**Supplementary Data**

**Supplementary table 1. Patient indications for treatment with cannabis-based medicinal products**. Clinicians diagnosed patients with indications prior to receiving a CBMP prescription. PTSD = post-traumatic stress disorder.

|  |  |
| --- | --- |
|  | **Diagnosis, n (%)** |
| **Condition** | **Primary** | **Secondary** | **Tertiary** |
| Chronic Non-Cancer Pain | 602 (56.3) | 25 (2.3) | 2 (0.2) |
| Neuropathic Pain | 126 (11.8) | 43 (4.0) | 2 (0.2) |
| Ehlers-Danlos | 30 (2.8) | 17 (1.6) | 8 (0.7) |
| Complex regional pain syndrome | 3 (0.3) | 3 (0.3) | 1 (0.09) |
| Fibromyalgia | 0 (0.0) | 58 (5.4) | 8 (0.7) |
| Anxiety | 0 (0.0) | 46 (4.3) | 8 (0.7) |
| Insomnia | 0 (0.0) | 10 (0.9) | 6 (0.6) |
| Depression | 0 (0.0) | 8 (0.7) | 18 (1.7) |
| Migraine | 0 (0.0) | 7 (0.7) | 4 (0.4) |
| Headache | 0 (0.0) | 4 (0.4) | 2 (0.2) |
| PTSD | 0 (0.0) | 3 (0.3) | 4 (0.4) |
| Autistic spectrum disorder | 0 (0.0) | 3 (0.3) | 3 (0.3) |
| Crohn’s disease | 0 (0.0) | 3 (0.3) | 2 (0.2) |
| Cancer pain | 0 (0.0) | 2 (0.2) | 0 (0.0) |
| Multiple sclerosis | 0 (0.0) | 2 (0.2) | 0 (0.0) |
| Parkinson’s disease | 0 (0.0) | 2 (0.2) | 0 (0.0) |
| Attention deficit hyperactivity disorder | 0 (0.0) | 1 (0.09) | 1 (0.09) |
| Agoraphobia | 0 (0.0) | 1 (0.09) | 0 (0.0) |
| Ulcerative colitis | 0 (0.0) | 1 (0.09) | 0 (0.0) |
| Eating disorder | 0 (0.0) | 0 (0.0) | 1 (0.09) |

**Supplementary table 2. Oil-based and dried flower CBMP product range.** Full product range of products included in the oils or dried flower CBMP category respectively. All products were Adven®. THC = tetrahydrocannabinol, CBD = cannabidiol. \*Although advertised as 0% CBD products, a small amount (<1% CBD) remains after the extraction process.

|  |  |
| --- | --- |
| **Oils** | **Dried flower** |
| 20 mg/ml THC isolate oil | 0% CBD/ 20% THC (hybrid) flos\* |
| 20 mg/ml THC full spectrum oil |  |
| 100 mg/ml THC full spectrum oil |  |
| 50 mg/ml CBD broad spectrum oil |  |
| 150 mg/ml CBD isolate oil |  |
| 10 mg CBD / 10 mg THC/ml full spectrum oil  |  |
| 100 mg CBD / 5 mg THC/ml full spectrum oil |  |
| 40 mg CBD / 20 mg THC/ml full spectrum oil  |  |
| 5 mg THC / 10 mg CBD full spectrum lozenges |  |
| 5 mg THC / 10 mg CBD full spectrum capsules |  |
| 10 mg THC / 10 mg CBD full spectrum capsules |  |
| 2.5 mg THC / 5 mg CBD full spectrum capsules |  |
| 25 mg CBD broad spectrum capsules |  |

**Supplementary table 3. Univariate analysis of variables affecting BPI Interference scores.** A univariate binary logistic regression model was used to assess the effect of age, body mass index (BMI), prior cannabis experience, gender, and treatment type on Brief Pain Inventory (BPI) Interference scores after 6 months relative to baseline. The BPI Interference score measures the interference of a patient’s pain on their daily life.

|  |  |  |
| --- | --- | --- |
| **Variable** | **Odds Ratio [95% Confidence Interval]** | **P-value** |
| **Age, years** |  |  |
| 18-30 | - | Ref |
| 31-40 | 2.041 [0.444 - 4.411] | 0.330 |
| 41-50 | 1.813 [0.487 - 8.567] | 0.375 |
| 51-60 | 1.905 [0.479 - 7.570] | 0.360 |
| 61-70 | 2.571 [0.565 - 11.712] | 0.222 |
| 71-80 | 1.000 [0.197 - 5.068] | 1.000 |
| 81+ | N/A |  |
| **BMI, kg/m2** |  |  |
| <20 | 2.045 [0.372 - 11.250] | 0.411 |
| 20-25 | - | Ref |
| 25-30 | 1.201 [0.456 - 3.163] | 0.710 |
| 30-35 | 1.000 [0.347 - 2.878] | 1.000 |
| 35+ | 0.606 [0.114 - 3.230] | 0.558 |
| **Cannabis status** |  |  |
| Current users | - | Ref |
| Ex-users | 0.525 [0.174 - 1.587] | 0.253 |
| Naïve  | 0.525 [0.454 - 2.058] | 0.930 |
| **Gender** |  |  |
| Female | - | Ref |
| Male | 1.315 [0.652 - 2.655] | 0.444 |
| **Treatment type** |  |  |
| Oils | - | Ref |
| Oils and dried flower | 1.587 [0.772 - 3.264] | 0.209 |
| Dried flower | 1.278 [0.230 - 7.100] | 0.779 |

**Supplementary table 4. Univariate analysis of variables affecting BPI Severity scores.** A univariate binary logistic regression model was used to assess the effect of age, body mass index (BMI), prior cannabis experience, gender, and treatment type on Brief Pain Inventory (BPI) Severity scores after 6 months relative to baseline. The BPI Severity score measures patient pain severity.

|  |  |  |
| --- | --- | --- |
| **Variable** | **Odds Ratio [95% Confidence Interval]** | **P-value** |
| **Age, years** |  |  |
| 18-30 | - | Ref |
| 31-40 | 2.00 [0.500 - 7.997] | 0.327 |
| 41-50 | 2.286 [0.627 - 8.338] | 0.211 |
| 51-60 | 1.357 [0.361 - 5.109] | 0.652 |
| 61-70 | 1.556 [0.381 - 6.357] | 0.538 |
| 71-80 | 3.00 [0.533 - 16.897] | 0.213 |
| 81+ | N/A |  |
| **BMI, kg/m2** |  |  |
| <20 | 0.326 [0.079 - 1.342] | 0.121 |
| 20-25 | - | Ref |
| 25-30 | 0.939 [0.353 - 2.497] | 0.900 |
| 30-35 | 0.572 [0.201 - 1.626] | 0.295 |
| 35+ | 0.978 [0.160 - 5.989] | 0.981 |
| **Cannabis status** |  |  |
| Current users | - | Ref |
| Ex-users | 1.023 [0.336 - 3.114] | 0.968 |
| Naïve  | 0.982 [0.488 - 1.979] | 0.960 |
| **Gender** |  |  |
| Female | - | Ref |
| Male | 1.210 [0.625 - 2.345] | 0.572 |
| **Treatment type** |  |  |
| Oils | - | Ref |
| Oils and dried flower | 1.169 [0.595 - 2.299] | 0.650 |
| Dried flower | 1.548 [0.280 - 8.567] | 0.617 |

**Supplementary table 5. Multivariate analysis of variables affecting BPI Interference scores.** A multivariate binary logistic regression model was used to assess the effect of age, body mass index (BMI), prior cannabis experience, gender, and treatment type on Brief Pain Inventory (BPI) Interference scores after 6 months relative to baseline. The BPI Interference score measures the interference of a patient’s pain on their daily life.

|  |  |  |
| --- | --- | --- |
| **Variable** | **Odds Ratio [95% Confidence Interval]** | **P-value** |
| **Age, years** |  |  |
| 18-30 | - | Ref |
| 31-40 | 1.295 [0.259 - 6.467] | 0.753 |
| 41-50 | 1.403 [0.320 - 6.151] | 0.653 |
| 51-60 | 1.530 [0.319 - 7.330] | 0.595 |
| 61-70 | 1.675 [0.314 - 8.933] | 0.546 |
| 71-80 | 0.581 [0.0890 - 3.792] | 0.570 |
| 81+ | N/A |  |
| **BMI, kg/m2** |  |  |
| <20 | 1.900 [0.318 - 11.336] | 0.481 |
| 20-25 | - | Ref |
| 25-30 | 1.063 [0.381 - 2.966] | 0.907 |
| 30-35 | 0.735 [0.230 - 2.350] | 0.604 |
| 35+ | 0.551 [0.093 - 3.265] | 0.512 |
| **Cannabis status** |  |  |
| Current users | - | Ref |
| Ex-users | 0.841 [0.225 - 3.140] | 0.797 |
| Naïve  | 1.478 [0.509 - 4.295] | 0.473 |
| **Gender** |  |  |
| Female | - | Ref |
| Male | 0.827 [0.343 - 1.995] | 0.672 |
| **Treatment type** |  |  |
| Oils | - | Ref |
| Oils and dried flower | 1.898 [0.681 - 5.291] | 0.220 |
| Dried flower | 1.606 [0.212 - 12.176] | 0.647 |

***Supplementary table 6. Quantity of adverse events for each treatment type categorized by both severity and a patient’s prior exposure to cannabis.*** *Naïve users had never used cannabis before, ex-users had previously used cannabis but were not using it at the time of their prescription. Current users were using non-prescription cannabis up until the time of their prescription. Patients only prescribed dried flower were not included due to insufficient sample size (N=1).*

|  |
| --- |
| **Oils** |
|  | **Prior Cannabis Use** |  |
| **Adverse Event Severity** | **Naïve** | **Ex-users** | **Current users** | **Total** |
| **Mild** | 317 | 42 | 28 | 387 |
| **Moderate** | 282 | 40 | 38 | 360 |
| **Severe** | 77 | 27 | 5 | 109 |
| **Life-threatening/Disabling** | 0 | 1 | 0 | 1 |
| **Adverse event incidence (%)** | 676 (281.7) | 110 (189.7) | 71 (142.0) | 857 (246.3) |
|  |
| **Patients with adverse events (%)** | 71 (29.6) | 12 (20.7) | 8 (16.0) | 91 (26.1) |  |
|  |  |
| **Oils and dried flower** |  |
|  | **Prior Cannabis Use** |  |  |
| **Adverse Event Severity** | **Naïve** | **Ex-users** | **Current users** | **Total** |  |
| **Mild** | 79 | 49 | 50 | 178 |  |
| **Moderate** | 63 | 34 | 70 | 167 |  |
| **Severe** | 15 | 22 | 33 | 70 |  |
| **Life-threatening/Disabling** | 0 | 0 | 0 | 0 |  |
| **Adverse event incidence (%)** | 157 (221.1) | 105 (169.4) | 153 (62.7) | 415 (110.1) |  |
|  |
| **Patients with adverse events (%)** | 21 (29.6) | 13 (21.0) | 22 (9.0) | 56 (14.9) |  |

***Supplementary table 7. Most common recorded adverse events across patients treated with oils or oils and dried flower for chronic pain.*** *Naïve users had never used cannabis before, ex-users had previously used cannabis but were not using it at the time of their prescription. Current users were using non-prescription cannabis up until the time of their prescription. Patients only prescribed dried flower were not included due to insufficient sample size (N=1).*

|  |  |  |  |
| --- | --- | --- | --- |
|  | Oils | Oils and dried flower | Total |
| Adverse Event Type | **Naïve** | **Ex-users** | **Current users** | **Naïve**  | **Ex-users** | **Current** |  |
| Fatigue |  |  |  |  |  |  |  |
| Mild | 18 | 3 | 1 | 5 | 6 | 2 |  |
| Moderate | 27 | 3 | 4 | 8 | 2 | 5 |  |
| Severe | 15 | 3 | 0 | 2 | 3 | 6 |  |
| Life-threatening/Disabling | 0 | 1 | 0 | 0 | 0 | 0 |  |
| Total | 60 | 10 | 5 | 15 | 11 | 13 | 114 |
| Somnolence |  |  |  |  |  |  |  |
| Mild | 0 | 0 | 0 | 0 | 0 | 0 |  |
| Moderate | 46 | 6 | 4 | 12 | 5 | 5 |  |
| Severe | 4 | 1 | 0 | 0 | 4 | 1 |  |
| Life-threatening/Disabling | 0 | 0 | 0 | 0 | 0 | 0 |  |
| Total | 50 | 7 | 4 | 12 | 9 | 6 | 88 |
| Dry Mouth |  |  |  |  |  |  |  |
| Mild | 36 | 6 | 4 | 11 | 4 | 9 |  |
| Moderate | 8 | 1 | 0 | 3 | 1 | 1 |  |
| Severe | 0 | 0 | 0 | 0 | 0 | 0 |  |
| Life-threatening/Disabling | 0 | 0 | 0 | 0 | 0 | 0 |  |
| Total | 44 | 7 | 4 | 14 | 5 | 10 | 84 |
| Lethargy |  |  |  |  |  |  |  |
| Mild | 22 | 0 | 1 | 5 | 6 | 2 |  |
| Moderate | 16 | 4 | 2 | 2 | 2 | 3 |  |
| Severe | 5 | 3 | 0 | 2 | 1 | 2 |  |
| Life-threatening/Disabling | 0 | 0 | 0 | 0 | 0 | 0 |  |
| Total | 43 | 7 | 3 | 9 | 9 | 7 | 78 |
| Headache |  |  |  |  |  |  |  |
| Mild | 17 | 1 | 2 | 5 | 3 | 4 |  |
| Moderate | 11 | 2 | 2 | 5 | 2 | 3 |  |
| Severe | 11 | 2 | 0 | 4 | 1 | 2 |  |
| Life-threatening/Disabling | 0 | 0 | 0 | 0 | 0 | 0 |  |
| Total | 39 | 5 | 4 | 14 | 6 | 9 | 77 |
| Nausea |  |  |  |  |  |  |  |
| Mild | 25 | 2 | 5 | 8 | 5 | 3 |  |
| Moderate | 15 | 2 | 1 | 4 | 4 | 2 |  |
| Severe | 0 | 1 | 0 | 0 | 0 | 0 |  |
| Life-threatening/Disabling | 0 | 0 | 0 | 0 | 0 | 0 |  |
| Total | 40 | 5 | 6 | 12 | 9 | 5 | 77 |
| Dizziness |  |  |  |  |  |  |  |
| Mild | 15 | 2 | 2 | 3 | 0 | 1 |  |
| Moderate | 25 | 1 | 3 | 4 | 0 | 3 |  |
| Severe | 2 | 2 | 0 | 2 | 3 | 1 |  |
| Life-threatening/Disabling | 0 | 0 | 0 | 0 | 0 | 0 |  |
| Total | 42 | 5 | 5 | 9 | 3 | 5 | 69 |
| Insomnia |  |  |  |  |  |  |  |
| Mild | 10 | 1 | 2 | 4 | 2 | 0 |  |
| Moderate | 14 | 1 | 2 | 5 | 2 | 5 |  |
| Severe | 8 | 0 | 1 | 2 | 2 | 7 |  |
| Life-threatening/Disabling | 0 | 0 | 0 | 0 | 0 | 0 |  |
| Total | 32 | 2 | 5 | 11 | 6 | 12 | 68 |
| Concentration impairment |  |  |  |  |  |  |  |
| Mild | 22 | 3 | 2 | 3 | 4 | 1 |  |
| Moderate | 10 | 0 | 2 | 1 | 2 | 2 |  |
| Severe | 1 | 0 | 0 | 0 | 0 | 1 |  |
| Life-threatening/Disabling | 0 | 0 | 0 | 0 | 0 | 0 |  |
| Total | 33 | 3 | 4 | 4 | 6 | 4 | 54 |
| Vertigo |  |  |  |  |  |  |  |
| Mild | 13 | 0 | 2 | 5 | 0 | 2 |  |
| Moderate | 13 | 2 | 3 | 3 | 1 | 0 |  |
| Severe | 2 | 0 | 0 | 1 | 1 | 0 |  |
| Life-threatening/Disabling | 0 | 0 | 0 | 0 | 0 | 0 |  |
| Total | 28 | 2 | 5 | 9 | 2 | 2 | 48 |

***Supplementary table 8****.* ***Univariate analysis model assessing factors contributing to the chance of experiencing adverse events.*** *A binary logistic regression model univariately assessed the effect of age, body mass index (BMI), cannabis status, gender, and treatment type on the chances of experiencing adverse events by calculating odds ratios and 95% confidence intervals. Ref = reference group. \* p<0.050, \*\* p<0.010, \*\*\* p<0.001.*

|  |  |  |
| --- | --- | --- |
| **Variable** | **Odds Ratio [95% Confidence Interval]** | **P-value** |
| **Age, years** |  |  |
| 18-30 | - | Ref |
| 31-40 | 0.638 [0.333 - 1.220] | 0.174 |
| 41-50 | 0.724 [0.386 - 1.358] | 0.314 |
| 51-60 | 1.364 [0.728 - 2.555] | 0.332 |
| 61-70 | 1.417 [0.711 - 2.822] | 0.322 |
| 71-80 | 2.294 [1.069 - 4.919] | 0.033\* |
| 81+ | 2.179 [0.774 - 6.139] | 0.140 |
| **BMI, kg/m2** |  |  |
| <20 | 0.550 [0.241 - 0.474] | 0.156 |
| 20-25 | - | Ref |
| 25-30 | 0.685 [0.416 - 1.129] | 0.138 |
| 30-35 | 0.828 [0.459 - 1.493] | 0.530 |
| 35+ | 0.881 [0.466 - 1.669] | 0.699 |
| **Cannabis status** |  |  |
| Current users | - | Ref |
| Ex-users | 2.316 [1.296 - 4.137] | 0.005\*\* |
| Naïve  | 3.697 [2.359 - 5.794] | <0.001\*\*\* |
| **Gender** |  |  |
| Female | - | Ref |
| Male | 0.320 [0.213 - 0.481] | <0.001\*\*\* |
| **Treatment type** |  |  |
| Oils | - | Ref |
| Oils and dried flower | 0.493 [0.340 - 0.714] | <0.001\*\*\* |