OBSERVATIONAL, LONGITUDINAL STUDY OF CANNABIDIOL (CBD) IMPACT ON PAIN, ANXIETY, AND SLEEP

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Principal Investigator Endo-C, LLC

Bountiful, UT

- Co-owner of **Regenerative Stem Cell and Wellness Center**
  - Bountiful, UT focusing on orthopedic umbilical cord derived stem cells, amniotic, and Wharton's Jelly products. Doing aesthetic procedures with stem cells, PRP, dermal fillers, and peptides.
- Co-founder of **Tame the Flame Now®**
  - The anti-inflammatory and anti-radical approach to anti-aging and weight loss
- Principal Investigator – **Endo-C®**
  - Dedicated to doing research on CBD, CBD/THC, and other nutraceutical products
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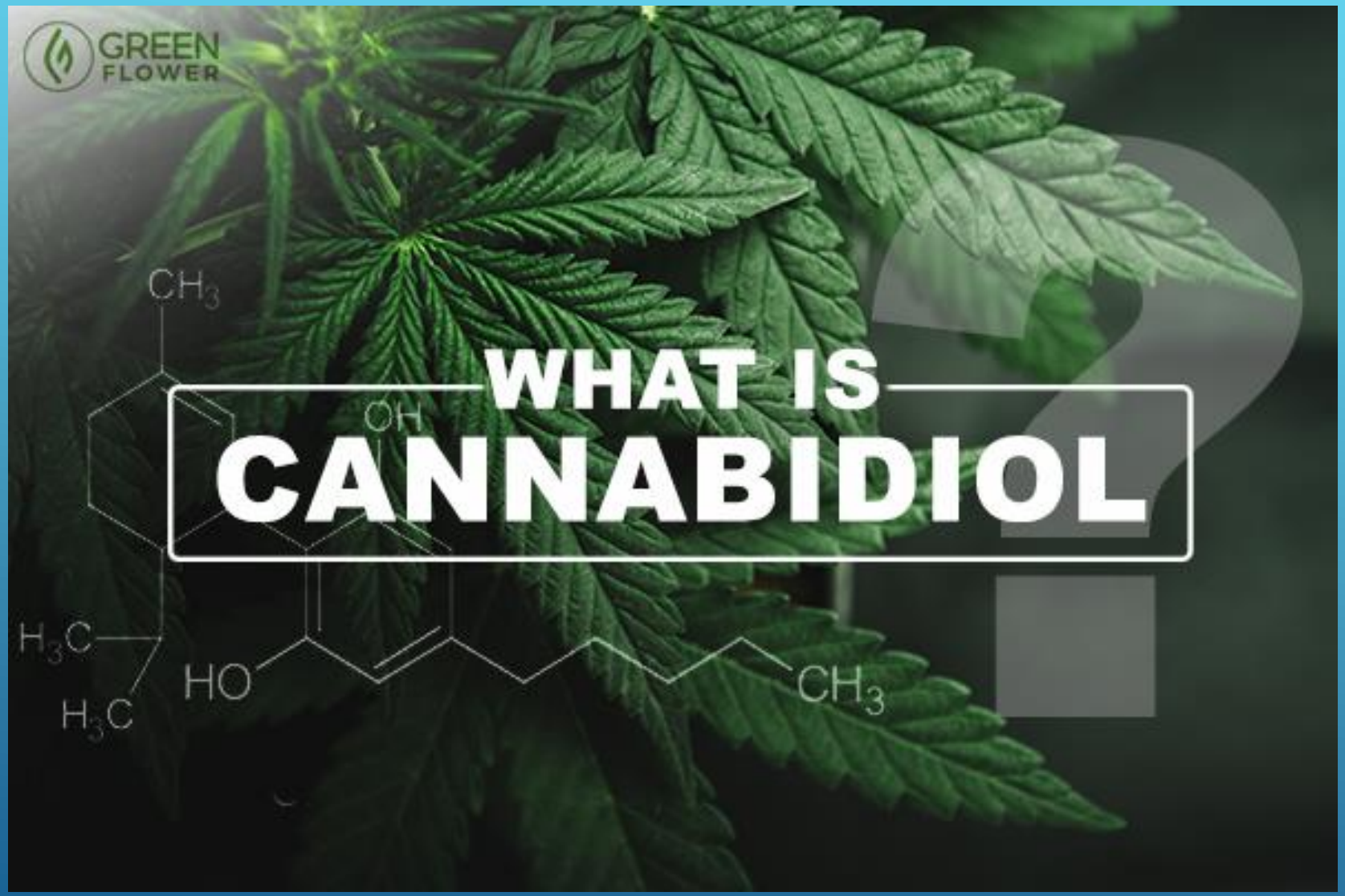
BACKGROUND OF STUDY

- **Nature** has the answers with analgesic plants
  - **Cannabis** - THC CBD and more
  - **Opium poppy** - morphine, codeine
  - **Chile peppers** - capsaicin
  - **Willow bark** - aspirin


GREEN
FLOWER
WHAT IS
CANNABIDIOL

CANNABIS AND CBD

- Over 400 unique chemicals found in this botanical plant
- Over 70 non-psychogenic but potent bioactive cannabinoids
- We synthesize our own cannabinoids and have an extensive endocannabinoid system in our body.

CANNABIS AND CBD

These play a significant role in regulating:

- Inflammation, pain, appetite, sleep, mood
- Fat and energy metabolism, insulin sensitivity
- Boosting immune system, and improving many neurological disorders

THE RECEPTORS IN THE BRAIN RESPOND TO CANNABIS AND CANNABIDIOL



MECHANISMS OF ACTION

Two basic endogenous arachidonic acid derived molecules known as endocannabinoids – anandamine (AEA) and 2-arachidonylethanolamide (2-AG) very active on glutamatergic and GABA-ergic synapses

THC – two G-protein coupled receptors

CB1-R –located mainly in the brain and nervous system and modulate neurotransmitter release to reduce pain, reduce inflammation, regulates sensory perception, memory and cognitive function

CB2-R – immune system, GI tract, bone, activated microglia in the CNS

CBD MECHANISM OF ACTION

- CBD has a very low affinity and shows little agonist activity at the G protein-coupled endocannabinoid system (ECS) receptors, CB1-R, CB2-R
- Opioid receptors (ORs) are $G_{i/o}$ protein-coupled receptors that bind opiates

  CBD may serve as an allosteric modulator at mu and δ ORs

Phytocannabinoid Cell Targets

PROF of POT

THC		CBD
	Cannabinoid System	
Partial Agonist	CB1	Negative Allo Modulator
Partial Agonist	CB2	Weak Antagonist
Not Tested	FAAH	Weak Inhibitor
Inhibitor	FABP	Inhibitor
	Atypical Cannabinoid Receptors	
Agonist	GPR18	Antagonist
Agonist	GPR55	Antagonist
	Serotonin Receptors	
No effect	5-HT1A	Full agonist
No effect	5-HT2A	Weak Partial Agonist
Negative Allo Modulator	5-HT3A	Negative Allo Modulator
	Dopamine Receptors	
Not Tested	D2High	Partial agonist
	Opioid Receptors	
Negative Allo Modulator	uOR	Negative Allo Modulator
Negative Allo Modulator	δOR	Negative Allo Modulator
	Adenosine System	
Inhibitor	ENT1	Inhibitor
	Glycine Receptors	
Positive Allo Modulator	GlyR	Positive Allo Modulator
	GABA Receptors	
Not Tested	GABA-A	Positive Allo Modulator
	Acetylcholine Receptors	
No Effect	α7-AChR	Negative Allo Modulator
	TRP Channels	
No Effect	TRPV1	Agonist
Agonist	TRPV2	Agonist
Agonist	TRPV3	Agonist
Agonist	TRPV4	Agonist
Agonist	TRPA1	Agonist
Antagonist	TRPM8	Antagonist
	Nuclear Receptors	
Agonist	PPARγ	Agonist

MECHANISM OF ACTION OF CBD

- Indirect effect on the CB1 Receptors – stopping the enzymatic breakdown of anandamide – allowing it to stay around longer

  Strong affinity for three kinds of fatty acid binding proteins (FABP) acting like an anandamine reuptake inhibitor
- Mild effect on CB2 receptors in the periphery in lymphoid tissue - mediates the release of cytokines to help reduce inflammation and pain
- Stimulation of the vanilloid pain receptors (TRPV-1 receptor) which are know to mediate pain perception, inflammation and body temperature
- Adenosine reuptake inhibitor which cause a broad anti-inflammatory effect
- Activates at higher doses the 5-HT1A serotonin receptor (G-coupled protein) –anti-anxiety

MECHANISMS OF ACTION OF CBD

- Antagonist at the potentially new third cannabinoid receptor GRP55, GRP18, GRP119, (G protein-coupled receptor) GRP55 expressed in the brain and immune system
- Activates PPARS (peroxisome proliferator activated receptors) especially PPAR-gamma
- Acts as a positive allosteric modulator enhancing the GABA-A receptor affinity for GABA increasing its calming effect
- Negative allosteric modulators of mu and delta opioid receptors decreasing their activity
- Inhibits glutamate neurotoxicity
- Antioxidant activity greater than vitamin C or vitamin E
- Inhibits Tumor Necrosis Factor-alpha

OTHER CANNABINOIDS NON PSYCHO-ACTIVE

- CBC (cannabichromene) - Anti-inflammatory, Antibiotic, Antifungal
- CBG (cannabigerol) affinity for CB1 CB2 GABA uptake inhibitor lipoxygenase Inhibits COX-2 blocking pain killing benefits
- THCA strong anti inflammatory not psychoactive
- THCV reduces appetite not psychoactive
- CBN elevated if old product
- Precursor to many classical phytocannabinoids anti-inflammatory, antibiotic, antifungal

TERPENES

- Beta-caryophyllene (BCP) - anti-inflammatory selective CB1 agonist gastric protective
- Myrcene - analgesic (can be blocked by naloxone) blocks inflammation via PGE-2 muscle relaxant
- Alpha-pinene - inhibits PGE-1 promoted alertness inhibits breakdown of acetylcholinesterase
- Linalool - local anesthetic effects anti anxiety
- D-Limonene – anti depressant, improve mood
- Phytol - sedating
- Many of these terpenes have calming or sleep-induced effects

  Action is through GABA-A receptor

FLAVONOIDS

- Apigenin - inhibits TNF-alpha anticholinesterase activity inhibition of ICAM (Intercellular Adhesion Molecule 1) and TNF-alpha, inhibition of inducible nitric oxide synthase (iNOS) and COX-2
- Cannflavin A - inhibits PGE-2 thirty times more potent than ASA
- Beta-sitosterol - reduces topical inflammation and chronic edema
- Kaempferol
- Quercetin - iNOS inhibition, COX-2 inhibition, C-protein inhibition, NF-kB suppression

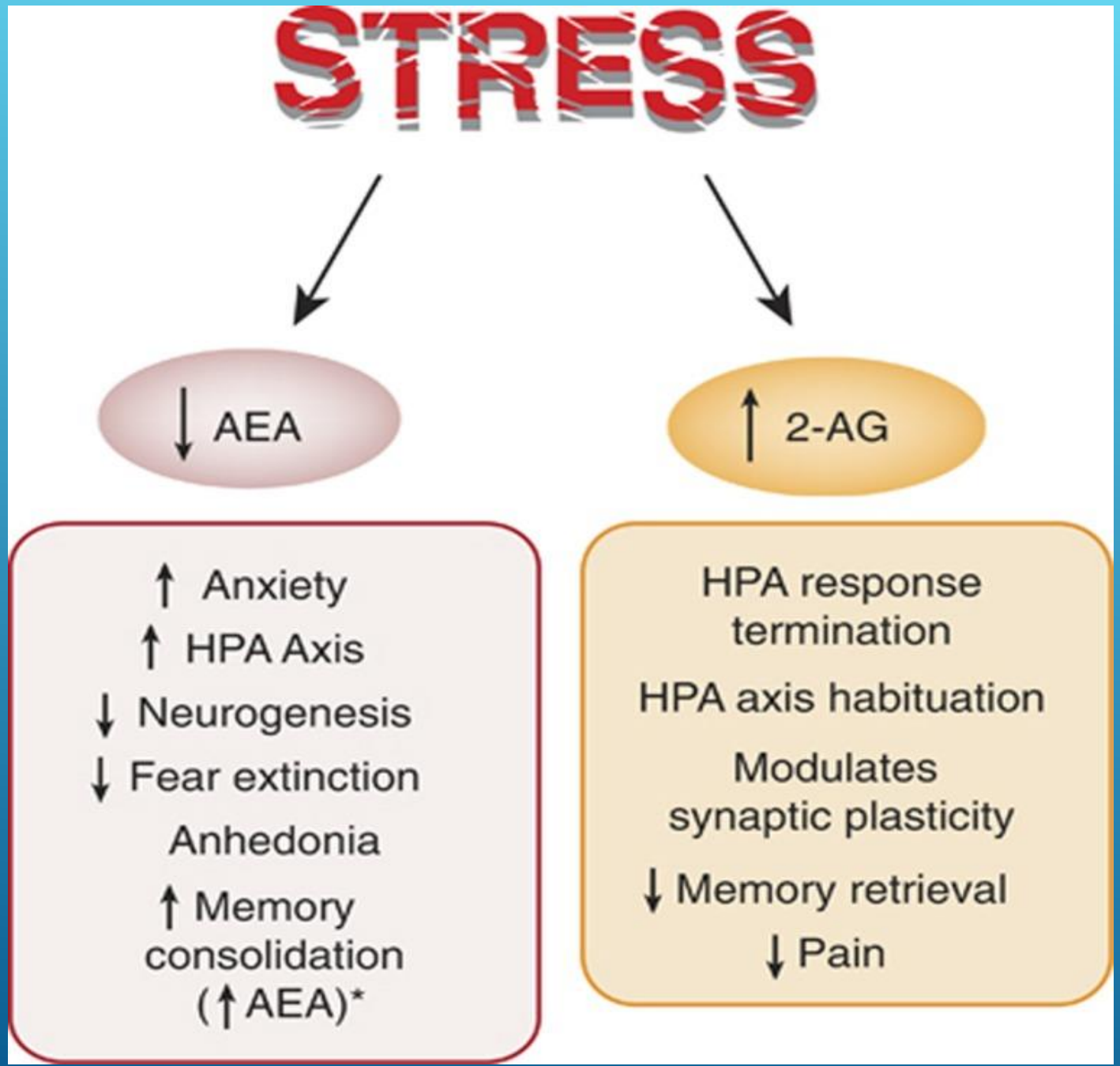
PROBLEMS WE FACE AS A SOCIETY

- Chronic pain – billions spent treating it as well as secondary damage from opioid abuse serious consequences on the patient's life, CP has a severe detrimental effect on their social and family environment, as well as on health care services.
- Chronic anxiety – a major problem in our society "everyone seems anxious" Anxiety disorders make up almost one third of the $148 billion annually spent on mental health in the US Anxiety can be felt physically as well as mentally.
- Sleep deprivation – resulting in major societal consequences Harvard scientists estimated in 2011 that sleep deprivation costs the U.S. economy about $63.2 billion in lost productivity annually. Affect all aspects of our health

ANXIETY - ENDOGENOUS SYSTEM

- Anandamide (AEA) and 2-AG both limit stress response gatekeeper roles
  - AEA controls initiation of the stress response
  - 2-AG controls the stress response after it has started
- Controls the BLA whether it can relay a stress signal to the HPA
- Acute stress causes Amygdala which coordinates the body's stress response – the basolateral amygdala (BLA) – hypothalamus to the HPA axis – cortisol
- AEA a rapid reduction in the AEA level (CRH induce activity of FAAH enzyme which metabolizes the AEA bring the levels down) increases cortisol
- 2-AG levels go up after acute and chronic stress (driven by increase in glucocorticoids)

Morena, M, et.al. Neurobiological Interactions Between Stress and the Endocannabinoid System, **Neuropsychopharmacology**. 2016 Jan; 41(1): 80–102


STRESS
↓ AEA
↑ 2-AG
↑ Anxiety
↑ HPA Axis
↓ Neurogenesis
↓ Fear extinction
Anhedonia
↑ Memory consolidation (↑AEA)*
HPA response termination
HPA axis habituation
Modulates synaptic plasticity
↓ Memory retrieval
↓ Pain

STUDIES ON CBD ON ANXIETY

- Neural basis of anxiolytic effects of cannabidiol (CBD) in generalized social anxiety disorder: a preliminary report
- Investigated patients with generalized SAD looking at regional cerebral blood flow – in a double-bind cross over study they found that CBD (400 mg) was associated with significantly decreased subjective anxiety and increased activity in the limbic and paralimbic areas.

Crippa, et al **Journal of Psychopharmacology** 2011, Jan 25(1) 121-30

CBD AND ANXIETY

- Cannabidiol reduces the anxiety induced by simulated public speaking in treatment-naïve social phobia patients

  Pre treatment with CBD significantly reduced anxiety, cognitive impairment and discomfort in their speech performance, and significantly decreased alert in their anticipatory speech. 600 mg of CBD (Bergamaschi, M, Costa Queiroz, R, et.al. Cannabidiol reduces the anxiety induced by simulated public speaking in treatment-naïve social phobia patients **Neuropsychopharmacology**, 2011, May 36(6): 1219-1226.)

- Antidepressant-like and anxiolytic-like effects of cannabidiol: a chemical compound of cannabis sativa (de Mello, de Oliveira, et.al. **CNS Neurology disorder and Drug Targets**, 2014;13(6):953-60)

  results suggest that CBD exhibited anti-anxiety and anti-depressant effects in animal models working on the 5-HT1A neuro-receptor

CBD AND ANXIETY

- Cannabidiol as a potential treatment for anxiety disorders A recent study found that existing preclinical evidence strongly supports CBD as a treatment for generalized anxiety disorder, panic disorder, social anxiety disorder, obsessive-compulsive disorder, and post-traumatic stress disorder when administered acutely.

  (Blessing, E., Steenkamp, M, **Neurotherapeutics** (2015) 12: 825-836)

- The anxiolytic effect of cannabidiol on chronically stressed mice depends on hippocampal neurogenesis: involvement of the endocannabinoid system (Campos, A, et.al. **International Journal of Neuropsychopharmacology** 2013 Jul 16(6):1407-19)

STUDIES ON CBD AND PAIN

- CBD gel on rats decreased inflammation and overall pain mouse pad study they induced monoarthritic knee pain in the rats and used 0.6, 3.1, 6.2, 62.3 mg/day of a CBD gel for 4 consecutive days. Joint circumference and immune cell invasion in histological sections were measured. They also examined paw withdrawal latency in response to heat stimulation and looked at exploratory behavior for animal's activity levels.
- Findings –significant reduction in joint swelling, immune cell infiltration, synovial membrane thickening. Saw reductions in pro inflammatory biomarkers
- (Hammell, d et.al. Transdermal cannabidiol reduces inflammation and pain-related behaviours in a rat model of arthritis **European Journal of Pain**, 2016 Jul 20 (6) , 936-948)

STUDIES ON PAIN AND CBD

- Cannabidiol as an emergent therapeutic strategy for lessing the impact of inflammation on oxidative stress (Booz, G **Free Radical Biology and Medicine** 2011 September 1; 51(5): 1054-1061)
- Cannabinoids in the management of difficult to treat pain (Russo, E **Therapeutics and Clinic Risk management** 2008: 4(1): 245-259)
- The analgesic potential of cannabinoids (Elikottil, J et. al. **Journal of Opioid Management** 2009; 5(6): 341-357)
- Is cannabis an effective treatment for joint pain? (Miller, R and Miller, R **Clinical and Experimental Rheumatology** 2017; 35 (suppl. 107): s59-s67)

CBD- PHARMACOLOGY INTERACTIONS

- CBD inhibits CYPs 1A1, 2B6, 2C9, 2C19, 3A4, and 3A5
- Increases activity CYPs 2B10 and 2B13 (usually seen with high doses of CBD)
- NSAIDs- work by inhibiting COX2 reduce inflammation and promote activity at the endocannabinoid receptors metabolized by CYP2C9 so CBD COULD DECREASE THE METABOLISM OF NSAIDs AND INCREASE THEIR SIDE EFFECTS. However does not appear to be the case
- INCREASES THE ANALGESIA EFFECT Ibuprofen modifies the endocannabinoid signaling even more not only inhibiting COX 2 but it also inhibits fatty acid amide hydrolase (FAAH) which increases anandamide levels
- High doses of CBD can interact with opioids via CYP3A4\CBD reduces cue-induced heroin-seeking
- Need to be aware that there can be interaction

LABELING ACCURACY

- Major concern is labeling accuracy of CBD extracts – 84 products were examined
  - 43% were under labeled
  - 26% were over labeled
  - 31% were accurate
  - 21% had detectable THC

Bonn-Miller, M, et.al. Labeling Accuracy of Cannabidiol Extracts Sold Online. **JAMA** (2017) 7:1708-9

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CoA # 17030523
CoA Date 03/24/2017
CoA Status Final

CERTIFICATE OF ANALYSIS

Customer	Love Hemp LTD	**Date Received**	3/17/2017
Address		**Condition**	Good
		Temp	Ambient
Sample Name	4.0g CBD / 10ml Tincture	**PO #**	
Sample Lot #	LH-031703-SB	**Remarks**	

Analysis	Specification	Result	Test Method	Test Date
Cannabidiol (CBD)	N/A	4459.8mg / 10mL	HPLC/UPLC	03/22/2017
Cannabigerol (CBG)	N/A	Not Detected	HPLC/UPLC	as above
Cannabinol (CBN)	N/A	Not Detected	HPLC/UPLC	as above
Cannabidiolic Acid (CBD-A)	N/A	Not Detected	HPLC/UPLC	as above
Cannabichromene (CBC)	N/A	Not Detected	HPLC/UPLC	as above
Tetrahydrocannabinol (THC)	N/A	Not Detected	HPLC/UPLC	as above
Tetrahydrocannabinolic (THC-A)	N/A	Not Detected	HPLC/UPLC	as above
alpha pinene	N/A	Not Detected	GC	03/17/2017
Camphene	N/A	11µg / g	GC	as above
ß-myrcene	N/A	1049.9µg / g	GC	as above
ß-Pinene	N/A	20.8µg / g	GC	as above
delta-3-Carene	N/A	70.4µg / g	GC	as above
alpha-Terpinene	N/A	12.1µg / g	GC	as above
Ocimene	N/A	Not Detected	GC	as above
d-Limonene	N/A	13.5µg / g	GC	as above
p-Cymene	N/A	Not Detected	GC	as above
ß-Ocimene	N/A	Not Detected	GC	as above
Eucalyptol	N/A	14.1µg / g	GC	as above
gamma-Terpinene	N/A	Not Detected	GC	as above
Terpinolene	N/A	Not Detected	GC	as above
Linalool	N/A	277.4µg / g	GC	as above
Isopulegol	N/A	Not Detected	GC	as above
Geraniol	N/A	Not Detected	GC	as above
ß-Caryophyllene	N/A	3004.1µg / g	GC	as above
alpha-Humulene	N/A	933.5µg / g	GC	as above
Nerolidol (Cis)	N/A	2446.7µg / g	GC	as above
Nerolidol (Trans)	N/A	3332.0µg / g	GC	as above
Guaiol	N/A	Not Detected	GC	as above
Caryophyllene oxide	N/A	38.5µg / g	GC	as above
alpha-Bisabolol	N/A	Not Detected	GC	as above
TPC	N/A	<10 cfu/g	AOAC 986.23	03/17/2017
Yeast	N/A	<10 cfu/g	FDA BAM, 8th Ed	as above
Mold	N/A	<10 cfu/g	FDA BAM, 8th Ed	as above
Coliforms	N/A	<10 cfu/g	AOAC 991.14	as above
E. Coli	N/A	Negative	AOAC 991.14	as above
Salmonella	N/A	Negative	AOAC 989.13	as above

Authorized by
Murali Muniandy, Laboratory Manager

These results apply only to the items tested. This certificate of analysis shall not be reproduced except in full without written consent of iLab.
Estimation of uncertainty of measurement is available upon request.

OBSERVATIONAL LONGITUDINAL STUDY OF CBD IMPACT ON PAIN, ANXIETY, AND SLEEP

- This is an ongoing observational study in the state of Utah.
- The purpose of the study is intended to confirm, and determine how significantly a highly bio-available precisely dosed CBD product will alter the research subject's pain levels and with the lessening of the pain, anxiety and if they will be able to better manage their sleep.
- This is an IRB approved and monitored study
- Patients were either physician referred or self – referred
- A comprehensive history was obtained from the patients including demographics, past medical history, review of systems, medications currently taking, prior medications, history of substance abuse, using marijuana, CBD currently, opioid or benzo usage, current diagnoses, supplements, and allergies. The patients online complete three vetted questionnaires - BPI: Questionnaire for Pain and Function; PSQ-3: Questionnaire for Pain and Sleep; and Generalized Anxiety Disorder 7 – item (GAD-7) Scale.

OBSERVATION AL LONGITUDINAL STUDY OF CBD ON PAIN, ANXIETY, AND SLEEP

- Each month the patients fill out online a follow up survey using the same questionnaires before receiving their next dose.
- Doses can be increased or decreased based on patient's reported signs and symptoms each month up to a maximum of 300mg/day

OBSERVATIONAL LONGITUDINAL STUDIES

Advantages

- They are effective in determining variable patterns over time.
- They can ensure clear focus and validity.
- They are very effective in doing research on developmental trends.
- They are more powerful than cross-sectional studies.
- They are highly flexible. They can provide high accuracy when observing changes.

Disadvantages

- They require huge amounts of time.
- They risk gathering data that is not 100% reliable
- They would risk experiencing panel attrition.
- They can be more expensive compared with cross-sectional studies.

LIMITATIONS

It was a dose adjustment study -the dosage could change once a month depending on patient's perceived need

Financial constraints (though hardship program available) patients paid to be in the study (the product was not sold)

PCR HEMP OIL



PHYTO-CANNABIDIOL RICH (PCR) HEMP OIL

- Industrial hemp is the non-psychoactive, low to no-THC, genetically distinct varieties of the plant *Cannabis sativa*. Hemp has absolutely no use as a recreational drug. Section 7606 of the Farm Bill defines industrial hemp as "the plant *Cannabis sativa L.* and any part of such plant, whether growing or not, with a delta-9 tetrahydrocannabinol concentration of not more than 0.3 percent on a dry weight basis.“
- Utah passed legislature that allows the use of farm bill hemp in any IRB studies regard the use of CBD for medical purposes.

PCR HEMP OIL

- PCR (Phyto- Cannabinoid Rich) hemp oil - full spectrum
- Optimal ratio of CBD to BCP (beta-caryophyllene) to bio activate the CBD
- Enhanced water solubility
- Soft gel capsule 25 mg of CBD/334 mg / 6 mg BCP/limonene

PCR HEMP OIL WITH BCP



PCR HEMP OIL

- The "entourage effect" is the potential therapeutic actions ascribed to a full range of cannabinoids contained in CBD PCR hemp oil which may positively help address conditional needs related to joint pain, anxiety, inflammation, but also may have broader therapeutic, health and healing properties.
- We take a lipid-based, natural, hemp oil product with the full entourage of cannabinoids and deliver them in a water soluble form with no loss in bio-efficacy or absorption.
- **VEDD** delivery system is a patented micelle technology that has been shown to improve the oral bioavailability of water insoluble compounds. **VEDD** is a natural water soluble **V**itamin **E** **D**erivative **D**imer technology that combined with **PCR** **(P**hyto-Cannabinoid Rich) oil. This delivers a water soluble hemp oil in a soft gel capsules.





Figure 2 - Difference between micelles, liposomes and VESIsorb® colloidal droplets

Nano-droplets composed of an oily core surrounded by a hydrophilic shell(emulsifiers). Compared a micellar system, this colloidal system contains lower amounts of surfactant and high amounts of oil

Result of Certificate of Analysis
Type: Phytocannabinoid Rich Hemp Oil
Extraction Method: SMB Liquid Chromatography
Potency Results

	Wt.(%)	(mg/g)
CBD	61	610
CBG	0.5%	< 1
CBN	0.30%	< 1
THC	Absent	Absent
CBC	0.30%	< 1
THC-A	Absent	Absent
CBD-A	< 0.1%	< 1
TOTAL THC	Absent	Absent
TOTAL CBD	61	610

TERPENES

	Wt. (%)			Wt. (%)
d-Limonene	.01-0.5		Myrcene	< 0.1
Eucalyptol	0.1-0.2		A-Bisabolol	< 0.1
a-Humulene	0.1-10		Phytol	< 0.1
a-Pinene	0.1-0.5		Linalool	< 0.1
β-Caryophyllene	0.1-0.5		Nerdilol	< 0.1

Pesticides

	ppm			ppm
Acequinocyl	Not Detected		Spinosad	Not Detected
Pyrethrium	Not Detected		Spirotetramat	Not Detected
Spiromesifen	Not Detected		Bifenazate	Not Detected
Abamectin	Not Detected		Fenoxycarb	Not Detected
Imidacloprid	Not Detected		Paclobutrazol	Not Detected

Ethanol	Not Detected

Heavy Metal Results
Microbiology

	ppm			ppm
Cadmium	< 0.005 ppm		TPC	10 cfu/g
Lead	< 0.005 ppm		Yeast and Mold	< 20 cfu/g
Arsenic	< 0.005 ppm		E. Coli	Negative
Mercury	< 0.005 ppm		Salmonella	Negative

STUDY PROTOCOL PROCESS FOR PAIN, ANXIETY & SLEEP

- Create an account
- Complete the intake form with medical history
- Complete the informed consent
- Primary Investigator (MD) signs off
- Complete follow up survey form each subsequent month

RESEARCH DESIGN

- Compare participant responses on intake survey with response on follow up survey.
- A Likert scale of 0-10 was used as measure
- A repeated ANOVA
  - Pain, Anxiety & Sleep scales are dependent variables
  - Group by Gender
  - Group by Usage of Opioid medication

MEASUREMENT SCALES

- Pain
  - On a scale of 0-10, with 0 meaning no pain and 10 meaning severe pain, please rate your pain

- Activity (combined to a single score for analysis)
  - In the past week rate how much interference pain has had on your general activity
  - In the past week rate how much interference pain has had on your ability to walk
  - In the past week rate how much interference pain has had on your productivity

- Anxiety (combined to a single score for analysis)
  - In the past week rate how much interference pain has had on your mood
  - Over the past 2 weeks I have been feeling nervous, anxious or on edge
  - Over the past 2 weeks I have been feeling down, depressed, or hopeless
  - Over the past 2 weeks I have been feeling little interest or pleasure in doing things
  - Over the past 2 weeks I have been worrying too much about different things
  - Over the past 2 weeks I have had trouble relaxing
  - Over the past 2 weeks I have becoming easily annoyed or irritable
  - Over the past 2 weeks I have been feeling something awful might happen

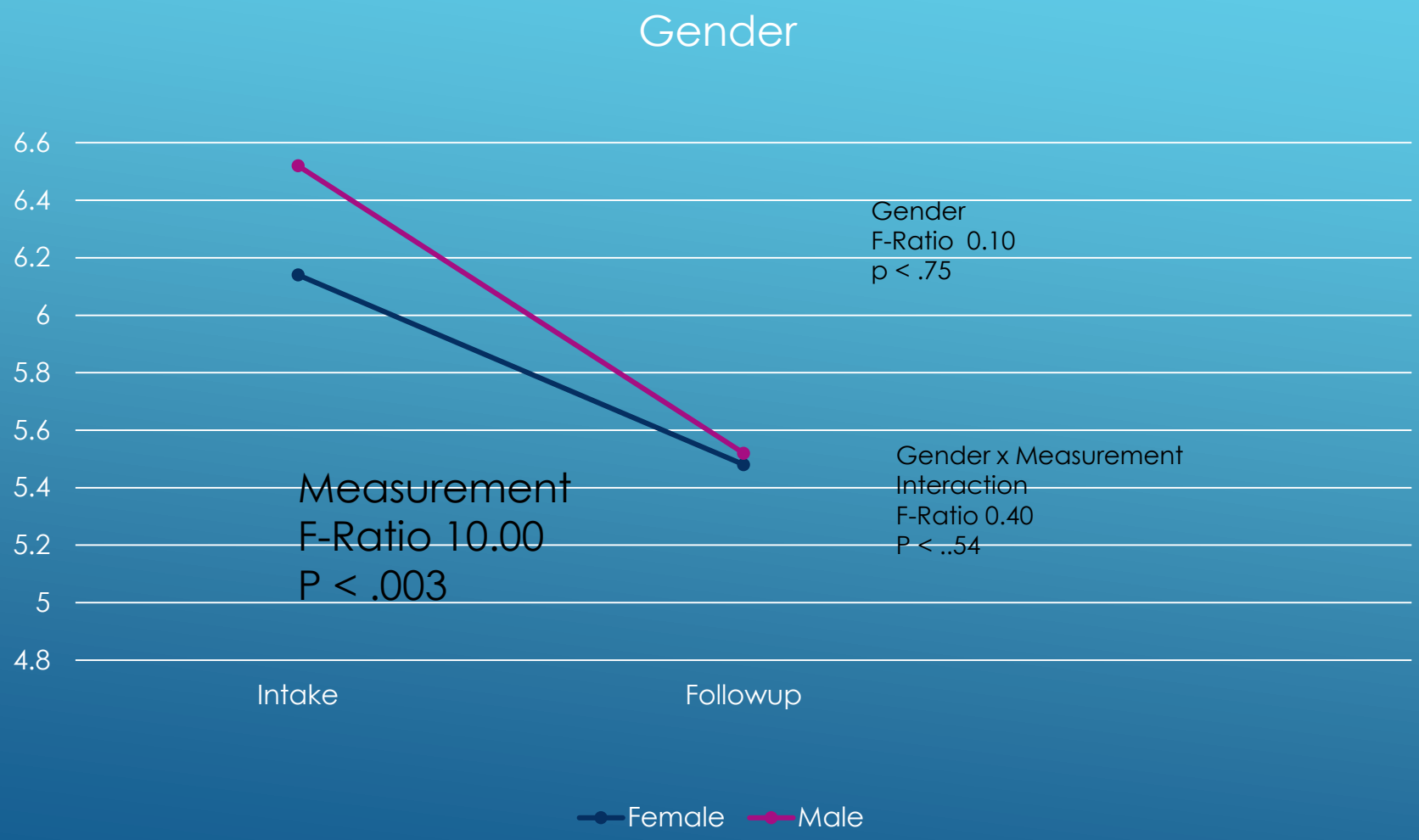
- Sleep (combined to a single score for analysis)
  - In the past week rate how much interference pain has had on your productivity
  - Over the past 2 weeks I have had difficult falling asleep
  - Over the past 2 weeks I have had trouble staying asleep
  - Over the past 2 weeks I feel rested when waking
  - How often do you use a sleeping aid

SUBJECT DEMOGRAPHICS

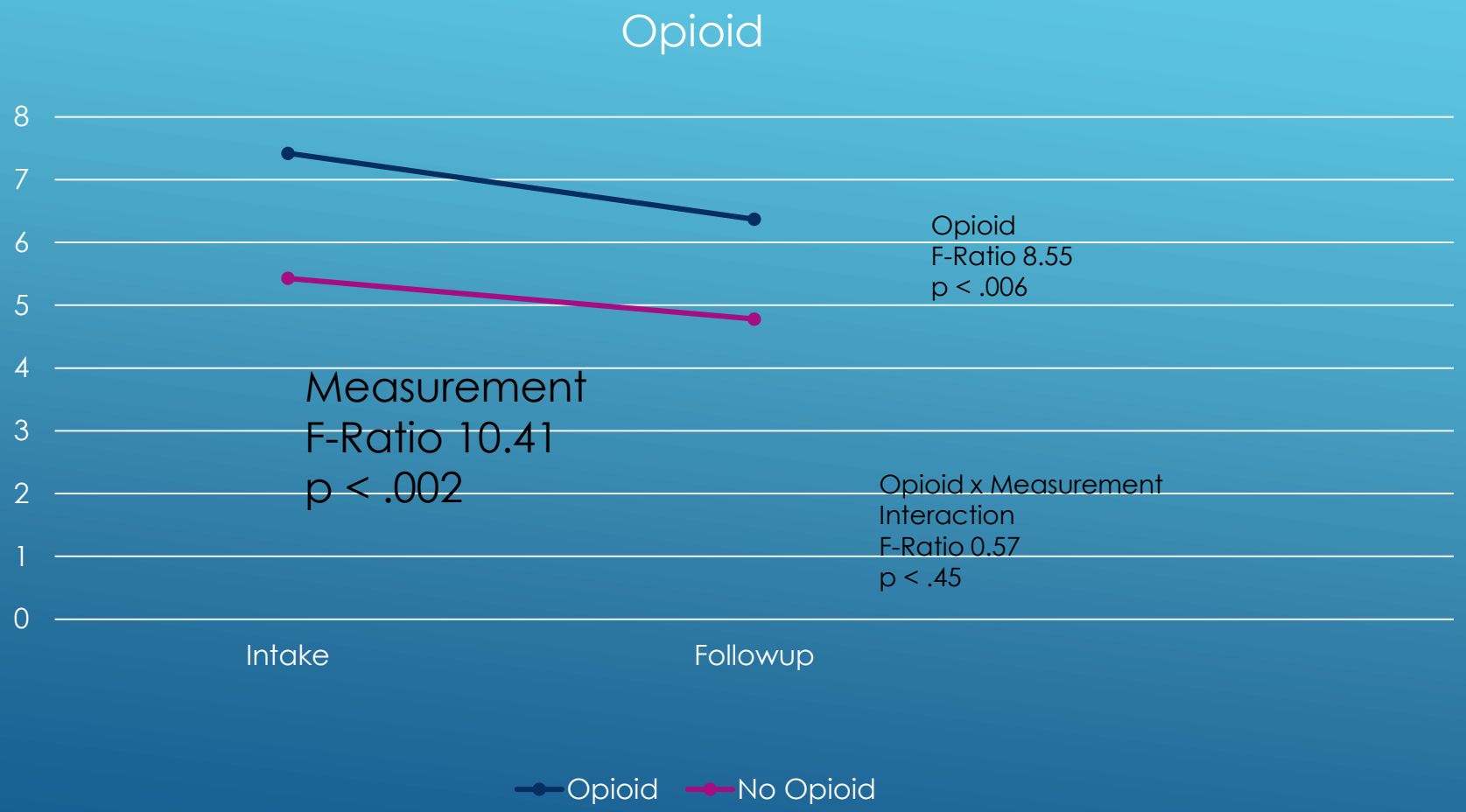
WOMEN AVERAGE AGE = 48.62
MEN AVERAGE AGE = 51.48
ON OPIOIDS AVERAGE AGE = 56.68
NO OPIOIDS AVERAGE AGE = 44.57



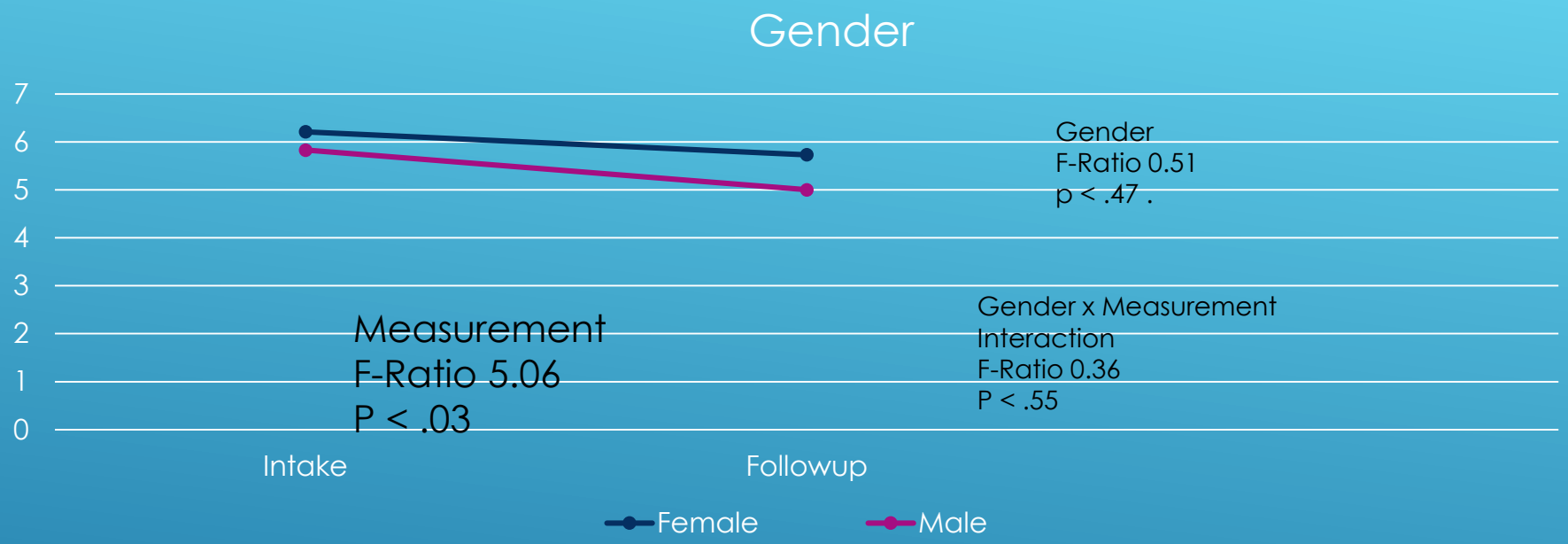
PAIN LEVEL

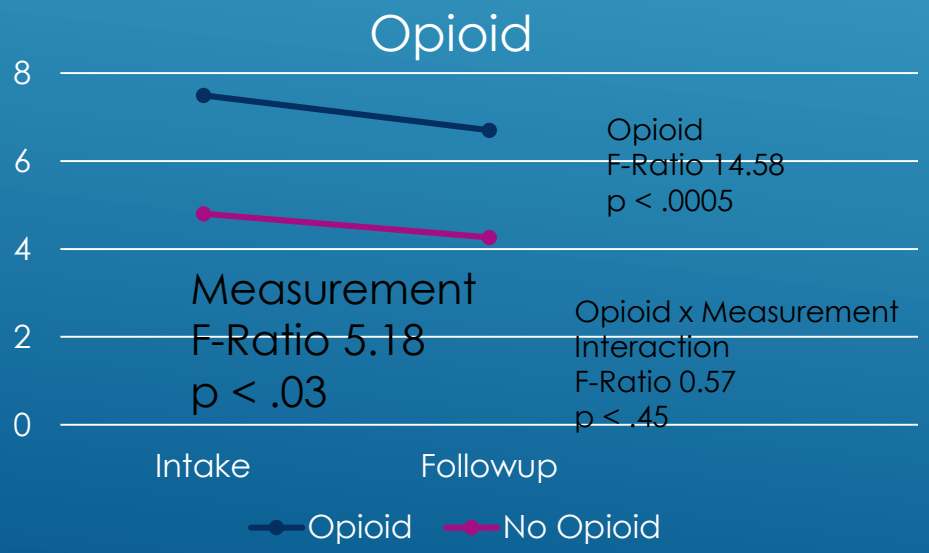

Gender
6.6
6.4
6.2
6
5.8
5.6
5.4
5.2
5
4.8
Intake
Followup
Female
Male
Gender
F-Ratio 0.10
p < .75
Gender x Measurement
Interaction
F-Ratio 0.40
P < ..54
Measurement
F-Ratio 10.00
P < .003

PAIN LEVEL

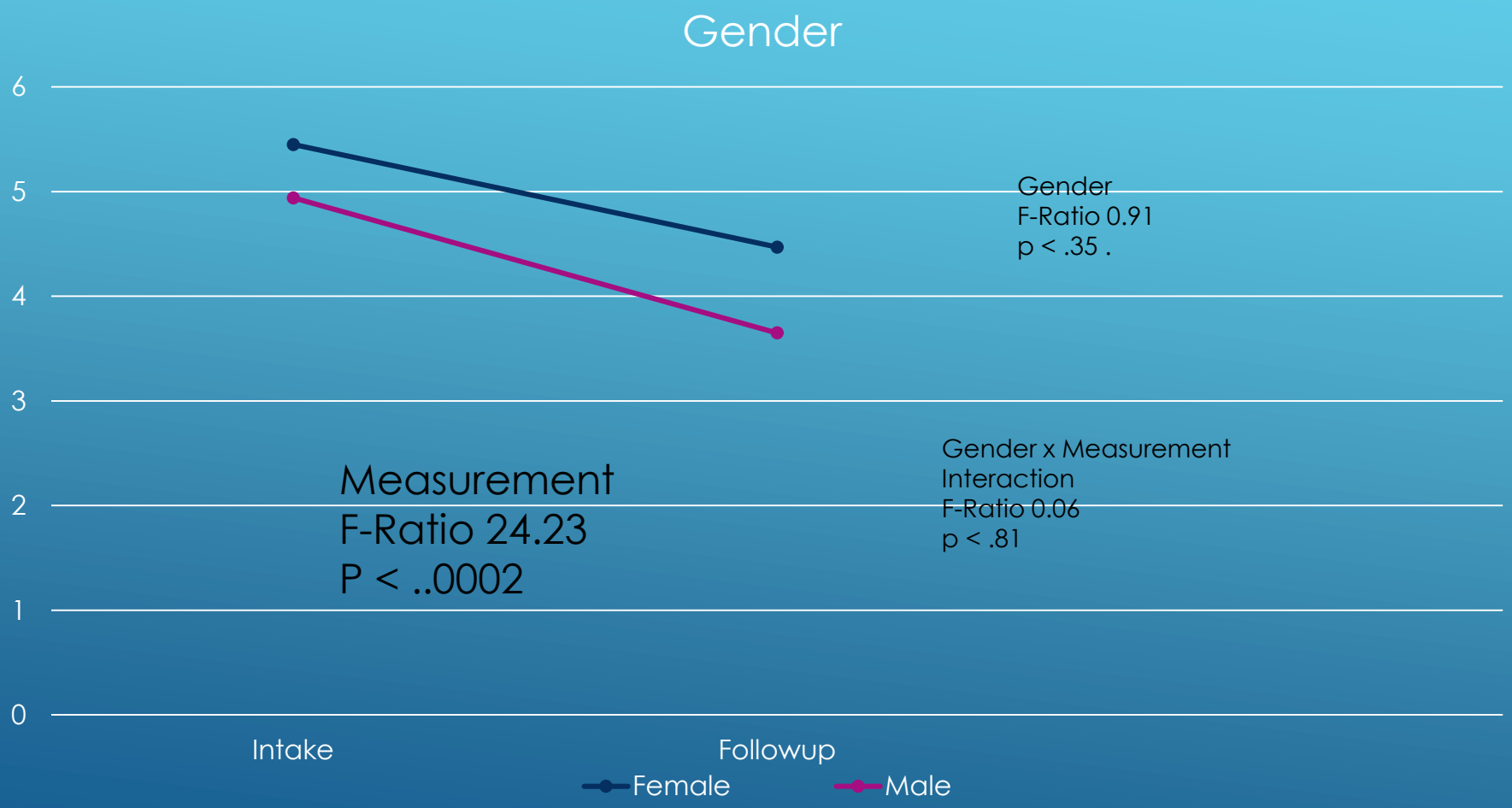

Opioid
8
7
6
5
4
3
2
1
0
Intake
Followup
Opioid
F-Ratio 8.55
p < .006
Measurement
F-Ratio 10.41
p < .002
Opioid x Measurement
Interaction
F-Ratio 0.57
p < .45
Opioid
No Opioid

ACTIVITY SCALE

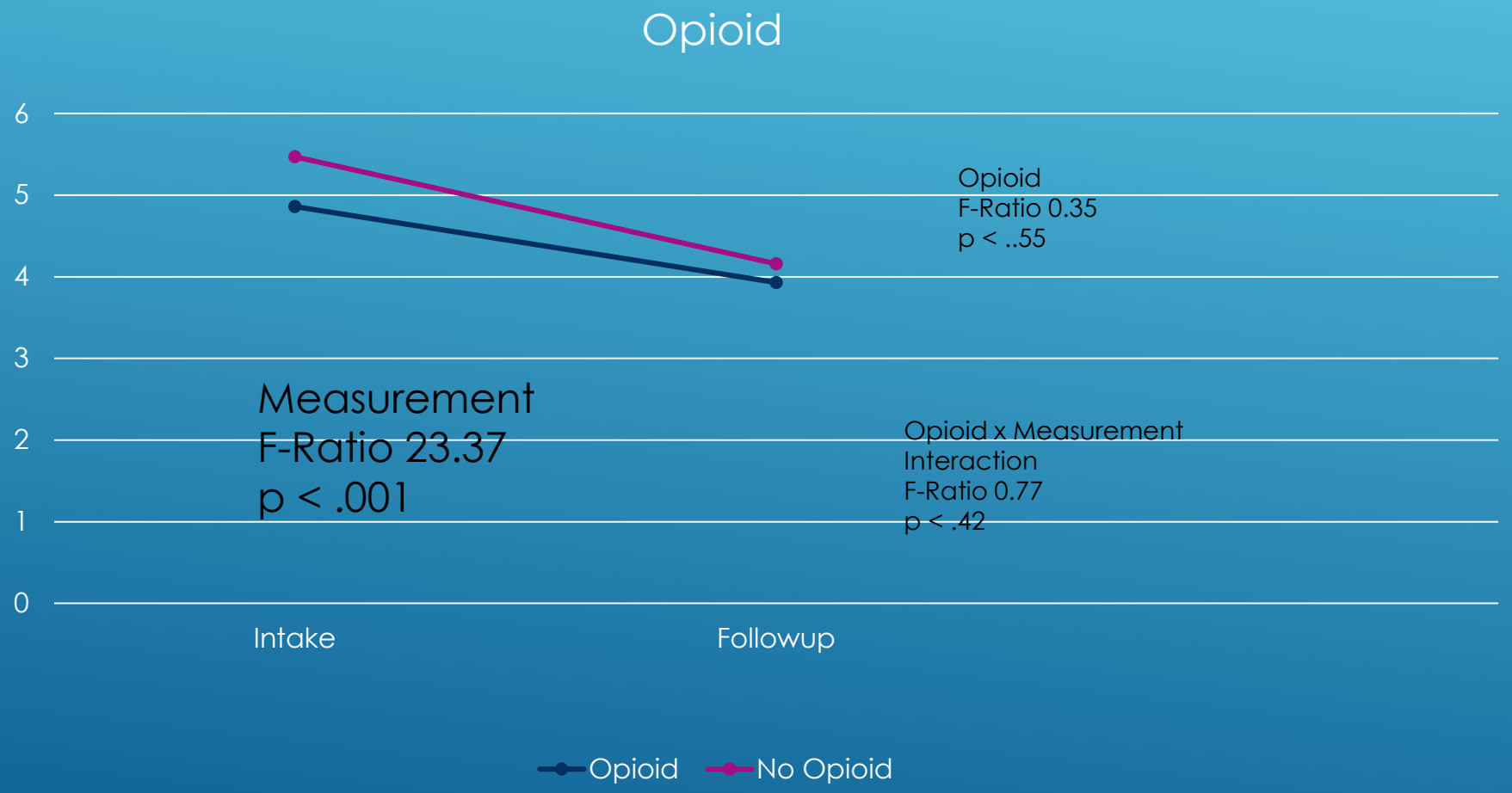




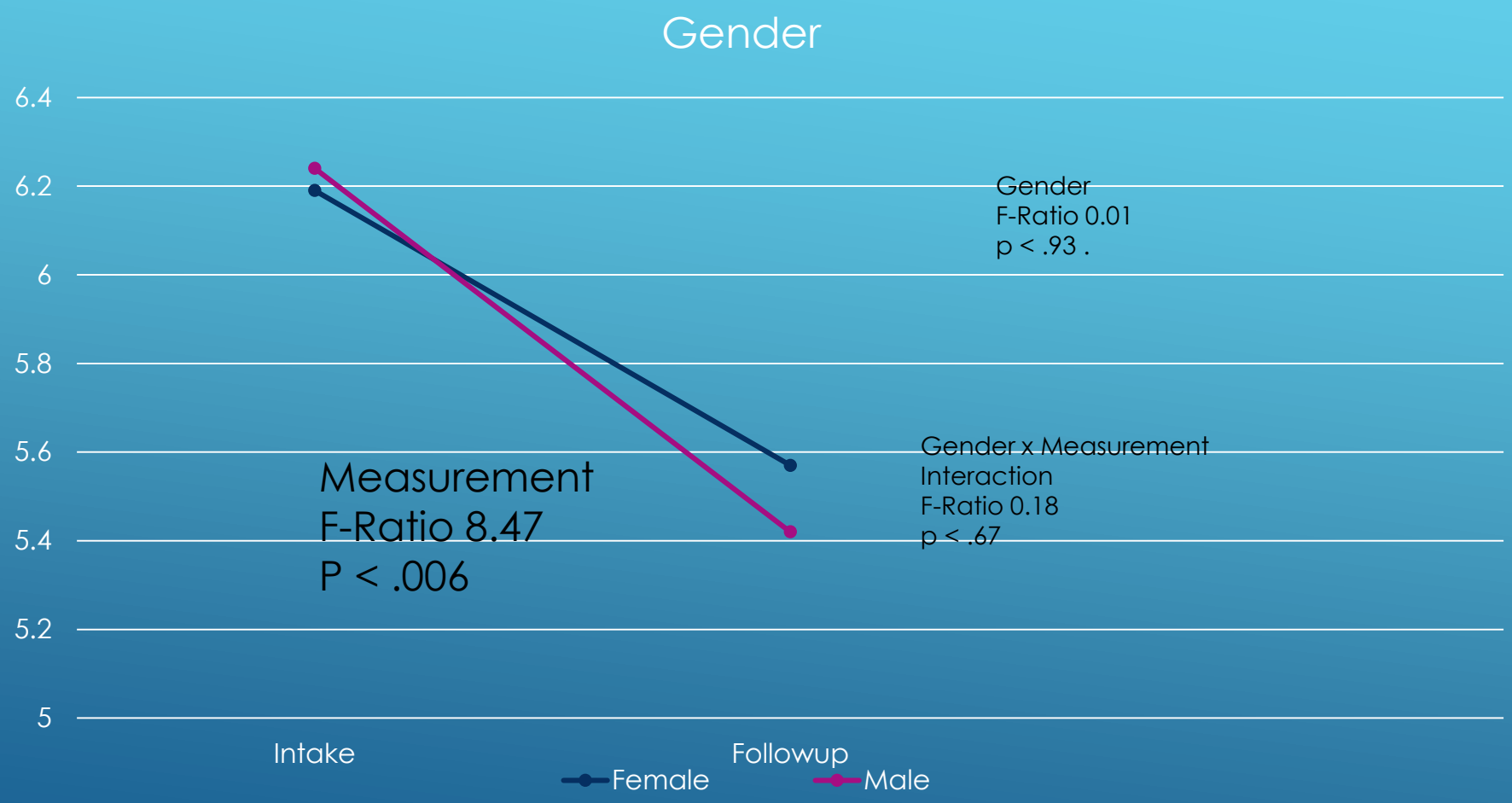
ANXIETY SCALE



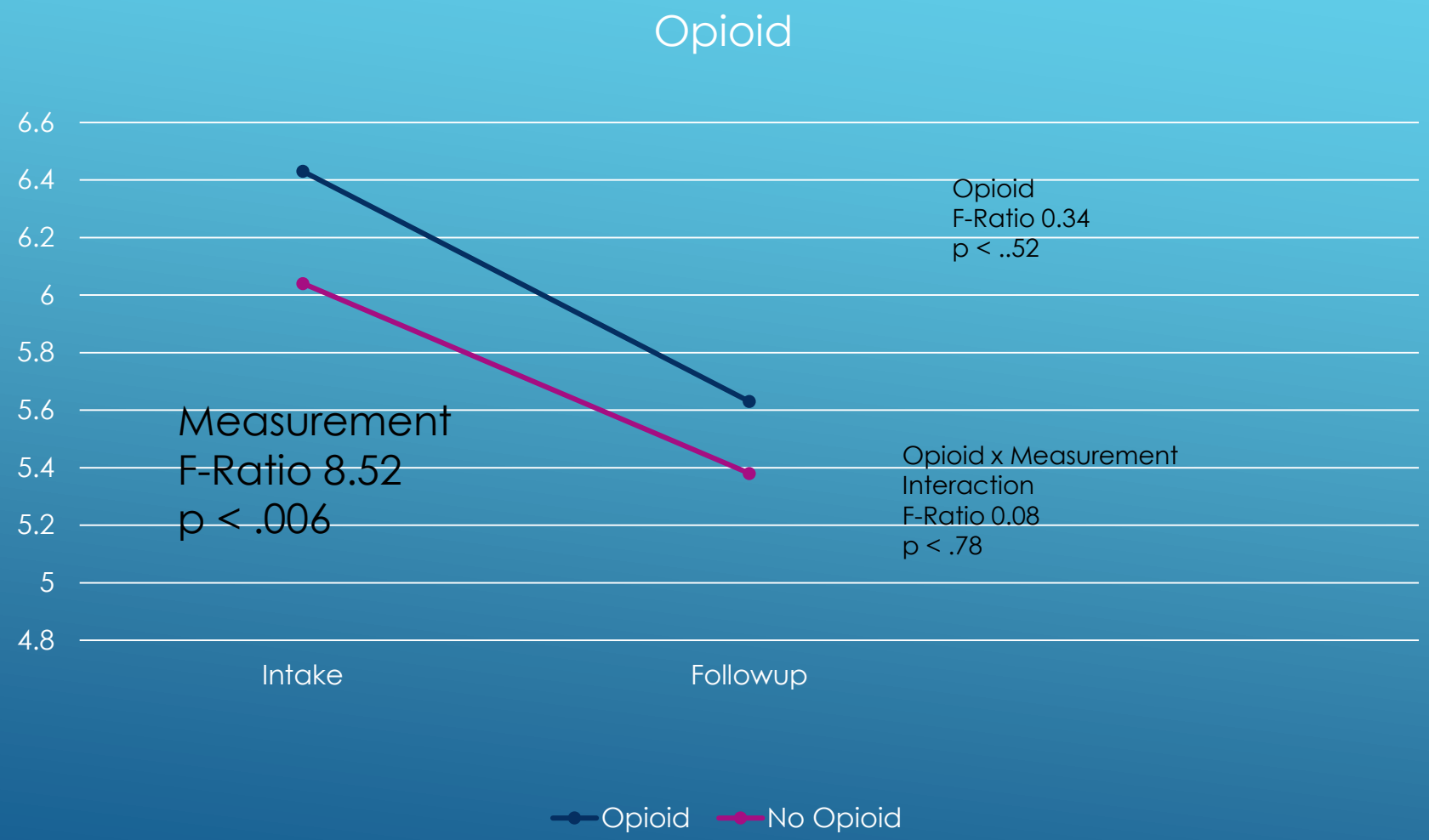
ANXIETY SCALE



SLEEP SCALE


Gender
6.4
6.2
6
5.8
5.6
5.4
5.2
5
Intake
Followup
Female
Male
Gender
F-Ratio 0.01
p < .93 .
Gender x Measurement
Interaction
F-Ratio 0.18
p < .67
Measurement
F-Ratio 8.47
P < .006

SLEEP SCALE


Opioid
6.6
6.4
6.2
6
5.8
5.6
5.4
5.2
5
4.8
Intake
Followup
Opioid
F-Ratio 0.34
p < ..52
Measurement
F-Ratio 8.52
p < .006
Opioid x Measurement
Interaction
F-Ratio 0.08
p < .78
Opioid
No Opioid

INITIAL OBSERVATIONS

- Initial 25mg Gel Cap 2X daily dose is effective
  - Consistent across pain, anxiety & sleep measures
- Consistent effect across gender
- Consistent effect across opioid and non opioid usage
  - Mitigates against a placebo effect interpretation

BENEFITS OF CBD



Rudroff and Sosnoff, Cannabidiol to Improve Mobility in People with Multiple Sclerosis Frontiers in Neurology 2018 Mar 22; 9:183

SUBSTITUTION FOR PHARMACEUTICAL AGENTS FOR PAIN, ANXIETY, AND SLEEP

- 1513 dispensary members did an online survey
- Respondents who regularly used opioids - 76.7% indicated that they reduced their use since starting medical cannabis
  - 71.8% decreased their use of anti-anxiety medications
  - 66.7% decreased their use of migraine medications
  - 65.2% decreased their use of sleep medications

  (patients who used alcohol and/or antidepressants did not reduce their use as much)

Piper, BJ et.al. Substitution of medical cannabis for pharmaceutical agents for pain, anxiety, and sleep. **Journal of Psychopharmacology** (2017) 31(5):569-75.

COMMENTS

- Anxiety is much lower mood is better feel much better than before overall well
- I have reduced my pain meds by a gigantic margin I can actually exercise again
- I wake up refreshed my left hip pain is almost gone to non existent
- I haven't had a flair up while using the CBD
- I have been taking a capsule twice a day and my doctor has cut my suboxone by 4 mg and cut my Effexor dose in half
- My muscle spasms went way down definite improvement in my ability to handle stress I have stopped needing my rescue medication at work due to anxiety
- sleeping better only one muscle spasm since starting my anxiety has calmed enough that I actually called family this month
- I decreased my Percocet this month from 4 a day to 3 a day and looking forward to decreasing it more I felt better this past week than I've felt in years

COMMENTS

- The change in dose by 1 tablet seems to help me go longer between doses of oral pain med and a lower dose.
- The days that I took another CBD mid day, I was able to not take my baclofen my sleep is much better as I dream and feel rested upon waking
- Feeling better and less anxious I feel like it is finally working and helping
- I feel better and have not had a mini headache since taking the CBD!!
- I have stage 4 carcinoid cancer of the liver and I have had nausea for 2 ½ years. The CBD has made the nausea so much better. It is almost gone. Overall my pain, anxiety and sleep is a lot better my wife says I don't complain as much
- It does help me go longer between pain med doses, my doctor is decreasing the dose of Percocet

COMMENTS

- Joints are more comfortable sleep is better it helps
- Able to do more exercise with less pain
- Migraine headaches are gone
- My body (back, knees) has decreased significantly
- The plantar fasciitis is not as bad
- I have not had as many migraine headaches as I usually do I have also not had to have a cortisone injection in my thumb where I have a nerve and tendon compressed in my wrist I have also not had to wear my wrist and thumb brace
- I have increased my activity level, with only some pain, but I can tolerate it easier than before. I can feel the difference with the CBD medicine

CONTINUED PLANS

- Expanding the study to multiple states
- Examine closer the reduction in opioid, anti-anxiety, sleeping medications
- Determine the dose for different symptoms
- Determine the maintenance dose
- Separate out the different types of pain acute chronic neuropathic
- Determine other secondary benefits