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### Objective & Study Design

### Results

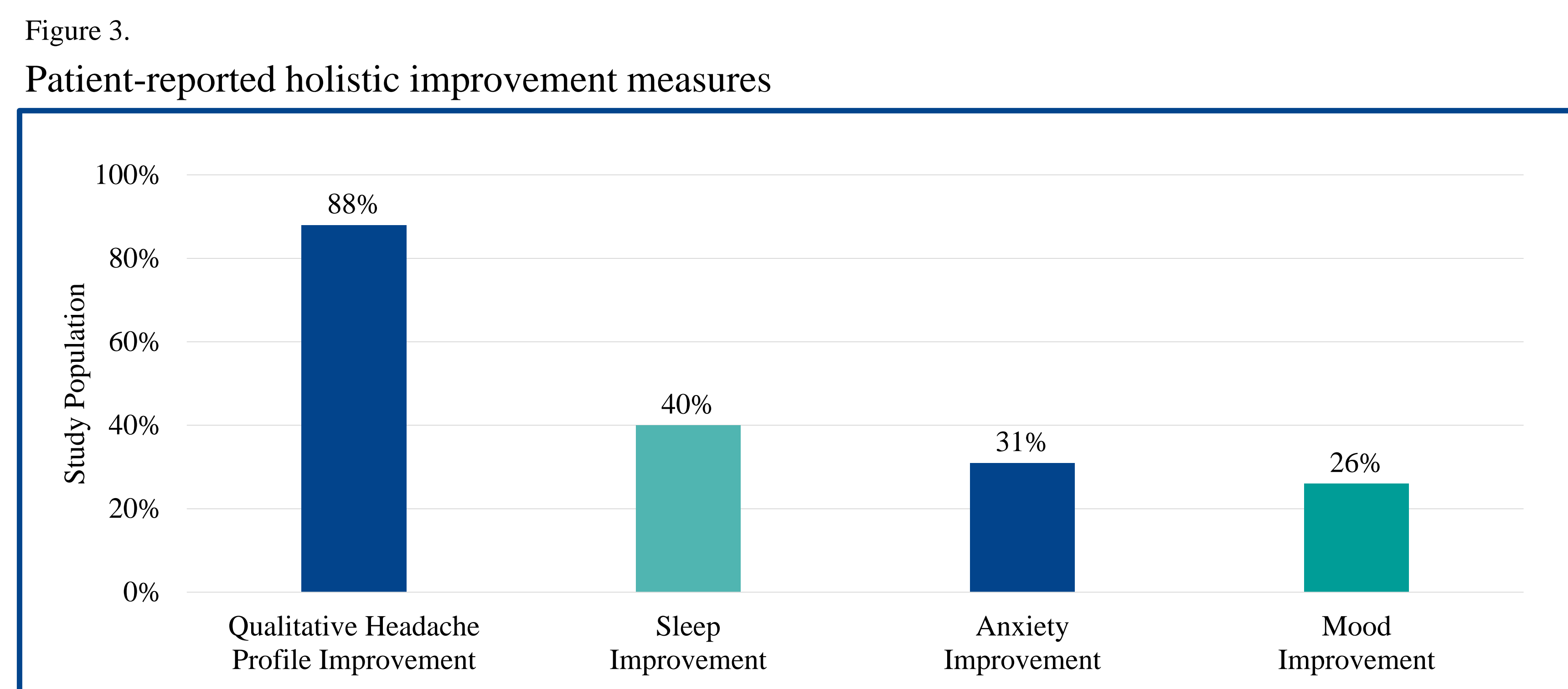
### Discussion

**Objective:**  
Medical cannabis (MC) is currently approved in 33 states for use in patients with chronic pain, and is used in the treatment of chronic migraine (CM). We report the results of a retrospective chart review of patients presenting with CM treated with MC.

**Methods:**  
316 patients met our criteria. Patients with a diagnosis of CM, as defined by the International Classification of Headache Disorders Third Edition, who had at least one follow-up visit after ≥1 month on New York State MC were eligible. Charts were reviewed for monthly headache days (MHD) and migraine days (MMD), at the start of MC and subsequent visits. Changes in patient-reported (headache) HA profile, anxiety, mood, sleep, HA medicines, opioid pain medicines, MC dosing, and adverse effects (AE) were also recorded.

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| <p><b>Inclusion/Exclusion Criteria</b></p> <ul style="list-style-type: none"> <li>Certified for New York State MC by UCNS board certified physicians or their nurse practitioner/physicians assistant team.</li> <li>Patients were on MC for at least one month treatment.</li> <li>At least 21 years of age.</li> </ul> | <p><b>Subjects</b></p> <ul style="list-style-type: none"> <li>316 patients diagnosed with CM and were certified for MC</li> <li>Patients were excluded due to lack of follow-up or inability to initiate MC treatment</li> <li>81.6% were female, 18.4% were male</li> <li>The average age was 47.2 years old, between 21 and 89</li> </ul> | <p><b>Study Population</b></p> <ul style="list-style-type: none"> <li>316 patients meet inclusion criteria and initiated MC treatment.</li> <li>Reasons for failure to initiate MC treatment included:                     <ul style="list-style-type: none"> <li>Financial barriers</li> <li>Employment restriction</li> </ul> </li> </ul> |
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Approved by the Western Institutional Review Board.



The results of this study indicate that incorporation of MC into a comprehensive CM treatment from a UCNS-certified headache medicine physician may be beneficial for patients, particularly for opioid pain medication reduction, anxiety, sleep, and mood. The study population reported these changes with an average of 169 ± 131 days of MC while 77% utilized on concomitant conventional prophylactic headache medication, including botulinum toxin and topiramate. All MC use was an out-of-pocket expense, with a monthly average cost of \$242. Patients are able utilize up to three MC ratios at a time, but no significance was found in outcomes between patients utilizing one versus multiple products, similarly no significance was found in outcomes between the three available routes of administration: tincture, vaporized inhalation, or capsule.

MC has several known mechanism of actions, including inhibition of cyclooxygenase-2 enzyme, increase in serotonin, inhibition of L-type calcium voltage-gated channel, increase in GABA, supplementation for AEA, and prevalence of CB1R within the nervous system. However, the absence of guidelines forces physicians to practice within a large clinical evidence gap or to avoid both risks and benefits associated with MC.

This study shows that a correlation exists between overall HA qualitative profile improvement and factors associated with CM such as anxiety, sleep, and mood in patients exposed to a Type I or III cannabis chemovars. Patients using Type I ratios were also more likely to reduce their consumption of HA medications. No correlation between routes of administration was observed. One in four patients reported AE. These AE were largely tolerable, with 1.3% of patients discontinuing due to adverse effects and no severe AE reported.

### Results

Table 1. Adjusted differences between MC chemovars

Patient Outcomes	High:low vs Equal Type I vs II (THC:CBD)	Low:high vs Equal Type III vs II (THC:CBD)
Qualitative Headache Profile Improvement	p = 0.1278	p = 0.5254
Headache Medication Dosage Reduction	* p = 0.0049 RR = 1.95	p = 0.4843
Anxiety Improvement	* p = 0.0003 RR = 2.13	* p = 0.0028 RR = 1.91
Mood Improvement	* p = 0.0066 RR = 1.93	* p = 0.0081 RR = 1.91
Sleep Improvement	* p = 0.0093 RR = 1.54	* p = 0.0093 RR = 1.51
Adverse Effects	p = 0.1605	p = 0.1000

Figure 4. Observed opioid pain medication dosage changes for CM-related pain

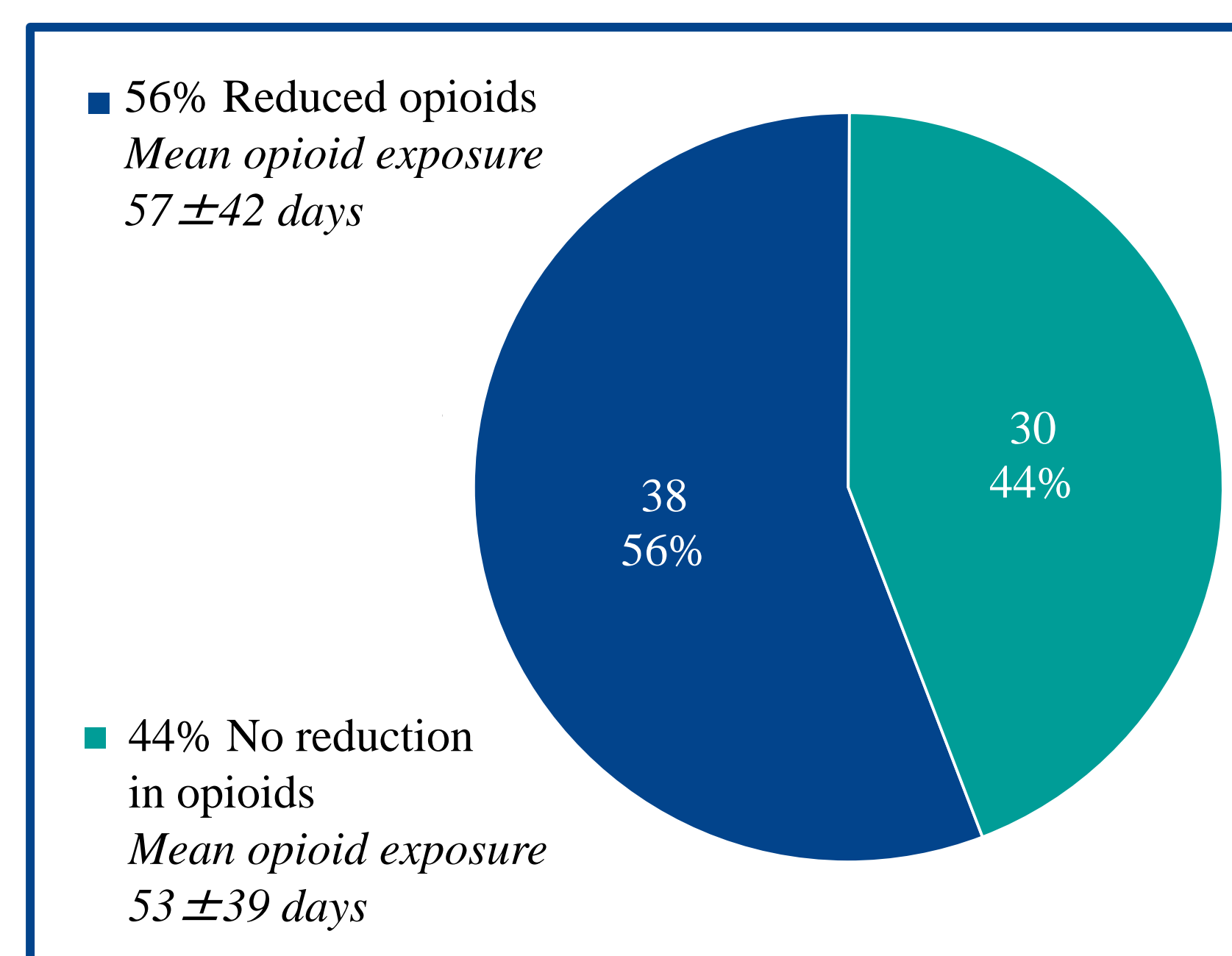


Figure 1. Observed changes in MMD and MHD frequency profiles

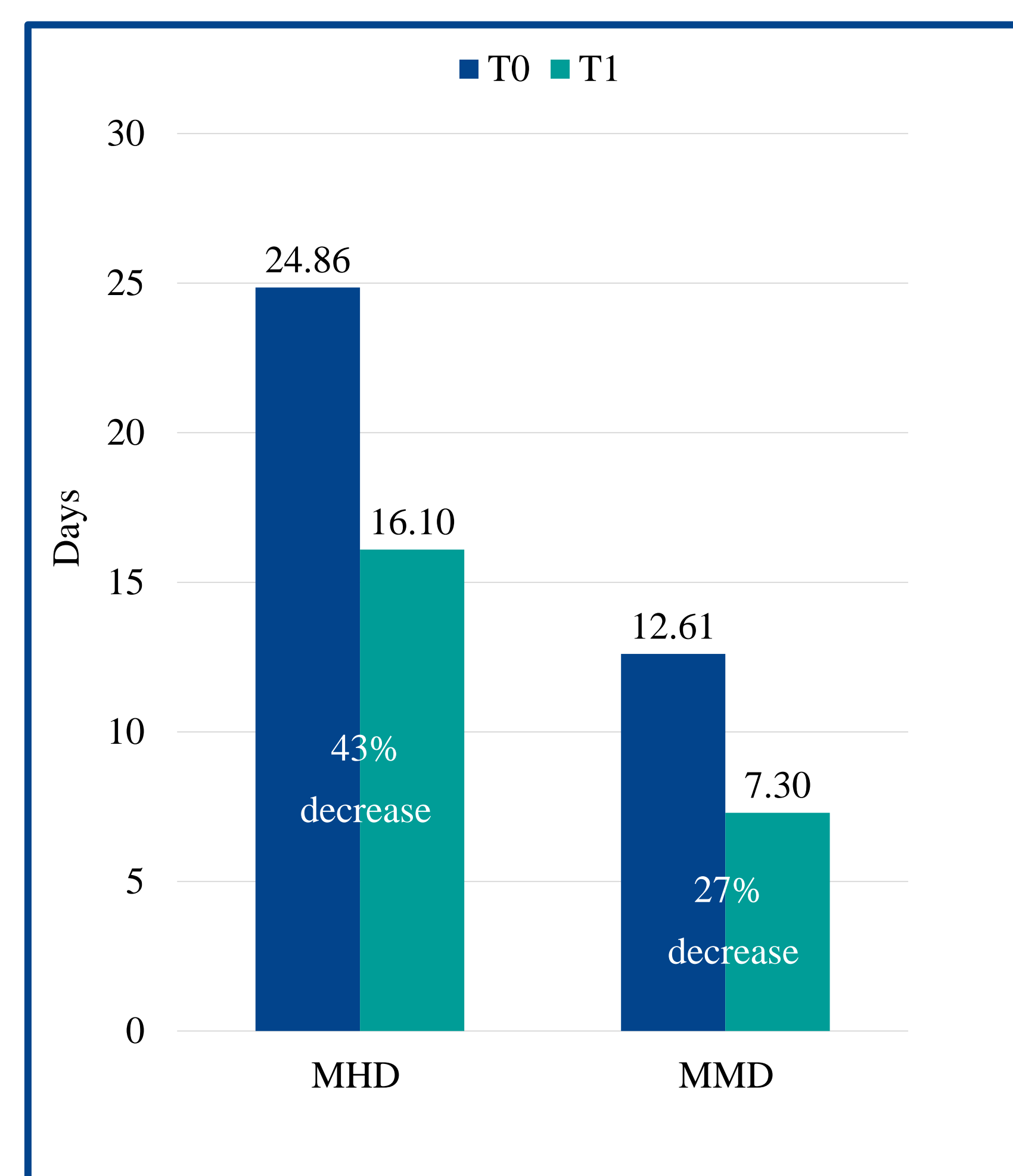
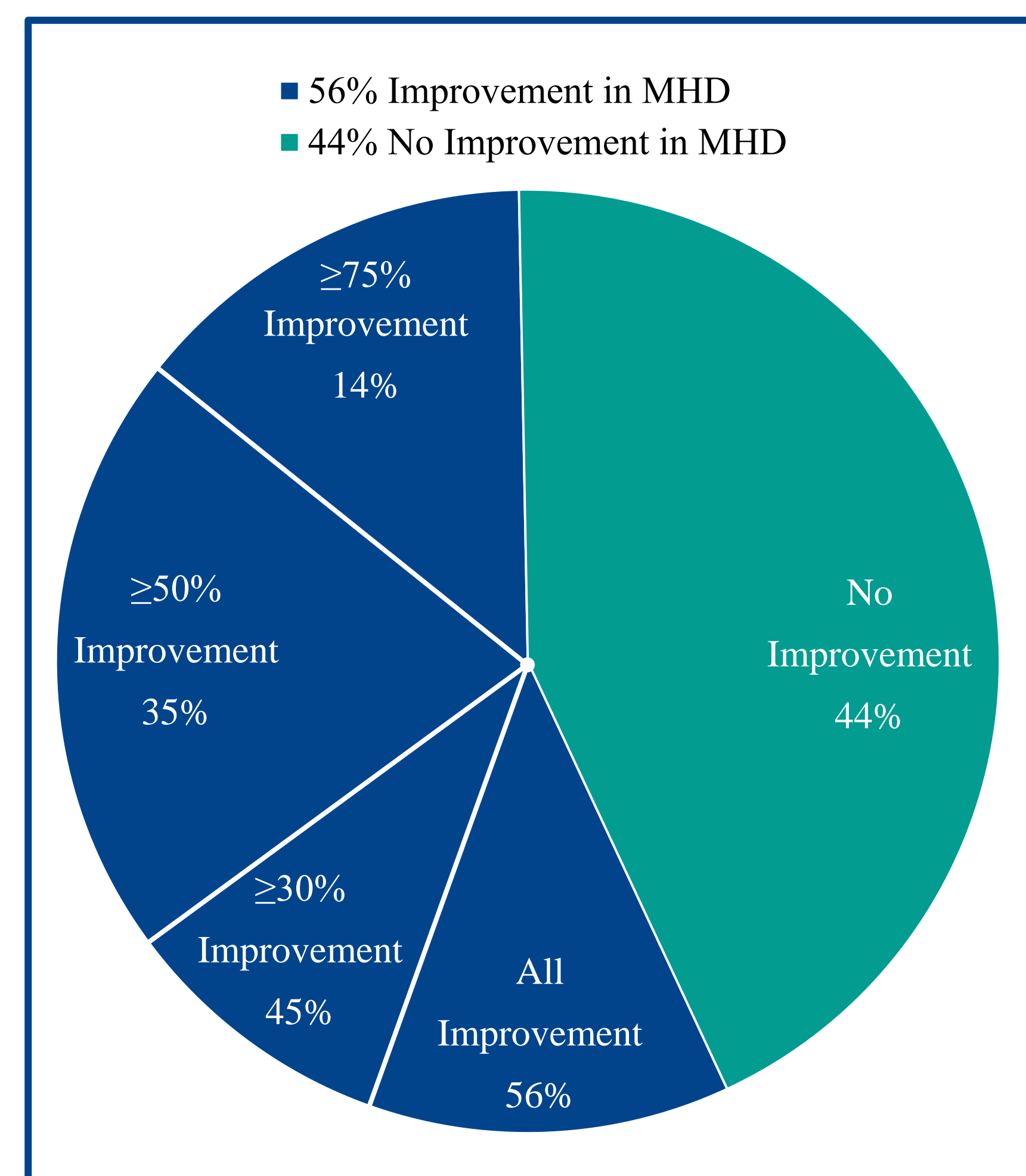


Figure 2. Observed MHD frequency profile response rates



### Conclusion

MC may be effective in reducing the frequency of both HA and migraine HA as a part of a comprehensive CM regimen. MC may offer unique relief from CM, a multi-faceted disease, in improvements to sleep, anxiety, and mood with a minimal side effect profile. MC-associated opioid reduction was observed in CM patients. With this additional retrospective information on MC, we hope to help generate a substantial line of inquiry for future prospective studies on MC effect and dosing for CM. As the country's interest in MC grows and states evaluate MC treatment programs, research must advance to allow for evidence-based public action.

### Acknowledgements & References

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Akerman, Simon, Philip R. Holland, and Peter J. Goadsby. "Cannabinoid (CB1) receptor activation inhibits trigeminovascular neurons." *Journal of Pharmacology and Experimental Therapeutics* 320.1 (2007): 64-71.

Ali, Ramez M., et al. "Effects of cannabidiol on contractions and calcium signaling in rat ventricular myocytes." *Cell calcium* 57.4 (2015): 290-299.

Lochte, Bryson C., et al. "The use of cannabis for headache disorders." *Cannabis and cannabinoid research* 2.1 (2017): 61-71.

Nicolodi M, Sandoval V, Terrine A. Therapeutic use of cannabinoids - Dose Findings, Effects in Chronic Migraine and Cluster Headache. 3rd Congress of the European Academy of Neurology (EAN)

Rubin, Rita. "Medical marijuana is legal in most states, but physicians have little evidence to guide them." *Jama* 317.16 (2017): 1611-1613.

Ruhaak, Lucia Renee, et al. "Evaluation of the cyclooxygenase inhibiting effects of six major cannabinoids isolated from Cannabis sativa." *Biological and Pharmaceutical Bulletin* 34.5 (2011): 774-778.

Sarchielli, Paola, et al. "Endocannabinoids in chronic migraine: CSF findings suggest a system failure." *Neuropsychopharmacology* 32.6 (2007): 1384.

Sigel, Erwin, et al. "The major central endocannabinoid directly acts at GABAA receptors." *Proceedings of the National Academy of Sciences* 108.44 (2011): 18150-18155.

Author Disclosures:  
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Dr. McVige: Speaker for Amgen, Avanir, GammaCore, Supernus, and Teva  
Dr. Saikali: Speaker for Allergan, Amgen, Assertio, Avanir, Cefaly, Egalet, GammaCore, Pernix, Promius, Supernus, and Teva  
All other authors report no disclosures.