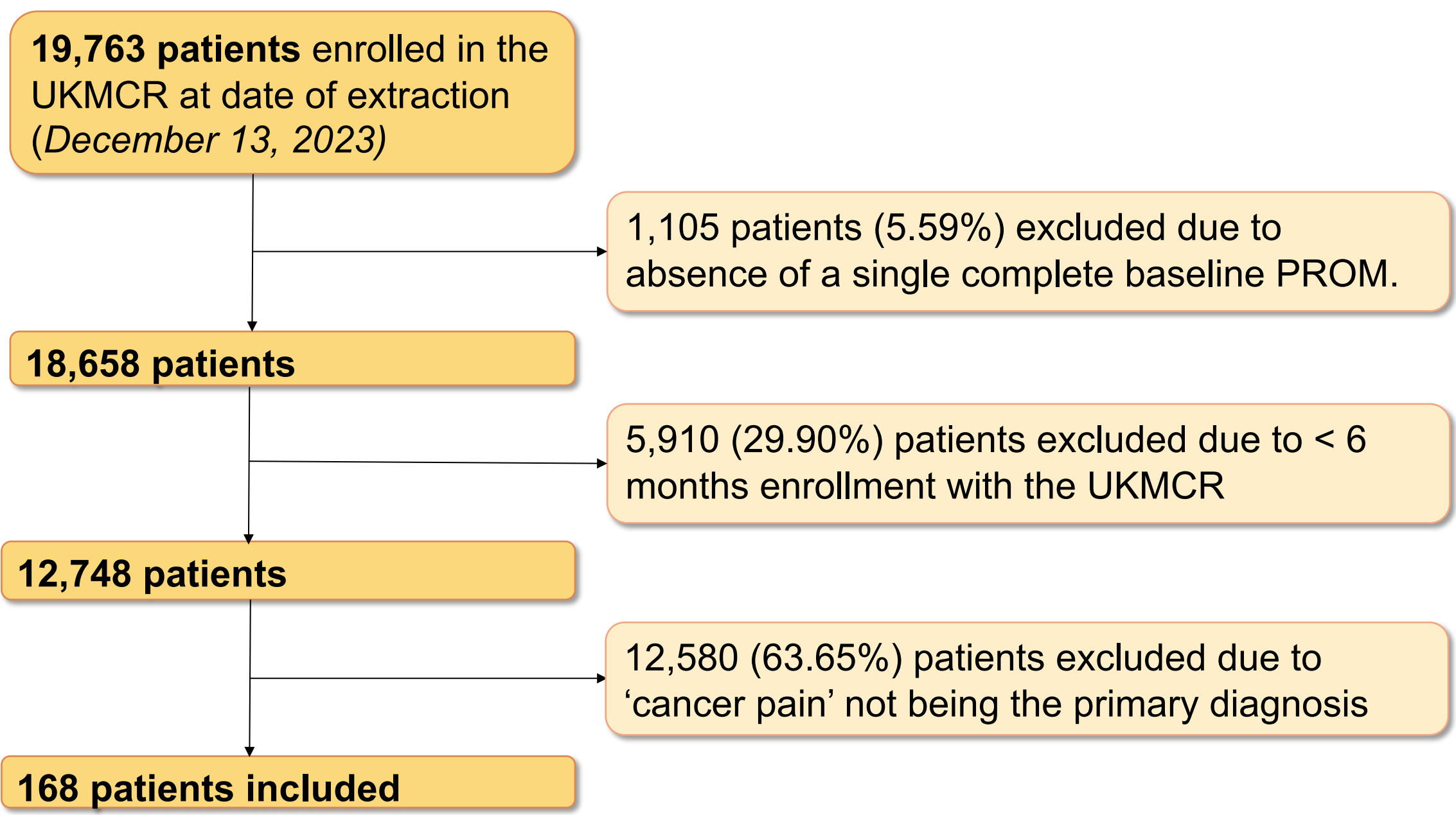


Table 3 – Summary of patient baseline demographic data.

Baseline Demographics	n (%) / mean ± S.D. / median [IQR]
Male	102 (60.71)
Female	66 (39.29)
Age (years)	54.20 ± 14.64
Body mass index (kg/m²)	25.48 ± 5.78
Charlson Comorbidity Index	8.00 [6.00 - 11.00]
Cannabis Status:	
Current user	69 (41.07)
Ex-user	28 (16.67)
Never used	71 (42.26)

References

- (1) Snijders RAH, Brom L, Theunissen M, van den Beuken-van Everdingen, Marieke H J. Update on Prevalence of Pain in Patients with Cancer 2022: A Systematic Literature Review and Meta-Analysis. *Cancers*. 2023; 15 (3): 591. 10.3390/cancers15030591.
- (2) Wiffen PJ, Wee B, Derry S, Bell RF, Moore RA. Opioids for cancer pain - an overview of Cochrane reviews. *Cochrane Database of Systematic Reviews*. 2017; 2020 (2): 10.1002/14651858.CD012592.pub2.
- (3) Anand U, Anand P, Sodergren MH. Terpenes in Cannabis sativa Inhibit Capsaicin Responses in Rat DRG Neurons via Na+/K+ ATPase Activation. *International Journal of Molecular Sciences*. 2023; 24 (22): 16340. 10.3390/ijms242216340.
- (4) Nielsen S, Picco L, Murnion B, Winters B, Matheson J, Graham M, et al. Opioid-sparing effect of cannabinoids for analgesia: an updated systematic review and meta-analysis of preclinical and clinical studies. *Neuropsychopharmacology: Official Publication of the American College of Neuropsychopharmacology*. 2022; 47 (7): 1315-1330. 10.1038/s41386-022-01322-4.
- (5) Wang L, Hong PJ, May C, Rehman Y, Oparin Y, Hong CJ, et al. Medical cannabis or cannabinoids for chronic non-cancer and cancer related pain: a systematic review and meta-analysis of randomised clinical trials. *BMJ*. 2021; n1034. 10.1136/bmj.n1034.

Ethics

The UK Medical Cannabis Registry has received favourable ethical opinion from Central Bristol Research Ethics Committee (22/SW/0145)

Conflicts of Interest

All authors are employed or work on a contractual basis with Curaleaf Clinic