



Medical Marijuana  
Awareness Webinar

# DOSING AND MEDICAL MARIJUANA

Marc Matoza

Marijuana Med Today

Turner Davis

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MMTC





## Medical Cannabis Today- Finding Your Dose

Cameron Vance PharmD, CIO

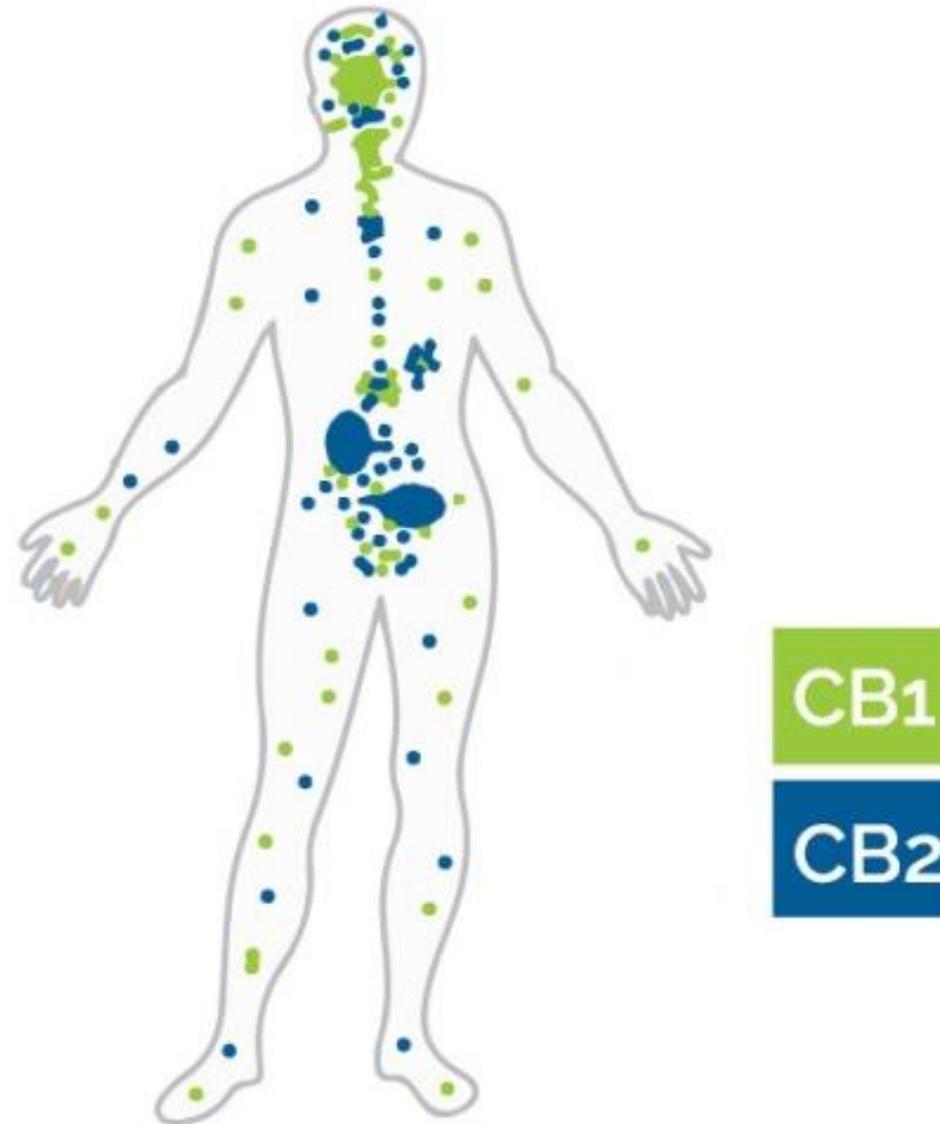
Medical Marijuana Treatment Clinics of Florida

cameronv@mmtcfl.com

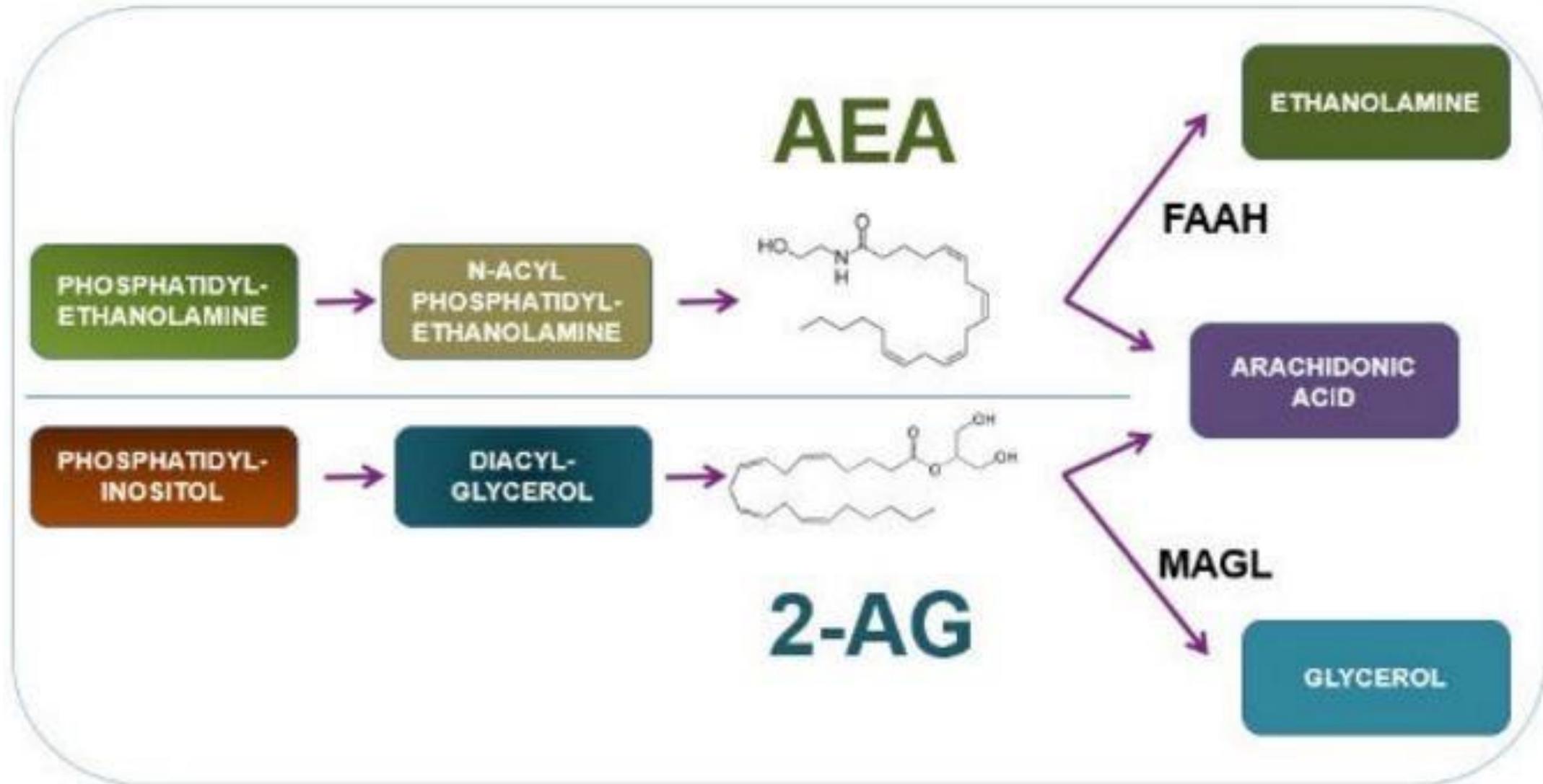
# The Endocannabinoid System



# Receptors & The Cannabis Plant



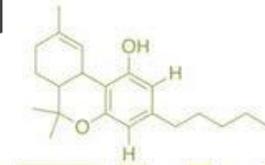
# Endocannabinoids



# WHAT IS MEDICAL CANNABIS/MARIJUANA ?

## THC – Tetrahydrocannabinol

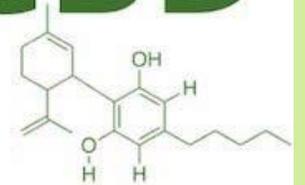
Psychoactive cannabis chemical



THC



CBD

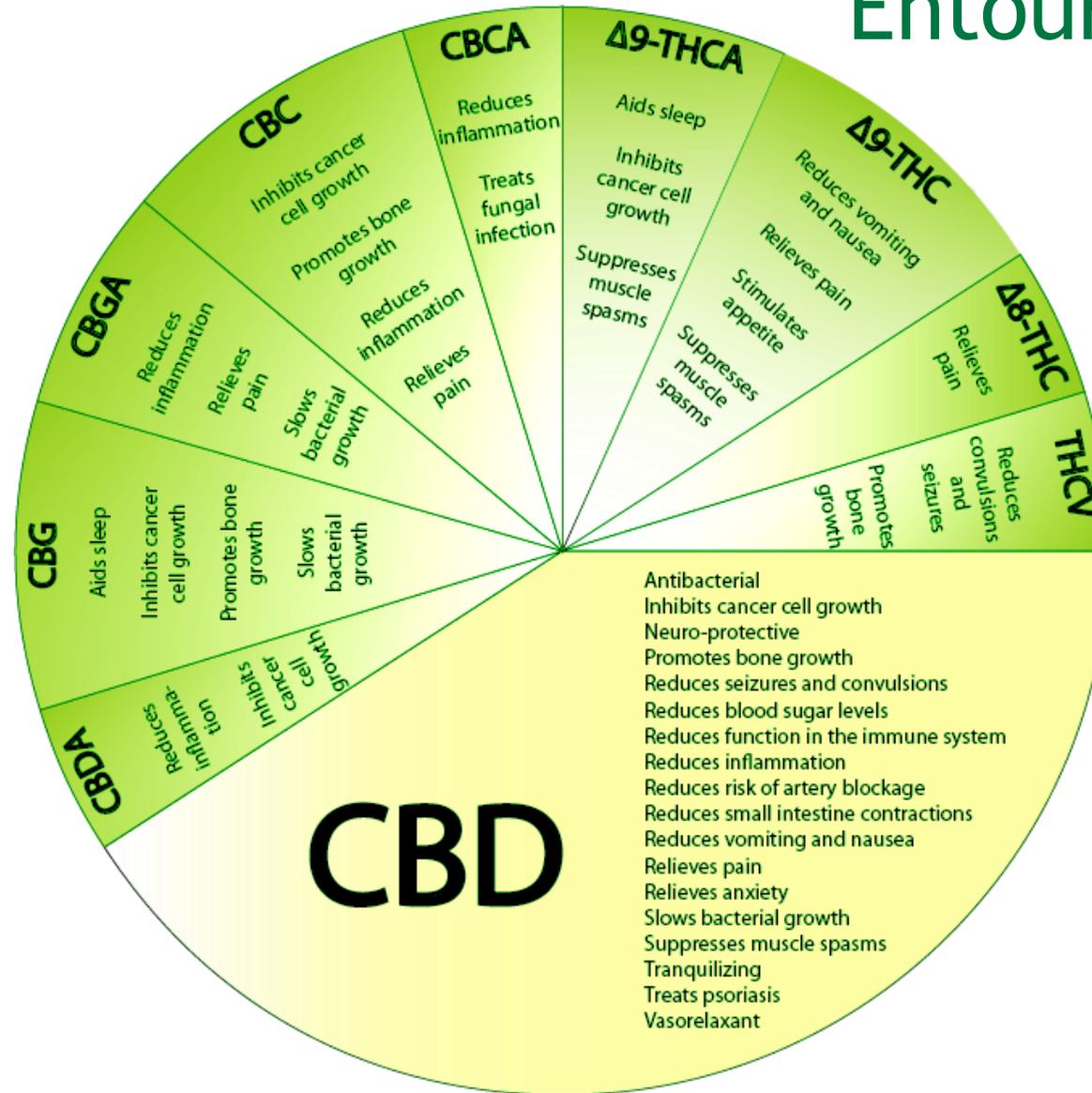


## CBD- Cannabidiol

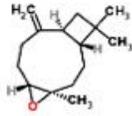
Non-Psychoactive cannabis chemical

– Also found in Hemp

# Entourage Effect

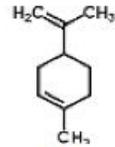


# Entourage Effect



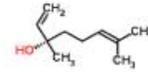
## Caryophyllene Oxide

- antifungal in onychomycosis
- decreases platelet aggregation



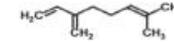
## Limonene

- antidepressant
- antifungal
- antimicrobial
- antispasmodic
- anxiolytic
- gastroprotective
- immunostimulant



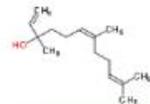
## Linalool

- analgesia
- anticonvulsant
- antiepileptic
- antineoplastic
- antipsychotic
- anxiolytic
- sedative



## $\beta$ -Myrcene

- analgesic
- anti-inflammatory
- antipsychotic
- antispasmodic
- hypnotic
- muscle relaxant
- sedative



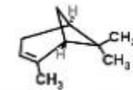
## Nerolidol

- antimicrobial
- sedative



## Phytol

- aids in lowering cholesterol
- increases GABA via SSADH inhibition



## $\alpha$ -Pinene

- Acetylcholinesterase inhibitor
- anti-inflammatory
- gastroprotective



# The Cannabis Plant



With medical cannabis, *I got my life back.*



Affordable and accessible  
cannabis treatment

**844-682-8261**



*Medical Cannabis  
Online information*

**Turner Davis, RPh COO MMTC**



# MEDICAL MARIJUANA USERS

## NEW YORK TIMES

*“When Retirement Comes With a Daily Dose of Cannabis” by Winnie Hu Sept 2017*



Ruth Brunn, 98 years old finally says “yes” to marijuana.

She pops a green pill filled with cannabis oil into her mouth with a sip of vitamin water. Then Ms. Brunn, who has neuropathy, settles back in her wheelchair and waits for the jabbing pain in her shoulders, arms and hands to ebb.

# MEDICAL MARIJUANA USERS

CBS NEWS May 1, 2016, 9:30 AM

Seniors and marijuana



Kerry Stiles, 78, wears a pacemaker. And he discovered pot at the Rossmoor retirement community in Walnut Creek, across the bay from San Francisco. "I drop it under my tongue, about five or six drops, and that helps me sleep," Stiles said.

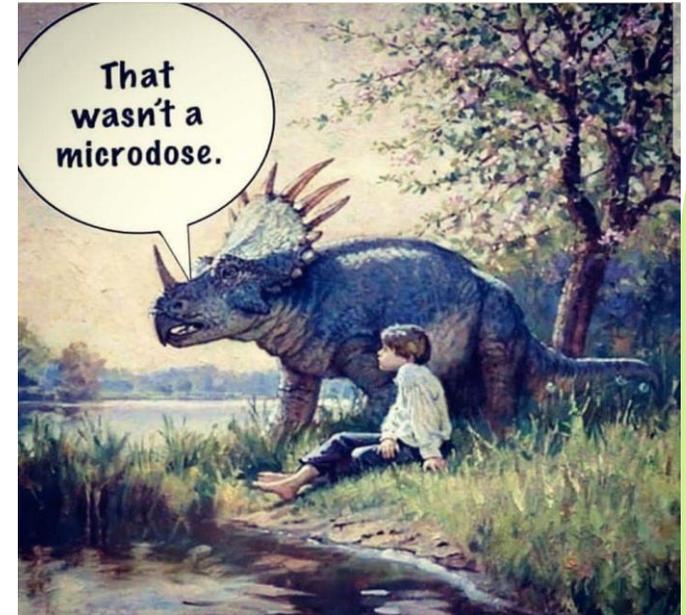
# Dosing Concepts

## *BB Gun or Shotgun? (i.e. Less is More)*

Medical Marijuana – The Goal is Relief with minimal side-effects(intoxication).

This is called **Microdosing**

Definition: the action or practice of taking or administering very small amounts of a drug in order to test or benefit from its physiological action while minimizing undesirable side effects.



# Dosing Concepts

## *Microdosing*



- People report better mood, reduced anxiety, improved focus, enhanced resilience to stress, less pain (and/or less bothersome pain), and other benefits without any adverse effects.
- Most consumers find that 1-5 mg of total cannabinoid works well for this purpose. Some emerging evidence even suggests that a practice like this could be protective against the damage of a heart attack[v],[vi] or brain injury![vii],[viii],[ix]

# Dosing Challenges

## *Individual Variation – Cannabis is Unusual*

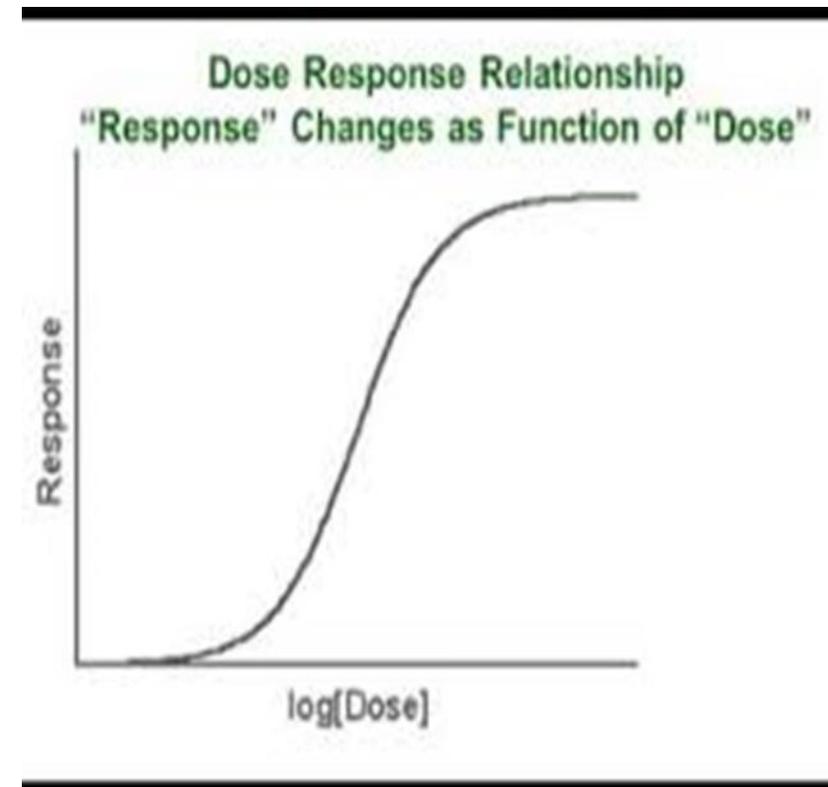
- Some patients effectively use tiny amounts of cannabis, while others use incredibly high doses.
- Some adult patients achieve therapeutic effects at 1 mg of total cannabinoids daily, while others consume over 2,000 mg daily without adverse effects.
- While a 2000-fold dosing range is unusual for a medication, researchers have failed to kill monkeys at doses even 300 times higher[i]



# Dosing Challenges

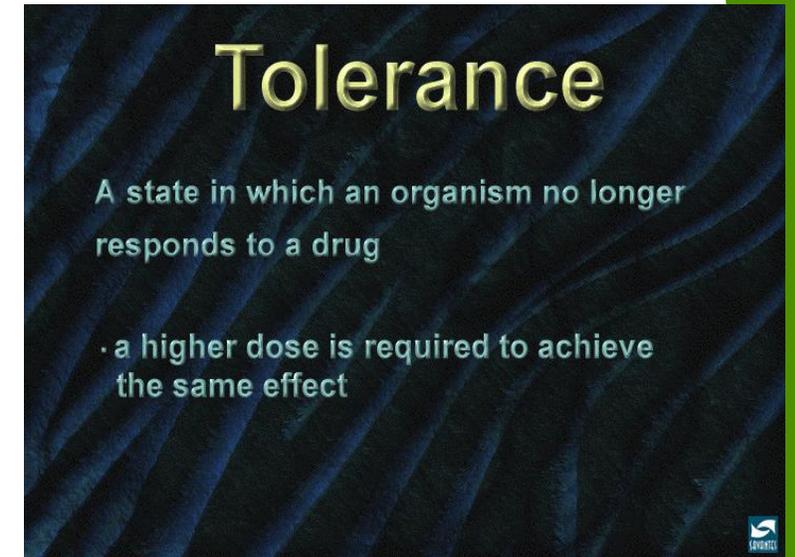
## *Multiphasic dose-response relationships*

- Cannabis exhibits an unusual relationship between the dose and the expected response.
- For most medications, a higher dose will result in a stronger therapeutic effect and a higher likelihood of adverse effects; this is described as a monophasic dose-response relationship.
- Cannabis simply does not follow this pattern.



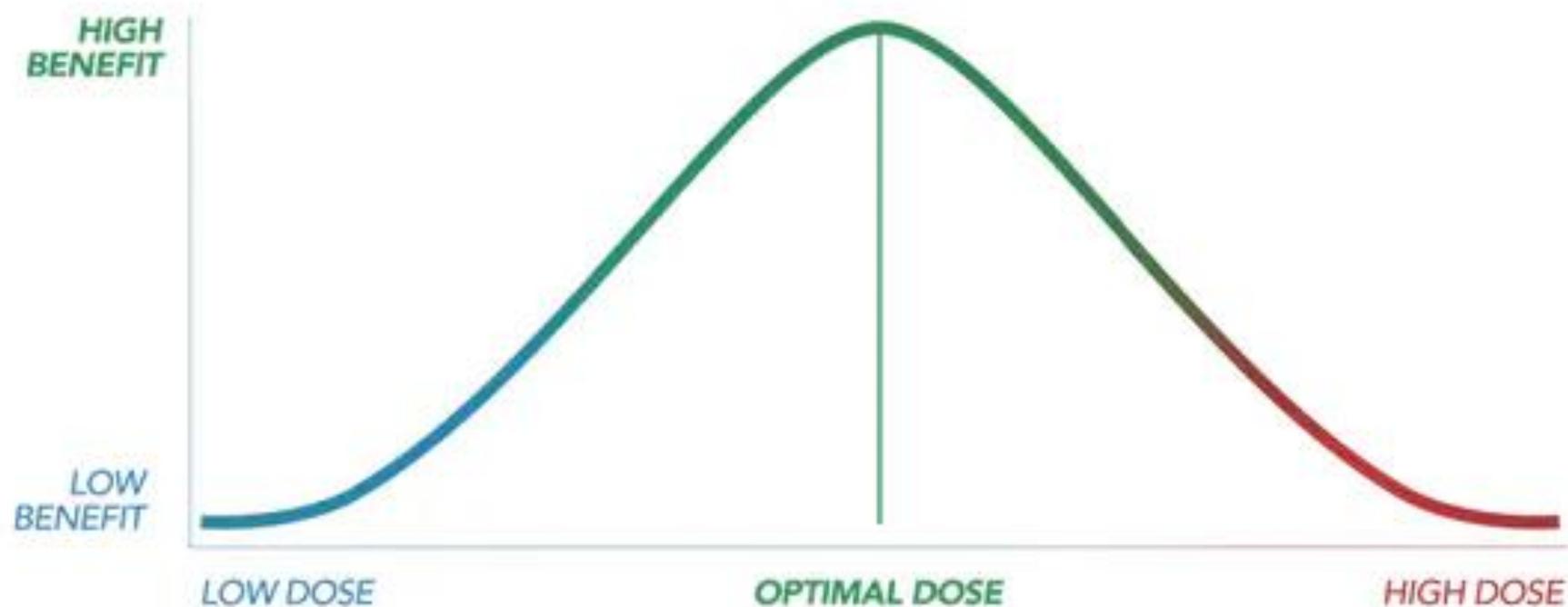
# Are Higher Doses More Effective?

- For most cannabis consumers, gradually increasing their dose will at first result in stronger effects; but after a certain point - tolerance(unique to each individual)
- Subsequent dosage increases can result in weaker and weaker therapeutic effects, accompanied by an increase in unwanted effects.
- Consumers who continue to increase their dosage to very high levels can often reclaim some or all of the previously lost benefit, and sometimes find additional therapeutic effects not achieved at the lower doses.



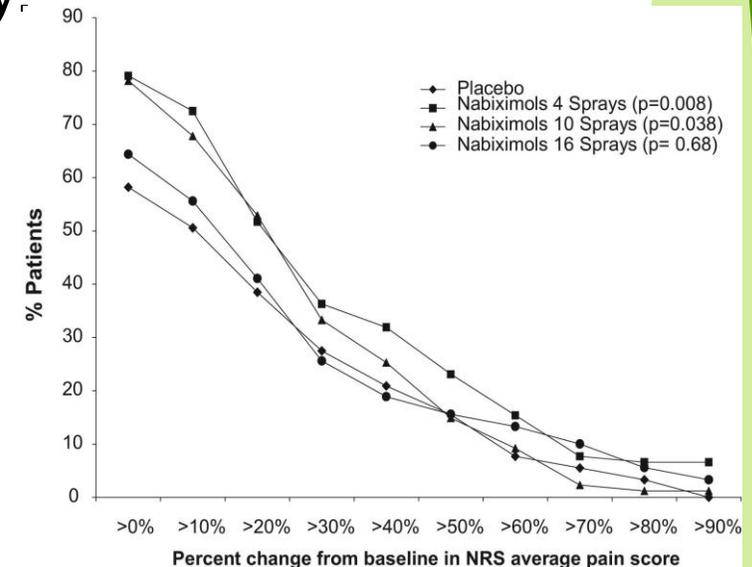
# Are Higher Doses More Effective?

Ultra-high doses are more expensive and produce more unwanted side effects. Most patients do much better at the lowest effective dose (Microdosing)



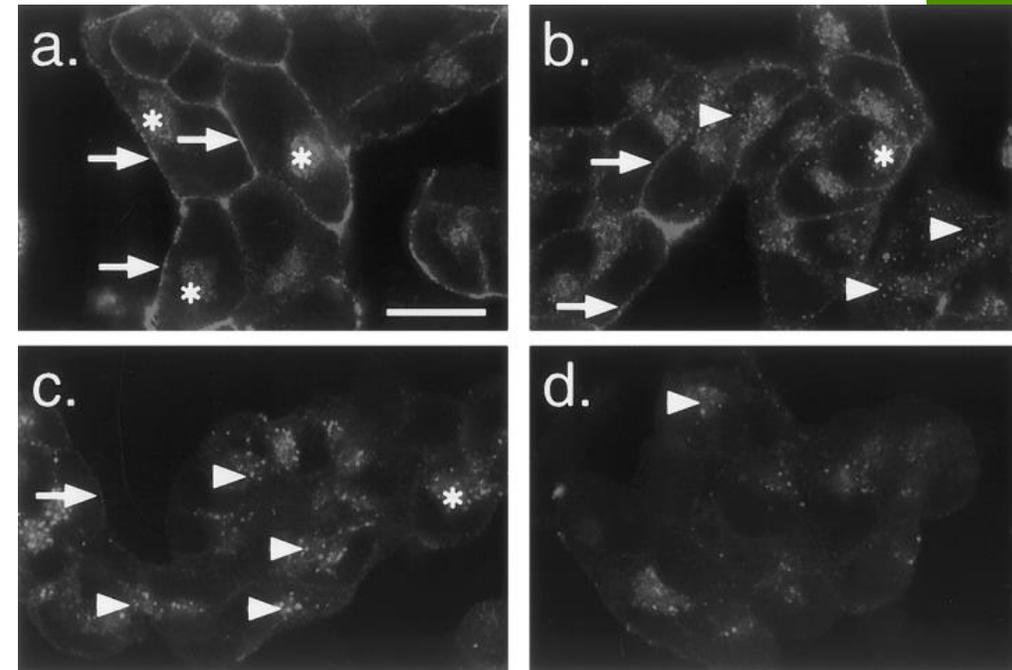
# Are Higher Doses More Effective?

- For many cannabis users, this means that less can be more.
- In a study of 263 opioid-treated cancer patients with poorly controlled pain, the group receiving 21 mg of combined THC and CBD each day experienced significant improvements in pain levels, more so than the group that received 52 mg daily.
- The group that received 83 mg daily reduced their pain no better than placebo, but experienced more adverse effects.[ii]



# How is this possible??

- The endocannabinoid system is a sensitive, highly tuned physiologic infrastructure designed to maintain balance at a cellular level.
- When the cannabinoid receptors become overstimulated by high doses of cannabis, the cells pull the receptors inside, where they are either recycled or degraded.[iii]
- As cannabinoid receptor levels diminish, the effects of cannabis will diminish as well, even (or especially) in the face of dose escalation.
- This is known as “tolerance-building,” something that many regular cannabis users have experienced.



## THE HUMAN ENDOCANNABINOID SYSTEM

***CBD, CBN and THC fit like lock and key into existing human receptors.*** These receptors are part of the endocannabinoid system which impact physiological process affecting pain modulation, memory and appetite plus anti-inflammatory effects and other immune system responses. The endocannabinoid system comprises two types of receptors, CB1 and CB2, which serve distinct functions in human health and well-being.

CB1 receptors are primarily found in the brain and central nervous system, and to a lesser extent in

Receptors are found on cell surfaces

## THE HUMAN ENDOCANNABINOID SYSTEM

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CB2 receptors are mostly in the peripheral organs especially cells associated with the immune system.



source: [www.be-better-solution.org](http://www.be-better-solution.org)

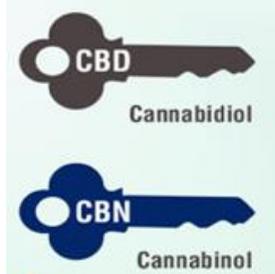


# Combining CBD and THC

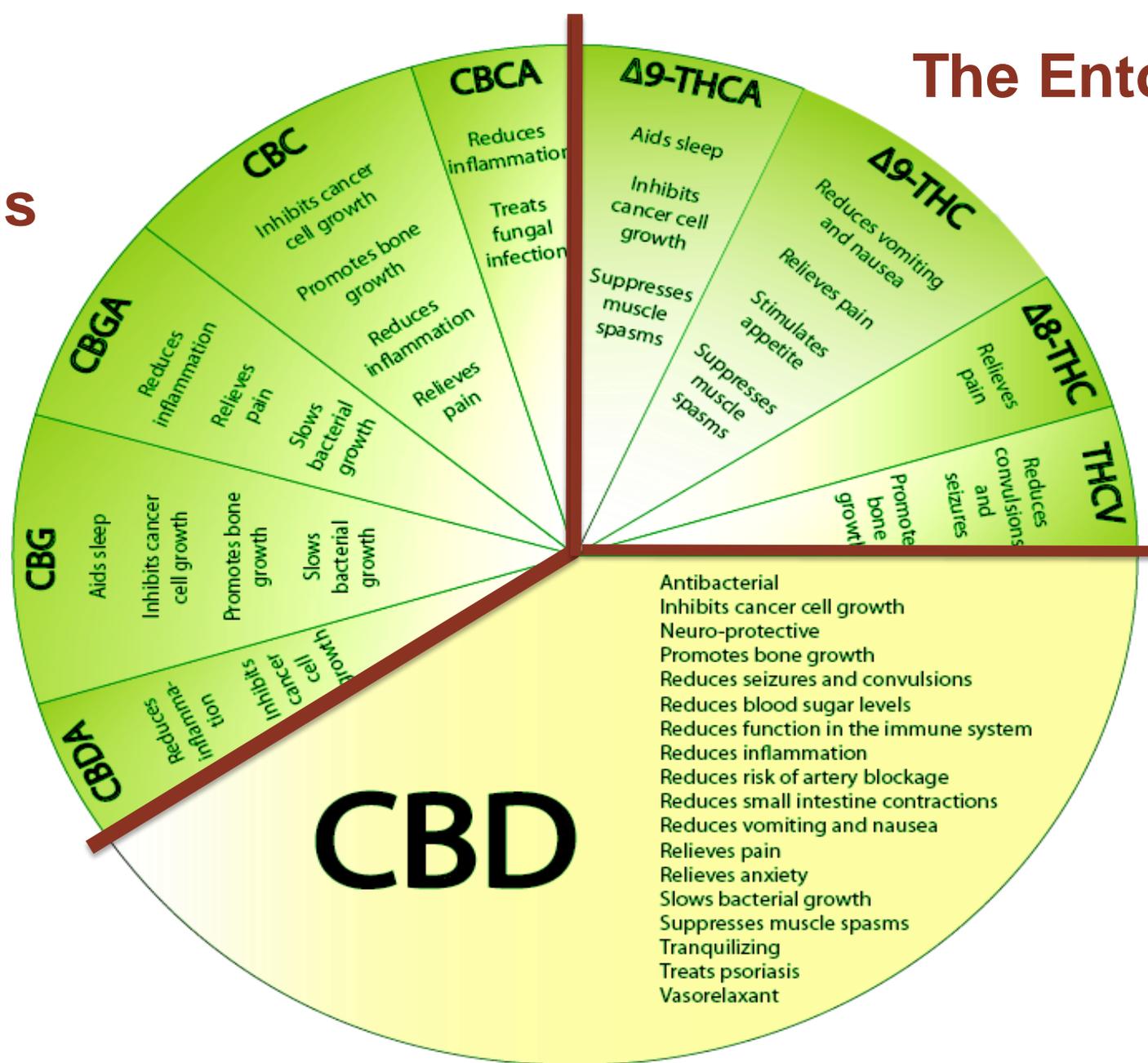
- CBD and THC have many overlapping therapeutic qualities, including relief of pain, anxiety, seizures, and nausea, although they work via different mechanisms of action.
- When combined, CBD and THC can enhance each other's benefits while reducing unwanted effects, including the psychoactive or impairing effects of THC.
- This is great news for cannabis users who want health benefits while maintain optimal performance at home or work.



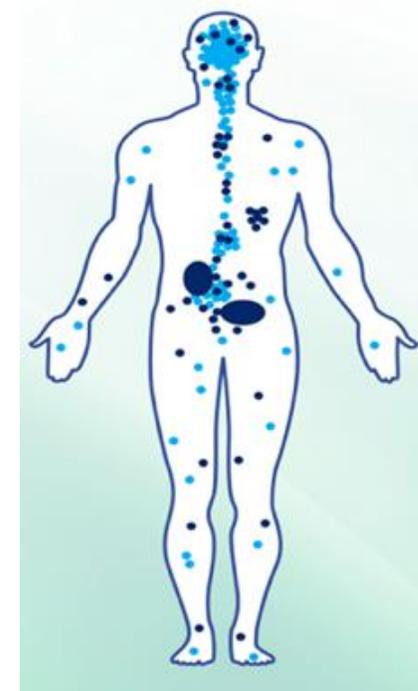
# CBD in Hemp & Cannabis



# The Entourage Effect

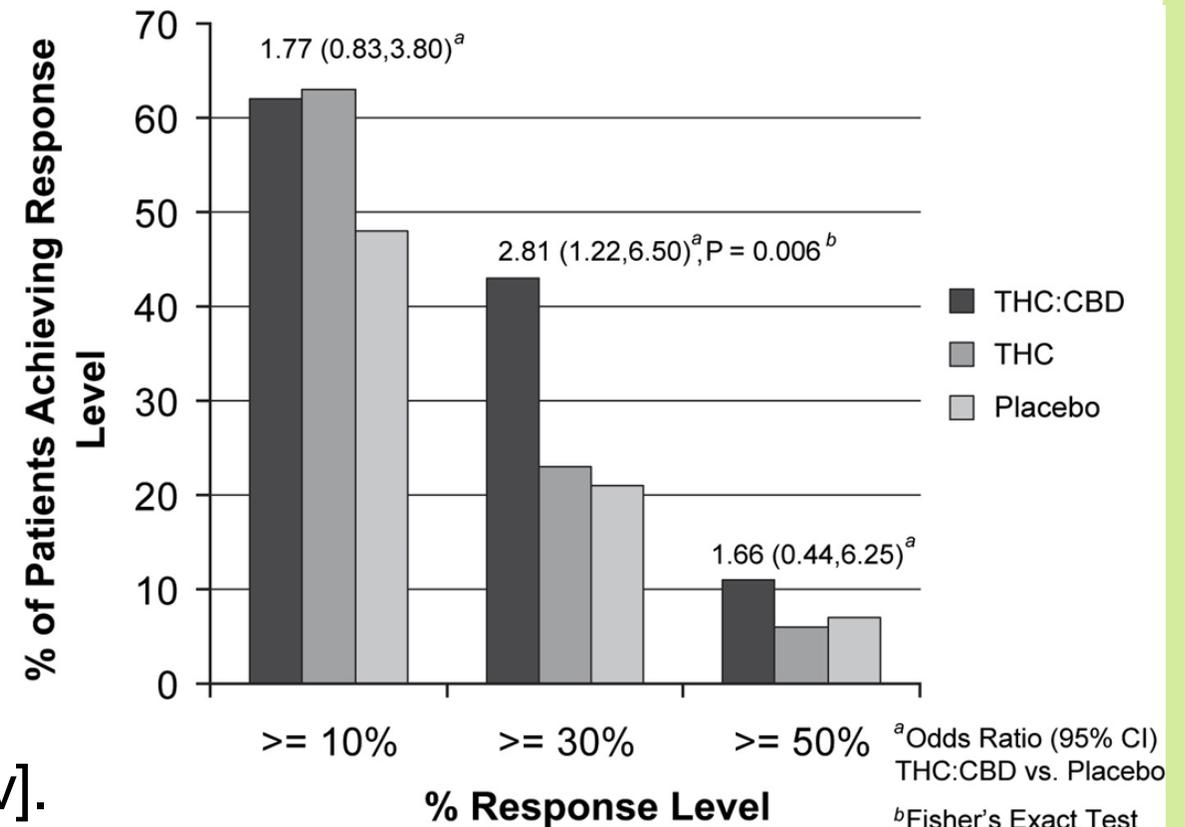


**THC**



# Combining CBD and THC

- In a study of 177 patients with cancer pain, one group received an oral spray of THC, while another group received an oral spray of combined THC and CBD at an approximate 1:1 ratio.
- Both groups were allowed to gradually increase their dose until they experienced satisfactory relief.
- The THC group ended up using an average of 27 mg daily, while the CBD+THC group used close to 60 total mg daily, but the CBD+THC group had a superior reduction in pain.[iv].



# Options for achieving CBD and THC balance

- Combining CBD and THC will produce optimal benefits, but be prepared to take (and purchase) higher overall dosages.
- THC products can ONLY be purchased with a Florida Medical Marijuana Card approved by a physician and purchased from a Florida licensed dispensary.
- CBD products are available without a medical marijuana card, and can be purchased at a lower cost outside of a dispensary.
- MMTC physicians generally recommend Full Spectrum CBD products to maximize the entourage effect

# Options for achieving CBD and THC balance

- Full Spectrum CBD products contain a wide variety of cannabinoids other than THC
- This allows maximum engagement of the endocannabinoid system
- Full spectrum CBD is available at \$0.06 - \$0.08 per mg as opposed to \$0.12 - \$0.20 per mg at Florida dispensaries.
- MMTC offers full spectrum CBD in clinic and online at:



[WWW.MYBOTANICAWELLNESS.COM](http://WWW.MYBOTANICAWELLNESS.COM)

[1<sup>st</sup> Time Buyers Receive 20% Off](#)

[MMTC Patients always receive 10% Purchases](#)



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# Dosing Suggestions

*How much should I take?*

*What about Formulations? Strains?*

## Factors that influence dosing

- *Method of Administration*
- *Safety, Tolerability, Efficacy*
- *Potency*
- *Isolate vs. Whole Plant Extract*
- *Tolerance / “ECS Tone”*

Symptom relief



Impairment



## Original Article

# Multicenter, Double-Blind, Randomized, Placebo-Controlled, Parallel-Group Study of the Efficacy, Safety, and Tolerability of THC:CBD Extract and THC Extract in Patients with Intractable Cancer-Related Pain

Jeremy R. Johnson, MB ChB, Mary Burnell-Nugent, MB BChir,  
Dominique Lossignol, MB ChB, MRCG, DRCOG,

Elena Doina Ganae-Motan, MD, Richard Potts, BSc (Hons), MICR, and  
Marie T. Fallon, MB ChB, MD, FRCP (E), FRCP (Glasg)

*Severn Hospice (J.R.J.), Shrewsbury, Shropshire, and St. Luke's Hospice (M.B.-N.), Turnchapel, Plymouth, United Kingdom; Association Hospitaliere De Brussels (D.L.), Centre des Tumeurs de l'ULB, Brussels, Belgium; Emergency Department (E.D.G.-M.), Hospital "Sf. Ioan cel Nou," Suceava, Romania; GW Pharma Ltd. (R.P.), Ely, Cambridgeshire; and Edinburgh Cancer Research Centre (M.T.F.), University of Edinburgh, Edinburgh, United Kingdom*

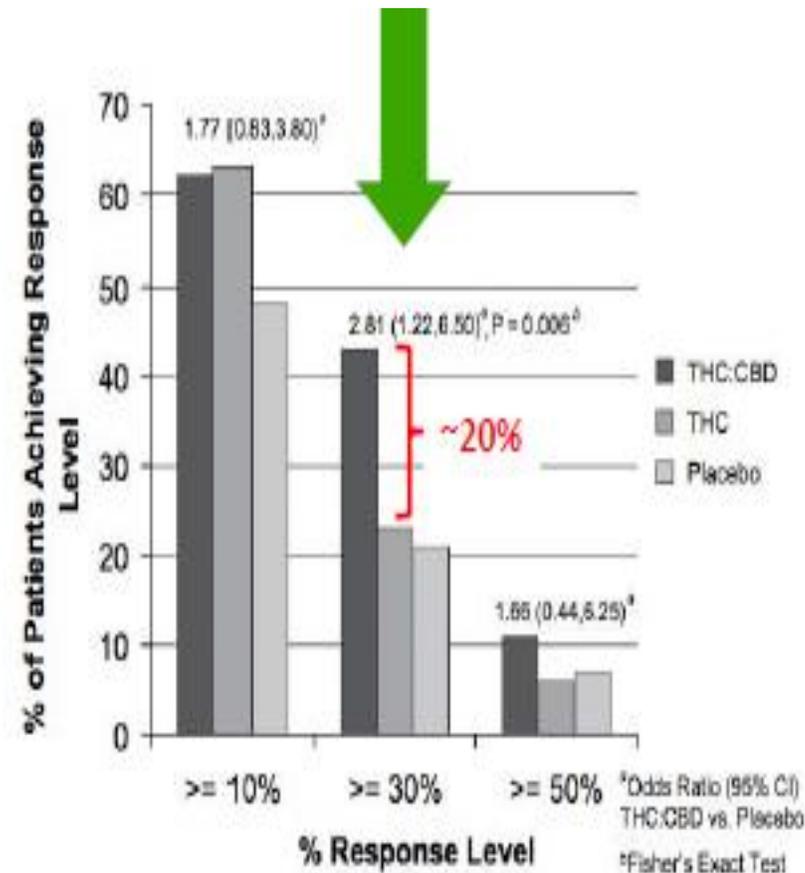


Fig. 3. Pain 0–10 Numerical Rating Scale scores: responder analysis (ITT analysis). <sup>a</sup>Odds ratio (95% CI) THC:CBD vs. placebo; <sup>b</sup>Fisher's exact test.





# STANDARD DOSING FORMS

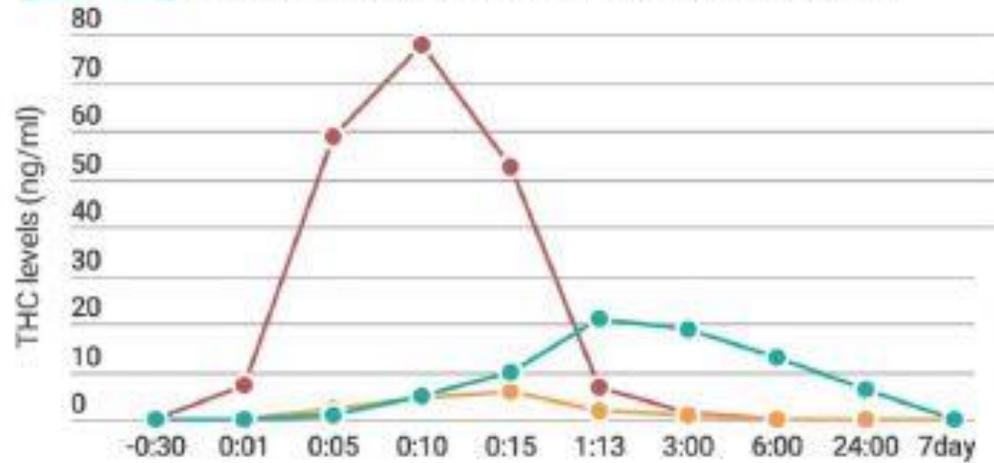
| FORM                             | TIME TO WORK       | EFFECTIVENESS | COMMENTS  |
|----------------------------------|--------------------|---------------|---|
| SUBLINGUAL DROPS/ TINCTURE       | 15-40 Min          | 4-6 Hours     | Taking cannabis in through the mouth under your tongue, absorbs via the digestive system or blood vessels in the mucous membranes in the mouth.                 |
| VAPE PEN                         | Almost Immediately | 2-4 Hours     | Electronic vaporizing device <sup>[SEP]</sup> Inhaling through the lungs  |
| CAPSULES                         | 30 min - 2 hours   | 5-8 Hours     | When taking cannabis in through the mouth, it enters the bloodstream after being digested or broken down in the stomach and absorbed into the digestive system. |
| EDIBLES                          | 15-40 Min          | 4-6 Hours     | Gummies, brownies, dots, cookies, et al   |
| TOPICALS                         | Almost immediately | 1-2 Hours     | A topical medicine is applied to the skin directly 'on top' of the place where it is needed.  |
| TRANSDERMAL PATCH                | 10 min - 1 Hour    | 8 - 72 Hours  | A topical medicine is applied to the skin directly 'on top' near the neck, inside of legs, top of hands /feet, back of neck                                     |
| SPRAY                            | Almost Immediately | 2-4 Hours     | Absorbs via the digestive system or blood vessels in the mucous membranes in the mouth.   |
| FLOWER                           | Almost Immediately | 1-5 Hours     | <b>REQUIRES A FL STATE FORM</b><br>Inhaling through the lungs<br><b>2.5oz/35 days: 4oz in possession</b>  |
| CRUMBLE <sup>[SEP]</sup> SHATTER | Almost Immediately | 1-6 Hours     | Inhaling through the lungs  |



# Inhalation versus Ingestion



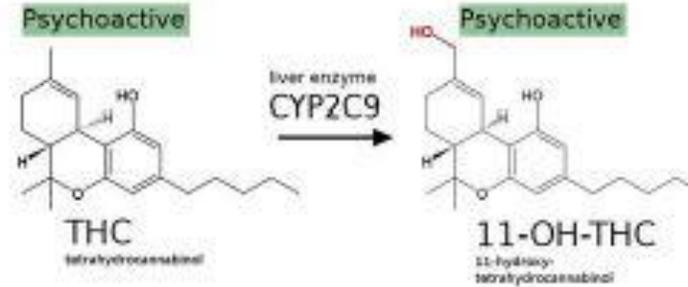
Average concentration of **delta-9-THC** and its metabolites after **INHALATION** of 15.8 mg (= one joint) of THC. Measured from half an hour before inhalation until 7 days after.



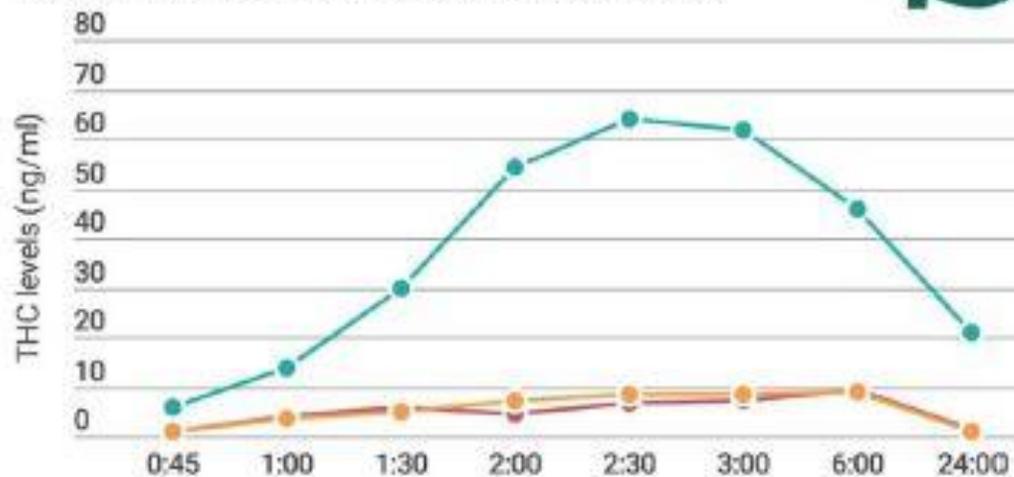
Inhalation

- Delta-9-THC
- 11-OH-THC
- 11-COOH-THC

Source: SeplenSoup Blog; Grotenhermen F. Pharmacokinetics and pharmacodynamics of cannabinoids. Clin Pharmacokinet. 2003;42(4):327-60. Review. PubMed PMID: 12648025.; Lindgren JE, Ohlsson A, Agurell S, et al. Clinico effects and plasma levels of delta 9-tetrahydrocannabinol (delta 9-THC) in heavy and light users of cannabis. Psychopharmacology [Berl]. 1981;74(3):208-12.



Average concentration of **delta-9-THC** and its metabolites after **INGESTION** of 20 mg (= one chocolate cookie) of THC. Measured from 45 minutes until 24 hours after consumption.

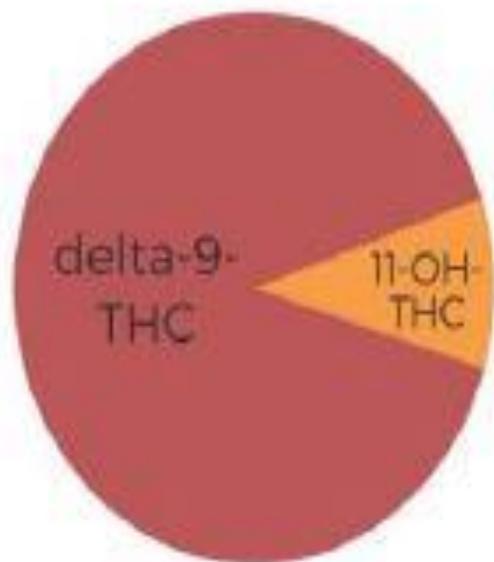


[4]



# Route of Administration Matters

WHEN INHALED



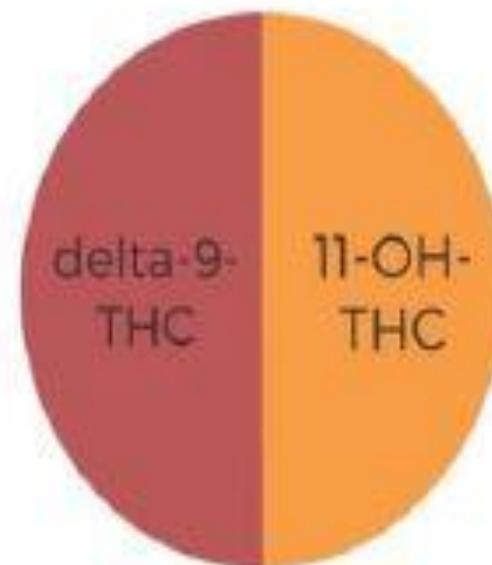
## PROPORTION matters

**11-OH-THC** passes the brain barrier more easily than **delta-9-THC**.



**11-OH-THC** is 3 to 7 times more potent than **delta-9-THC** in activating receptors in the brain.

WHEN INGESTED



# World Health Organization

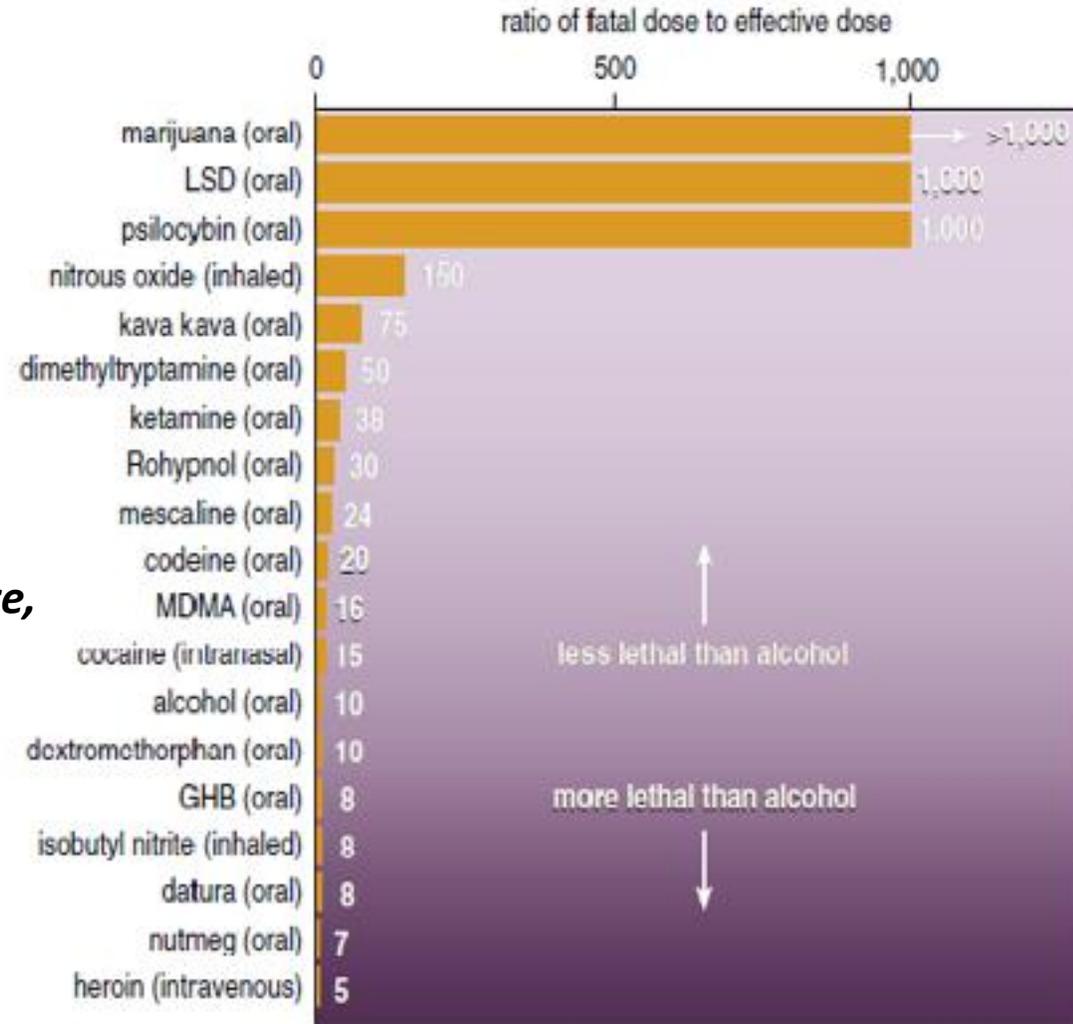
PUBLICATION: “The Health and Social Effects of Non-medical Use Cannabis”, 2016

*“There are no reports of fatal overdoses in the epidemiological literature”*

Ranking psychoactive substances by their ratios of lethal dose to effective dose gives a general picture of how likely each is to precipitate an acute fatal reaction. ***By this measure, many illicit drugs are considerably safer than alcohol.***



World Health Organization



# Potential Adverse Effects

## Affecting more than 1 in 10 people

- Feeling dizzy or tired.

## Affecting less than 1 in 10 people

- Eating more or less than usual.
- Changed sense of taste or a dry mouth, mouth ulcers, burning
- Constipation, diarrhea, or nausea
- Feeling abnormal or drunk.
- Loss of balance or falling over.
- Red Eyes, Blurred Vision
- Dizziness
- Anxiety

# Safety Profile

## RESEARCH

### Adverse effects of medical cannabinoids: a systematic review

Tongtong Wang MSc, Jean-Paul Collet PhD MD, Stan Shapiro PhD, Mark A. Ware MBBS MSc

∞ See related article page 1685

#### ABSTRACT

**C**annabis (*Cannabis sativa*) is widely used as a recreational drug, with an estimated worldwide annual prevalence (defined as use at least once per year) of 160

**A systematic review of 31 studies (23 randomized controlled trials and 8 observational studies) found that 96.6% of adverse effects were “not serious”.**

events and to facilitate future cannabis research initiatives. We critically evaluated the quality of published studies with a view to identifying ways to improve future studies.

**Results:** A total of 321 articles were eligible for evaluation. After excluding those that focused on recreational cannabis

Pharmaceuticals], which contains  $\Delta$ -9-tetrahydrocannabinol and cannabidiol in an oromucosal spray); dronabinol (synthetic  $\Delta$ -9-tetrahydrocannabinol, marketed as Marinol [Solvay Pharmaceuticals]); nabilone (a synthetic derivative of  $\Delta$ -9-tetrahydrocannabinol, marketed as Cesamet [Valeant Pharmaceuticals International]); and the herbal form of cannabis



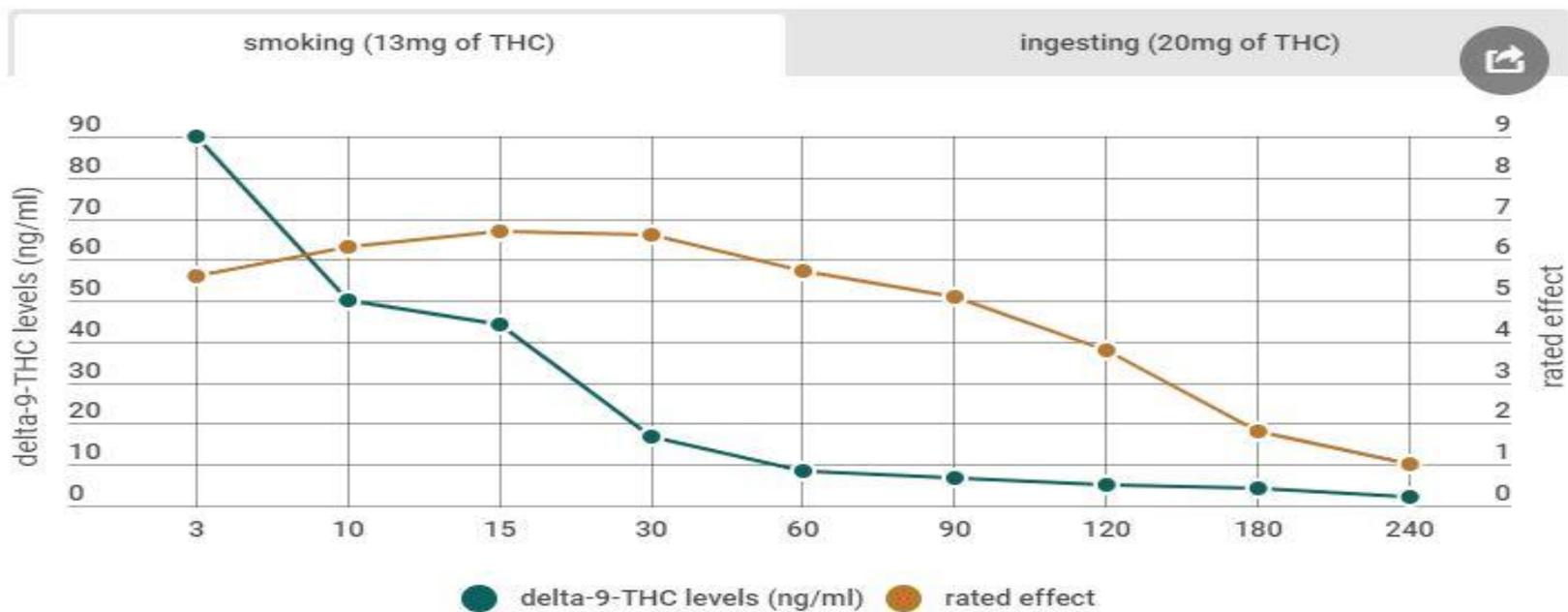
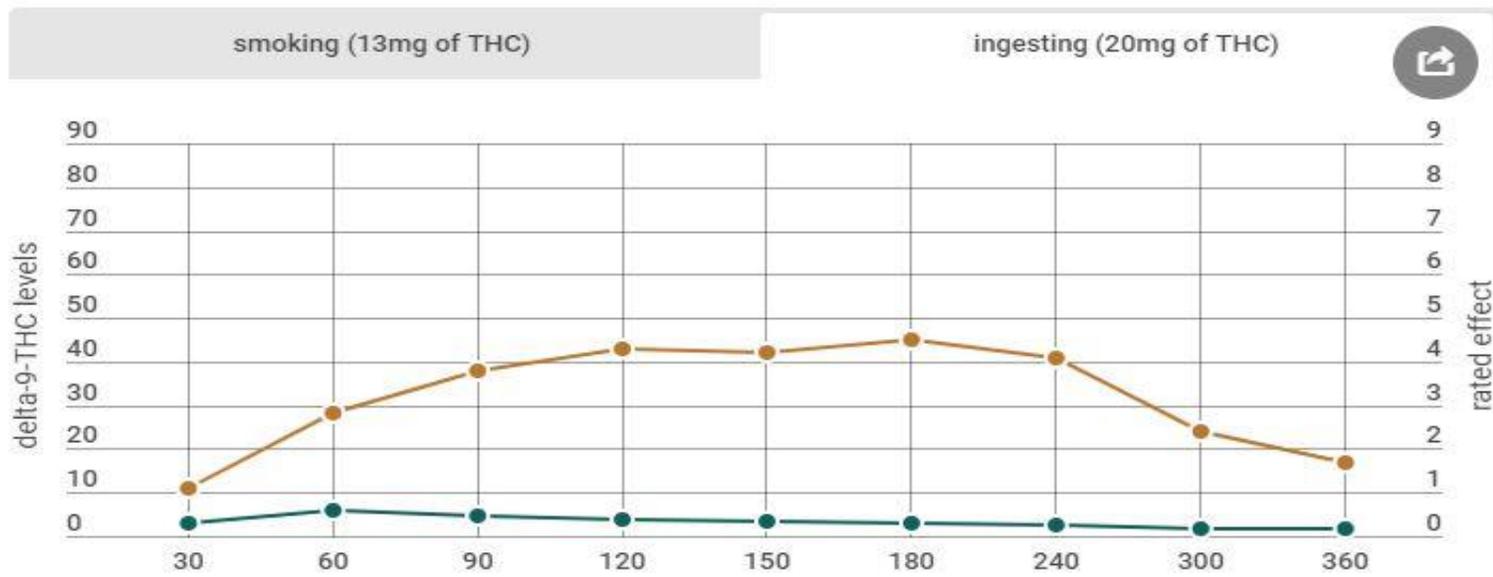
# References



- [i] Thompson GR, et al. Oral and intravenous toxicity of  $\Delta^9$ -tetrahydrocannabinol in rhesus monkeys. *Toxicology and Applied Pharmacology*. 1974;27(3):648-665.
- [ii] Portenoy RK, et al. Nabiximols for opioid-treated cancer patients with poorly-controlled chronic pain: A randomized, placebo-controlled, graded-dose trial. *The Journal of Pain*. 2012;13(5):438-449.
- [iii] Hsieh C, et al. Internalization and recycling of the CB1 cannabinoid receptor. *Journal of Neurochemistry*. 1999;73(2):493-501.
- [iv] Johnson JR, et al. “Multicenter, double-blind, randomized, placebo-controlled, parallel-group study of the efficacy, safety, and tolerability of THC: CBD extract and THC extract in patients with intractable cancer-related pain.” *Journal of Pain and Symptom Management*. 2010;39(2): 167-179.
- [v] Waldman M, et al. An ultra-low dose of tetrahydrocannabinol provides cardioprotection. *Biochemical Pharmacology*. 2013;85(11):1626-1633.
- [vi] Johnson-Sasso CP, Kao D, Walker LA. marijuana use and short-term outcomes in patients hospitalized for acute myocardial infarction. *Journal of the American College of Cardiology*. 2016;67(13):569.
- [vii] Fernández-Ruiz J, Moro MA, Martínez-Orgado J. Cannabinoids in neurodegenerative disorders and stroke/brain trauma: From preclinical models to clinical applications. *Neurotherapeutics*. 2015;12(4):793-806.
- [viii] Nguyen BM, et al. Effect of marijuana use on outcomes in traumatic brain injury. *The American Surgeon*. 2014;80(10):979-983.
- [ix] Di Napoli M, et al. Prior cannabis use is associated with outcome after intracerebral hemorrhage. *Cerebrovascular Diseases*. 2016;41(5-6):248-255.

# THANK YOU





# PRICING



## MMTC PHYSICIAN

- Initial Visit \$299 – Includes Exam, Registration and 210 day order  
*if you do not qualify, there is no cost*
- 1<sup>st</sup> Follow Up \$99
- Every Follow Up thereafter - \$199

**Total Yearly Cost - \$398/year**

\* **MMTC accepts credit cards**

**FLORIDA ID CARD(STATE) - \$75/year**

\* **State of Florida accepts credit cards**

**MEDICATION - \$150/mo**

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**TYPICAL MONTHLY COST- \$190**