

EMBRACING WOMEN'S HEALTH



New Developments in
Evidence-Based Solutions

PRESENTED
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EMBRACING WOMEN'S HEALTH

TODAY'S SESSION WILL EXPLORE

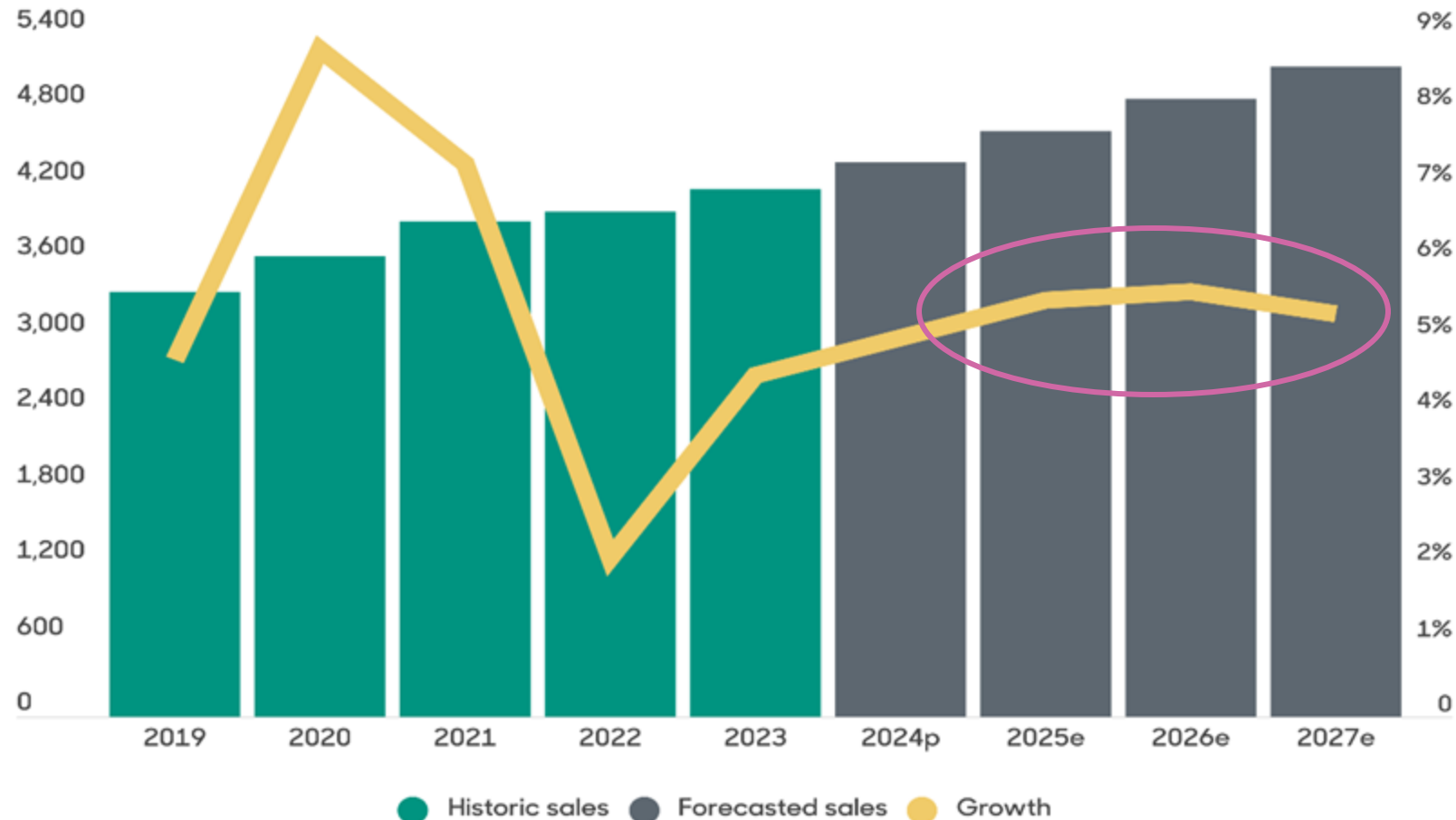
- Overview of the Women's Health dietary supplement market
- Top Concerns: Sleep, Stress, Mood, Anxiety, Hormonal Health
- Hormone Balance: Differences in PMS and PMDD
- Enter Venetron-a botanical based clinically researched solution
- Clinical research review
- PMS and Menstruation study
- NEW! Venetron® study on Sleep, Stress and Mood



VENETRON[®]

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U.S. Women's Health Supplement Sales and Growth 2019 – 2027e



Source: Nutrition Business Journal (\$mil, consumer sales)

Note: This chart combines data from the following NBJ conditions: Women's General Health, Menopause, Pre and Postnatal, and Women's Sexual Health supplements.

	2019	2020	2021	2022	2023	2024	2025	2026	2027
Pre- and Postnatal supplement sales	770.6	751.6	779.3	758.1	764.7	776.3	802.7	832.3	872.4
Pre- and Postnatal supplement growth	2.9%	-2.5%	3.7%	-2.7%	0.9%	1.5%	3.4%	3.7%	4.8%
Menopause supplement sales	557.3	564.8	589.6	603.5	635.0	684.3	741.2	807.1	871.9
Menopause supplement growth	3.9%	1.3%	4.4%	2.4%	5.2%	7.8%	8.3%	8.9%	8.0%
Women's General Health supplement sales	1,801	2,098	2,294	2,368	2,488	2,614	2,746	2,882	3,007
Women's General Health supplement growth	7.0%	16.5%	9.3%	3.2%	5.1%	5.1%	5.0%	5.0%	4.3%
Women's Sexual and Reproductive Health supplier	226.1	235.2	253.7	268.2	288.0	310.1	334.6	361.1	391.9
Women's Sexual and Reproductive Health supplier	5.0%	4.0%	7.8%	5.7%	7.4%	7.7%	7.9%	7.9%	8.5%
	2019	2020	2021	2022	2023	2024	2025	2026	2027
Women's health supplements	3,355	3,650	3,917	3,997	4,176	4,385	4,624	4,882	5,143
Growth	4.7%	8.8%	7.3%	2.1%	4.5%	5.0%	5.5%	5.6%	5.3%
Source: <i>Nutrition Business Journal</i> (\$mil, consumer sales)									

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Women's Health Applications

RANK	WHICH OF THESE HEALTH GOALS IS IMPORTANT TO YOU?
1	Getting better sleep
2	Longevity and aging in good health
3	Managing stress
4	Improving energy levels
5	Achieving a healthier weight
6	Supporting mood and mental health
7	Improving immunity
8	Improving digestion
9	Improving skin
10	Optimizing fitness and performance
11	Reducing hunger and managing insulin peaks
12	Supporting hormonal health and fertility
13	Supporting menopause
14	None of these

- 1 Getting better sleep
- 2 Longevity and aging in good health
- 3 Managing stress
- 4 Improving energy levels
- 5 Achieving a healthier weight
- 6 Supporting mood and mental health
- 7 Improving immunity
- 8 Improving digestion
- 9 Improving skin
- 10 Optimizing fitness and performance
- 11 Reducing hunger and managing insulin peaks
- 12 Supporting hormonal health and fertility
- 13 Supporting menopause
- 14 None of these

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Google Says: Top Functional Concerns for Women

TOP CONCERNS BY INCREASE

Trend	Volume	Increase	YOY
Sleep	149.9K	+25.1K	+20.1%
Parasite	69.4 K	+16.7K	+31.5%
Anxiety	92.5K	+16.4K	+21.5%
Constipation	78.0K	+12.4K	+19.0%
Blood Pressure	67.2K	+9.1K	+15.7%
Menopause	34.9K	+8.5K	+32.1%
Migraine	22.2K	+7.9K	+55.7%
Hair Loss	95.5K	+7.5K	+8.5%
Hormone Balancing	7.3K	+4.8K	+193.8%
Pregnancy	152.7K	+4.5K	+3.0%

TOP CONCERNS BY YEAR OVER YEAR

Trend	Volume	Increase	YOY
Mature Skin	510	+508	+29.8%
Hyperthyroidism	720	+717	+27.7%
HPV	950	+946	+22.3%
Leptin Resistance	1.1K	+840	+280.0%
Vaginal Dryness	910	+650	+250.5%
Crepey Skin	4.0K	+2.9K	+243.4%
Endometriosis	1.2K	+800	+195.1%
Hormone Balancing	7.3K	+4.8K	+193.8%
Diabetes	940	+602	+178.3%
Brittle Nails	1.9K	+1.2K	+157.0%

Source: Google Search data, average monthly search volume, average monthly search volume increase and year-over-year growth compared to the previous 12 months.

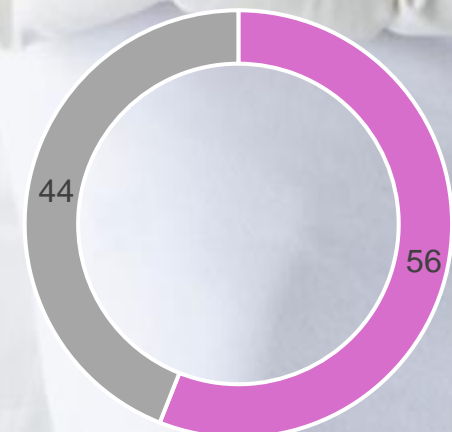
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Sleep: What To Know

- Stress and “Mental Load” play a role in falling and staying asleep
- Women are 40% more likely to experience insomnia
- Women experience fragmented, worse quality sleep more often than men
- Mood is influenced by hormonal fluctuations, sleep quality, and stress levels
- PMDD is linked to a decreased response to melatonin during luteal phase
- Menstruation impacts the quality of stage 2 and REM sleep
- Women report pain as a sleep disruptor during menstruation and pregnancy

Suni, E., Truong, K. 100+ Sleep Statistics, Sleep Foundation, September 26, 2023.

Monthly Sleep Aid Usage %



■ Sleep Aid Users ■ Non-Users

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Stress: What to Know

- Women are disproportionately affected by stress due to factors such as
 - hormonal fluctuations
 - societal pressures
 - caregiving responsibilities
 - work-life balance challenges
- Fastest growing stress-relief application
 - Functional foods & beverages targeting women
- The market data says
 - Global stress management market may exceed \$20 billion by 2030
 - Global stress relief supplements market is growing at 6.75% CAGR and may reach \$900 million by 2032
 - Women's health and wellness supplements are expected to grow at a 7-9% CAGR
- Products need to deliver a high perceptual experience



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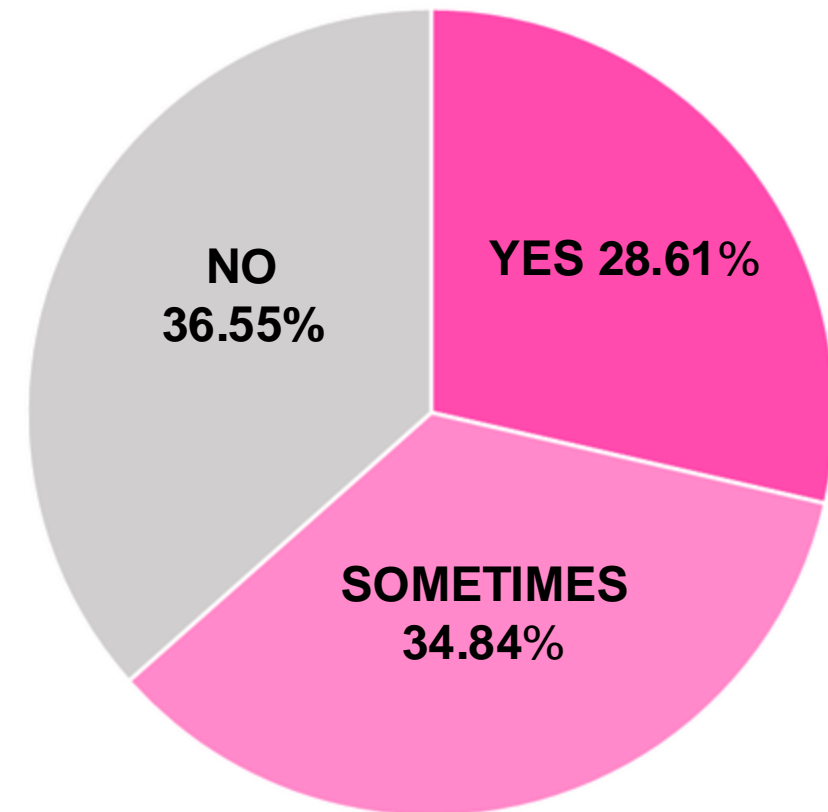
Menstruation and PMS: What to Know

Q: Do your **premenstrual symptoms interfere** with your daily life?

A: **63.45%** of women report PMS interferes with their daily lives to some degree.

Did You Know?

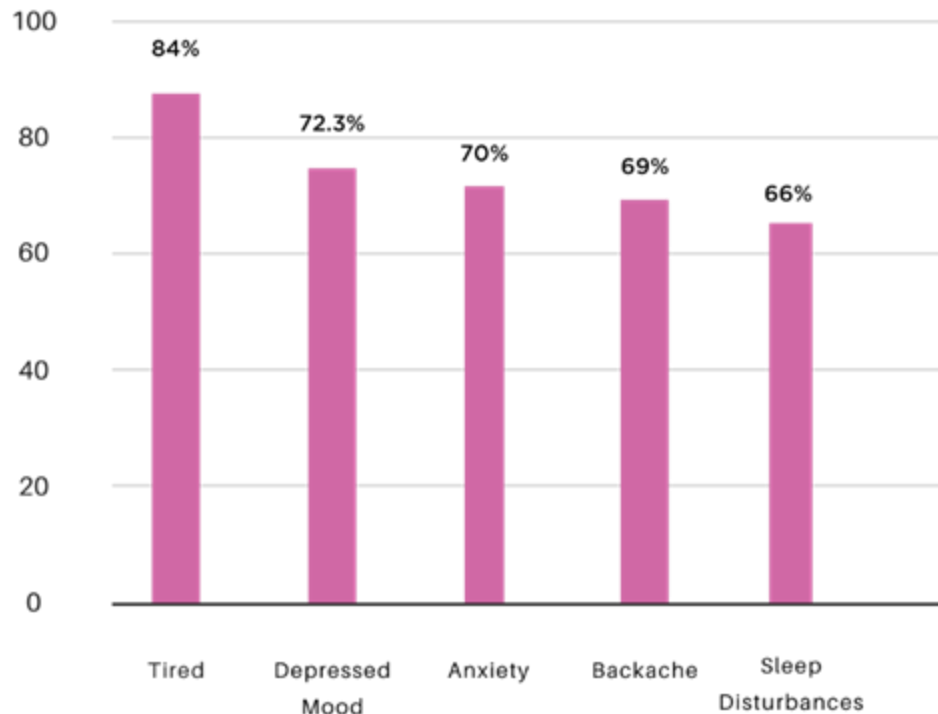
Menstrual symptoms are associated with approximately **9 days of lost productivity** per woman per year.



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PMS and PMDD: What Are They?

Symptoms of PMDD (Premenstrual Dysphoric Disorder)



Symptoms of PMS (Premenstrual Syndrome)

Emotional & Psychological Symptoms

Severe mood swings
Intense irritability or anger
Depression or hopelessness

Anxiety or tension
Extreme sensitivity to rejection
Difficulty concentrating

Behavioral Symptoms:

Increased conflicts with others
Loss of interest in usual activities
Fatigue or low energy

Sleep disturbances
Appetite changes or food cravings

Physical Symptoms:

Breast tenderness or swelling
Headaches
Bloating

Joint or muscle pain
Hot flashes or night sweats

Clinically studied low-dose botanical extract for sleep, mood, stress and concentration without any interactions

- Patented, purified, powdered extract of *Apocynum venetum* (Rafuma Leaf)
- Standardized to contain at least 4% hyperoside and isoquercitrin
- Finalist: Innovation in Women's Health in the 2024 Nutraingredients-USA Awards

Ingredient Highlights:

- Does not affect the CYP3A pathway
- Active at a low 50mg dose
- Prevents the degradation of serotonin
- Promotes production of melatonin at night
- Works synergistically with GABA
- Provides a high perceptual experience



Formulation

Low Daily Dose



Taste Profile



Delivery Formats



Status



Two Forms

Venetron® and Venetron®-W (water-soluble)

Mechanism of Action

Mode of Action 1

GABA receptor agonist
Reduces chromogranin-A secretion



Mode of Action 2

Serotonin degradation inhibition to
promote melatonin production at night



Product Claims

- Helps maintain comfort during the menstrual cycle
- Helps support hormonal balance and menstrual health
- Promotes a positive mood and emotional well-being
- Helps maintain emotional well-being during occasional stress
- Promotes relaxation without drowsiness
- Promotes a sense of calm before bedtime
- Helps maintain a healthy sleep cycle
- Promotes relaxation for a better night's sleep



Research Summary

Clinical trial 1: Anti-depression, anti-anxiety, insomnia improvement on 39 people

Clinical trial 2: Safety study on 30 people

Journal of Nutritional Food. 12, 1-9 (2009)

Clinical trial 3: Anti-stress by co-ingestion of GABA and VENETRON® on 12 males

Japanese Journal of Physiological Anthropology 14(3), 151-155 (2009)

Clinical trial 4: Sleep improvement on 8 people

J. Nutr. Sci. Vitaminol. 61(2), 182-187 (2015)

Clinical trial 5: Sleep improvement, concentration maintenance, anti-stress on 17 people

Jpn Pharmacol Ther. 46(1), 117-125 (2018)

Clinical trial 6: Psychological and physical symptoms associated with menstruation on 42 women

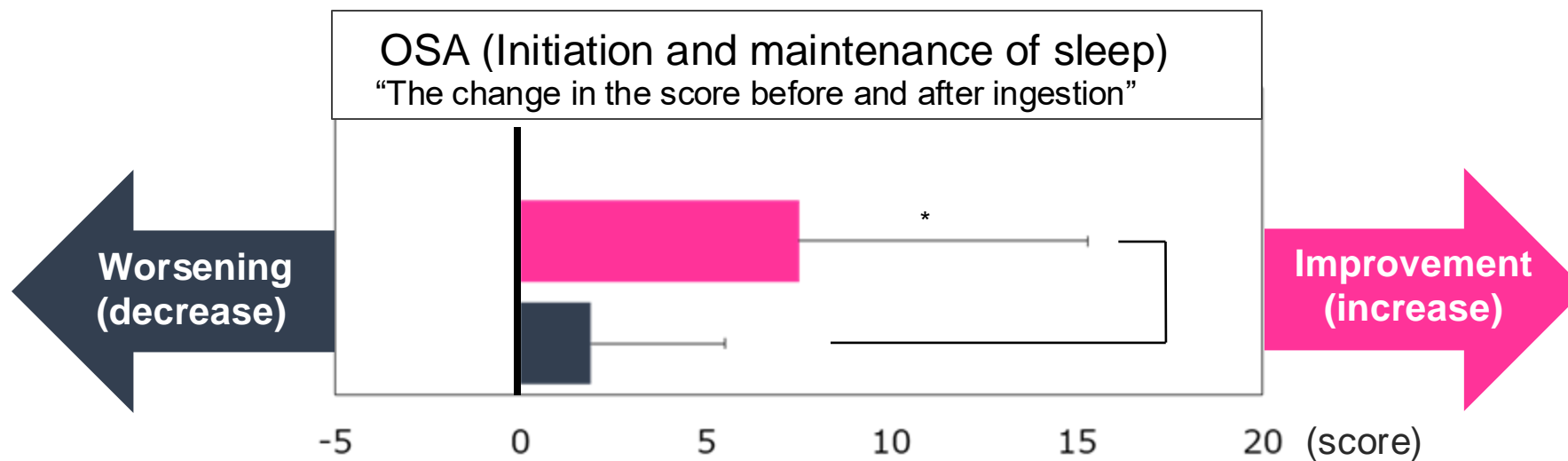
Clinical trial 7 – NEW! Assessing the Effects of VENETRON on Sleep, Stress and Anxiety on 476 people

Clinical Research Trial #5: Sleep Quality



Result 1: Sleep Quality Improvement

Participants reported a higher score on the sleep quality questionnaire. This indicates an improvement of sleep quality and suggests the improvement of sleep quality is related to deep (non-REM) sleep and sleep initiation by ingestion.



■ VENETRON[®] (n=11)

■ Placebo (n=11)

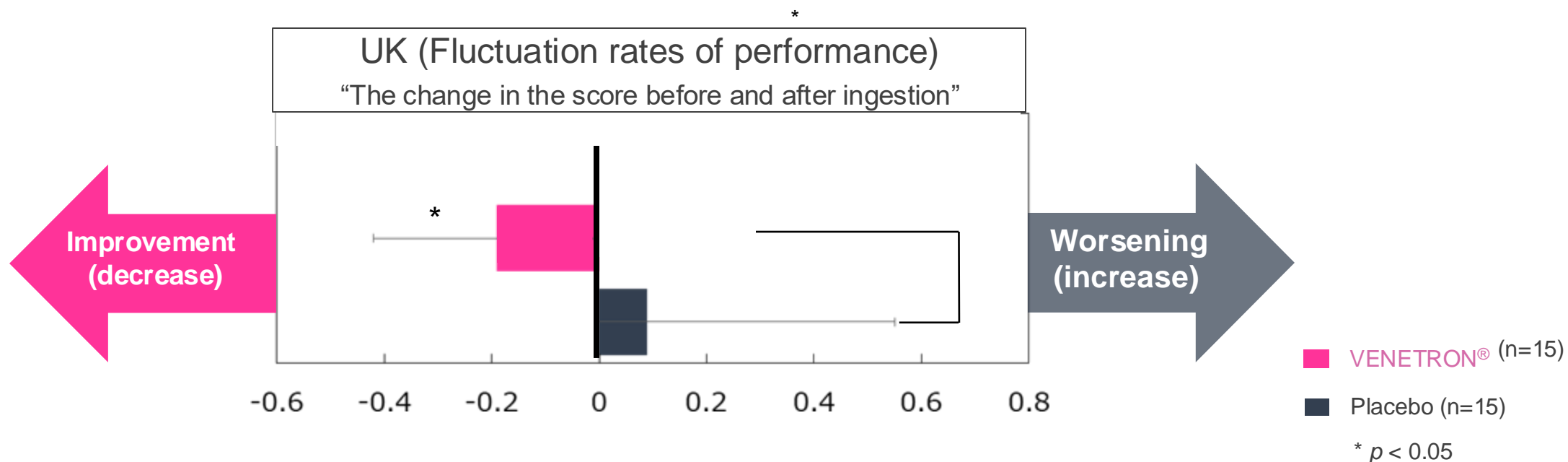
* $p < 0.05$

Clinical Research Trial #5: Sleep Quality



Result 2: Concentration Maintenance

Participants' work performance was measured as an index of psychological stress. The lower numbers indicates improvement of concentration. The result suggests that Venetron® promotes recovery from fatigue induced by desk work, improvement of concentration, and provides stability of work performance.



Clinical Research Trial #5: Sleep Quality

Result 3: Stress Support

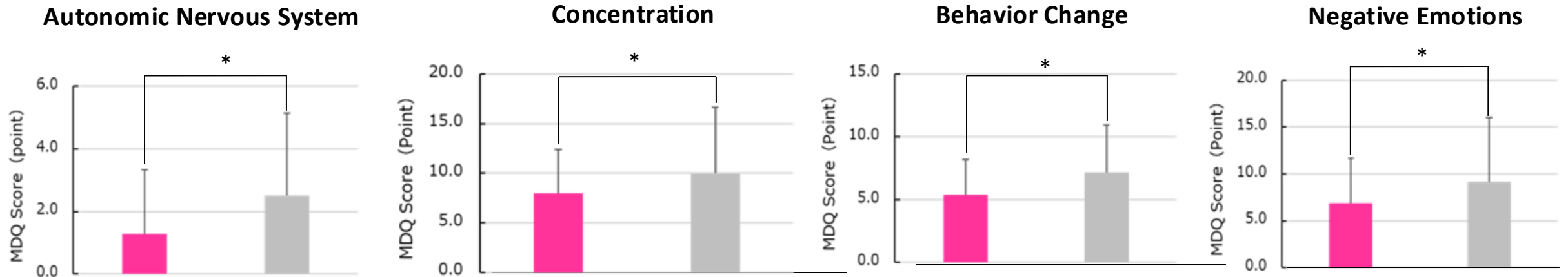
The lower numbers indicate improvement of reported stress levels. The result suggests that Venetron® supplementation supports relief of psychological stress.

UKQ (The change in the score before and after ingestion)			
Items	VENETRON®	Placebo	<i>P value</i>
Nervous	-0.5±0.7	0.2±0.9	0.015
Restless	-0.5±0.9	0.3±1.2	0.038
Irritated	-0.6±1.1	0.1±0.7	0.038
<i>n=17</i>	Improvement (decrease)	Worsening (increase)	

Clinical Research Trial #6: PMS and Menstruation Symptoms

Result 1: Reduction in Common PMS Symptoms

Pre-menstrual ingestion of Venetron® saw improvement in the autonomic nervous system, reduction in negative emotions, improved concentration and behavioral changes (performance and sociability).



■ Venetron® (n=21)

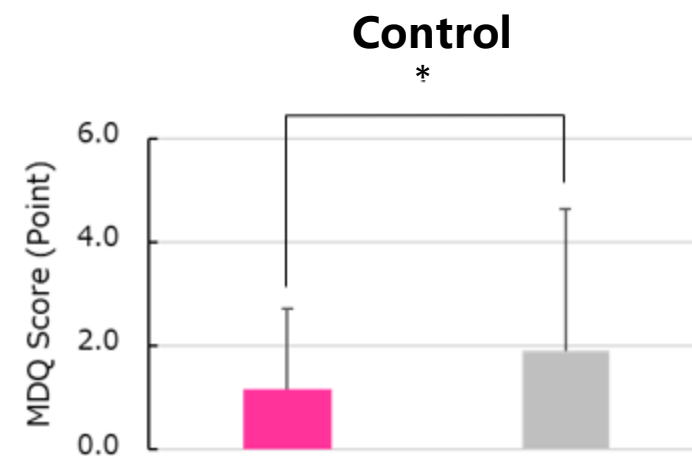
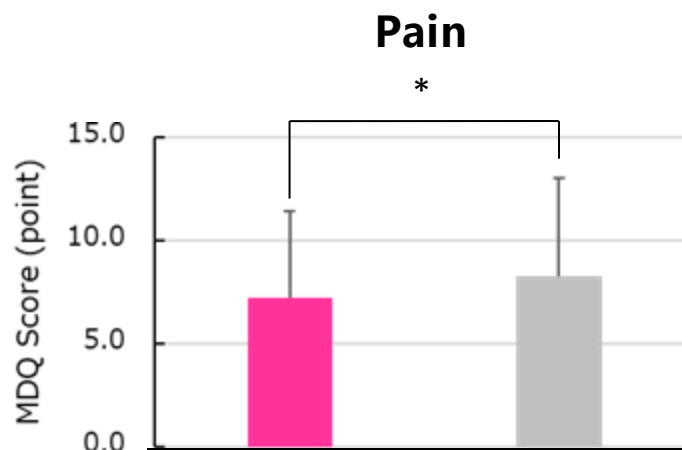
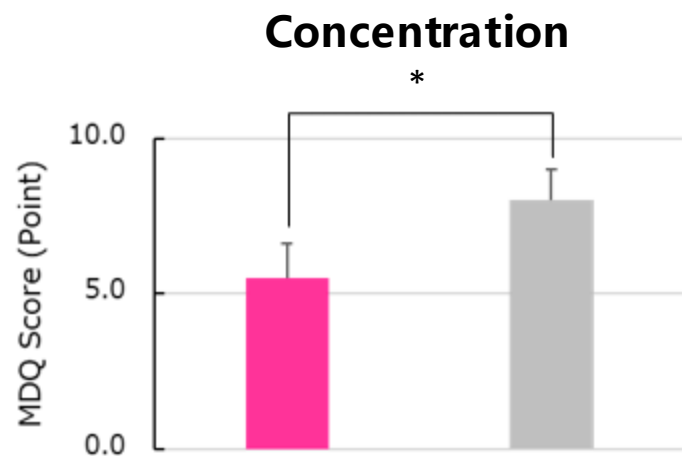
■ Placebo (n=21)

* $p < 0.05$

Clinical Research Trial #6: PMS and Menstruation Symptoms

Result 2: Reduction in Common Menstruation Complaints

During Menstruation, ingestion of Venetron® improved pain, poor concentration, and control with fewer complaints on symptoms associated with menstruation.



■ VENETRON® (n=21)

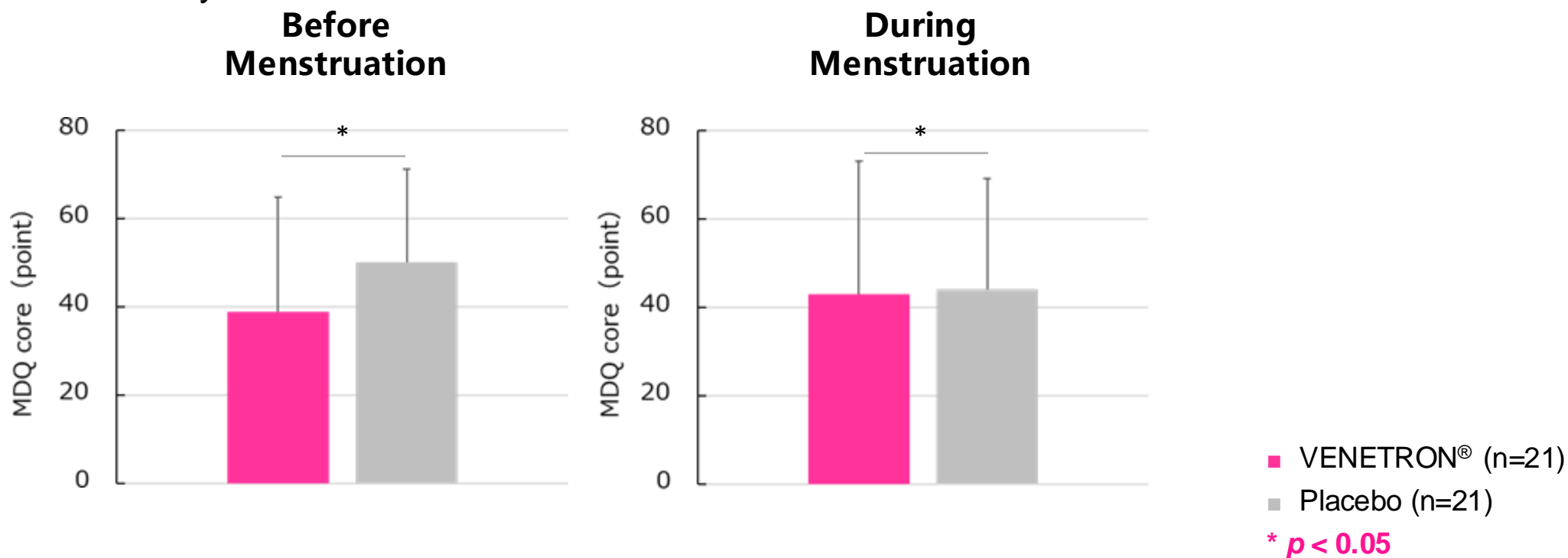
■ Placebo (n=21)

* $p < 0.05$

Clinical Research Trial #6: PMS and Menstruation Symptoms

Result 3: Venetron® is effective at easing symptoms of the menstruation cycle.

Ingestion of Venetron® significantly improved participants discomfort before and during menstruation indicating that Venetron® is effective at easing common symptoms associated with PMS and the menstrual cycle.



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Evidence for:**

1. R&D
2. Claims
3. Target Marketing

Article

A Randomized, Placebo-Controlled, Double-Blind Trial to Assess the Effects of *Apocynum venetum* L. (*A. venetum*) Venetron® on Sleep and Stress in those expressing Feelings of Anxiety

Kaitlyn P. White¹, Susan Hewlings^{1*}, Corey Bryant¹, Megan Moseley¹, Christopher R. D'Adamo², Christopher S. Colwell³, Jeff Chen³ and Emily K. Pauli³

¹ Radicle Science, Inc., Del Mar, CA 92014, USA; Kaitlyn.white@radiclescience.com; corey.bryant@radiclescience.com

² Department of Family and Community Medicine, University of Maryland School of Medicine, Baltimore, MD 21201, USA

³ Department of Psychiatry & Biobehavioral Sciences, University of California-Los Angeles, Los Angeles, CA 90095, USA

* Correspondence: susan.hewlings@radiclescience.com

Abstract:

Background/Objectives: Anxiety and stress are interrelated and connected to reduced health-related quality of life. Botanicals such as *Apocynum venetum* L. (*A. venetum*) have been shown to improve health outcomes. No human studies have been conducted in a diverse large group of healthy adults in the US. The purpose of this randomized, double-blind, placebo-controlled study was to evaluate the effects of Venetron® *Apocynum venetum* leaf extract on self-reported anxiety levels and overall health outcomes compared to placebo. **Methods:** Healthy adults (N = 476) seeking improvement in self-reported anxiety and stress were randomly assigned to receive 50 mg of *A. venetum* (n = 234) or placebo (n = 242) for 6 weeks. Feelings of anxiety were assessed at baseline and weekly using Patient-Reported Outcomes Measurement Information System (PROMIS™) Anxiety 8A. Perceived stress, sleep quality, and cognitive function were evaluated at baseline and weekly using validated assessments. A linear mixed-effects regression model was used to compare the change in health outcome scores between active and placebo groups. **Results:** There was a significant difference between the groups in the rate of improvement of perceived stress and sleep disturbance. The active group was significantly more likely to experience a Minimal Clinically Important Difference (MCID) in their perceived stress and marginally significantly more likely to experience an MCID in their feelings of anxiety. Participants who reported experiencing side effects did not significantly differ between arms. **Conclusion:** Venetron® may be safe and effective therapy for stress and sleep disturbance among those suffering from feelings of anxiety.

Keywords: *Apocynum venetum*; *A. venetum*; flavonoids; feelings of anxiety; real world evidence; virtual study; RCT; dietary supplement

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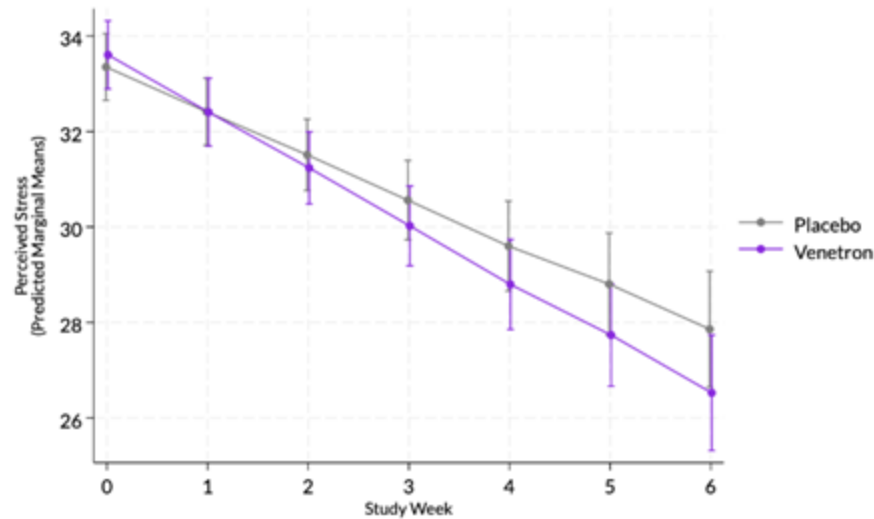
Citation: To be added by editorial staff during production.

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Were there significant differences in effect between the product and placebo arm?

There was a **significant difference** in average effect between Venetron and placebo. In other words, we found evidence that there was a significantly sharper decline in perceived stress among those who took Venetron relative to those who took the placebo.

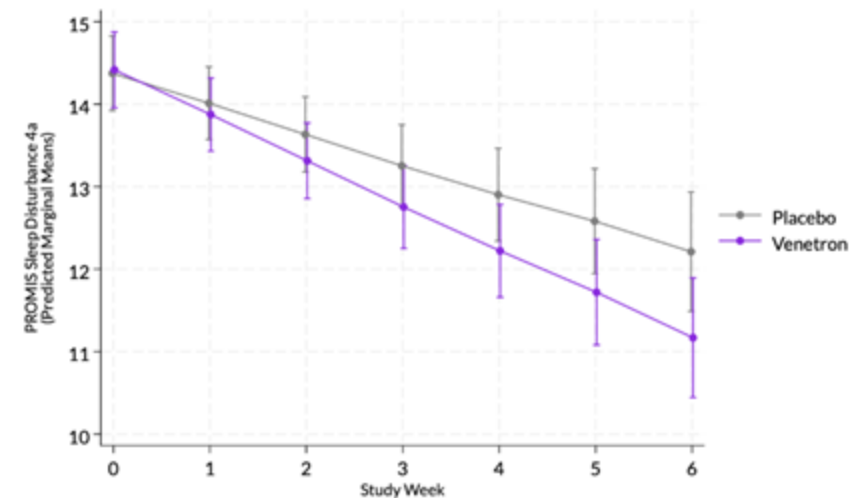


Perceived Stress

Sleep Quality

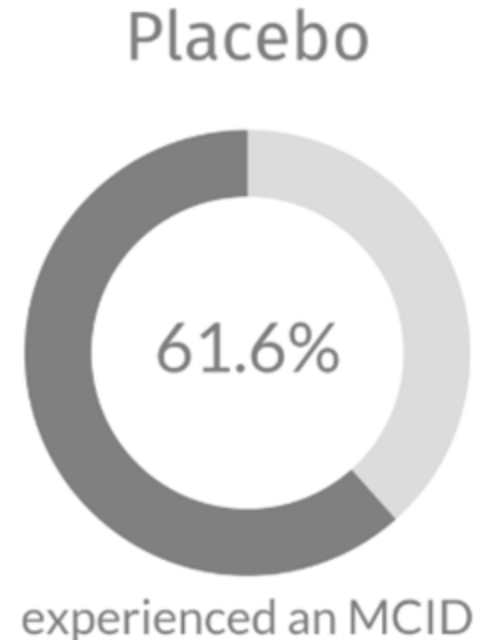
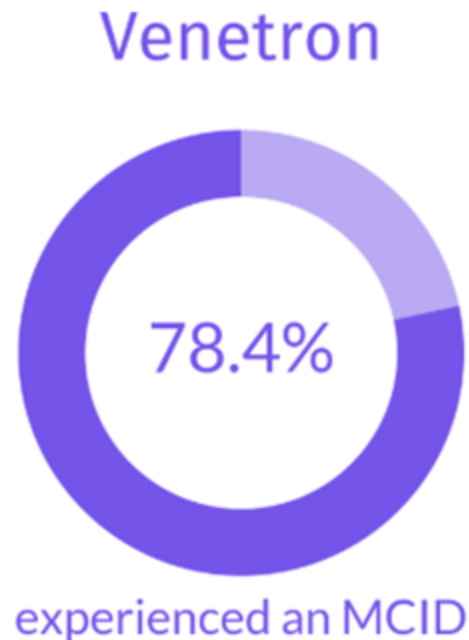
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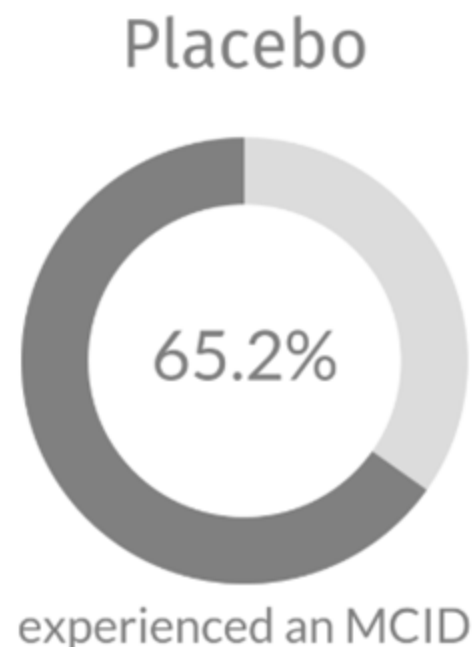
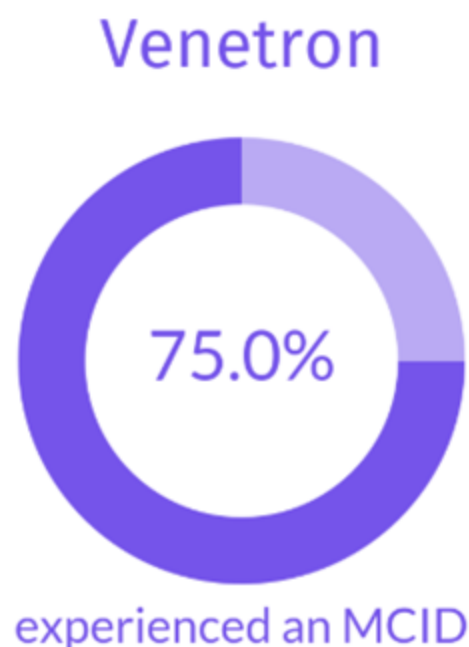
Were people more likely to experience clinically meaningful change in certain arms?

The majority (78%) of participants in the Venetron arm experienced a minimal clinically important difference (MCID) in their Perceived Stress score^a, meaning that they experienced a meaningful change that could warrant a change in their symptom management. By comparison, approximately 62% of participants in the placebo group experienced an MCID. Those assigned to Venetron were **significantly more likely** to experience an MCID in stress relative to placebo control.



Were people more likely to experience clinically meaningful change in certain arms?

The majority (75%) of participants in the Venetron arm experienced a minimal clinically important difference (MCID) in their PROMIS Anxiety 8a score^a, meaning that they experienced a meaningful change that could warrant a change in their symptom management. By comparison, approximately 65% of participants in the placebo group experienced an MCID. There was a **marginally significant difference** in the likelihood of experiencing an MCID such that participants assigned to Venetron were more likely to experience an MCID relative to the placebo control at the $\alpha = .05$ level ($p = 0.052$).





CONTACT

Lauren Clardy

Sr. Director, Branded Ingredients

(914) 251-0701 x147

Lauren.Clardy@Maypro.com

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MOOD, STRESS, SLEEP, CONCENTRATION

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