A Day of Education and Connection

AMN-PEI

Atlantic Mentorship Networks

Project Overview

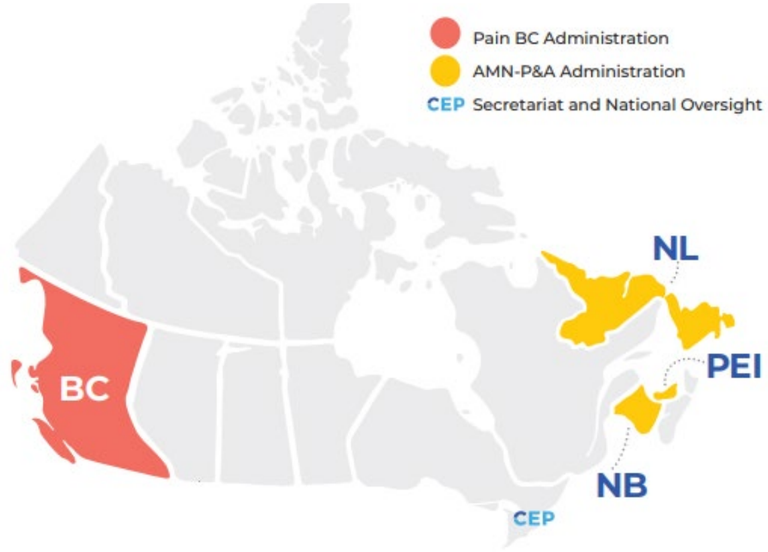
A National Initiative to build Adaptive Mentoring Networks

- Used successfully in Canada for the last 18 years to build primary care capacity

The initiative is a collaboration between:

- Atlantic Mentorship Network – Pain and Addiction (AMN-P&A)
- Pain BC
- Center for Effective Practice (CEP)

…to build Adaptive Mentoring Networks in NS, NL, NB, & PEI



Grant-funded from Health Canada through March 2025

AMN's "Why/What/How"

VISION

Health care providers in the Atlantic provinces are engaged fully, confidently, and effectively in mental illness, chronic pain, and addiction care.

MISSION

Growing capacity to assess and meet the health care needs of people with or at risk of developing mental illness, chronic pain, and/or addiction in the Atlantic provinces.

CORE ROLE/ STRATEGY

Enabling and supporting health care providers in the Atlantic provinces to engage fully, confidently, and effectively in care for mental illness, chronic pain, and addiction.

PRIORITIES/ DIRECTION

Adaptive Mentoring

A specific form of mentoring with the following features:

1. Mentoring that adapts to goals, needs, and preferences of each mentee
2. Mentorship grounded in fostering a compassionate and safe professional relationship environment
3. Mentoring that provides bi-directional value for mentors and mentees.

Disclosure of Financial Support

- This program receives funding from Health Canada's Substance Use and Addictions Program (SUAP).
- This program has not received in -kind support

Objectives of the Day

Following the workshop, attendees will:

- Acquire clinical knowledge updates in chronic pain, mental illness, and substance use that are relevant to primary care.
- Make professional connections coupled to clinical expertise that will allow them to help individual complex patients and populations in a variety of settings.

Agenda

Timeline	Session
9:00-9:15	Opening Remarks
9:15-10:00	Into the Weeds: The Overgrown Landscape of Health Considerations Around Marijuana
10:00-11:00	Opioid Use Disorder: Treatment options in the context of medical, social, and geographical complexities
11:00-11:15	**BREAK**
11:15-12:15	Update on Interventions for Chronic Pain Conditions
12:15-1:15	Access to Means…To What?...End??: Lessons about suicidality from the intersection of medical toxicology and psychiatry
1:15-2:00	**LUNCH**

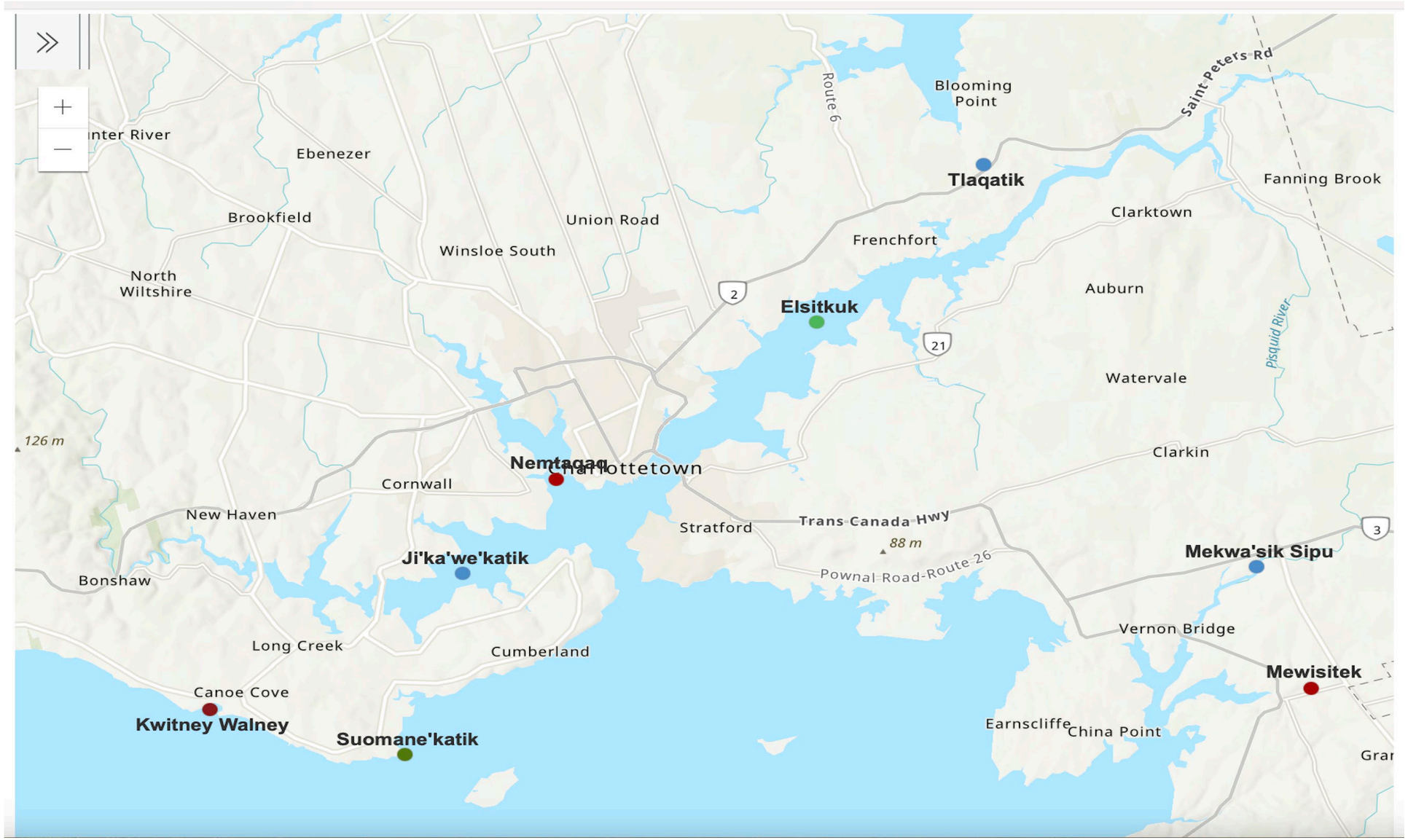
AMN-PEI Mentor / Mentee Meeting @ 2pm

Copy of Slides

Housekeeping

- Washrooms
- Wifi – Holman Grand Meeting Room
- Cell Phones
- Respectful of Time
- Certificate of Attendance
- Evaluations

Land Acknowledgement



https://lnuey.ca/reconciliation/epekwitk-place-names/

Into the Weeds: The Overgrown Landscape of Health Considerations Around Marijuana

Dr. J.J. Rasimas

Into the Weeds:

The overgrown landscape of health considerations around marijuana

AMN - PEI Education Day, April 19, 2024

J.J. Rasimas, Ph.D., M.D., F.A.A.C.T., F.A.C.L.P., F.A.C.M.T., F.A.C.Psych.
MH&A Co-Occurring Disorders Program Lead, Nova Scotia Health
Professor of Psychiatry & Emergency Medicine
Dalhousie University, University of Minnesota, & Penn State College of Medicine

Disclosures: J.J. Rasimas

- I have no relevant conflicts of interest around recreational substances, medicinal products, medical treatments or financial interests related to them
- I'm from the U.S.
- I have formal certification in addiction medicine and medical toxicology – both make me more attuned to negative consequences of ingesting things, not automatically prone to see exposures as therapeutic even when it feels good

Overview

- Cannabis pharmacology / toxicology
  - Dialogue
- “Medical” marijuana
  - Dialogue
- Practicalities, Legalities, and Good Medicine
  - Summary

Marijuana = Dried & Shredded Cannabis

- Family Cannabaceae
- Two (?) species of the Cannabis genus
  - *sativa*
  - *indica*

flowers, stems, seeds, leaves…

smoked, cooked, brewed…

Forms of Usable Cannabis

- Marijuana
- Hash
- Resin
- Oil
- Tincture
- Capsules

Shennong (Shen-Nung)

- Emperor of Ancient China born in the 28th century B.C.E.
- Father of Chinese agriculture
  - Invented the plow (?)
- Documented 365 species of medicinal plants in *Pen Ts'ao*
- Used by a Chinese surgeon Hua T'o in 2nd century C.E.
  - Anesthetic
  - Resin combined with wine

U.S. in 19th and Early 20th Centuries

Clinical effects - Neuropsychiatric

“Desirable”

- Euphoria: *“high”*
- Anxiolysis: *“mellowing out”*

“Toxic”

- Disorientation
- Unsteady gait
- Impaired coordination
- Amotivation
- Memory loss
- Altered perception
- Decreased consciousness

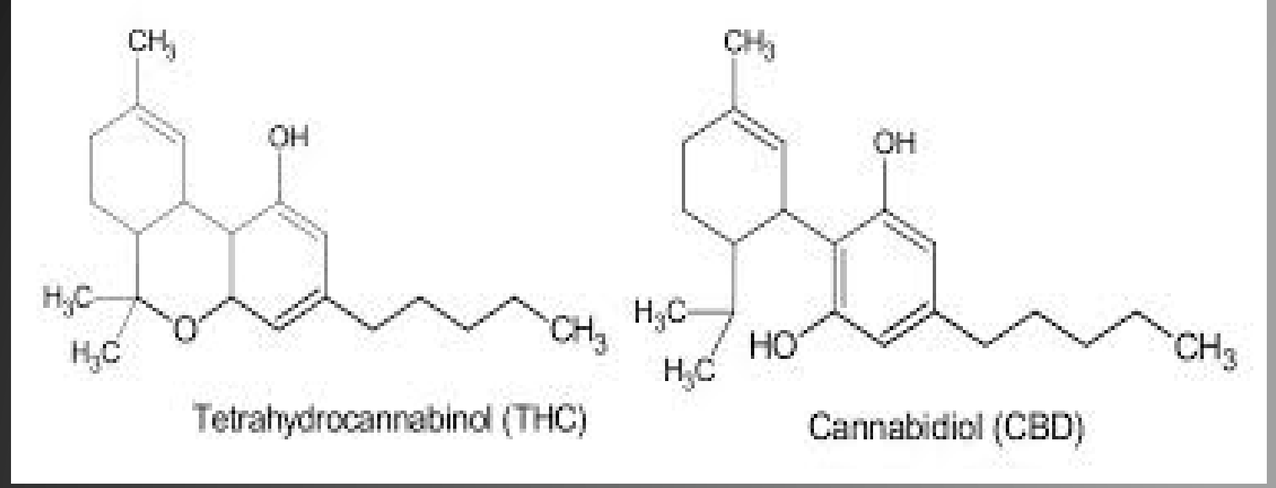
Clinical effects - Somatic

"Desirable"		"Toxic"
Anti-emetic		Xerostomia, hypohydrosis
↓ intra-ocular tension		Conjunctival Irritation
Analgesic		Bronchopulmonary Irritation
Muscle relaxant		Tachycardia
Anticonvulsant		Hypertension
Anti-inflammatory		Endocrine changes
↑appetite: "the munchies"		↓ Immunomodulation

Chemical Constituents of Marijuana

- Cannabinoids (66)
- Nitrogenous cmpds. (27)
- Amino acids(18)
- Proteins/ enzymes (11)
- Sugars (34)
- Hydrocarbons (50)
- Simple alcohols (7)
- Simple aldehydes (12)
- Simple ketones (13)
- Simple acids (21)
- Fatty acids (22)
- Simple esters/lactones (13)
- Steroids (11)
- Terpenes (20)
- Non-cannabinoid phenols (25)
- Flavonoids (21)
- Vitamins (1)
- Pigments (2)
- Elements (9)

483 total identified compounds



- Delta-9-tetrahydrocannabinol
- Major psychoactive
- Metabolites
  - Hydroxy – THC
  - Carboxy – THC
- Dronabinol = synthetic THC
- Nabilone = close analog

- Cannabidiol (CBD)
- Somatic
- More amphipathic
  - Peripheral actions
- Nabiximols = mixture
  - ~ 1:1 THC : CBD

Cannabigerol, Cannabinol,…
> 50 other cannabinoids

The Little We Know – THC

- Smoking
  - 18-50% absorbed
  - Onset 6-15 mins
  - Peak 30 min - 2 hours
- Oral
  - 5-10% absorbed
  - Onset 30-60 mins
  - Peak 1-3 hours
  - First pass → OH – THC
- Hepatic (CYP) metabolized
- Elim: 35% urine, 65% feces

- Psychotropic effects lag plasma levels after inhalation
- Psychotropic threshold: 25 ng/mL
- Peak plasma levels > 100 ng/mL drop to < 2 ng/mL in 4 hours
  - Lipid distribution
  - Depot / ongoing release

“Dose”
Cannabinoid Receptor Agonism

- Cannabinoid receptors: CB1 and CB2
- G-protein coupled receptors
  - Endogenous ligands activate them (more later)
- In addition to (mostly) minor 5-HT activity, immediate effects are referable to CB1 agonism

Effects by CB1 location

- Prefrontal cortex
  - Reasoning
- Hippocampus
  - Memory
  - Attention
- Mesolimbic area
  - Vigilance / Fear
  - Perception
  - Reinforcement
- Basal ganglia & Cerebellum
  - Coordinated movement
- Hypothalamus
  - Hunger & Sex
- Spinal Cord
  - Pain sensation

Not expressed in medulla
No respiratory depression

Adverse Effects

- Cardiac
  - Tachycardia and myocardial stress
  - 5-fold increase in risk of MI in the hour after smoking
  - Contributor to development of CAD with chronic use ?
- Pulmonary
  - Lung irritant and carcinogen burden
  - Phlegm, cough…increased bronchial infection risk
  - Studies quote 50-70% ”more” carcinogens than tobacco
  - Deeper inhalation / longer breath-holding increase exposure
- Overwhelming neuropsychiatric symptoms
  - Accidental trauma rates increase in the hours after use

NIDA

Possible Link to Psychosis

- Induces symptoms that mimic schizophrenia
  - Altered awareness and thinking patterns, paranoia, hallucinations
- Heavy cannabis use appears to increase the risk of persistent psychotic symptoms → SCZ **2-fold**
  - COMT polymorphisms may compound risk
- Cannabis use is higher among those with psychotic illnesses than the general population
  - Subjective coping with symptoms ?
    - Cannabis --→ Psychosis
    - Psychosis ←-- Cannabis

Further Explication of Risk

- Individuals “at risk” for psychosis and who use cannabis 10-fold more likely to develop psychotic illness than users without identified risk.

- Meta-analysis in 2007 found increased OR of 1.41 (95% CI, 1.2-1.65) for psychosis in people who had ever used cannabis.
  - Also found OR of 2.09 (95% CI, 1.54-2.84) for more frequent users (daily, weekly, more than 50 times total)
  - ***Sola dosis facit venenum***

- One factor in complex web of gene × environment interaction

Developmental Vulnerability

- Initiation before age 17
  - Lower verbal IQ scores
  - Impaired working memory
  - Smaller whole brain and cortical gray matter volumes
- Causality?
  - Puberty is a period of brain reorganization / pruning
  - Cannabinoid use affects GABA and glutamate activity resulting permanent physiologic changes

Earlier Development…

- Half of women who use cannabis continue that use into pregnancy
- Pregnancy outcomes
  - Anemia and perhaps more precipitous labors
  - No associations with: Gestational diabetes or HTN, Excessive weight gain, Hyperemesis gravidarum, PROM, prolonged labor, hemorrhage
- Neonatal outcomes
  - Decreased birth weight (M > F), NICU admissions
  - Little to no data on behavioral outcomes
- Conclusions limited by use of other substances
  - Most women get no counseling, ACOG urges abstinence

Gunn JK. BMJ Open. 2016; 6(4):e009986
Holland CL. Obstet Gynecol. 2016; 127(4):681-7.

Debatable ?

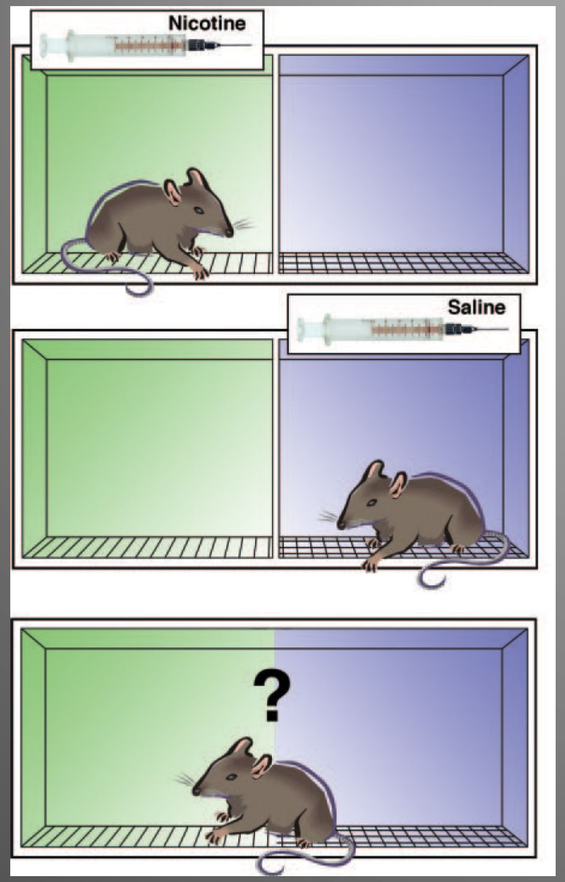
- 50 years ago, when THC concentrations were low…
  - And we subsequently had ”diagnostic” words like:
    - Abuse
    - Dependence
  - And we focused on tolerance and withdrawal
- Now with THC % in marijuana regularly north of 20…
  - And we say “use disorder” to emphasize impact on life
  - And treatment admissions equal those for cocaine & heroin
  - And there’s a recognized withdrawal syndrome for good measure

Nope.

Like Other Drugs of Abuse

Preclinical data

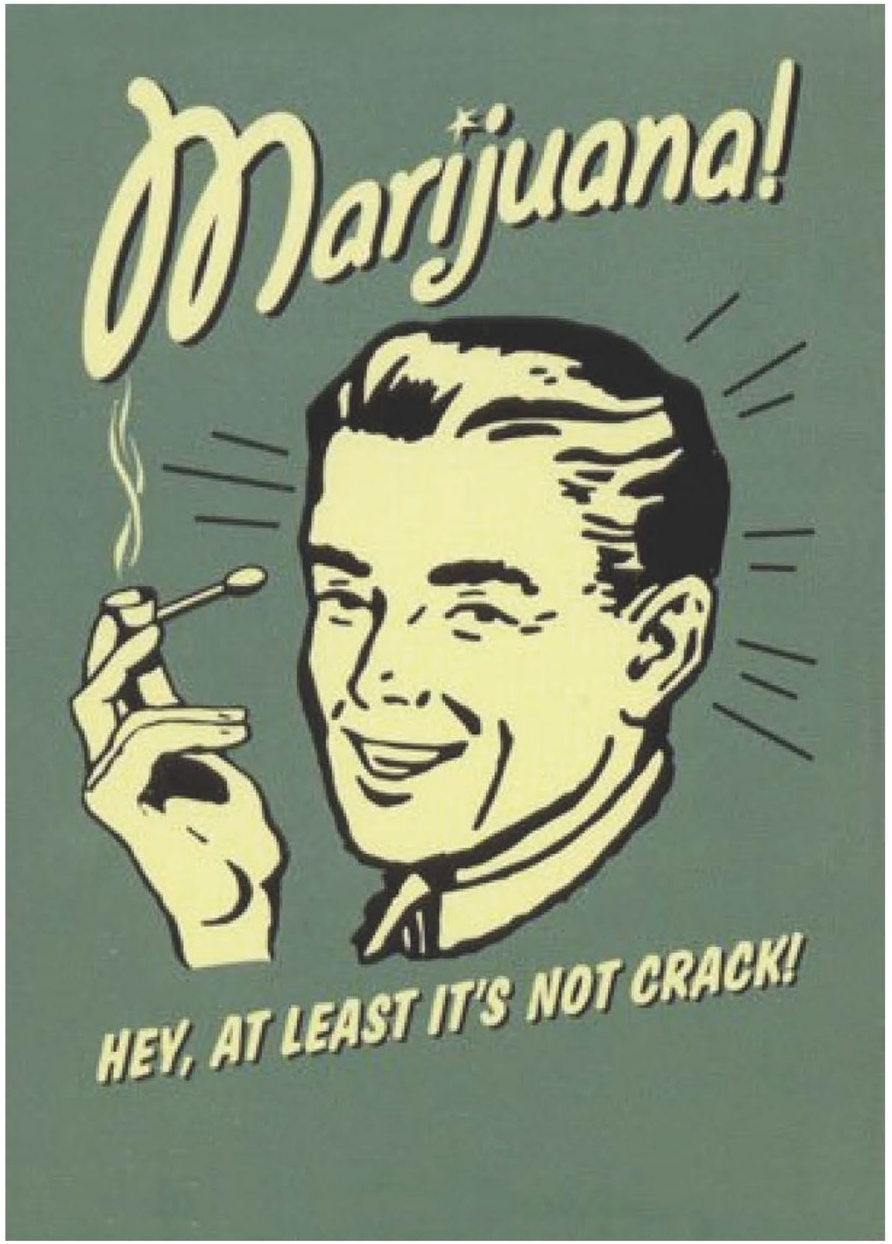
- ✓ Is self-administered
- ✓ THC seeking can be reinstated after delay
- ✓ ↑CRF & BSR ("brain stimulation reward")
- ✓ Dopamine increase
- ✓ Produces Conditioned Place Preference (CPP)



Clinical data

- Tolerance: rapid on/off PK smoked
- Withdrawal syndrome: atypical, mild → very real
- Dependence: at least 9% of those who have ever used …and growing

Le Foll & Goldberg 2005


Marijuana!
HEY, AT LEAST IT'S NOT CRACK!

Pre-wired:
The Endocannabinoid System

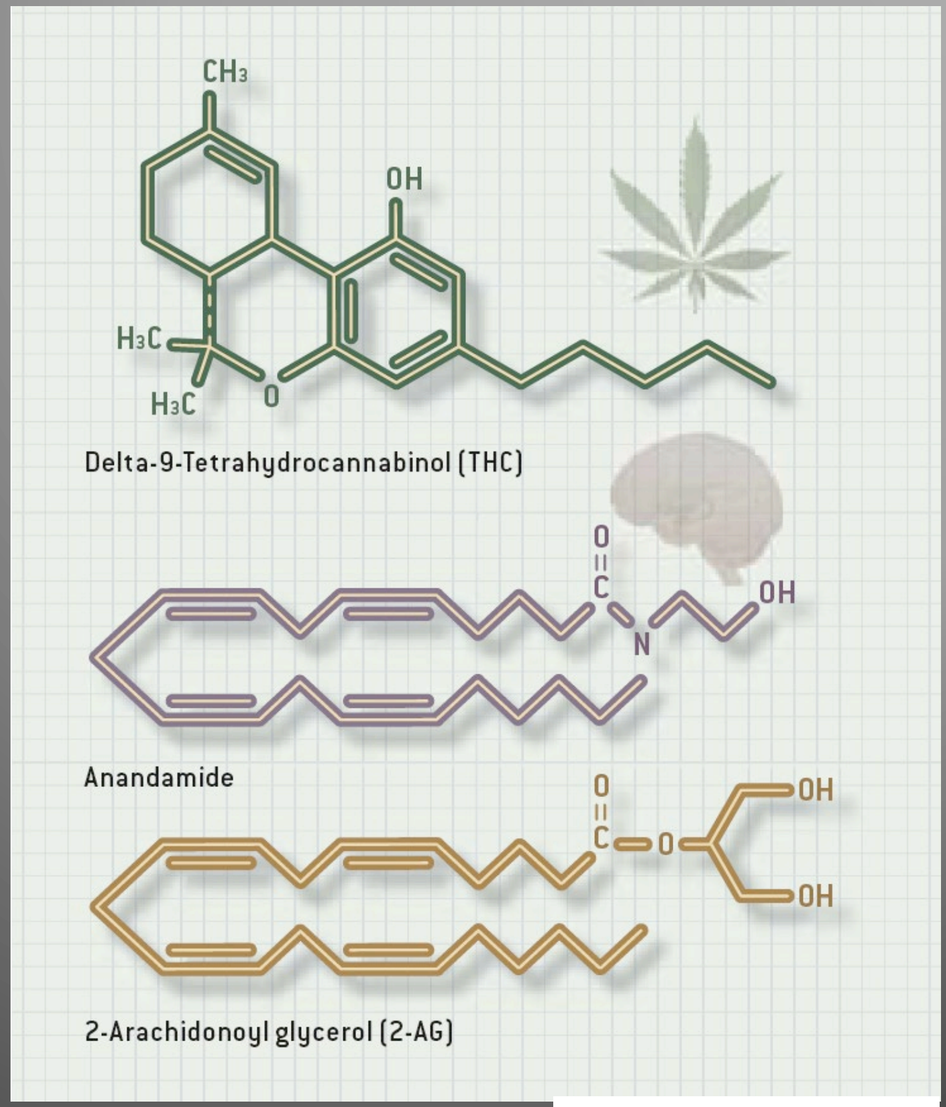
- Cannabinoid (CB1 and CB2) receptors
  - G-protein coupled, 7 membrane-spanning segments
  - CB1: mainly located in CNS -- hippocampus
    - Also in frontal cortex, basal ganglia, hypothalamus, cerebellum
  - CB2: mainly in immune system -- B-lymphocytes
    - Also on macrophages
    - Modulate cytokine release
  - Both also located in GI tract (duodenum), liver, muscle, fat, reproductive, cardiovascular, and endocrine systems

Endocannabinoids

- Bind CB1 > CB2
- Structured like prostaglandins

- Anandamide
(arachidonyl-ethanolamid)

- 2-Arachidonoylglycerol (2-AG)
more abundant, less potent

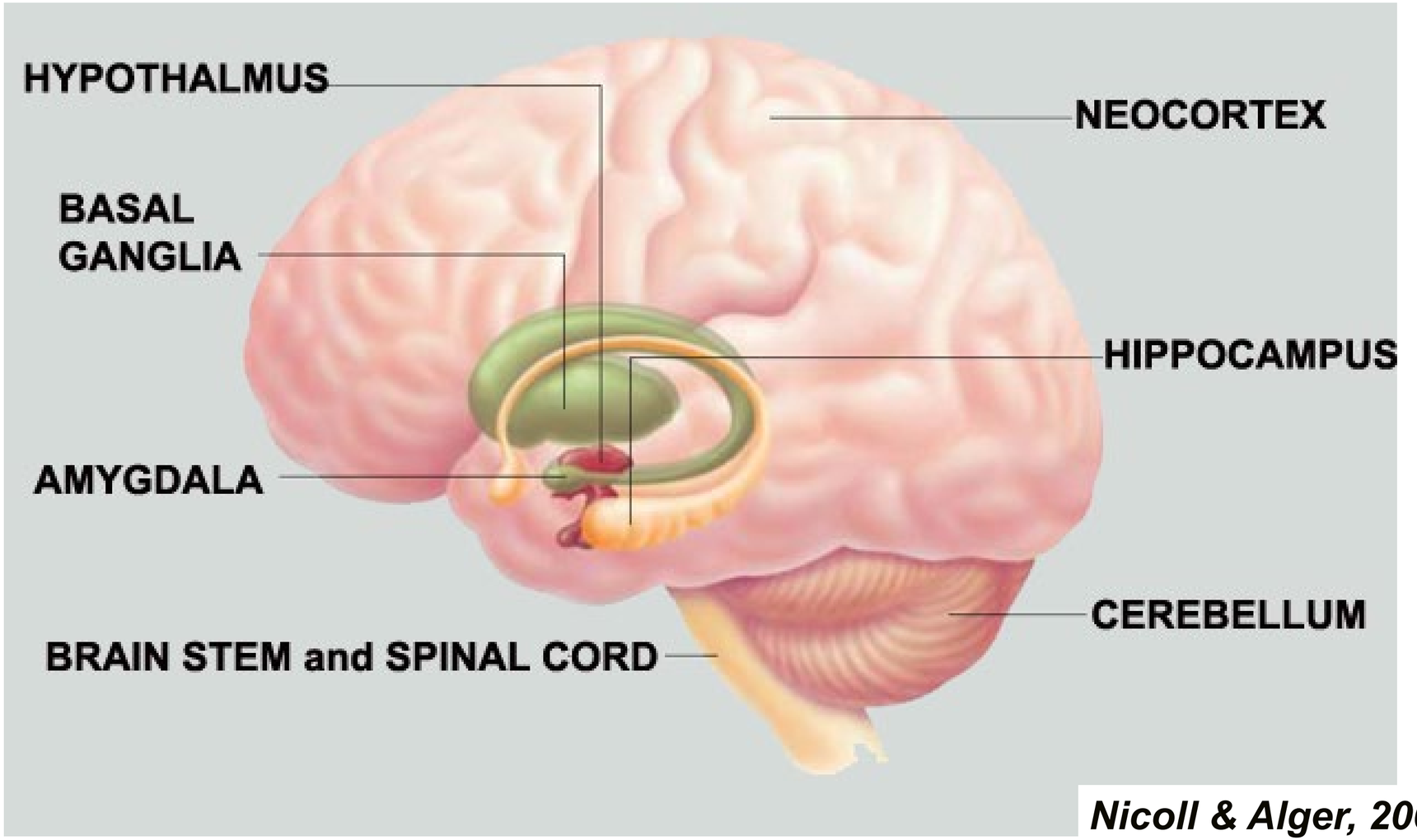


Nicoll & Alger, 2004

CB1 receptor density in the brain

Higher density: Basal Ganglia, Cerebellum, Hippocampus, Nucleus Accumbens, Mid-Prefrontal, Parietal Cortex

Lower density: Amygdala, Spinal Cord, Brainstem



Nicoll & Alger, 2004

Basic Endocannabinoid Summary

- Anandamide and 2-archidonoylglycerol
- Naturally bind CB receptors that compounds in cannabis target (mostly THC, little CBD)*
- Messengers and modulators of post-synaptic signaling with presynaptic feedback potential
- Present in all major CNS NT pathways
  - GABA
  - Glutamate
  - Dopamine
  - Acetylcholine

***Systemic effects difficult to ascertain and quantify**

Medicinal Marijuana Throughout History

- Ancient History
  - **Chinese** medicine dating back >10,000 years, still in Traditional Chinese Medicine
  - Ancient **Egypt**: Hemorrhoids and inflammatory conditions
  - **India**: Insomnia, pain, digestive problems
  - Ancient **Greece**: Extensive veterinary uses, also in humans for nosebleeds, tapeworms
  - **Middle East**: Antiemetic, diuretic, antiepileptic, anti-inflammatory
- Western Medicine
  - **Europe**: Muscle spasms, stomach cramps
  - **America**: Widespread in “patent medicines”
- Modern Times
- Advocates Support:
  - Insomnia
  - Pain
  - Anxiety
  - Depression
  - Nausea and vomiting
  - Appetite w/ weight loss
  - Crohn’s disease
  - Muscle spasms
  - Epilepsy
  - Glaucoma
  - Many others

~~Medical~~ Marijuana

- Medicinal Cannabis

Current or Potential Oral Cannabinoid Modulators

- Agonists
  - Cannabis itself
  - Synthetic Tetrahydrocannabinol (THC)
    - Dronabinol, Nabilone, and analogs
  - Selective CB1 or CB2 agonists
- Antagonists, partial agonists
  - Rimonabant, Taranabant, etc.
- Modifiers of endocannabinoid metabolism
  - FAAH inhibitors (anandamide)
  - Monoglyceride lipase (MGL) inhibitors (2-AG)

Dronabinol (Marinol) – Synthetic THC

- Haney et al, showed increase in caloric intake and weight gain in HIV-positive patients
  - Dronabinol was more effective at improving sleep than placebo
- Cooper et al, compared analgesic effects of marijuana vs. dronabinol vs. placebo
  - Decreased pain scores in both active arms
  - Longer duration of effect for dronabinol
- BMJ study in 2004, showed modest benefit on neuropathic pain in patients with Multiple Sclerosis

Dronabinol (Marinol) – Synthetic THC

- 2013 Lancet study looked at dronabinol for impact on progression of Multiple Sclerosis
  - Well tolerated, but no significant effect on disease
- In 2007, Meiri et al. studied dronabinol vs. ondansetron vs. combination in chemotherapy patients with nausea and vomiting.
  - Similar effectiveness at cessation of nausea in all groups
  - Intensity of N/V better controlled in dronabinol group
  - Combination offered no advantage
- 2017 preliminary study showed improvement in OSA

JCSM 14(4):679-681, 2018

Nabilone (Cesamet) – THC analog

- Available in the United Kingdom, Canada
  - Indicated for nausea from chemotherapy refractory to standard Rx and Anorexia with weight loss in AIDS
  - Same indications as dronabinol in the U.S.

- Improved QOL in lung cancer patients, not head & neck
- No impact on post-operative nausea and vomiting
- Effective adjunct for neuropathic pain in MS
- Preliminary RCT data in:
  - Headaches, Sleep in fibromyalgia, Nightmares in PTSD
  - Substitution therapy for cannabis addiction…

Nabiximols (Sativex)
Cannabis sativa extract oral spray

- Available in the United Kingdom, Canada, Oz, Spain,…
- Roughly THC:CBD equal ratio

- Improved opioid refractory cancer pain
- Effective for neuropathic pain and spasticity in MS
  - Active study in post-stroke spasticity
- Preliminary RCT data
  - Substitution therapy for cannabis addiction…

A similar product marketed by Parke Davis as a "narcotic, analgesic, and sedative" was available for a brief period in the U.S. in the 1930s.

Cannabidiol (CBD)

- Natural constituent of cannabis plants
- Comprises up to 40% of marijuana extracts
  - Breed of plant
  - Extraction method
- Devoid of typical psychological effects of THC
- Attenuation of psychoactive effects of THC when both compounds are administered concomitantly?

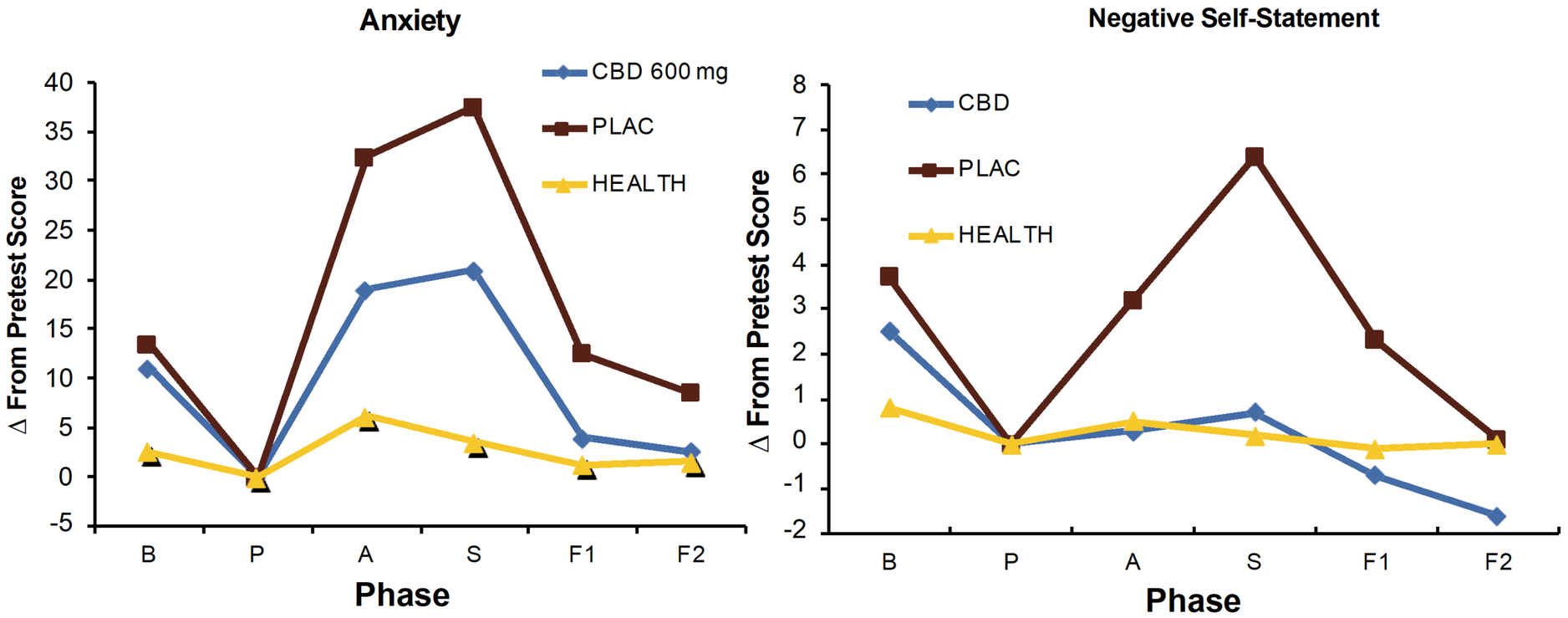
Possible MOAs of CBD

- Little potential to activate CB1 or CB2
- Desensitizes transient receptor potential channels (e.g., TRPV1): antinociceptive to inflammatory pain?
- Blocks GPR55, which may also play a role in neuropathic and inflammatory pain
- Enhances glycine receptor activity: anticonvulsant?
- Inhibits FAAH: increase availability of anandamide?
- Enhances 5HT1A receptor activity: anxiolytic effect?
- Modulates cytochrome P450 2C metabolism of THC to the more psychoactive 11-hydroxy-THC ?

Suggested CBD Therapeutics

- Anti-inflammatory
- Analgesic
- Anti-emetic
- Sedative / Hypnotic
- Antipsychotic
- Anticonvulsant
- Neuro-protective
- Anxiolytic

CBD Reduces Anxiety Induced by Simulated Public Speaking in Treatment-Naïve Social Phobia

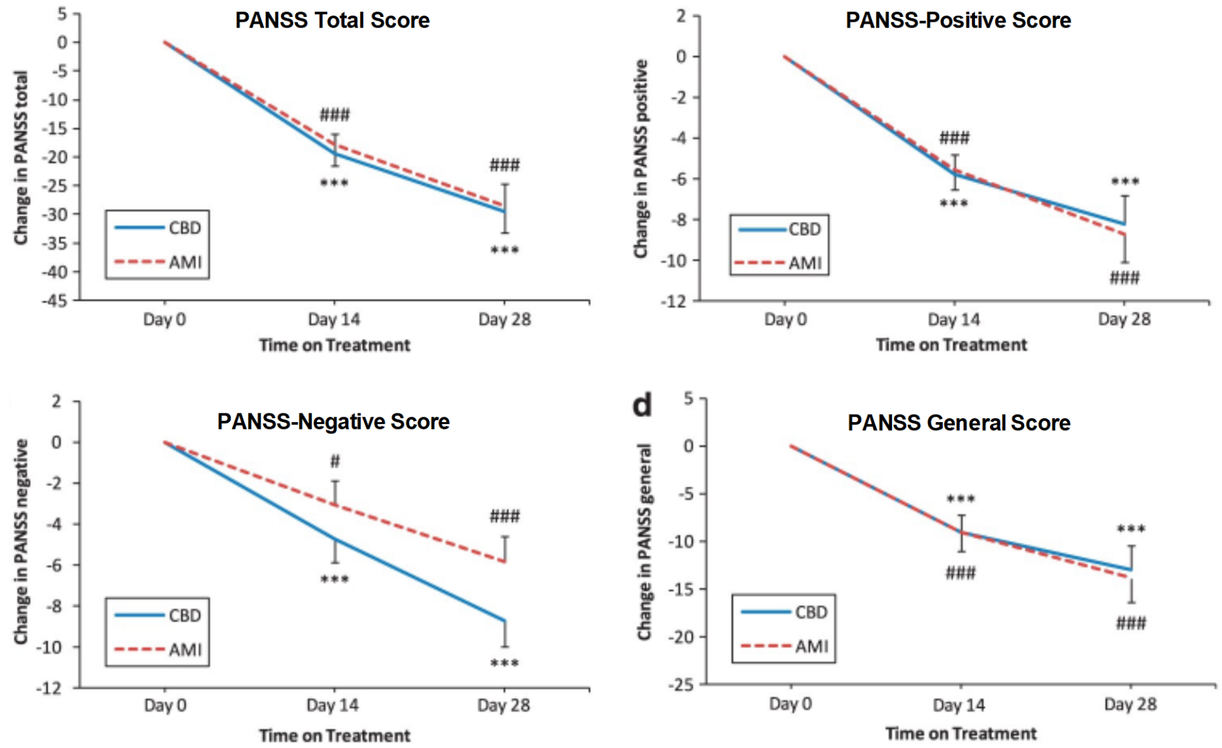


Bergamaschi MM, et al. *Neuropsychopharmacology*. 2001;36(6)1219-1226.

Slide information courtesy of Dr. José Alexandre de Souza Crippa, Department of Neurosciences and Behavior, Ribeirão Preto Medical School, University of São Paulo, Brazil.

CBD Improves Positive and Negative Symptoms of Schizophrenia

42 Cases Randomized to Receive 800 mg/d CBD or Amisulpride



PANSS = Positive and Negative Syndrome Scale.
Leweke FM. *Transl Psychiatry*. 2012;2:e94.

Data show predicted means and side effects. Statistical significance is calculated between groups and versus baseline, that is, 0. (*CBD, #AMI; #$P < 0.001$; ***/###$P < 0.05$).

National Academies Report (2017)
Evidence for Therapeutic Benefits of Cannabis

- Substantial/conclusive evidence of cannabinoid efficacy in:
  - Chronic pain
  - Spasticity of multiple sclerosis (MS)
  - Control of nausea
- Moderate evidence of cannabinoid efficacy in:
  - Improving sleep in those with chronic medical conditions (e.g., chronic pain, fibromyalgia) **-- insufficient data for sleep apnea.**
- Limited evidence of cannabinoid efficacy in:
  - Treatment of certain anxiety disorders and posttraumatic stress disorder
  - Promoting appetite and weight gain
- No or insufficient evidence of cannabinoid efficacy in:
  - Treatment of cancers, irritable bowel syndrome, epilepsy, movement disorders due to Huntington disease or Parkinson's disease, schizophrenia

National Academies of Sciences, Engineering, and Medicine. 2017. *The Health Effects of Cannabis and Cannabinoids: The Current State of Evidence and Recommendations for Research*. Washington, DC: The National Academies Press. https://doi.org/10.17226/24625.

Mark Gold, by permission, 2019

What About Antagonism ?

- CB1 antagonism blocks the direct reinforcing effects of some drugs of abuse and food

- CB1 antagonism blocks the motivational effects of most drugs of abuse
  - Addiction relapse prevention ?

Obesity
A hyperactive endocannabinoid system ?

- Endocannabinoids and cannabis
  - Induce appetite (orexigenesis)
  - Reduce satiety
  - Stimulate lipogenesis
  - Reduce energy expenditure
  - Increase hedonic reward value of palatable food

A CB1 antagonist should have opposite effects…

Specific Antagonists

- CB1
  - SR 141716 (Rimonabant)
  - MK-0364 (Taranabant) – inverse agonist
  - AM 281, AM 251

  - **In 2008, U.S. Pharma halted most projects due to concern for emergent depression, anxiety, suicidality.**

- CB2
  - SR 144528
  - Under investigation – complex clinical chemistry

WHERE WE STAND

- Medicines are potentially harmful until proven safe
- Drugs are potentially beneficial until proven harmful

In the absence of facts, we rely upon belief…

COMMENTS / QUESTIONS ?

Medicalization / Decriminalization / Legalization

- Recognizes reality of medicinal history
- Offers potential benefit
- Quality control on products

- Enlists medicine without data or education
- Downplays expertise
- False veneer of safety

- Responds to societal demands, including medicinal
- Fits with reality of current medical science

- Alters public health landscape without preparation
- Despite regulatory attempts, leaves the market to set course
- Illegal sales increase (Canada)
  - Legality provides “cover"

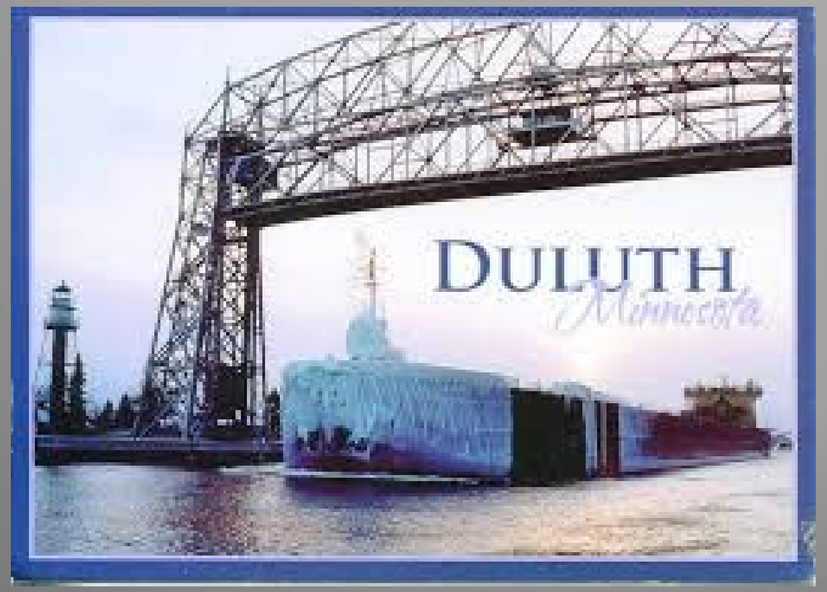
Decriminalization

- Cannabis would not be ”marketable” in legal fashion
  - Not subject to standard drives for monetary gain
  - Advertising would not have the power to exploit the vulnerable
- Address concerns about unfairness of criminalization for drug offenses, allowing “medicinal” cultivation/possession
- Avoid conflating medical, medicinal, and recreational ahead of having data to guide “progress”
- Allow time to head off the tragic errors made around tobacco where aggressive marketing and false narratives around lack of risk led to widespread public health harms

Quality control would require different solutions

A Gateway ?

- Marijuana is known as the “gateway drug”…
- Use is **associated** with increased risk for abuse of and addiction to other drugs
- However, **causality** has not been proven
- This does not mean we are unclear on certain realities…

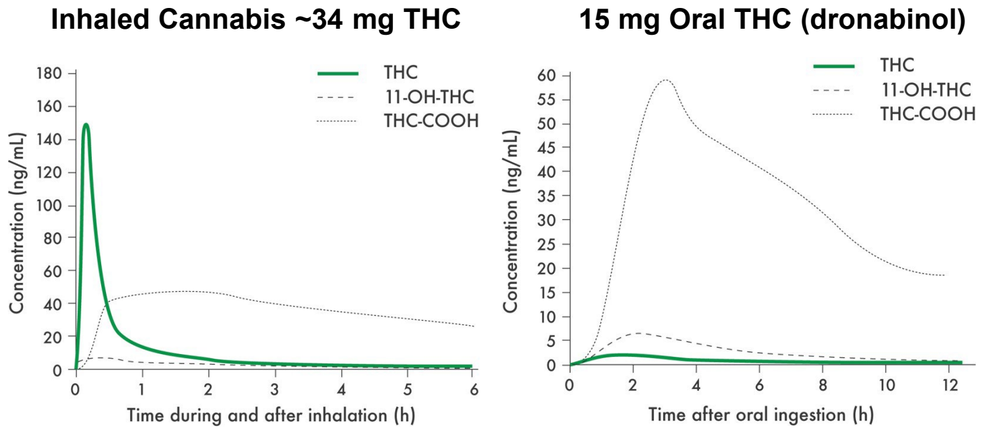


Common Sense ← → Common Ground

- Marijuana delivery system is much more harmful than the substance itself (1999 IoM report)
  - The problem with smoking weed is learning to smoke
  - It's not so much a gateway drug as a gateway procedure
- Relative to other illicit and legal psychoactive substances, the abuse and addictive potential of cannabis is modest
  - Higher potencies and synthetics are more problematic
- Secondhand smoke is firsthand smoke without consent
- Smoking is a problem we should be able to mobilize agreement to control

Watson SJ, et al. Arch Gen Psych 57(6):547-52, 2000.

Dose and Route of Administration



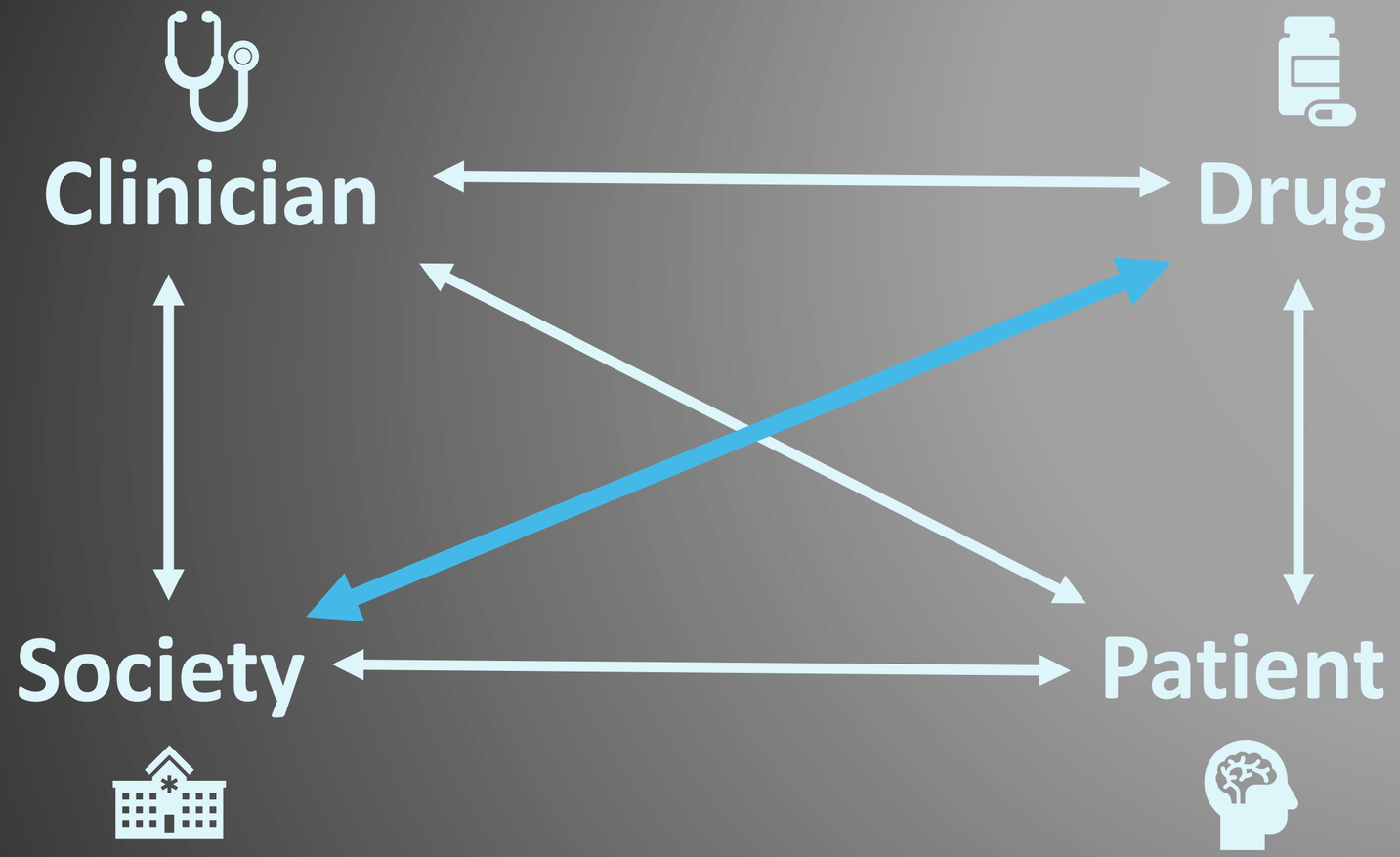
Mean plasma concentrations of Δ9-THC, 11-OH-THC, and 11-nor-9-carboxy-THC (THC-COOH) following administration smoked cannabis versus oral dronabinol.
THC bioavailability from oral averages 6%, versus up to 50% inhaled.

Grotenhermen F, et al. *Clin Pharmacokinet*. 2003;42(4):327-360.

Mode of Cannabinoid Administration May Influence Efficacy, Duration of Action, and Side Effect Profile

Other open questions

- Intoxicated driving – distraction, slower reaction times
  - Impacts seen in Colorado, California, Washington, and their neighboring states… **on PEI half of DWI cases involved cannabis**
  - How to best assess?
- Does legalization make it appear safe to youth?
  - Will teenagers think it is (even more) “OK” to use when it may actually be the most dangerous time for them to try?
- Lack of firm regulation makes labeling and retailing risky in terms of toxic exposure to minors
  - Accidental exposure calls to PCCs about edibles have risen



Issues are bigger than all of what we have discussed

…and the evolution of all these relationships is at stake.

Summary

- Endocannabinoids exert homeostatic influence in many systems: nervous, immune, CV, etc.
  - Modulators have therapeutic potential
- Legal impediments have slowed medical progress
  - THC efficacious in neuropathic pain, spasticity, nausea/anorexia
  - CBD shows promise in anxiety, psychosis, some pain conditions
- Exogenous cannabinoids and synthetic psychoactive analogues are not wholly safe
  - Unfortunately, addiction is a more real threat now
  - *Dosis facit venenum*, though timing and ROI also matter
- Medicine and society have much to learn…

Acknowledgements

Pamela Hudson, M.D.

Mark S. Gold, M.D.

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Christina Wichman, D.O., F.A.C.L.P.

John Wermager, M.D.

- Rotating residents at Pinnacle Toxicology (Harrisburg, PA)
- Staff of the Philadelphia and Minnesota Poison Centers
- Many, many, many patients…

Comments / Questions / Complaints ?

References

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Supplemental Materials

- For a few of your FAQs

Find What You're Looking For – THC

- **Screening** - Immunoassay: Threshold is 50 ng/mL, does not discriminate THC from the metabolites

Detection Time:	
Single use:	1-3 days
Moderate use (4x/week)	5-7 days
Daily use	10-15 days
Long-term heavy use	>30 days

False Positives: **Efavirenz, Promethazine, NSAIDs, PPIs, B2…**

- **Confirmation** - Gas chromatography / specific methods
- Plasma but not urine concentrations are correlated with time and amount used

MMWR Weekly September 16, 1983 / 32(36);469-71

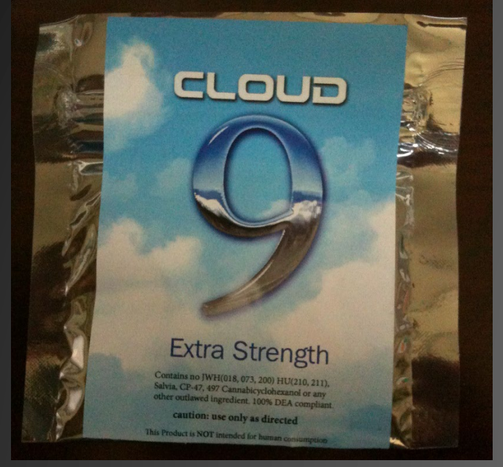
NHTSA Fact sheet 2002

Synthetic Cannabinoids

What's So Much Fun, Anyway?

- Delta-9-THC, mostly…
  - Marijuana contains between 0.5% & 22% THC
  - Resin > 35%, Hash Oil > 50%
- CB1 and CB2 receptor agonism (brain and spinal cord)
- Intoxication
  - Calm, slowed thinking with memory impairment
  - Time flow distortion and mild perceptual alterations
  - Conjunctival injection, pupils that will not accommodate
  - Increase in heart rate
  - Impaired coordination / ataxia
  - Unless there's a "bad trip"…


A · C · M · T
Sola Dosis Facit Venenum



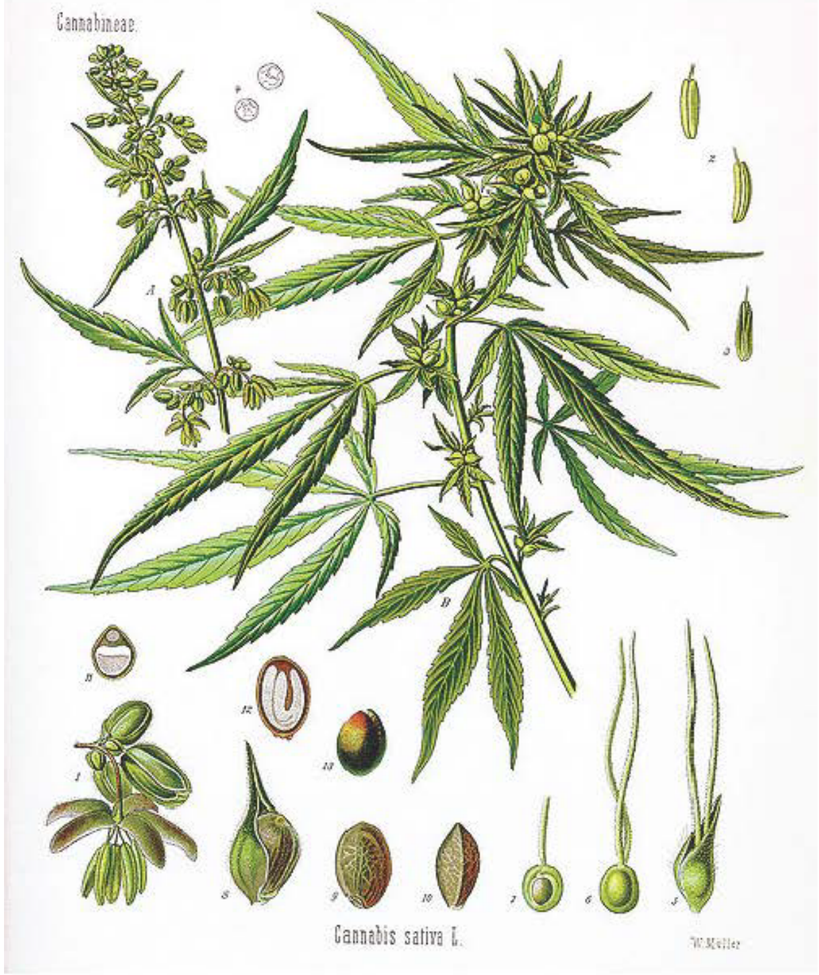
Beyond Fun

More potent than cannabis
Similar duration (3-6 hours)

- Tachycardia
- Hypertension
- Hyperthermia
- Hallucinosis
- Conjunctival injection
- Nausea / Vomiting
- Paresthesias
- Seizures

More serotonergic
Greater risk of persistent symptoms

Missouri Dept. Health, 2010 and Auwarter, et al. *J Mass Spectrom.* 2009.


Cannabineae.
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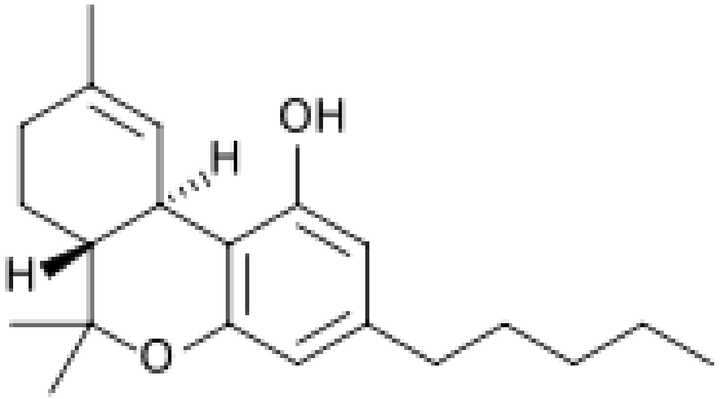
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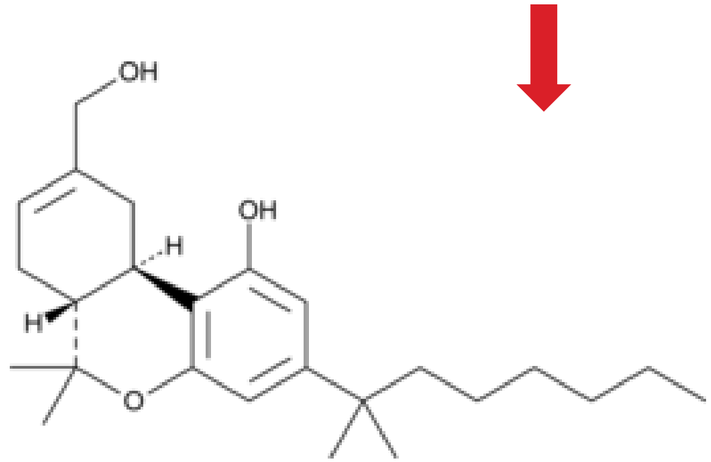
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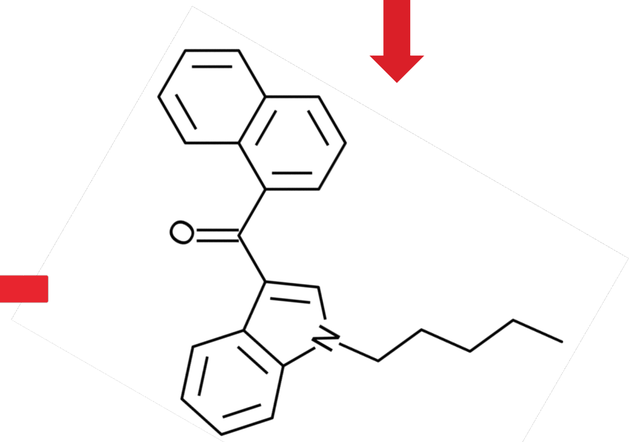
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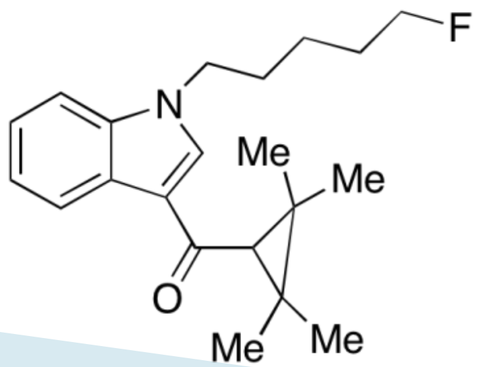
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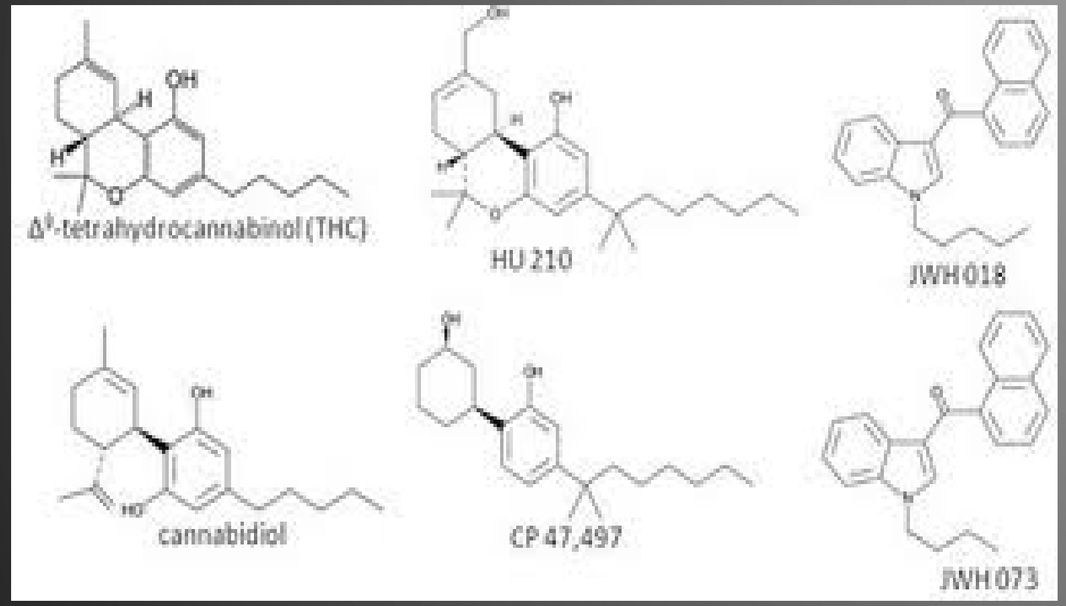
Synthetic cannabinoids



- K2, Spice, Incense, etc.
- Agonists at cannabinoid receptors causing similar symptoms as THC
- Tend to be more potent
- Constantly changing to stay ahead of laws and detection

Non-Medicinal Synthetic Cannabinoids

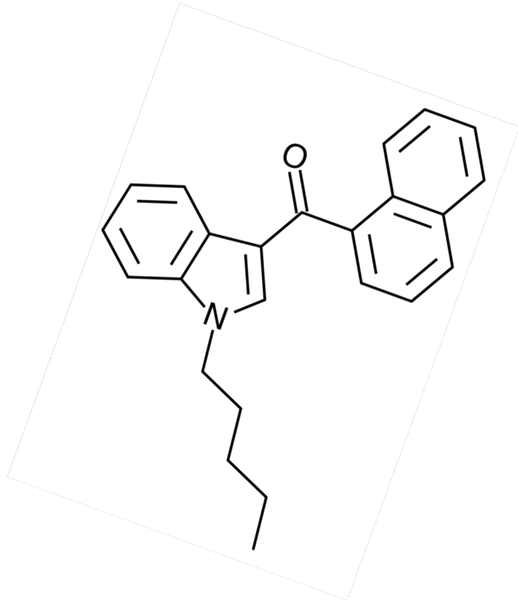
- CP-55940
  - developed by Pfizer in 1974 but never marketed
  - full agonist at CB_1 and CB_2 receptors
  - mimics the effects of THC (but up to 45x more potent)
- Dimethylheptylpyran
  - invented in 1949
  - insoluble in water but dissolves in alcohol
  - stronger analgesic and anticonvulsant effects than THC
  - weaker psychological effects than THC
- HU-210
  - first synthesized in 1988 at Hebrew University
  - (+) enantiomer has cannabinoid acitivity
  - (-) enantiomer is an NMDA antagonist with neuroprotective effects
  - ingredient discovered to be in "Spice" products in 2009

Non-Medicinal Synthetic Cannabinoids

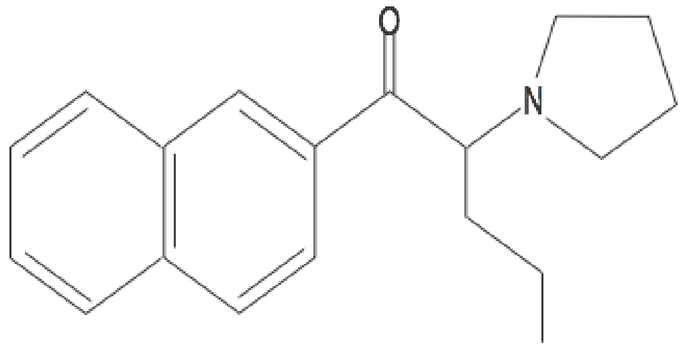
- JWH-018 (“K2” or “Spice”)
- Levonantradol
  - analog of dronabinol
  - agonist of CB_1 and CB_2 receptors
  - potential anti-emetic and analgesic effects
  - limited by central side effects
- WIN 55,212-2
  - potent analgesic
  - may prevent inflammation caused by Amyloid beta proteins involved in Alzheimer's Disease

The Future?

- Note similarity between this synthetic cannabinoid and…



- **Naphyryone**
- Substituted phenylethylamine
- Monoamine releaser
- Serotonin receptor agonist
- Triple reuptake inhibitor
- NET > DAT > SERT



Naphyrone
(RS)-1-naphthalen-2-yl-2-pyrrolidin-1-ylpentan-1-one
(napthylpyrovalerone, O-2482, NRG-1)

It’s all the same…

- Hallucinations and stimulation almost always involve enhanced serotonin neurotransmission
- Based on this serotonergic mechanism of designer drugs, serotonin syndrome could theoretically occur after the use of any of them
  - More severe monoaminergic effects from phenethylamines
- Attend to ABCs, vital signs, and mental status
- Diagnosis often established by history and physical examination alone
- Drug screens, even if positive, confirm use, not toxicity
  - And don’t come back in time to impact care

General Management Strategy

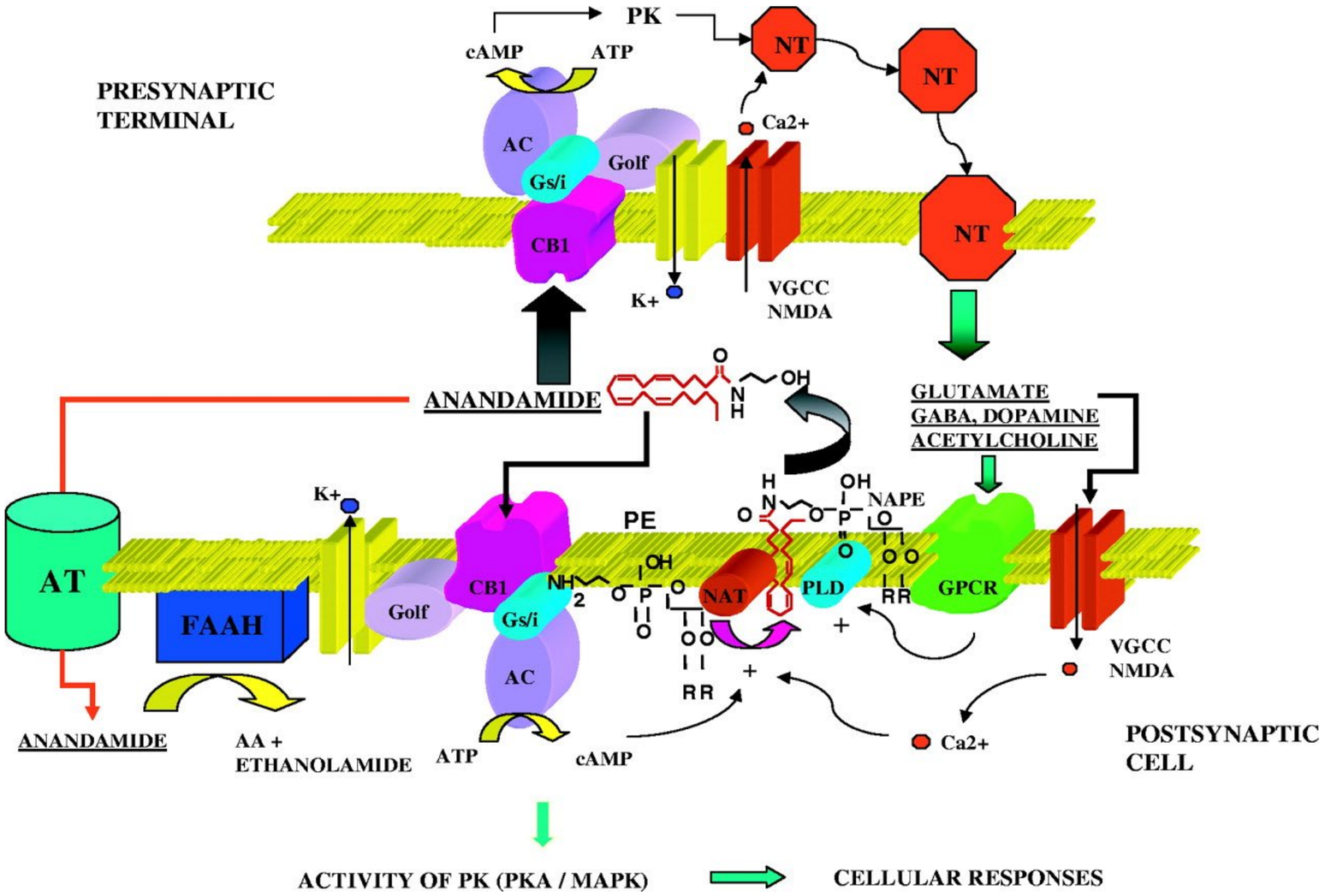
- Hallucinogenic / psychostimulant effect alone
  - Fully alert, oriented, and aware under the influence
  - Euphoria, dysphoria, and emotional lability
  - Supportive care, perhaps Rx BZDs …or Haloperidol
- Psychosis / agitation
  - Hallmark of more robust central effect
  - BZDs first and early (targeting the mechanism), then haloperidol
  - More H if only psychobehavioral symptoms persist

But if there's more…

Serotonergic / Monoaminergic Toxicity

- Hyperautonomia / Abnormal Neurologic Exam
  - Mydriasis, diaphoresis
  - Ataxia
  - Hypertension
  - Tachycardia
  - Hyper-reflexia / Clonus
  - Delirium
- BZDs the core of Rx, Adjunctive haloperidol prn once autonomic indices begin to respond
  - If they do not, phenobarbital…propofol…dexmedetomidine…

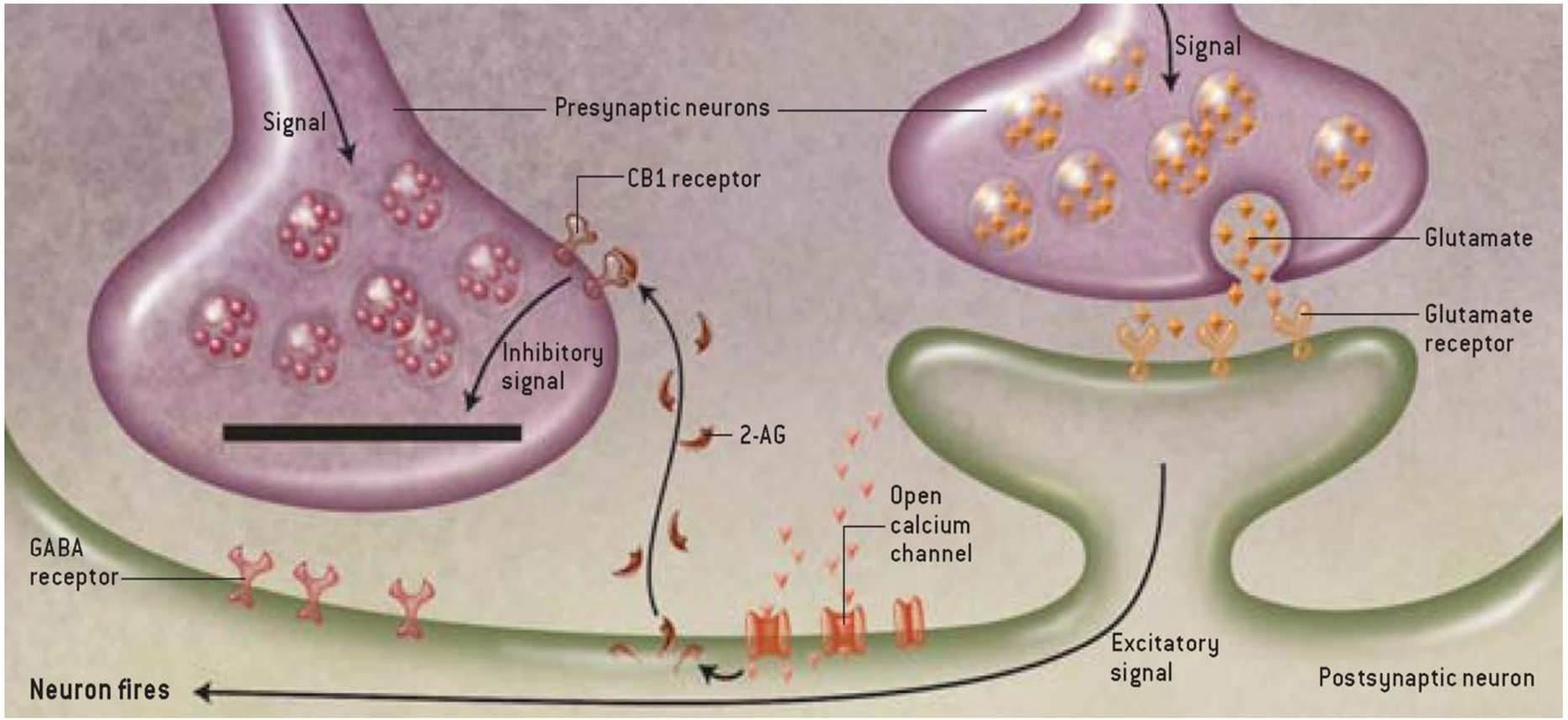
Anandamide



RODRÍGUEZ de FONSECA F et al.
Alcohol and Alcoholism 2005;40:2-14

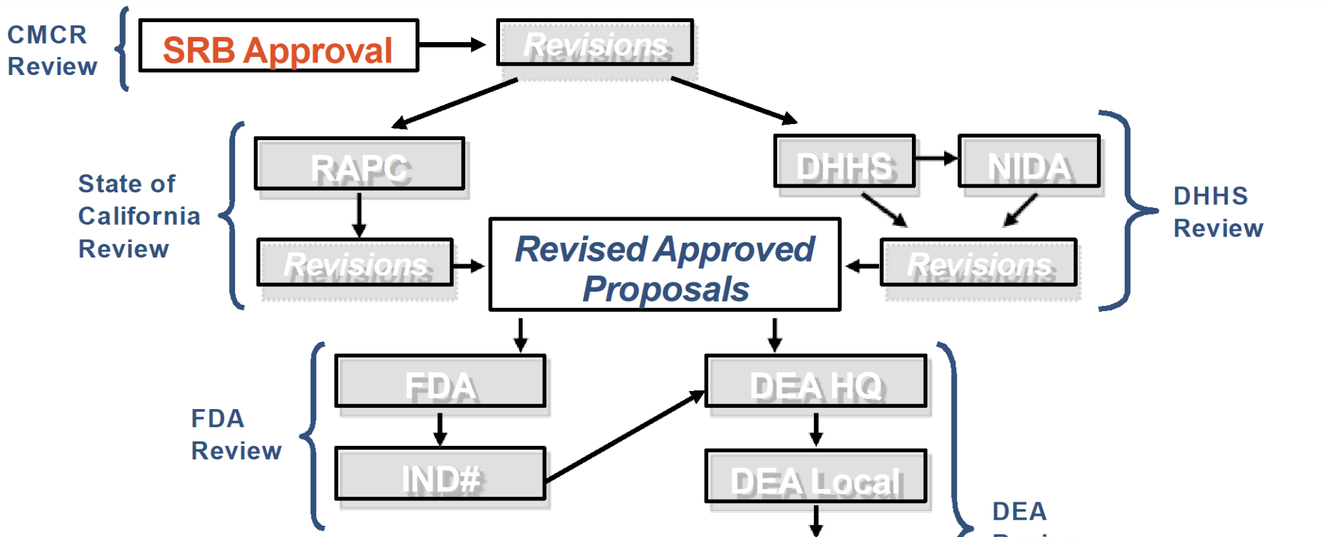
Depolarization-induced suppression of inhibition

POSTSYNAPTIC endocannabinoid release inhibits PRESYNAPTIC GABA and glutamate release



Nicoll & Alger, 2004

Because Cannabis Is a Schedule 1 Drug, and the Only Legal Source Is the Federal Government, Studies Are Challenging



Time from submission of CMCR-approved study to state and federal regulators to study initiation was ~1 year (range, 6-18 months).

CMCR = Center for Medicinal Cannabis Research at University of California, San Diego; DEA = Drug Enforcement Administration; DHHS = Department of Health & Human Services; FDA = Food and Drug Administration; HQ = headquarters; IND = investigational new drug; NIDA = National Institute on Drug Abuse; RAPC = Research Advisory Panel of California; SRB = scientific review board.

Mark Gold, by permission, 2019

Completed U.S. Clinical Studies

Site	Disorder	Design	N	Dose (% THC)	Result
UCSD Mark Wallace	Healthy Volunteers (Experimentally-Induced Pain)	Crossover RCT	15	0%, 2%, 4%, 8%	+
UCSF Donald Abrams	HIV Neuropathy, Experimental Pain	Paralle l Group s RCT	50	0%, 3.5%	+
UCSD Ronald Ellis	HIV Neuropathy	Crossover RCT	28	0%, 1-8%	+
UCD Barth Wilsey	Neuropathic Pain, Experimental Pain	Crossover RCT	33	0%, 3.5%, 7%	+
UCD Barth Wilsey	Neuropathic Pain	Crossover RCT	39	0%, 1.29%, 3.53% (Vaporized)	+
UCSD Jody Corey-Bloom	MS Spasticity	Crossover RCT	30	0%, 4%	+
UCSD Mark Wallace	Diabetic Neuropathy	Crossover RCT	16	0%, 2%, 4%, 7%	+

Mark Gold, by permission, 2019

I am not a crook…

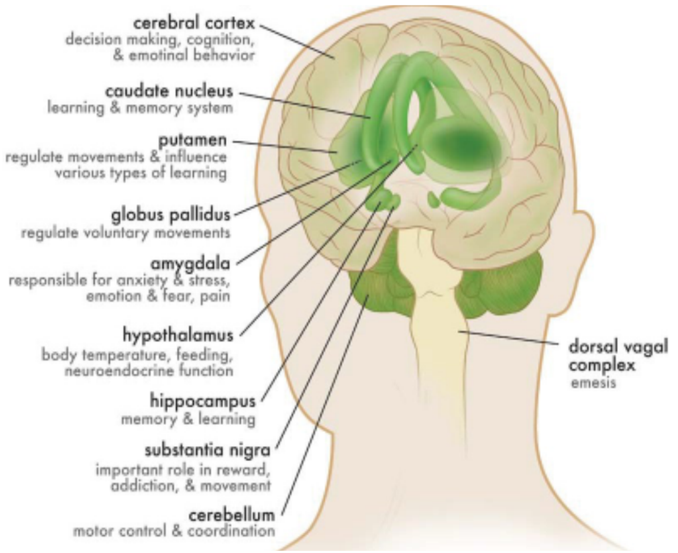
Schedule I under the Controlled Substances Act

''…high potential for abuse, no currently accepted medical use and a lack of accepted safety'' = illegal.

Cannabis Comes in from the Cold: A Tale of Science and Politics

- Persistent anecdotal reports of benefits
- Political shifts favoring medicinal access (in the U.S., most states now provide for some measure of access)
- Discovery of the endocannabinoid system
  - CB1 and CB2 receptors
  - Anandamide[1]
  - 2-arachidonoylglycerol[2,3] and other signaling molecules
  - Development of synthetic molecules: agonists, partial agonists, antagonists, and other modifiers
    (e.g., inhibitors of fatty acid amide hydrolase [FAAH]. FAAH breaks down anandamide)

CNS Distribution of CB1 Receptors



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“Medical Marijuana” in MN

CHAPTER 311--S.F.No. 2470

- Authorized producing businesses
  - Minnesota Medical Solutions
  - LeafLine Labs
  - Each grow in 1 location, distribute from up to 4
- Qualifying conditions
  - Medical involvement
- Consumer application process
- Authorized dispensaries
  - Pharmacist distribution / dose titration
  - Law defines preparations available

Qualifying Medical Conditions

- Cancer[1]
- Glaucoma
- HIV/AIDS
- Tourette syndrome
- Autism
- PTSD
- ALS
- IBD, including Crohn’s
- Seizures, including those characteristic of epilepsy
- Severe and persistent muscle spasm, including those characteristic of MS
- Terminal illness with a probable life expectancy of less than one year[1]
- Intractable Pain
- Obstructive Sleep Apnea
- Alzheimer's disease

[1]To qualify for the program, your cancer, or its treatment, must be accompanied by severe/chronic pain, nausea or severe vomiting, or cachexia or severe wasting. Or you must be diagnosed with a terminal illness, with a life expectancy of less than one year, if the illness or treatment produces severe/ chronic pain, nausea or severe vomiting, cachexia or severe wasting.

Certification

- Medical Practitioner: M.D., D.O., P.A., A.P.R.N.
- Practitioner must enroll via the MN Department of Health website in the Medical Cannabis Registry
- Practitioner certifies that the “patient” does have a qualifying medical condition
  - Prompts the delivery of an email to the “patient” with an enrollment application

Application

- Proof of Minnesota Residence
- $200 application fee
  - Renewed annually
  - Reduced to $50 with proof of SSI, SSDI, Medicaid, or MinnesotaCare status
- A caregiver (parent / guardian) must pass a background check
- The result, after 30 days, the “patient” is given a “medical marijuana card”

Receipt (i.e. buy the product)

- Fill out a “Patient Self-Evaluation Form”
- Go to an authorized dispensary
  - One of 8 “Cannabis Patient Centers”
  - Closest one to us here is in Hibbing
- Interact with a dispensing expert (i.e. pharmacist)
- Receive cannabis: pills, oils, liquids
  - No edibles, hash, flower, flower vapor, or any IN delivery
- Pay the “Cannabis Product Fee”
  - The part that reminds us that this is a business, not standard medical care

What Ailments Qualify for Medical Cannabis in Pennsylvania?

Patients in Pennsylvania diagnosed with one of the following severe, debilitating, or life-threatening medical conditions, are afforded legal protection under the Pennsylvania Medical Marijuana Law

- Cancer
- Positive status for HIV/AIDS
- Amyotrophic lateral sclerosis (ALS)
- Parkinson's disease
- Multiple sclerosis
- Damage to the nervous tissue of the spinal cord with objective neurological indication of intractable spasticity
- Epilepsy
- Inflammatory bowel disease (including Crohn's disease & ulcerative colitis)
- Neuropathies
- Huntington's disease
- Glaucoma
- Post-traumatic stress disorder (PTSD)
- Intractable seizures
- Sickle cell anemia
- Severe chronic or intractable pain of neuropathic origin or severe chronic or intractable pain in which conventional therapeutic intervention or opiate therapy is contraindicated or ineffective
- Chronic inflammatory Demyelinating Polyneuropathy
- Autism
- Terminally ill, where a medical prognosis of life expectancy of approximately one year or less if the illness runs its normal course
- Neurodegenerative Diseases
- Dyskinetic & Spastic Movement Disorders
- Opioid-Use Disorder

Getting Medical Marijuana. Available at https://www.pa.gov/guides/pennsylvania-medical-marijuana-program/#HowtoGetMedicalMarijuana. Accessed February 1, 2019

Mark Gold, by permission, 2019

The Lessons of History

Video

Opioid Use Disorder: Treatment options in the context of medical, social, and geographical complexities

AMN Day of Education, April 19th 2024

Pamela Hudson, MD CCFP

Objectives

- Review treatment options for opioid use disorder in the context of complex patient comorbidities and chronic pain
- Explore collaborative treatment approaches within rural and urban PEI communities

Case #1: Jimmy

- 72 yo male presents to primary care clinic for meet & greet appointment
  - Medical history includes chronic pain related to remote MVA involving b/l femur fractures and several vertebral fractures, otherwise healthy
    - Followed previously by pain clinic
    - Followed previously by PT and MT
  - Social History:
    - Currently on LTD, previously fished oysters
    - Single, no children
    - Smoking 1PPD, no Cannabis
    - Occasional etoh (with recent DUI)
    - No other substance use (apart from Rx next slide)
    - Rural community
    - Does not drive (recent DUI)

Case #1: Jimmy

- Medications:
  - Duloxetine 90mg PO daily
  - Pregabalin 150mg PO BID
  - Seroquel 100mg PO QHS
  - Oxycodone and Acetaminophen 10mg / 325mg PO QID PRN
  - Discloses that he typically purchases additional Rx for total approx. 8 tabs / day
  - Interested in increased dose to optimize pain control

Case #2: Becka

- 25 yo female, presents to primary care clinic: “I need help for my addiction”
  - Discloses Hydromorphone use 8mg 4-6 tabs / day
  - Route: IV
  - Last use: 3 hours prior to clinic appointment
  - No prior treatments / admissions for same
- Other substances:
  - Cocaine 1-2x/week, Tobacco 0.5ppd, Cannabis QHS, 1-2 drinks etoh / day
- Medical history:
  - Depression
  - Anxiety
  - PTSD
  - ADHD

Case #2: Becka

- Social History:
  - Lives with partner and 3yo daughter
  - Small urban community
  - Waitress at local pub
- Medications:
  - Sertraline 150mg PO Daily
  - Ativan 1mg SL Daily PRN

Initial Thoughts

- How would you approach your first appointment with Jimmy and / or Becka?
- What team member(s) do you involve?
- What medication changes do you suggest?

Substance Use Disorder

A *mild* substance use disorder is diagnosed if 3 of the following criteria are met. People meeting 4 or 5 criteria are classified as having *moderate* substance use disorder, and *severe* substance use disorder is diagnosed in cases where 6 or more of the criteria are met.

1. Taking the substance in larger amounts or for longer than you meant to
2. Wanting to cut down or stop using the substance but not managing to
3. Spending a lot of time getting, using, or recovering from use of the substance
4. Cravings and urges to use the substance
5. Not managing to do what you should at work, home, or school because of substance use
6. Continuing to use, even when it causes problems in relationships
7. Giving up important social, occupational, or recreational activities because of substance use
8. Using the substance again and again, even when it puts you in danger
9. Continuing to use, even when you know you have a physical or psychological problem that could have been caused or made worse by the substance
10. Needing more of the substance to get the effect that you want (tolerance)
11. Development of withdrawal symptoms, which can be relieved by taking more of the substance

Source: American Psychiatric Association, 2013.

Substance Use Disorder

- Use of a substance in larger amounts than intended
- Continued use despite wanting to cut back / stop
- Significant amount of time acquiring or using a substance
- Cravings or urges
- Functional impact at work, school, or home
- Continued use despite impact on relationships
- Continued use despite missing social, occupational, or work commitments
- Continued use despite involvement in high risk / dangerous situations
- Continued use despite medical condition caused or worsened by use
- Tolerance (requiring more substance to achieve the same effect)
- Withdrawal, relieved by taking the substance

American Psychiatric Association, 2013

Substance Use Disorder

- Use of a substance in larger amo
- Continued use despite wanting
- Significant amount of time acquiring or using a substance
- Cravings or urges
- Functional impact at wor
- Continued use despite im
- Continued use despite m nmitments
- Continued use despite in ations
- Continued use despite m use
- Tolerance (requiring mor)
- Withdrawal, relieved by

Specify if:
Mild: 3
Moderate: 4-5
Severe: 6+

Specify if:
Opioid
Stimulant
Nicotine
Alcohol
Cannabis
Sedative, Hypnotic, Anxiolytic
Inhalant
Hallucinogen
Non-substance addictive d/o

American Psychiatric Association, 2013

Substance Use Disorder as a Chronic Disease

- A chronic, relapsing and remitting condition with roots in co-morbid psychiatric conditions, chronic pain, genetics, socioeconomic stress, and trauma.

Why do people “use”?

- Genetic predisposition
- Comorbid mental health conditions: PTSD, Depression, Anxiety, Schizophrenia
- Comorbid medical conditions: Chronic pain
- Poverty / socioeconomic stress
- Personality: Impulsivity, sensation seeking, anxiety sensitivity, hopelessness
- Drug effect: Euphoria, calm, analgesia, comfort

(Deak & Johnson, 2021; Lo et al., 2020; Lo et al., 2021)

Treatment Approach

HARM REDUCTION:

Canadian Mental Health Association

An evidence-based, client-centered approach that seeks to reduce the health and social harms associated with addiction and substance use, without necessarily requiring people who use substances from abstaining or stopping (CMHA, 2019).

- *Pragmatism:* Harm Reduction recognizes that substance use is inevitable in a society and that it is necessary to take a public health-oriented response to minimize potential harms.
- *Humane Values:* Individual choice is considered, and judgement is not placed on people who use substances. The dignity of people who use substances is respected.
- *Focus on Harms:* An individual's substance use is secondary to the potential harms that may result in that use. [iv]

Treatment Approach

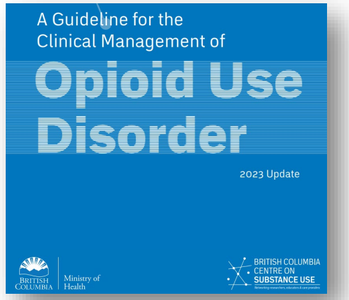
- **HARM REDUCTION:** Examples of harms related to opioid use

  - Intentional and accidental overdose
  - Impact on quality of life / family / community
  - IVDU related complications
    - Blood Borne Pathogens: HIV, HCV
    - Other infectious disease:
      Endocarditis, Osteomyelitis, Cellulitis/Abscess, Bacteremia
  - Associated health care costs

Treatment Approach

Table 1. Summary of Principles of Care

1.	Patient-centred Care: Clinicians should strive to provide care that is respectful of the unique needs, values, and preferences of each patient. Patients should be empowered as experts in their own care.
2.	Social Determinants of Health: Opioid use disorder should be viewed within a larger societal framework that is shaped by inequities in the social determinants of health. Where appropriate, clinicians should aim to address disparities in the socioeconomic determinants of health by connecting patients with resources that meet these needs (e.g., housing, food/nutrition, financial assistance, employment).
3.	Indigenous Cultural Safety and Humility: Clinicians should make a meaningful commitment to providing culturally safe care and practicing cultural humility in order to establish safe and positive partnerships with Indigenous patients, families, and communities.
4.	Anti-racist Practices: Confronting and interrogating racist structures in health care and building awareness of one's own position within oppressive systems can help improve care engagement and health outcomes for communities facing racism.
5.	Trauma- and Violence-informed Practice: Clinicians should be familiar with and incorporate the principles of trauma- and violence-informed practice in the care and clinical management of patients with OUD with the goal of creating a safe and respectful environment that minimizes the potential for harm and re-traumatization.



6.	Recovery and Self-defined Wellness: Clinicians should validate patients' goals in OUD treatment and care, which may include recovery and/or self-defined wellness.
7.	Harm Reduction: A harm reduction-oriented approach to OUD care involves the acknowledgement and support of any steps taken by patients to improve their health and well-being. Clinicians should respect patients' decisions and goals concerning substance use, and promote strategies to minimize opioid-related harms.
8.	Integrated Continuum of Care: Opioid use disorder is understood to be a chronic, relapsing and remitting condition. This guideline supports the use of a stepped and integrated approach, in which treatment options are continually adjusted to meet changing patient needs, circumstances, and goals.
9.	Comprehensive Health Management: Opioid use disorder should be managed within a broader framework of comprehensive health care and support, including routine and ongoing medical, mental health, and psychosocial assessments.
10.	Family and Social Circle Involvement in Care: Family and social circle[g] involvement in treatment planning and decision-making should be encouraged whenever possible, and when deemed appropriate by the patient and their care team.

BCCSU, 2023

Treatment Approach:

A <u>Multimodal</u> Approach:

- Withdrawal management
- 12 step programs (AA, NA)
- Counselling (CBT, DBT, Motivational Interviewing)
- SMART recovery
- Screening for and treatment of comorbid conditions
- Attention to social determinants of health (housing, employment, food security, etc.)
- Pharmaceutical treatment
- Harm reduction strategies

Treatment Options: Pharmaceutical Treatment
Opioid Agonist Therapy

- Mainstay of pharmaceutical treatment for moderate to severe opioid use disorder
- Part of a multimodal approach
- Associated with decreased morbidity and mortality
- Involves fully observed dosing with transition to take-home doses (for oral treatment)
- Involves scheduled and random urine drug screening

Treatment Options: Pharmaceutical Treatment
Opioid Agonist Therapy

- Methadone
- Buprenorphine / Naloxone (SL tab or film)
- Extended release subcutaneous Buprenorphine
- Suspended release oral Morphine (SROM)
- Subdermal Buprenorphine Implant

BCCSU, 2023

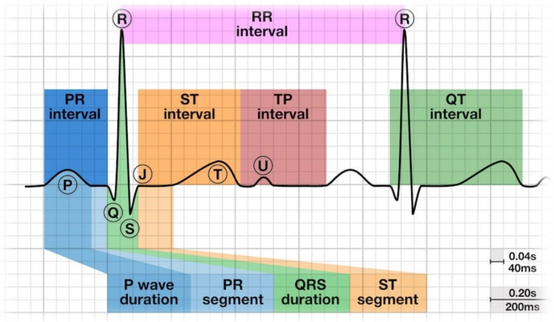
Opioid Agonist Therapies: Methadone

- Methadone: Full opioid agonist
  - Predominant action at the mu-opioid receptor
  - Some action at kappa- and delta- receptors
  - Antagonist at NMDA- receptor
- Contraindications to Methadone treatment:
  - Hypersensitivity to Methadone
  - Taking Monoamine oxidase inhibitors (MAOIs) or use within past 14 days
  - Severe respiratory compromise
- Onset of action: 0.5-1 hour

BCCSU, 2023

Opioid Agonist Therapies: Methadone

- Cautions:
  - Life-threatening respiratory depression
  - Comorbid respiratory conditions
  - Concurrent CNS depressant use
  - Life-threatening QTc prolongation
  - Caution re. accidental ingestion (*safe storage, lock box*)



- QTc: Time of ventricular depolarization and repolarization
  - Start of Q wave to end of T wave
  - Corrected QT is estimated QT interval at HR of 60 BPM
  - QT prolonged if > 440ms in men and > 460ms in women
  - Prolonged QTc increases risk of ventricular arrhythmias i.e., Torsades to Pointes
  - **EKG order with Methadone treatment with any of:**
    - 2 QTc prolonging medications
    - Hx of arrhythmia, syncope, hypokalemia, hypomagnesemia
    - Moderate / high dose Methadone

BCCSU, 2023

Opioid Agonist Therapies: Methadone

- Induction:
  - Starting dose is based on opioid tolerance (5mg-40mg PO daily)
  - Patient assessed weekly (ideally in person) during titration of medication
  - High tolerance: Increase by a maximum of 15mg every 3-5 days
  - Low tolerance: Increase by a maximum of 5-10mg every 3-5 days
    - Slow titration when 85mg is reached
  - Alternative dosing schedule for inpatient induction
  - Consider renal dosing

"After a dose increase, it can take several days for Methadone to reach a steady concentration and maximum therapeutic effect, which can also cause delayed emergence of serious adverse effects like respiratory depression" – BCCSU, 2023

BCCSU, 2023

Conversion from oral opioids to oral methadone:

Oral Morphine to Oral Methadone Conversion Factors

Total daily baseline oral morphine dose	Estimated daily oral methadone requirement as percent of total daily morphine dose
<100 mg	20% to 30%
100 to 300 mg	10% to 20%
300 to 600 mg	8% to 12%
600 to 1,000 mg	5% to 10%
>1,000 mg	<5%

(Connor, 2024)

Opioid Agonist Therapies:
Buprenorphine / Naloxone

- Buprenorphine: Partial opioid agonist at mu- receptor, antagonist at kappa- receptor
- Naloxone: Opioid antagonist at mu-, delta-, and kappa-opioid receptors, precipitates withdrawal with IV use and insufflation

Buprenorphine vs Methadone

- Lower all cause mortality and opioid related overdose relative to Methadone in first 4 weeks of treatment
- Lower treatment retention relative to Methadone (with low dose Buprenorphine/Naloxone 6mg or less compared to Methadone 40mg or less)
- No significant difference in retention rates at moderate or high dose treatment
- Lesser effect on QTc relative to Methadone

Buprenorphine carries a low risk of overdose (in absence of other CNS depressants) given ceiling effect on respiratory depression

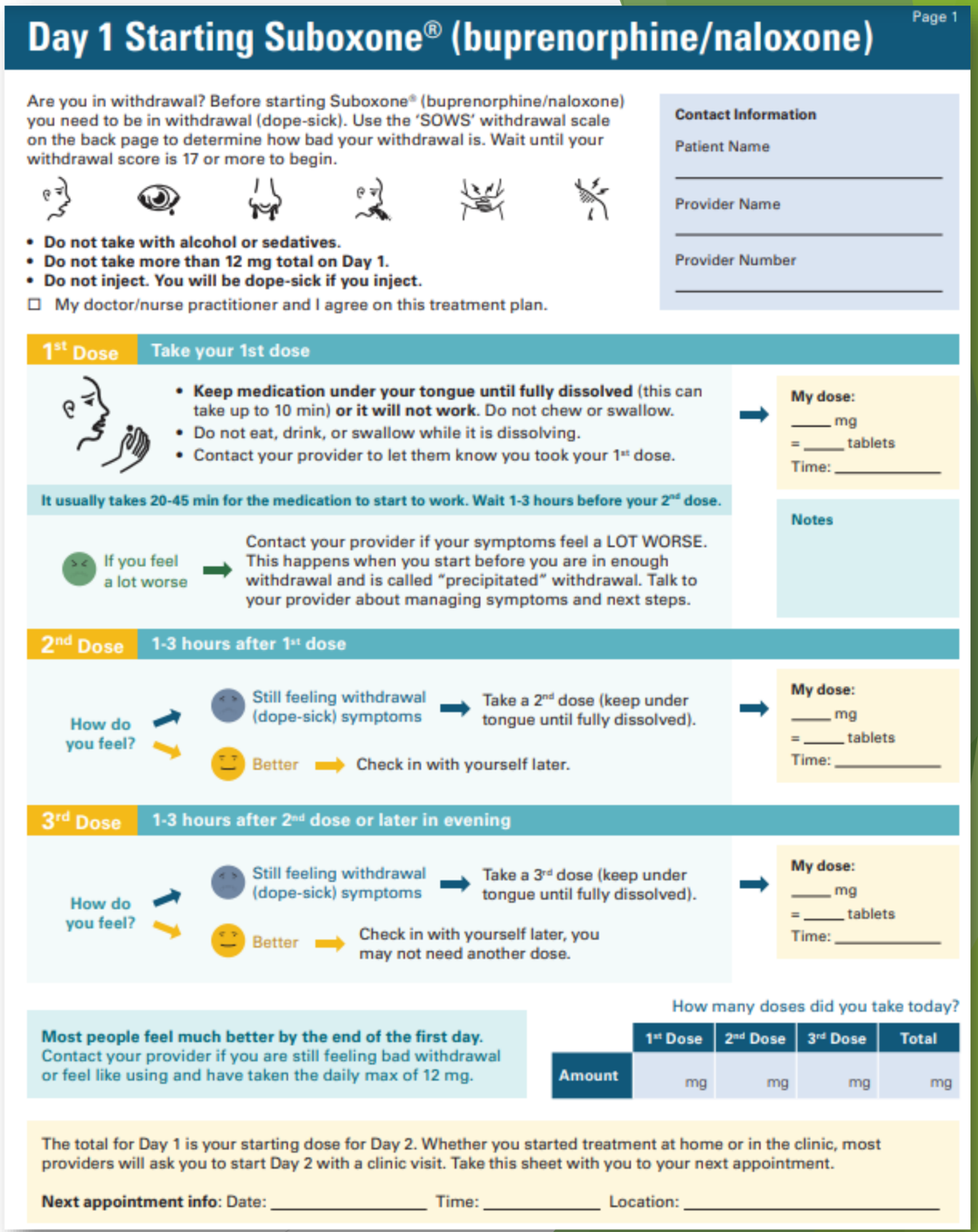
Opioid Agonist Therapies: Buprenorphine / Naloxone

- No renal dosing / adjustment required
- Hepatic impairment: Dose reduction by 50%

- Tablet strengths (sublingual):
  - 2mg = 2mg buprenorphine / 0.5mg naloxone
  - 8mg = 8mg buprenorphine / 2mg naloxone
  - Tablets can be split to achieve target dose

Opioid Agonist Therapies: Buprenorphine / Naloxone Induction

- Traditional approach:
  - Induction after period of opioid abstinence
  - Initiate Buprenorphine/Naloxone when patient is experiencing withdrawal symptoms
  - Rational: Avoid precipitated withdrawal



Page 1

Day 1 Starting Suboxone® (buprenorphine/naloxone)

Are you in withdrawal? Before starting Suboxone® (buprenorphine/naloxone) you need to be in withdrawal (dope-sick). Use the 'SOWS' withdrawal scale on the back page to determine how bad your withdrawal is. Wait until your withdrawal score is 17 or more to begin.

- **Do not take with alcohol or sedatives.**
- **Do not take more than 12 mg total on Day 1.**
- **Do not inject. You will be dope-sick if you inject.**

☐ My doctor/nurse practitioner and I agree on this treatment plan.

Contact Information

Patient Name _____

Provider Name _____

Provider Number _____

1st Dose Take your 1st dose

- **Keep medication under your tongue until fully dissolved** (this can take up to 10 min) **or it will not work**. Do not chew or swallow.
- Do not eat, drink, or swallow while it is dissolving.
- Contact your provider to let them know you took your 1st dose.

My dose: ____ mg = ____ tablets Time: _____

It usually takes 20-45 min for the medication to start to work. Wait 1-3 hours before your 2nd dose.

If you feel a lot worse → Contact your provider if your symptoms feel a LOT WORSE. This happens when you start before you are in enough withdrawal and is called "precipitated" withdrawal. Talk to your provider about managing symptoms and next steps.

Notes

2nd Dose 1-3 hours after 1st dose

How do you feel?

- Still feeling withdrawal (dope-sick) symptoms → Take a 2nd dose (keep under tongue until fully dissolved).
- Better → Check in with yourself later.

My dose: ____ mg = ____ tablets Time: _____

3rd Dose 1-3 hours after 2nd dose or later in evening

How do you feel?

- Still feeling withdrawal (dope-sick) symptoms → Take a 3rd dose (keep under tongue until fully dissolved).
- Better → Check in with yourself later, you may not need another dose.

My dose: ____ mg = ____ tablets Time: _____

Most people feel much better by the end of the first day.
Contact your provider if you are still feeling bad withdrawal or feel like using and have taken the daily max of 12 mg.

How many doses did you take today?

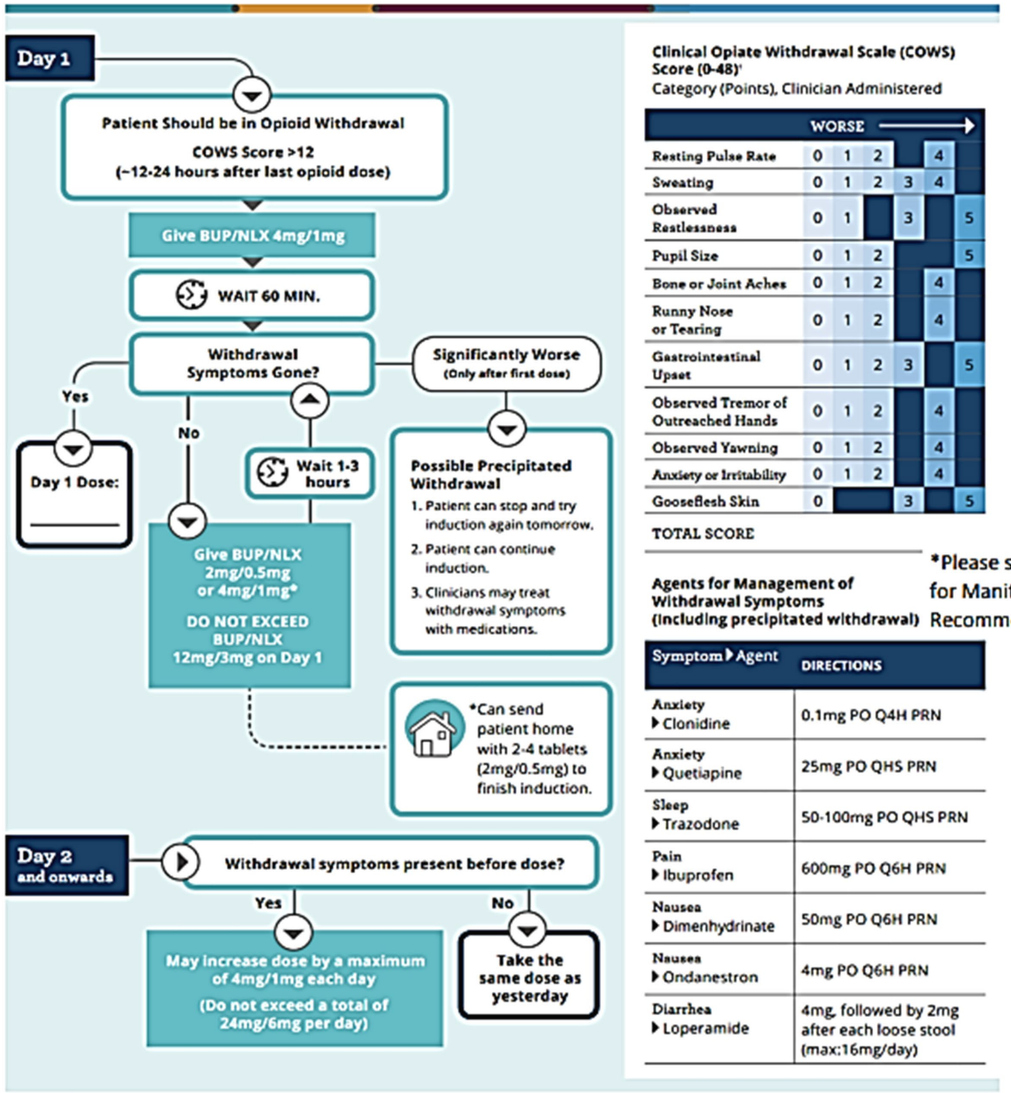
	1st Dose	2nd Dose	3rd Dose	Total
Amount	mg	mg	mg	mg

The total for Day 1 is your starting dose for Day 2. Whether you started treatment at home or in the clinic, most providers will ask you to start Day 2 with a clinic visit. Take this sheet with you to your next appointment.

Next appointment info: Date: _____ Time: _____ Location: _____

https://www2.gov.bc.ca/assets/gov/health/practitioner-pro/bc-guidelines/oud-induction-handout.pdf

Buprenorphine/Naloxone (BUP/NLX) Induction Flow Diagram



Clinical Opiate Withdrawal Scale (COWS) Score (0-48)[1]
Category (Points), Clinician Administered

	WORSE →					
Resting Pulse Rate	0	1	2		4	
Sweating	0	1	2	3	4	
Observed Restlessness	0	1		3		5
Pupil Size	0	1	2			5
Bone or Joint Aches	0	1	2		4	
Runny Nose or Tearing	0	1	2		4	
Gastrointestinal Upset	0	1	2	3		5
Observed Tremor of Outreached Hands	0	1	2		4	
Observed Yawning	0	1	2		4	
Anxiety or Irritability	0	1	2		4	
Gooseflesh Skin	0			3		5
TOTAL SCORE						

*Please see **Appendix O** for Manitoba Medication Recommendations

Agents for Management of Withdrawal Symptoms (including precipitated withdrawal)

Symptom ▸ Agent	DIRECTIONS
Anxiety ▸ Clonidine	0.1mg PO Q4H PRN
Anxiety ▸ Quetiapine	25mg PO QHS PRN
Sleep ▸ Trazodone	50-100mg PO QHS PRN
Pain ▸ Ibuprofen	600mg PO Q6H PRN
Nausea ▸ Dimenhydrinate	50mg PO Q6H PRN
Nausea ▸ Ondanestron	4mg PO Q6H PRN
Diarrhea ▸ Loperamide	4mg, followed by 2mg after each loose stool (max:16mg/day)

1 Full COWS Scoring Available at: https://www.drugabuse.gov/sites/default/files/files/ClinicalOpiateWithdrawalScale.pdf
For home induction, use patient administered Subjective Opiate Withdrawal Scale (SOWS) scoring available at: http://www.bccsu.ca/wp-content/uploads/2017/08/SOWS.pdf

Alberta College of Family Physicians

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Korownyk et al., 2019

Opioid Agonist Therapies:
Buprenorphine / Naloxone

Induction via microdosing / low dose induction

What is Microdosing?

The Bernese Method uses the principle of Microdosing to initiate a patient onto buprenorphine/naloxone (bup/nlx) maintenance therapy. The theoretical background of this method is based on the following principles:

1) Repetitive administration of very small buprenorphine doses with sufficient dosing intervals (e.g. 12 hours) should not precipitate opioid withdrawal
2) Because of the long receptor binding time, buprenorphine will accumulate at the opioid receptor
3) Over time, an increasing amount of a full μ-agonist will be replaced by buprenorphine at the opioid receptor

CMHA, 2019

Opioid Agonist Therapies:
Buprenorphine / Naloxone

Table 7. Sample 7-day Low-dose Induction Protocol

Day	Buprenorphine/naloxone Dose	Other opioids
1	0.5mg/0.125mg two times	Continue full agonist use
2	0.5mg/0.125mg three times	Continue full agonist use
3	1mg/0.25mg two times	Continue full agonist use
4	2mg/0.5mg two times	Continue full agonist use
5	2mg/0.5mg three times	Continue full agonist use
6	4mg/1mg three times	Continue full agonist use
7	12mg/3mg once	Stop other opioid use

BCCSU, 2023

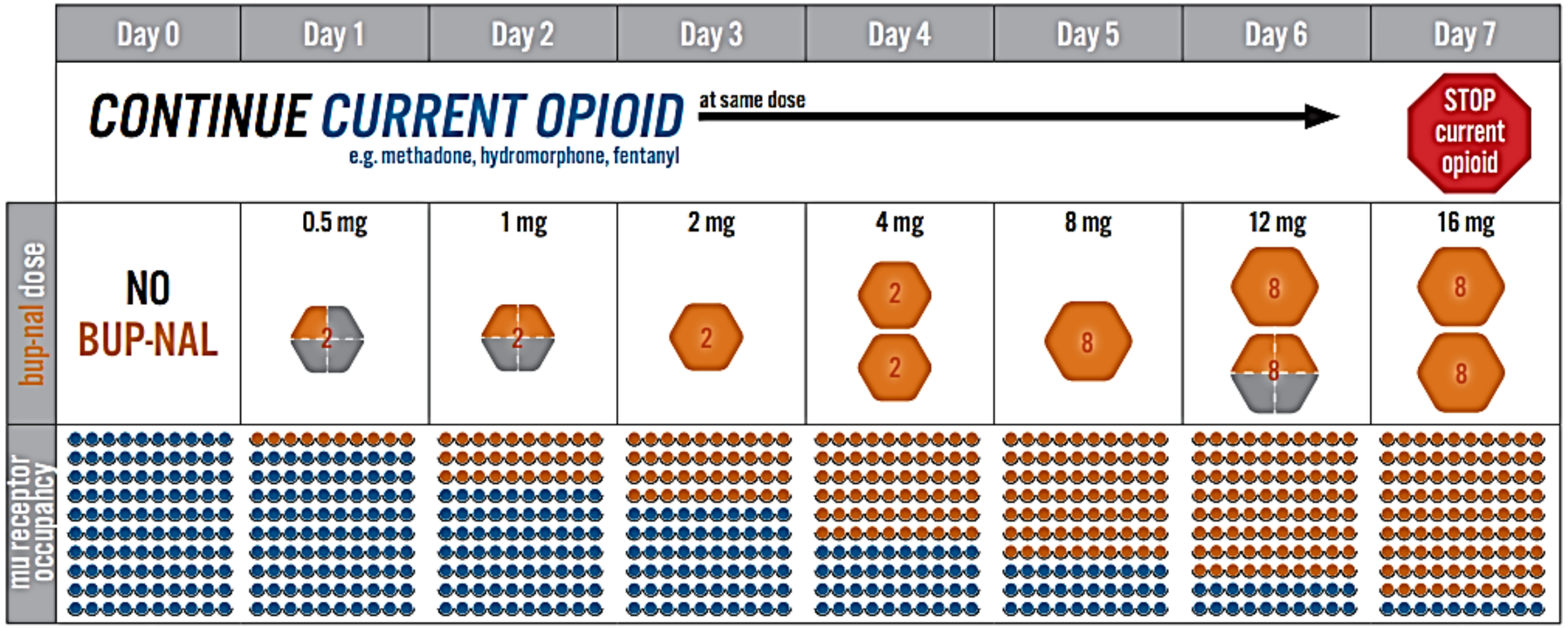
<u>Long-acting Opioid:</u> (Including Fentanyl, Fentanyl Patches, and Methadone)

Day	Buprenorphine	Opioid
1	0.5 mg daily	Maintain dose
2	1.0 mg daily	Maintain dose
3	1.5 mg daily	Maintain dose
4	2.0 mg daily	Maintain dose
5	2.5 mg daily	Maintain dose
6	3.0 mg daily	Maintain dose
7	4.0 mg daily	Maintain dose
If long- AND short-acting opioids, stop short-acting opioids here and maintain long-acting opioid dose. You may also choose to begin a taper of long-acting opioids at this point, though we have not found it necessary		
8	5.0 mg daily	Maintain dose
9	6.0 mg daily	Maintain dose
10	7.0 mg daily	Maintain dose
11	8.0 mg daily	Maintain dose
12	10.0 mg daily	Maintain dose
13	12.0 mg daily	Maintain dose
14	12.0 mg daily	Stop all remaining opioid therapy
Follow-up appointment at Day 7 to monitor progress and outline taper of long-acting opioid if you choose. See the patient on Day 14, after 12mg of Bup/Nlx, and give another 2mg every 1h until comfortable, to a max of 16mg that day.		

Patel, 2019

Micro-dosing Initiation of Buprenorphine-Naloxone (SUBOXONE)

Micro-dosing (a.k.a. Bernese Method) is the process of slowly and gradually introducing buprenorphine-naloxone (bup-nal) into the body when someone is currently using another opioid (e.g. methadone, hydromorphone, fentanyl). This is done to prevent precipitated withdrawal, which is the sudden onset of withdrawal symptoms that occurs when the first dose of bup-nal is taken when other opioids are still in the body.



These ◡ are 100 mu opioid receptors entirely occupied by the ● current opioid (e.g methadone). Bup-nal hasn't been started yet.

● Bup-nal is introduced in small amounts, slowly displacing the current opioid from the receptors. This helps prevent precipitated withdrawal.

As the dose of bup-nal increases, it occupies more and more opioid receptors.

The receptors are considered "fully-occupied" at a dose of 16 mg. At this dose the current opioid can be abruptly stopped with minimal to no withdrawal symptoms.

Micro-dosing initiation is considered off-label. Regimens can vary in length (usually 3-14 days) and bup-nal is usually given once or twice daily.

Rx FILES

Support for this infographic was provided by: Saskatchewan Health Authority
Stewardship and Clinical Appropriateness
Opioid Stewardship Program

Rx files

Opioid Agonist Therapies:
Extended release subcutaneous Buprenorphine

- Administered monthly via subcutaneous injection
- Patient must be clinically stable on 8mg-24mg of sublingual Buprenorphine-Naloxone for at least 7 days
- Associated with high treatment retention
- *Pharmacy -> health professional direct:
  - Forms solid mass upon administration
  - Serious harm or death with IV administration (tissue ischemia, thrombo-embolic event)

Month 1: 300mg

Month 2: 100mg or 300mg (if > 18mg Buprenorphine / Naloxone)

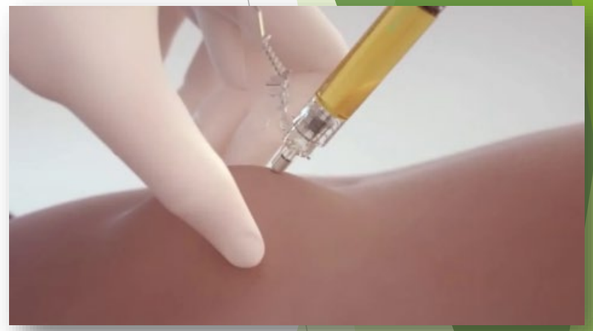
Month 3: 100mg or 300mg ongoing monthly

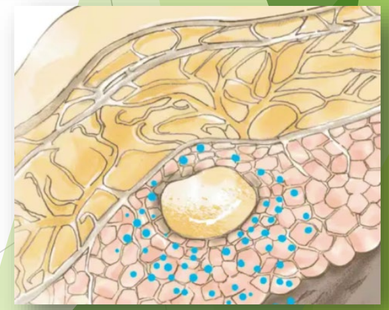
BCCSU, 2023; Indivior, 2023

Opioid Agonist Therapies:
Extended release subcutaneous Buprenorphine

- Stored at 2-8 degrees Celcius
- To be used within 7 days of removal from this temperature
- Medication released via diffusion from, and biodegration of, the depot
- Alternate sites monthly: RUQ / RLQ / LLQ / LUQ
- Apply ice to area prior to injection to avoid pain / burning with injection

- Discontinuation:
  - Plasma concentrations decrease slowly over 2-5 months
  - Patient may have detectable plasma levels of Buprenorphine for 12 months or longer





Indivior, 2023

Treatment Options: Considerations with Medical Comorbidities

- QTc prolongation
- Hepatic and renal function
- Frailty & history of falls
- GI side effects
- Comorbid respiratory conditions: OSA, COPD
- Comorbid chronic pain

Treatment Options: Considerations in Rural Communities

- Assess patient's access to transportation
- Locations of pharmacies and clinics
  - Does patient require daily observed dosing at pharmacy?
  - Does local pharmacy dispense OAT?
- Virtual care
  - Does patient have access to internet?

Language Considerations

Drug Abuse - > Illicit substance use

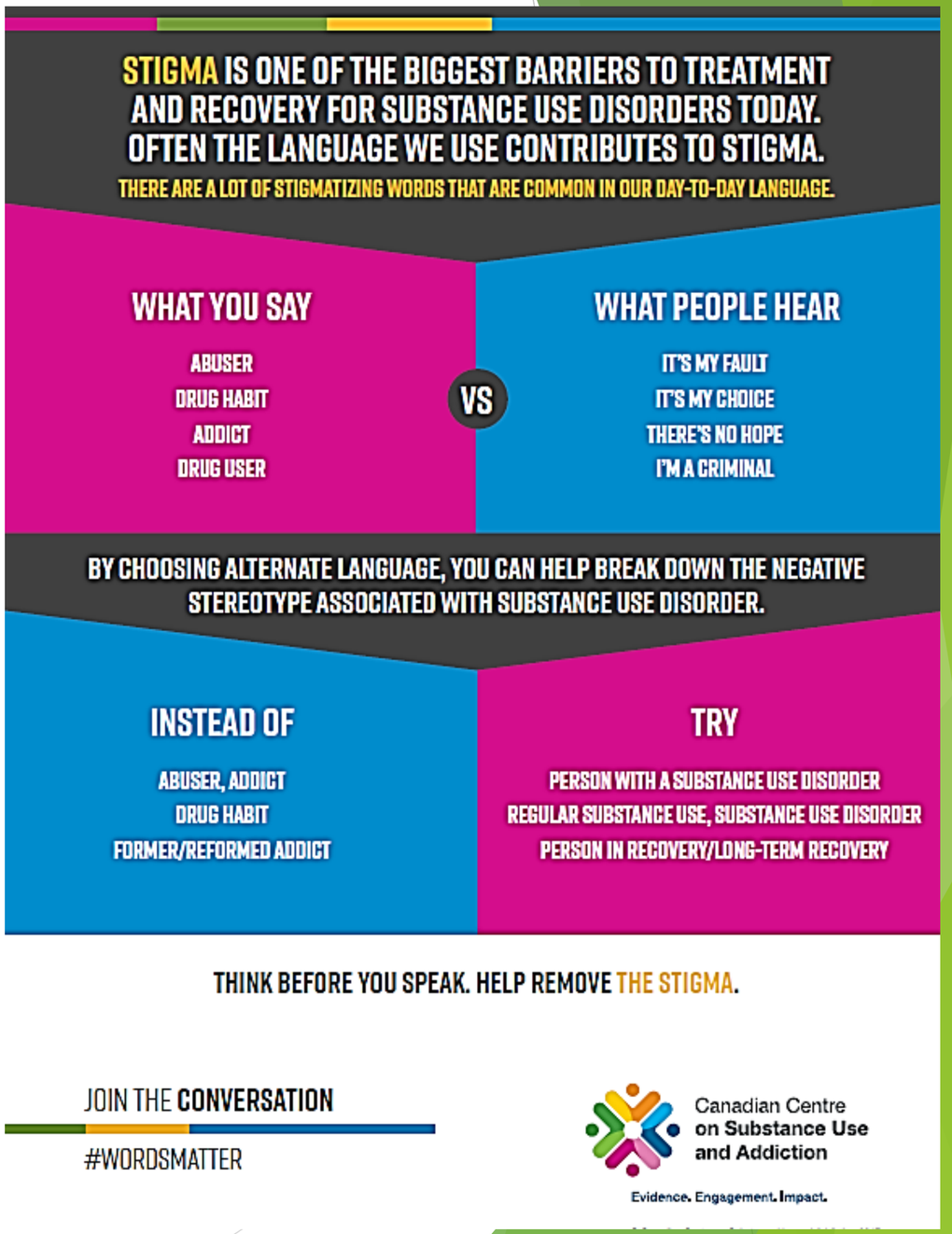
Dirty / Clean urines - > Positive / Negative Urine

“Addict” - > A Patient with a substance use disorder

Former Addict - > Person in recovery

Clean -> Abstinent / Not actively using X substance

Dirty -> Actively using X substance



Case Discussions: Jimmy and Becka

- Any additional thoughts?

Jimmy	Becka
72 yo male with chronic pain related to remove MVA	25 yo female seeking treatment for IV opioid use

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Questions?


Break Time
Be back in 15 min

Update on Interventions for Chronic Pain Conditions

Dr. Tim Fitzpatrick

IASP DEFINTION OF PAIN

- Pain is always a personal experience that is influenced to varying degrees by biological, psychological, and social factors.
- **Pain and nociception are different phenomena. Pain cannot be inferred solely from activity in sensory neurons**.
- Through their life experiences, individuals learn the concept of pain.
- **A person's report of an experience as pain should be respected**.
- Although pain usually serves an adaptive role, it may have adverse effects on function and social and psychological well-being.
- Verbal description is only one of several behaviors to express pain; inability to communicate does not negate the possibility that a human or a nonhuman animal experiences pain.
-

3 ACCEPTED MECHANISMS OF PERSISTENT PAIN

- NOCICEPTIVE
- NEUROPATHIC
- NOCIPLASTIC

SUICIDE RISK IN CHRONIC PAIN

IS THREE TIMES ABOVE OTHERS

PRIMARY MENTAL HEALTH DISORDERS AND PAIN

- DSM 5
- SOMATIC SYMPTOM DISORDER
- ILLNESS ANXIETY DISORDER
- FUNCTIONAL NEUROLOGICAL SYMPTOM DISORDER
- FACTITIOUS DISORDER
- OTHER/UNSPECIFIED

The Misery Industry

- Is there a real problem out there ?
- Why is the science so poor?
- How can you make reasonable decisions in this context?

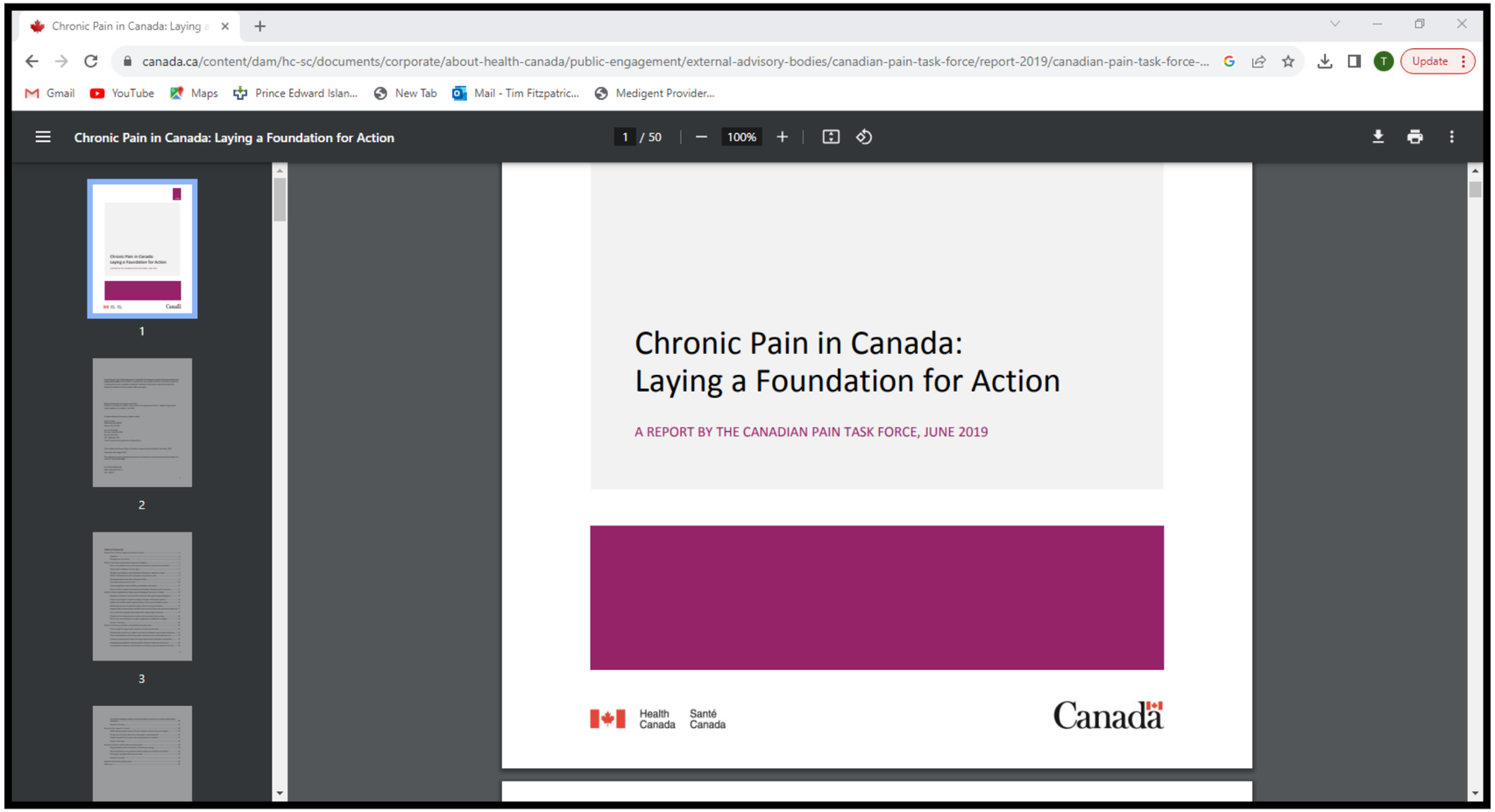
TIMELINE OF PAIN DISORDERS

- ACUTE LESS THAN 3 MONTHS
- CHRONIC OVER 3 MONTHS
- TRANSITIONAL….

TRANSITIONAL PAIN

- ACUTE EPISODE HEADING TO CHRONIC / ONGOING OPIATE USE
- STARTED AT U OF TORONTO

NATIONAL PICTURE;CANADIAN PAIN TASK FORCE



Goals of Canadian task force

- 1 Enable coordinated collaborative leadership across Canada
- 2 improve access to timely equitable and person centred pain care
- 3 improve awareness , education, and specialised training in pain
- 4 support pain research and strengthen related infrastructure
- 5 monitor population health and system quality
- 6 ensure equitable approaches for populations disproportionately affected by pain

CANADIAN PAIN MEDICINE SPECIALTY

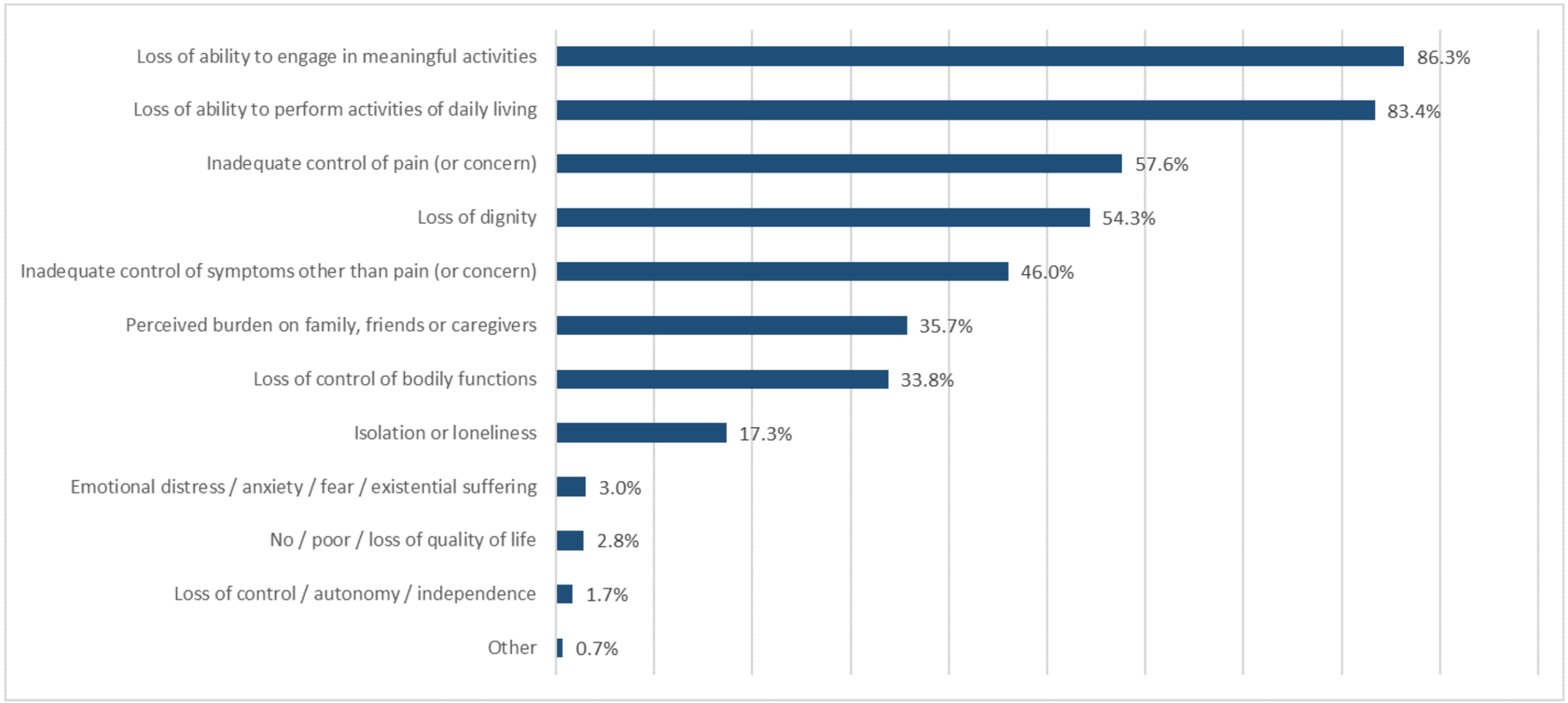
pain-medicine-otr-e.pdf

IDENTIFIED AT RISK GROUPS

- SENIORS esp in care facilities
- NATIVE PEOPLES
- WOMEN
- PEOPLE WHO USE DRUGS
- VETERANS
- PATIENTS WITH MENTAL HEALTH DISORDERS
- WORKING ADULTS

Children/interventions

MAID AND CHRONIC PAIN



PROVINCIAL PAIN MANAGEMENT UNIT

- POLYCLINIC AND DR MACKINNON/WHALEN
- CENTRAL INTAKE
- FULL INITIAL ASSESSMENT

KEYS TO INITIAL APPROACH

- ATTEMPT TO ACHIEVE A DIAGNOSIS OF AT LEAST TYPE OF PAIN
- ASSESS EMOTIONAL STATUS/MENTAL HEALTH/ADDICTION RISK
- SMART GOALS
- ATTEMPT PHYSICAL TX AND EXERCISE IF POSSIBLE
- LOW DOSE MUTI MODAL MEDICATIONS
- SELF MANAGEMENT REFERRAL AND CBT IF POSSIBLE

Sleep disorders

- Sleep apnea esp with opiates or depression
- Pain interference
- Often sleep quality is the first goal of the SMART programme
- I avoid benzos , use cbt/ thc/baclofen /tca

EMPOWERED RELIEF

- 2 HOUR VIRTUAL CBT SESSION FROM STANFORD
- AS EFFECTIVE AS FULL 8 WEEK COURSE
- IMPROVED FUNCTION /MEDICATION REDUCTION

Evidence from empowered relief

- Dr Beth Darnell Stanford
- Equivalent to 8 week CBT course
- Medication reduction / more successful surgery
- Used as standard in Cleveland Clinic pre op

EXERCISE PRESCRIPTION

- AQUA
- TAI CHI
- KATIE BECK

GET REAL RE EFFECTIVENESS OF MEDS

- GABA NNT 7 NNH 10 ish
- TCA NNT 4-5 nnh 14
- OPIATE NNT ? NNH ?
- CANNABINOIDS - MAY HELP SLEEP; C SPINE;PELVIS

OPIOIDS AND CHRONIC PAIN

- GENERALLY EVIDENCE SAYS THERE IS A SMALL ROLE FOR SOME PEOPLE
- TRIAL WITH CONTRACT/SCREENING/FUNCTIONAL GOALS
- DOSE ESCALATION NOT HELPFUL
- LONG ACTING COMPOUNDS ARE HIGHER RISK AND RARELY INDICATED

CANADIAN OPIOID GUIDELINES

2017 CANADIAN OPIOID PRESCRIBING GUIDELINE

KEY POINTS

Patients with chronic noncancer pain may be offered a trial of opioids only after they have been optimized on non-opioid therapy, including non-drug measures.

We suggest avoiding opioid therapy for patients with a history of substance use disorder (including alcohol) or current mental illness, and opioid therapy should be avoided in cases of active substance use disorder.

For patients beginning opioid therapy, we recommend restricting to under 90 mg morphine equivalents daily (MED) and suggest restricting the maximum prescribed dose to under 50 mg MED.

Patients already receiving high-dose opioid therapy (≥90 mg MED) should be encouraged to embark on a gradual dose taper, and multidisciplinary support offered where available to those who experience challenges.

GOOD PRACTICE STATEMENTS

Acquire informed consent prior to initiating opioid use for chronic noncancer pain. A discussion about potential benefits, adverse effects, and complications will facilitate shared-care decision making regarding whether to proceed with opioid therapy.

Clinicians should monitor chronic noncancer pain patients using opioid therapy for their response to treatment, and adjust treatment accordingly.

Clinicians with chronic noncancer pain patients prescribed opioids should address any potential contraindications and exchange relevant information with the patient's general practitioner (if they are not the general practitioner) and/or pharmacists.

RECOMMENDATION 1

When considering therapy for patients with chronic noncancer pain, we recommend optimization of nonopioid pharmacotherapy and nonpharmacologic therapy, rather than a trial of opioids (strong recommendation)

RECOMMENDATION 2

For patients with chronic noncancer pain, without current or past substance use disorder and without other active psychiatric disorders, who have persistent problematic pain despite optimized nonopioid therapy, we suggest adding a trial of opioids rather than continued therapy without opioids (weak recommendation)

Remark: By a trial of opioids, we mean initiation, titration and monitoring of response, with discontinuation of opioids if important improvement in pain or function is not achieved. The studies that identified substance use disorder as a risk factor for adverse outcomes characterized the conditions as alcohol abuse and dependence, and narcotic abuse and dependence, and sometimes referred to International Classification of Diseases, 9th revision (ICD-9) diagnoses. The mental illnesses identified in studies as risk factors for adverse outcomes were generally anxiety and depression, including ICD-9 definitions, as well as "psychiatric diagnosis," "mood disorder" and post-traumatic stress disorder.

RECOMMENDATION 3

For patients with chronic noncancer pain with an active substance use disorder, we recommend against the use of opioids (strong recommendation)

Remark: Clinicians should facilitate treatment of the underlying substance use disorders, if not yet addressed. The studies that identified substance use disorder as a risk factor for adverse outcomes characterized the conditions as alcohol abuse and dependence, narcotic abuse and dependence, and sometimes referred to ICD-9 diagnoses.

RECOMMENDATION 4

For patients with chronic noncancer pain with an active psychiatric disorder whose nonopioid therapy has been optimized, and who have persistent problematic pain, we suggest stabilizing the psychiatric disorder before a trial of opioids is considered (weak recommendation)

RECOMMENDATION 5

For patients with chronic noncancer pain with a history of substance use disorder, whose nonopioid therapy has been optimized, and who have persistent problematic pain, we suggest continuing nonopioid therapy rather than a trial of opioids (weak recommendation)

Remark: The studies that identified a history of substance use disorder as a risk factor for adverse outcomes characterized the conditions as alcohol abuse and dependence, and narcotic abuse and dependence, and sometimes referred to ICD-9 diagnoses.

RECOMMENDATION 6

For patients with chronic noncancer pain who are beginning opioid therapy, we recommend restricting the prescribed dose to less than 90 mg morphine equivalents daily, rather than having no upper limit or a higher limit on dosing (strong recommendation)

Remark: Some patients may gain important benefit at a dose of more than 90 mg morphine equivalents daily. Referral to a colleague for a second opinion regarding the possibility of increasing the dose to more than 90 mg morphine equivalents daily may therefore be warranted in some individuals.

RECOMMENDATION 7

For patients with chronic noncancer pain who are beginning opioid therapy, we suggest restricting the prescribed dose to less than 50 mg morphine equivalents daily (weak recommendation)

Remark: The weak recommendation to restrict the prescribed dose to less than 50 mg morphine equivalents daily acknowledges that there are likely to be some patients who would be ready to accept the increased risks associated with a dose higher than 50 mg in order to potentially achieve improved pain control.

RECOMMENDATION 8

For patients with chronic noncancer pain who are currently using opioids, and have persistent problematic pain and/or problematic adverse effects, we suggest rotation to other opioids rather than keeping the opioid the same (weak recommendation)

Remark: Rotation in such patients may be done in parallel with, and as a way of facilitating, dose reduction.

RECOMMENDATION 9

For patients with chronic noncancer pain who are currently using 90 mg morphine equivalents of opioids per day or more, we suggest tapering opioids to the lowest effective dose, potentially including discontinuation, rather than making no change in opioid therapy (weak recommendation)

Remark: Some patients may have a substantial increase in pain or decrease in function that persists for more than one month after a small dose reduction; tapering may be paused or potentially abandoned in such patients.

RECOMMENDATION 10

For patients with chronic noncancer pain who are using opioids and experiencing serious challenges in tapering, we recommend a formal multidisciplinary program (strong recommendation)

Remark: In recognition of the cost of formal multidisciplinary opioid reduction programs and their current limited availability/capacity, an alternative is a coordinated multidisciplinary collaboration that includes several health professionals whom physicians can access according to their availability (possibilities include, but are not limited to, a primary care physician, a nurse, a pharmacist, a physical therapist, a chiropractor, a kinesiologist, an occupational therapist, an addiction medicine specialist, a psychiatrist and a psychologist).

COLLABORATING FOR BETTER CARE

National medical organizations have come together to form the Pan-Canadian Collaborative for Improved Opioid Prescribing. This partnership seeks to connect prescribers with educational resources to help address the harms associated with prescription opioids –including addiction, overdose, and death. The Collaborative is also committed to helping ensure Canadians have timely and appropriate access to optimal treatment for acute and chronic pain.

The Collaborative is pleased to disseminate 2017 Canadian Guideline for Opioid Therapy and Chronic Noncancer Pain, coordinated by the Michael G. DeGroote National Pain Centre at McMaster University. The guideline is integral in assisting the practice decisions regarding use of opioids for chronic noncancer pain management based on the latest evidence and expertise.

Health care professionals will have access to an app available at https://www.magicapp.org/public/guideline/8nybOE that gives easy access to the evidence underpinning the recommendations. There will be a self-directed CME on the guideline and other tools that will be made available online.

These new prescribing guidelines are intended to increase patient safety; however, there may be unintended harms while reducing opioid prescribing levels. Becoming familiar with the risks of abrupt cessation of opioids, strategies for overdose prevention, and resources to guide tapering and assessment of opioid use disorder may mitigate risks associated with reducing opioid prescribing. The work seeks to support physicians and help them get the information they need, how they need it.

The Collaborative organizations will communicate with their members about new resources to support optimal patient care in this important area as they become available.

Canadian Centre on Substance Use and Addiction

Association Médicale Canadienne | Canadian Medical Association | 1867–2017 150

The College of Family Physicians of Canada | Le Collège des médecins de famille du Canada

MDcme.ca Credible. Accessible. Flexible. Crédible, accessible et souple.

McMaster University

Michael G. DeGroote National Pain Centre

Royal College of Physicians and Surgeons of Canada | Collège royal des médecins et chirurgiens du Canada

Cannabis for chronic pain

- My experience is that it is rarely helpful
- Cost and quality issues
- Low dose cbd with thc can aid sleep

MEASURING PAIN

SELF REPORT

VALIDATED SCORES

DIAGNOSTIC SCORES

MCGILL PQ

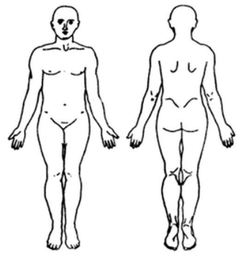
McGill Pain Questionnaire

Patient's Name _____ Date _____ Time _____ am/pm

PRI: S _____ (1-10) A _____ (11-15) E _____ (16) M _____ (17-20) PRI(T) _____ (1-20) PPI _____

1 FLICKERING QUIVERING PULSING THROBBING BEATING POUNDING	11 TIRING EXHAUSTING	
2 JUMPING FLASHING SHOOTING	12 SICKENING SUFFOCATING	
3 PRICKING BORING DRILLING STABBING LANCINATING	13 FEARFUL FRIGHTFUL TERRIFYING	
4 SHARP CUTTING LACERATING	14 PUNISHING GRUELLING CRUEL VICIOUS KILLING	
5 PINCHING PRESSING GNAWING CRAMPING CRUSHING	15 WRETCHED BLINDING	
6 TUGGING PULLING WRENCHING	16 ANNOYING TROUBLESOME MISERABLE INTENSE UNBEARABLE	
7 HOT BURNING SCALDING SEARING	17 SPREADING RADIATING PENETRATING PIERCING	
8 TINGLING ITCHY SMARTING STINGING	18 TIGHT NUMB DRAWING SQUEEZING TEARING	
9 DULL SORE HURTING ACHING HEAVY	19 COOL COLD FREEZING	
10 TENDER TAUT RASPING SPLITTING	20 NAGGING NAUSEATING AGONIZING DREADFUL TORTURING	
	PPI 0 NO PAIN 1 MILD 2 DISCOMFORTING 3 DISTRESSING 4 HORRIBLE 5 EXCRUCIATING	

BRIEF MOMENTARY TRANSIENT	RHYTHMIC PERIODIC INTERMITTENT	CONTINUOUS STEADY CONSTANT



E = EXTERNAL
I = INTERNAL

COMMENTS:

LANSS

APPENDIX

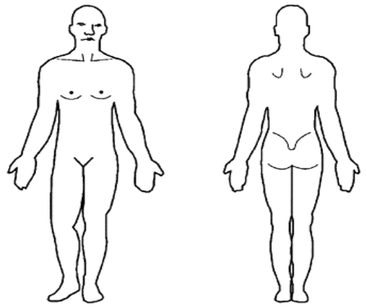
THE S-LANSS PAIN SCORE

Leeds Assessment of Neuropathic Symptoms and Signs (self-complete)

NAME_____ **DATE**_____

- This questionnaire can tell us about the type of pain that you may be experiencing. This can help in deciding how best to treat it.

- Please draw on the diagram below where you feel your pain. If you have pain in more than one area, **only shade in the one main area where your worst pain is.**



- On the scale below, please indicate how bad your pain (that you have shown on the above diagram) has been in the last week where:
'0' means no pain and '10' means pain as severe as it could be.

NONE 0 1 2 3 4 5 6 7 8 9 10 **SEVERE PAIN**

- On the other side of the page are 7 questions about your pain (the one in the diagram).

- Think about how your pain that you showed in the diagram has felt **over the last week.** Please circle the descriptions that best match your pain. These descriptions may, or may not, match your pain no matter how severe it feels.

- Only circle the responses that describe your pain. **Please turn over**.

BRIEF PAIN INVENTORY

Date: ____ /____ /____ Time: _____

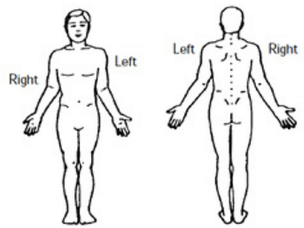
Name: _____ _____ _____

Last First Middle intial

1) Throughout our lives, most of us have had pain from time to time (such as minor headaches, sprains, and toothaches). Have you had pain other than these everyday kinds of pain today?

1. Yes 2. No

2) On the diagram, shade in the areas where you feel pain. Put an X on the area that hurts the most.



3) Please rate your pain by circling the one number that best describes your pain at its **worst** in the past 24 hours.

0 1 2 3 4 5 6 7 8 9 10
No pain — Pain as bad as you can imagine

4) Please rate your pain by circling the one number that best describes your pain at its **least** in the past 24 hours.

0 1 2 3 4 5 6 7 8 9 10
No pain — Pain as bad as you can imagine

5) Please rate your pain by circling the one number that best describes your pain on **average**.

0 1 2 3 4 5 6 7 8 9 10
No pain — Pain as bad as you can imagine

6) Please rate your pain by circling the one number that tells how much pain you have **right now**.

0 1 2 3 4 5 6 7 8 9 10
No pain — Pain as bad as you can imagine

7) What treatments or medications are you receiving for your pain?

_____

_____

8) In the past 24 hours, how much **relief** have pain treatments or medications provided? Please circle the one percentage that most shows how much relief you have received.

0% 10 20 30 40 50 60 70 80 90 100%
No relief — Complete relief

9) Circle the one number that describes how, during the past 24 hours, pain has **interfered** with your:

A. General activity

0 1 2 3 4 5 6 7 8 9 10
Does not interfere — Completely interferes

B. Mood

0 1 2 3 4 5 6 7 8 9 10
Does not interfere — Completely interferes

C. Walking ability

0 1 2 3 4 5 6 7 8 9 10
Does not interfere — Completely interferes

D. Normal work (includes both work outside the home and housework)

0 1 2 3 4 5 6 7 8 9 10
Does not interfere — Completely interferes

E. Relations with other people

0 1 2 3 4 5 6 7 8 9 10
Does not interfere — Completely interferes

F. Sleep

0 1 2 3 4 5 6 7 8 9 10
Does not interfere — Completely interferes

G. Enjoyment of life

0 1 2 3 4 5 6 7 8 9 10
Does not interfere — Completely interferes

PAIN CATASTROPHIZATION SCORE

Item	Components 1	2	3	*M*	*SD*	Item total *r*
Rumination						
11. I keep thinking about how badly I want the pain to stop.	.87	.01	.00	2.0	1.2	.70
8. I anxiously want the pain to go away.	.84	.04	.13	2.7	1.1	.57
9. I can't seem to keep it out of my mind.	.80	.04	−.11	1.7	1.6	.70
10. I keep thinking about how much it hurts.	.79	.00	−.12	1.9	1.1	.71
Magnification						
13. I wonder whether something serious may happen.	−.12	.76	−.14	1.3	1.0	.37
6. I become afraid that the pain may get worse.	.15	.64	−.04	1.4	1.0	.47
7. I think of other painful experiences.	−.01	.67	.12	0.6	0.9	.22
Helplessness						
2. I feel I can't go on.	−.11	−.07	−.86	0.7	0.8	.46
3. It's terrible and I think it's never going to get any better.	−.01	.11	−.68	0.9	0.9	.51
1. I worry all the time about whether the pain will end.	.11	.04	−.58	1.4	0.9	.51
4. It's awful and I feel that it overwhelms me.	.31	.05	−.53	1.1	0.9	.65
5. I feel I can't stand it any more.	.38	−.01	−.48	1.3	1.0	.64
12. There is nothing I can do to reduce the intensity of the pain.	.22	.30	−.31	1.3	0.9	.53

Note. $N = 425$; components: 1 = rumination, 2 = magnification, and 3 = helplessness. Items 1–5 were drawn from the Coping Strategies Questionnaire (described in Rosenstiel & Keefe, 1983); items 6, 7, and 13 were developed from descriptions of catastrophizing provided by Chaves and Brown (1978, 1987); and the remaining items were developed from descriptions of catastrophizing provided by Spanos et al. (1979). Items 1–5 are from the *Coping Strategies Questionnaire* by A. K. Rosenstiel and F. J. Keefe, 1983. Copyright 1983 by A. K. Rosenstiel and F. J. Keefe. Reprinted with permission. Copies of the Pain Catastrophizing Scale may be obtained from Michael J. L. Sullivan.

SPECIFIC SCORES FOR DIAGNOSES

- OSWESTRY DI FOR LOW BACK
- WOMAC FOR LARGE JOINT
- QUEBEC C SPINE
- ACR FIBROMYALGIA

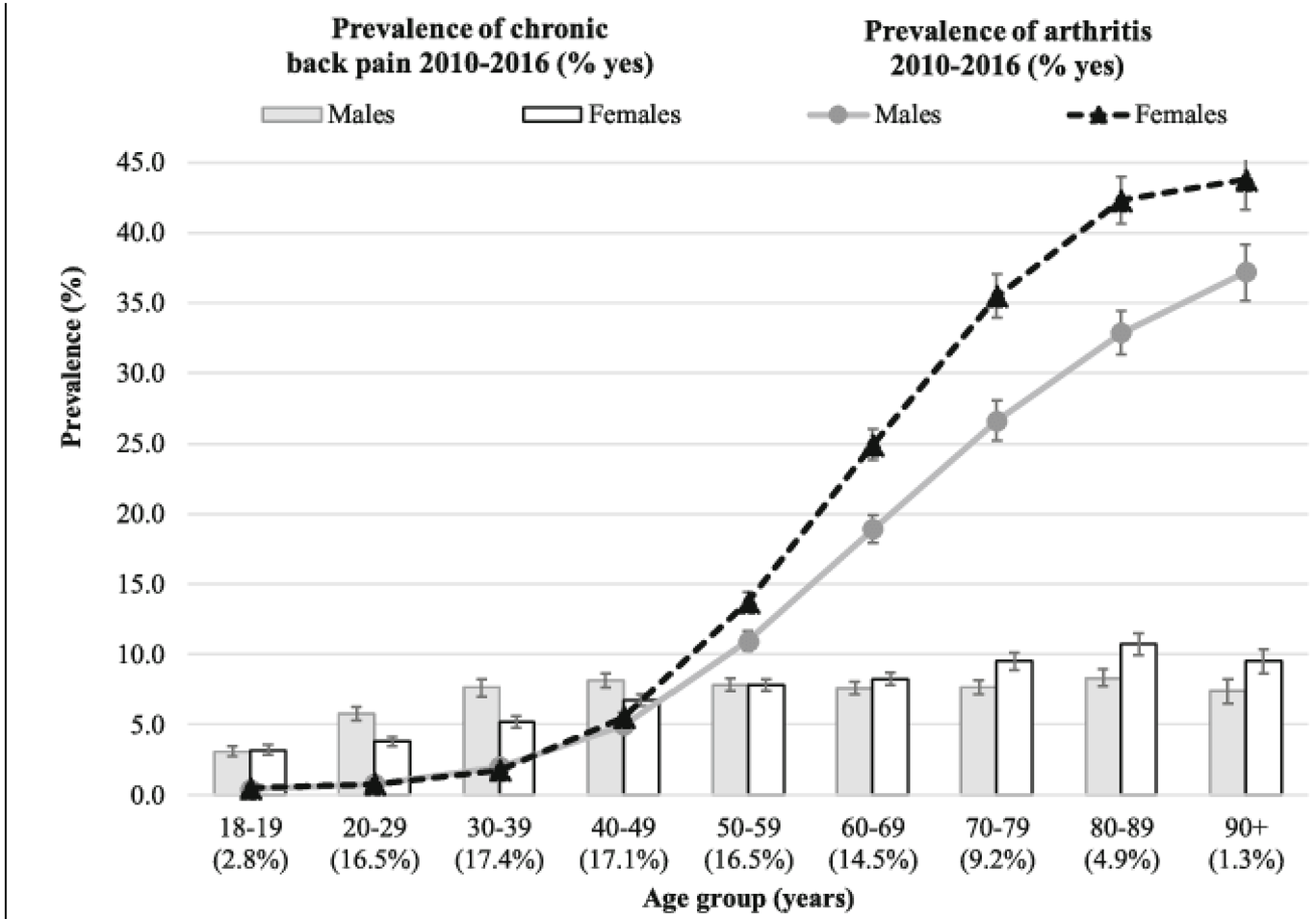
WHEN TO REFER

- SUSPECTED CRPS;DISC HERNIATION; COMPLEX MH ADDICTIONS
- SENIORS NOT RESPONDING TO INITIAL TX
- WORK DISABLED OR OTHER AT RISK POPULATION
- SEVERE NEUROPATHIC PAIN

ADULT BACK PAIN

- AXIAL CONSIDER FACET/DISC/SACROILIAC
- INFLAMMATORY VS DEGENERATIVE
- AGE AFFECTS LIKELIHOOD RATIO

AGE AND BACK PAIN



ETIOLOGY OF BACK PAIN WITH AGE

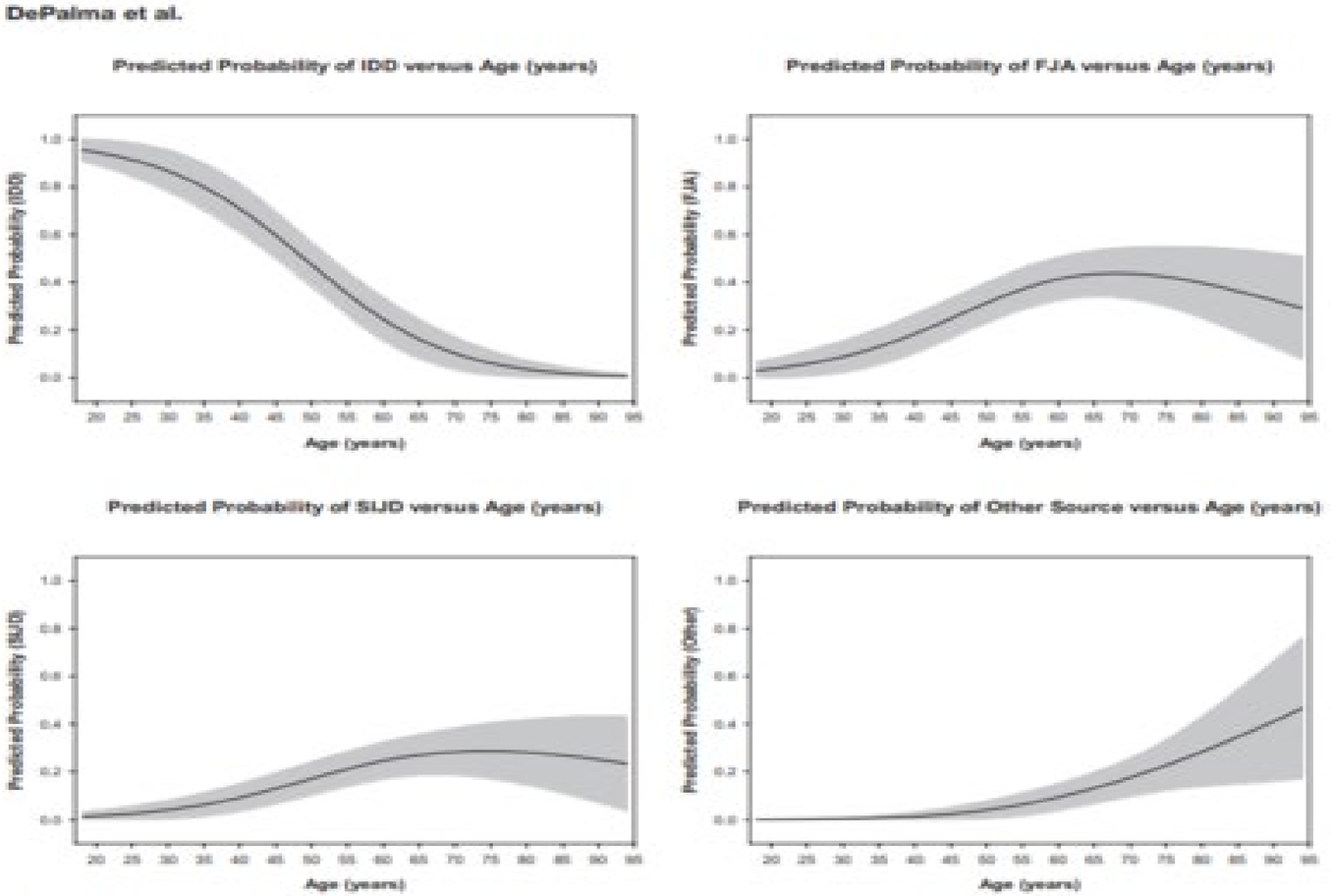
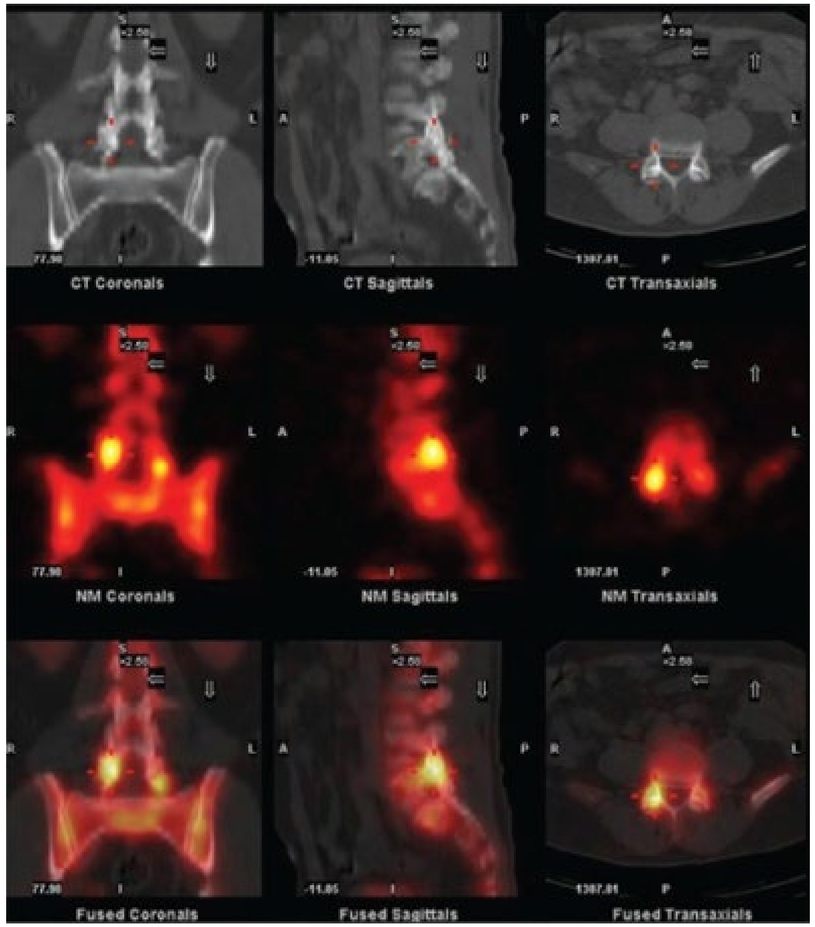


Figure 4 Predicted probabilities and 95% confidence intervals for internal disc disruption (IDD), facet joint pain (FJP), sacroiliac joint pain (SIJP), and other sources of low back pain (LBP) as a function of age.

IMAGING FOR BACK PAIN

- CT GOOD FOR AXIAL ISSUES/ASSESS STENOSIS
- MRI FOR RADICULAR PAIN /SURGICAL REFERRAL
- CT SPECT CAN BE HELPFUL FOR AXIAL/CAVEATS(SPECIFIC ONLY SO HIGH FASLE NEGATIVE)
- PLAIN FILM FOR ? FRACTURE
- SI JOINTS BEST SEEN WITH MRI
- ADD GAD FOR POST OP PATIENTS

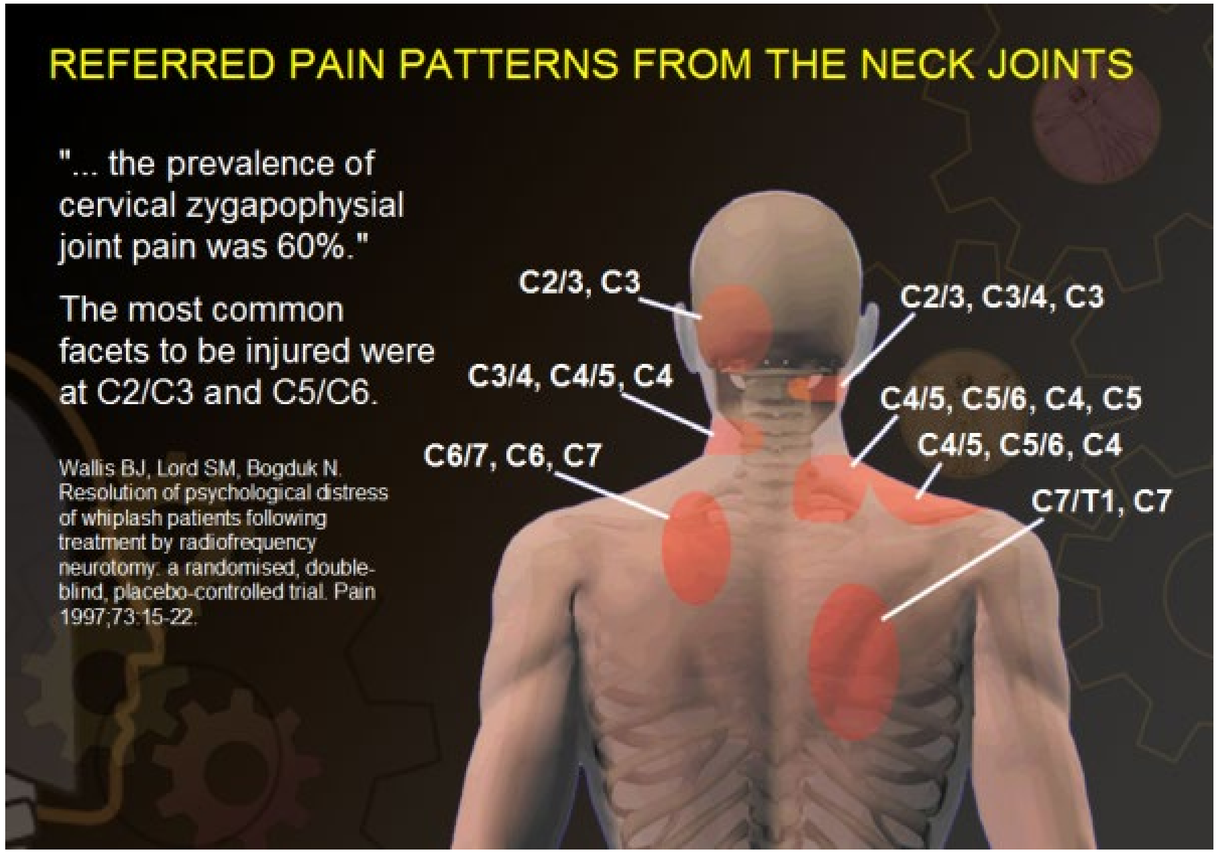
CT SPECT


CT Coronals
CT Sagittals
CT Transaxials
NM Coronals
NM Sagittals
NM Transaxials
Fused Coronals
Fused Sagittals
Fused Transaxials

NECK PAIN

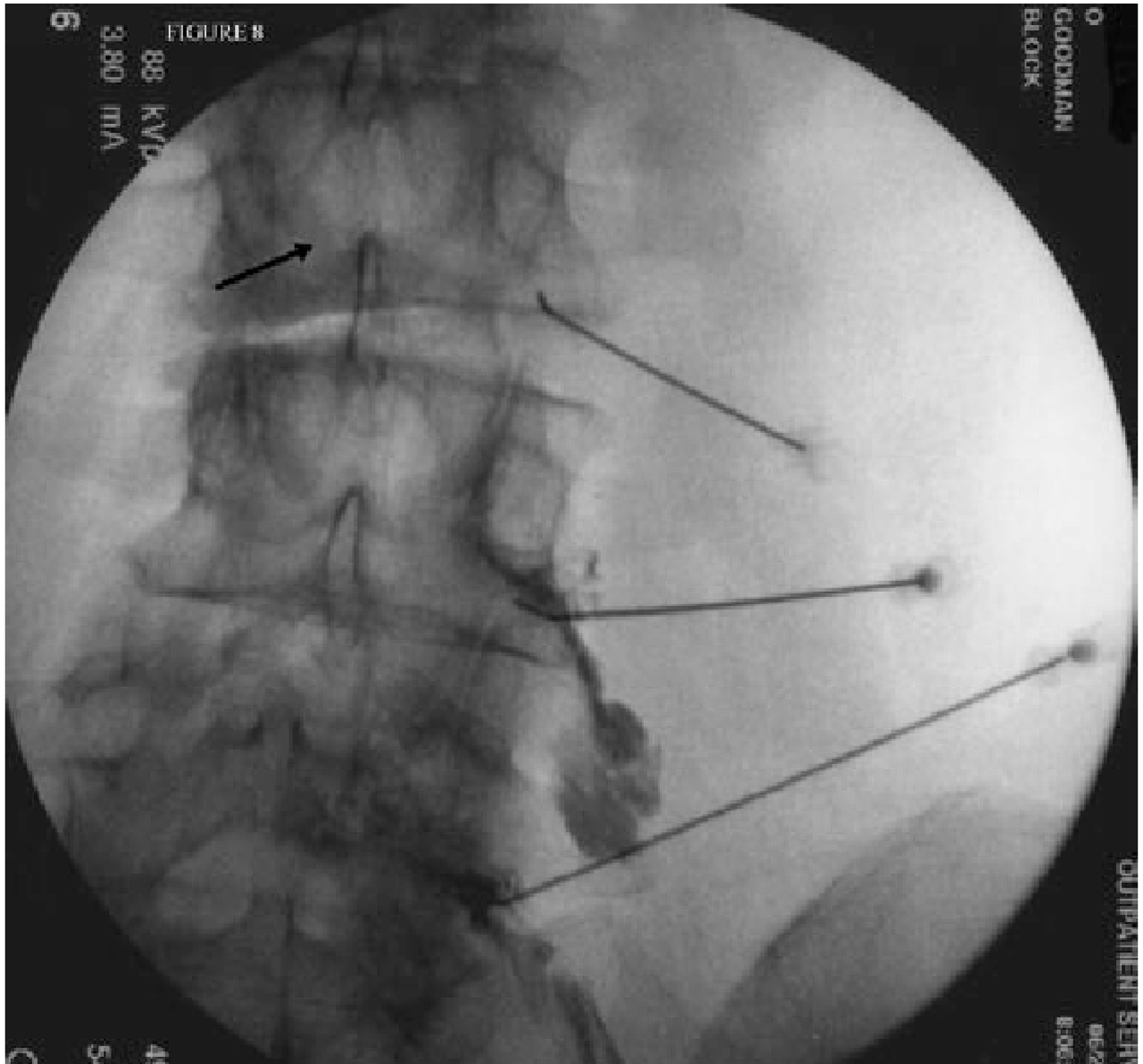
- AXIAL NECK PAIN IS ALMOST ALWAYS FACET
- MRI IS REQUIRED TO ASSESS FOR MYELOPATHY
- CERVICAL PROCEDURES HAVE SERIOUS RISKS BEYOND LUMBAR DUE TO THE VERTEBRAL ARTERY

CERVICAL FACET RADIATION

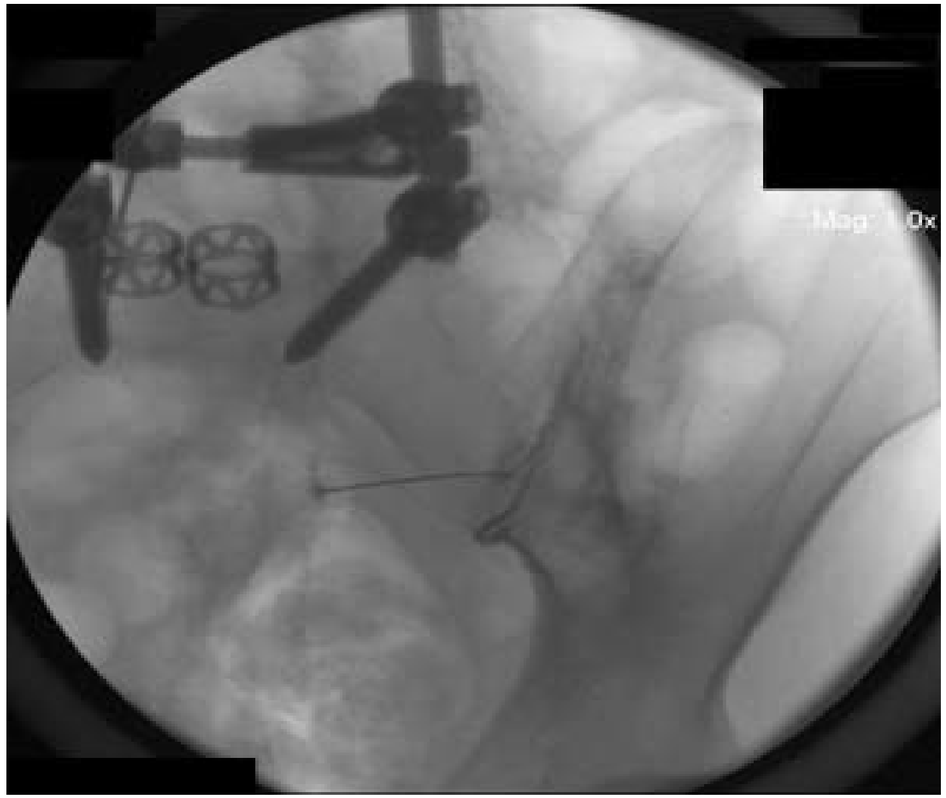


INTERVENTIONS WHICH ARE PROVEN HELPFUL

- FORAMINAL
- 2-3 MONTHS



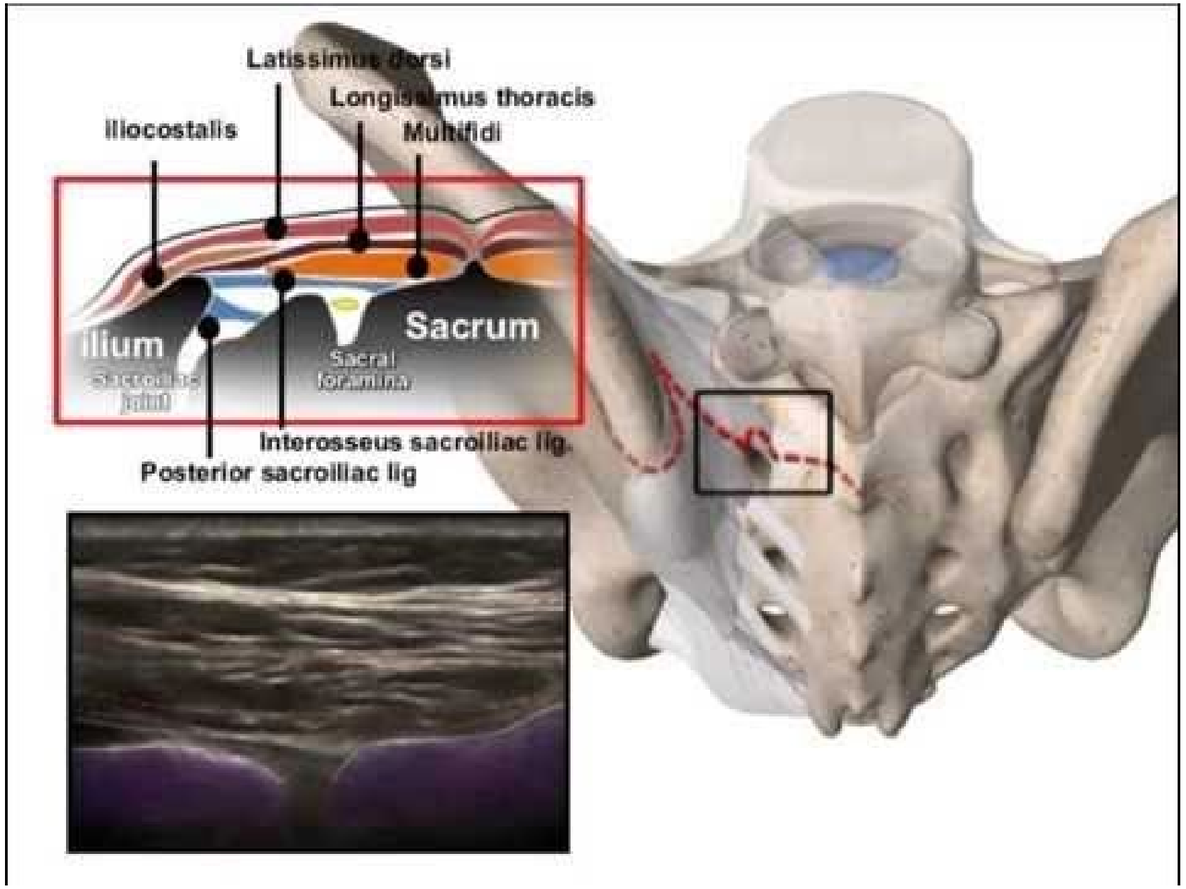
SACROILIAC INJECTIONS



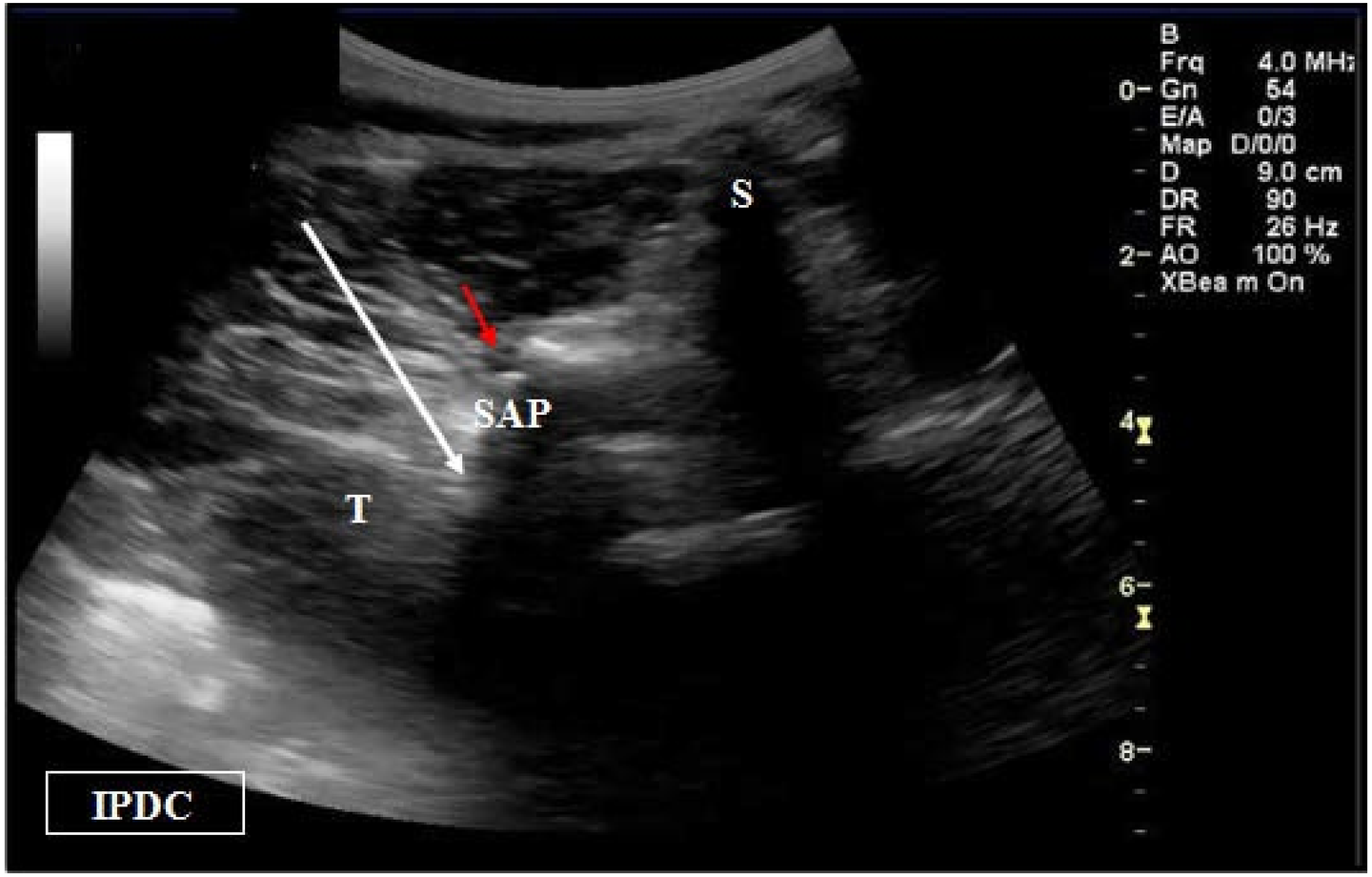
ULTRASOUND GUIDANCE

- EQUAL TO FLUORO IN ACCURACY FOR SACROILIAC AND FACETS
- CONVENIENT
- NO RADIATION

ULTRASOUND SCAROILIAC



ULTRASOUND FACET



RFA OF CERVICAL FACETS

SPINE SURGERY

- DISC/NERVE
- STENOSIS
- IS FUSION REQUIRED?
- WILL DALHOUSIE NEUROSURGERY REFUSE OUR PATIENTS?
- MONCTON- NEUROSX;COMSTOCK;LEBRETON
- ST JOHN MANSON

Some pain syndromes to be aware of

- Meralgia paresthetica
- Crps
- Anterior cutaneous nerve syndrome abdomen
- Intercostal neuralgia
- Foot entrapment neuropathies- tibial Morton’s
- Occipital neuralgia / c2-3 facets/whiplash
- Genitofemoral/ilio inguinal entrapment

CRPS MECHANISMS PROPOSED

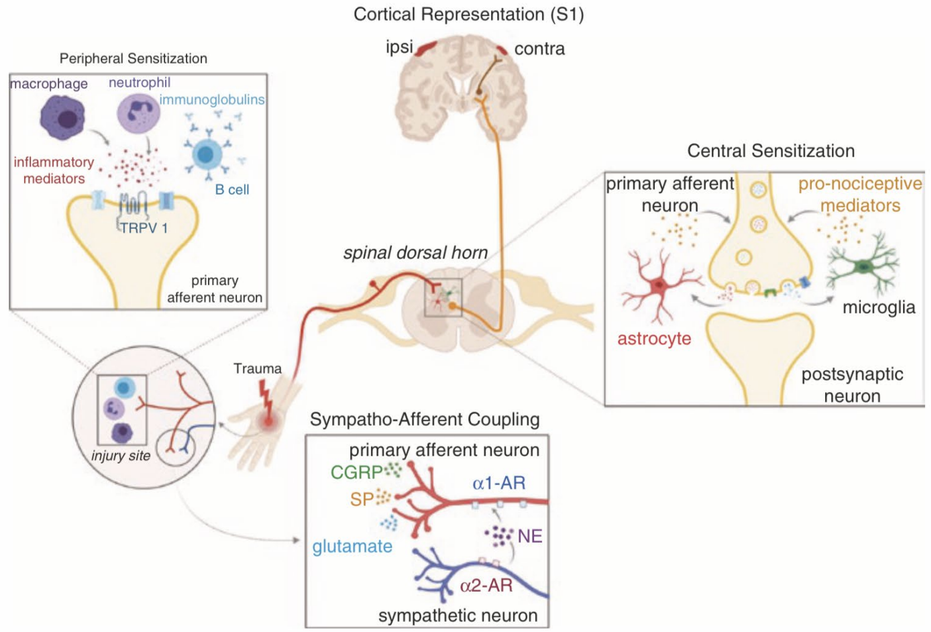


Fig. 1.1 Proposed pathophysiological mechanisms of complex regional pain syndrome (CRPS). Injury to a limb results in peripheral sensitization. Immune cells, such as macrophages and neutrophils, home to the site of injury and release inflammatory mediators that lead to the sensitization of pro-nociceptive channels (TRPV1 channel) on primary afferent neurons. B cells at the injury site release immunoglobulins that may target autoantigens and contribute to CRPS-related autoimmunity. Sympatho-afferent coupling may occur due to the expression of α1-AR on primary afferent neurons. Norepinephrine (NE) released by neighboring sympathetic neurons binds to the α1-AR, causing increased release of calcitonin gene-related peptide (CGRP), substance P (SP), and glutamate from primary afferent neurons. In the spinal cord dorsal horn, local neuroimmune cells such as astrocytes and microglia are activated by pro-nociceptive substances released from

Table 1.1 Budapest criteria for CRPS

Category	Symptom/sign
Sensory	Allodynia Hyperalgesia
Sudomotor	Asymmetric edema Sweating changes Sweating asymmetry
Vasomotor	Temperature asymmetry (>1 °C) Skin color changes Skin color asymmetry
Motor	Decreased range of motion Motor dysfunction (weakness, tremors, dystonia) Trophic changes (hair, nails, skin)
Continuing pain, disproportionate to the inciting event Must have 1 symptom in 3 of 4 categories Must have 1 sign in at least 2 categories at time of evaluation No other diagnosis better explains symptoms and signs	

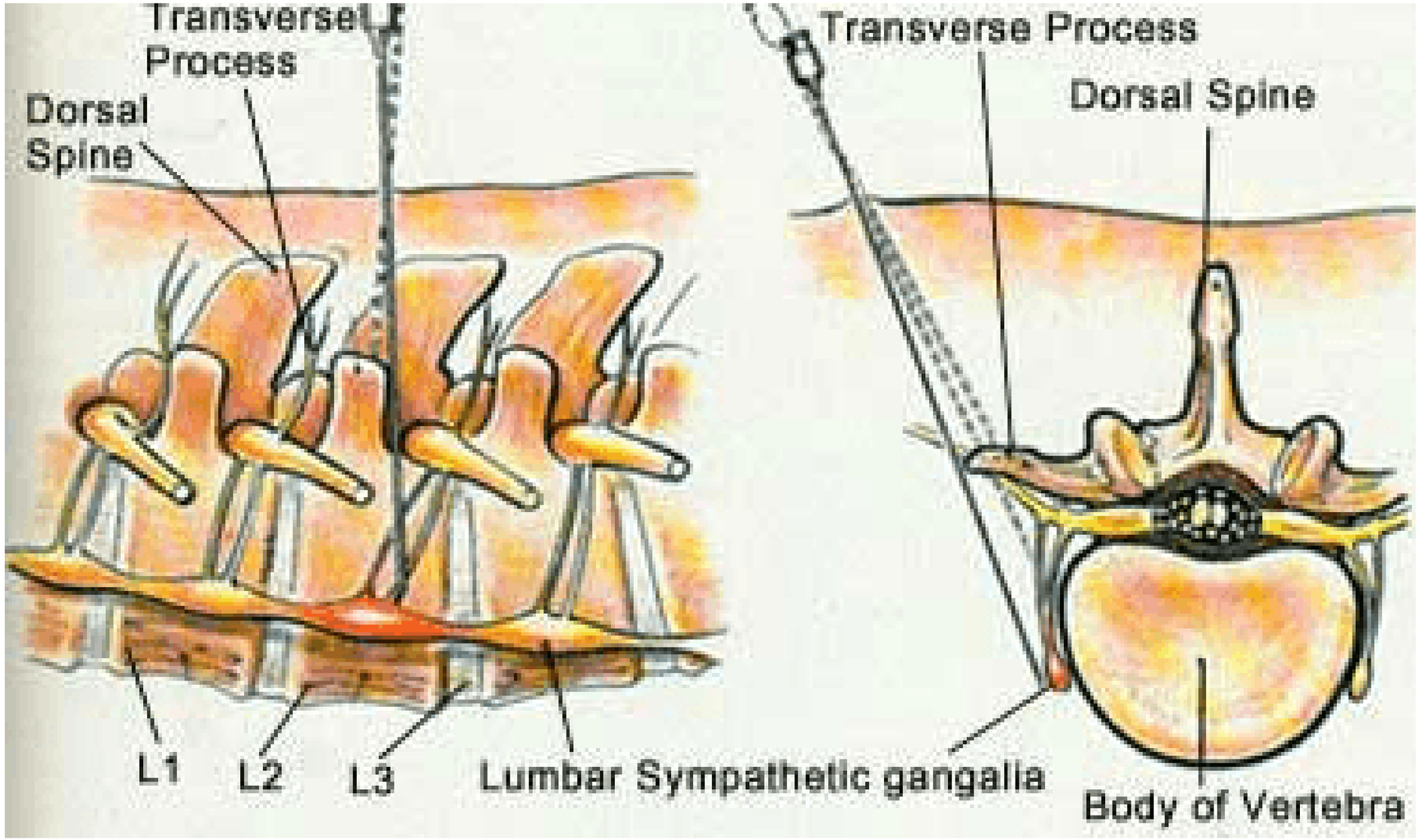
Adapted from: Harden et al. [39]

Table 1.2 CRPS severity score (CSS)

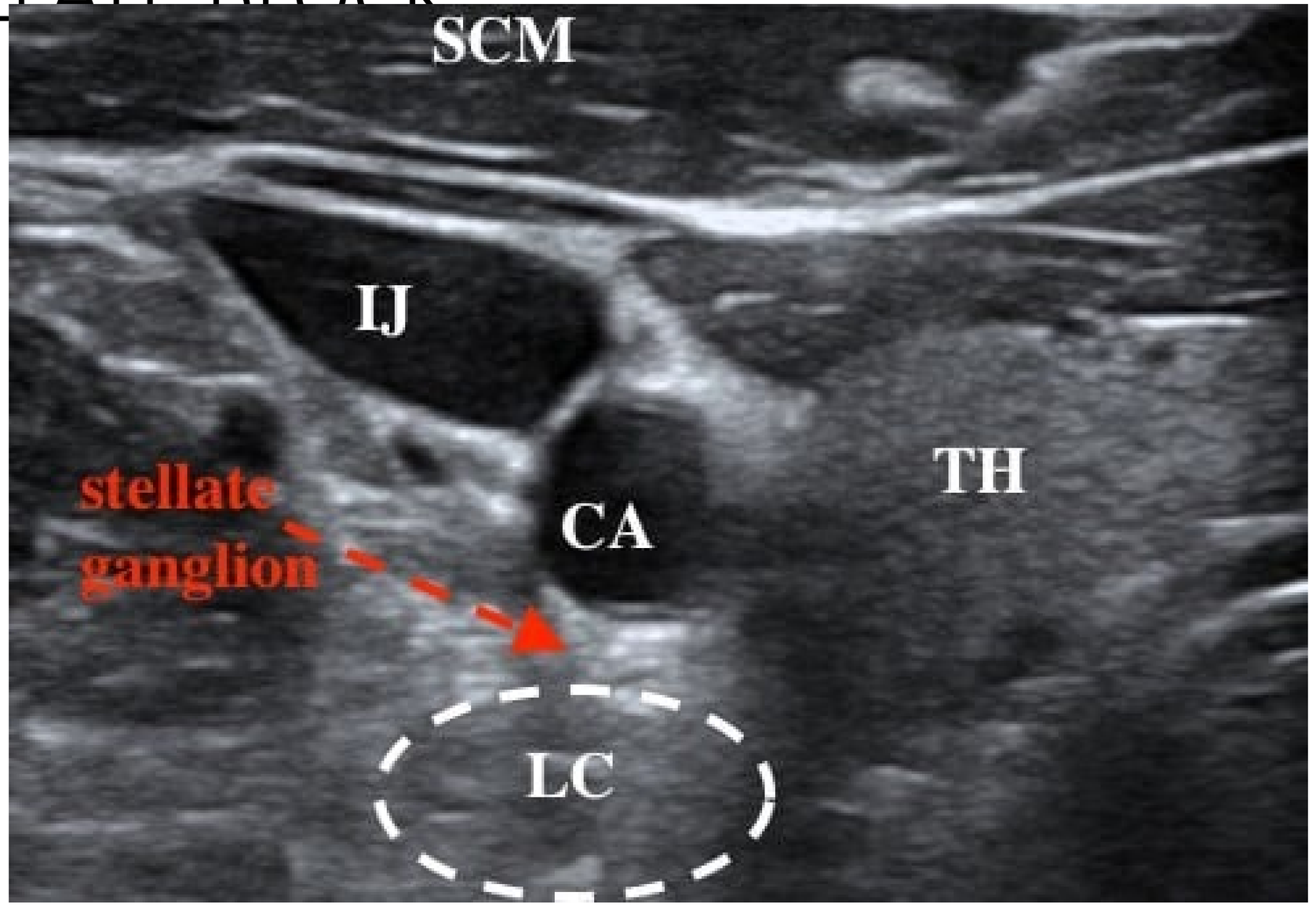
Self-reported symptoms	
Continuing disproportionate pain	
Sensory	Allodynia or hyperalgesia
Sudomotor	Asymmetric edema Sweating asymmetry or changes
Vasomotor	Temperature asymmetry Skin color asymmetry or changes
Motor	Motor dysfunction (weakness, tremors, dystonia) Trophic changes
Signs observed during evaluation	
Sensory	Allodynia Hyperalgesia to pinprick
Sudomotor	Asymmetrical edema Sweating asymmetry or changes
Vasomotor	Temperature asymmetry Skin color asymmetry or changes
Motor	Motor dysfunction (weakness, tremors, dystonia) Trophic changes

Adapted from: Harden et al. [40]

LUMBAR SYM PLEXUS



STELLATE BLOCK



2020 [82].

CRPS Spread

Non-dermatomal spreading of CRPS is a feared complication of CRPS, most common in patients with a young age of CRPS onset and those reporting a more significant impact of their CRPS [93]. CRPS spread was evaluated among 185 patients with a CRPS diagnosis; 89 patients had CRPS in multiple limbs, with 49% spreading to the contralateral limb, 30% spreading ipsilaterally, and 14% spreading diagonally [93]. Trauma to the region of spread was reported in 37% of patients with contralateral spread, 44% of patients with ipsilateral spread, and 91% of patients with diagonal spread. The risk of spread following trauma was higher in patients with more limbs affected. Proposed pathophysiologic mechanisms for spread include peripheral hyperexcitability causing hyperexcitability in the brainstem and higher brain regions, in addition to impaired pain modulation [26], and compromised response by the CNS to neurogenic inflammation [67].

Conclusions

CRPS is an enigmatic condition that typically develops after minor injury such as surgery or fracture, with a 3–4:1 female-to-male predominance. Our understanding of CRPS has evolved significantly since it was first described in the sixteenth century, creating more specific diagnostic criteria and targeted research. Distinct stages characterize CRPS—an acute stage mediated by peripheral factors such as sympathetic dysregulation and circulating pro-inflammatory mediators, and a

FIBROMYALGIA

- A BRAIN PROBLEM
- ACR CRITERIA

Journal of Clinical Neuroscience
Volume 38, April 2017, Pages 13-22

Review article

Alterations of brain activity in fibromyalgia patients

Passakorn Sawaddiruk [a, c], Sahattaya Paiboonworachat [a, c], Nipon Chattipakorn [a, b], Siriporn C. Chattipakorn [a, d]

https://doi.org/10.1016/j.jocn.2016.12.014

Highlights

- Fibromyalgia is a chronic pain syndrome.
- The summary of possible alterations of brain in fibromyalgia patients.
- The potential brain regions maintain pain of fibromyalgia patients.
- Insula plays an important role in pathophysiological changes in fibromyalgia.

Abstract

Fibromyalgia is a chronic pain syndrome, characterized by widespread musculoskeletal pain with diffuse tenderness at multiple tender points. Despite intense investigations, the pathophysiology of fibromyalgia remains elusive. Evidence shows that it could be due

International Journal of *Molecular Sciences*

MDPI

Review

Novel Approaches in Molecular Imaging and Neuroimaging of Fibromyalgia

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Abstract: Fibromyalgia (FM) represents a condition that is still controversial in its entity, pathophysiology, diagnosis and management. The aim of this review is to focus on imaging aspects of FM, especially on novel approaches in molecular imaging, with a special focus on neuroimaging. Novel functional and molecular imaging findings may represent, eventually, future biomarkers both in research settings and in terms of clinical practice. Several imaging techniques have already been tested in clinical trials in the FM field, including functional MRI, positron emission tomography (PET) imaging with ^{18}F-FDG in FM, PET imaging of the dopaminergic system, PET imaging of the GABAergic system, PET imaging with neuroinflammation and neuroimmune parameters, PET imaging of the opioid system and $H_2{}^{15}O$-PET activation studies. Therefore, the potential role in the FM field of fMRI and different PET tracers has been discussed in different settings, serving as a comprehensive guide of novel imaging options both in research and in the clinical field.

Keywords: positron emission tomography; fibromyalgia; functional MRI; molecular imaging

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1. Introduction

Fibromyalgia is defined by chronic widespread pain with further symptoms, such as joint stiffness, fatigue, and symptoms related to possible central nervous system (CNS) alterations, such as sleep disturbance, cognitive dysfunction, and depression. Fibromyalgia (FM) is also defined by widespread pain in the absence of identifiable peripheral pathology

https://www.physio-pedia.com/The American College of Rheumatology 2010 preliminary diagnostic criteria for fibromyalgia

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doi: 10.1093/pm/pnaa001
Advance Access Publication Date: 12 September 2020
Original Research Article

Low-Dose Naltrexone for the Treatment of Fibromyalgia: Investigation of Dose–Response Relationships

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Conflicts of interest: The authors have no conflicts of interest to declare.

Abstract

Objective. This study explores dose–response relationships when treating fibromyalgia with low-dose naltrexone.**Design**. A single-blinded clinical trial was carried out using the "up-and-down" method.**Subjects**. Subjects included women with a diagnosis of fibromyalgia aged 18–60 years who had been referred to treatment at a public pain clinic at a Danish university hospital.**Methods**. The test doses were in the range 0.75–6 mg, and the dosing interval was 0.75 mg. The method was sequential and allowed predicting the dose effective in 50% (ED50) and 95% (ED95) of the subjects when the dose had shifted direction 10 times, and six pairs of "up-and-down" data were available.**Results**. A total of 27 subjects were included in the study; two subjects were withdrawn. After inclusion of 25 evaluable subjects, the dose estimates were calculated as 3.88 mg for ED50 and 5.40 mg for ED95. As a secondary outcome, the effects on 10 common fibromyalgia symptoms were evaluated. A high interindividual variation was observed both in the symptom presentation at baseline and in which symptoms were reduced by low-dose naltrexone.**Conclusions**. This study is the first to explore dose–response relationships in the treatment of fibromyalgia with low-dose naltrexone. Future placebo-controlled randomized clinical trials are needed, and according to our findings, 4.5 mg, which has previously been used, seems to be a relevant test dose. We recommend that future studies include additional nonpain fibromyalgia symptoms as outcome measures.

Key Words: Fibromyalgia; Low-Dose Naltrexone; LDN; Dose–Response

Introduction

nociceptors and reduced central inhibition, leading to a

Journal of Pain Research

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open access to scientific and medical research

Open Access Full Text Article

METHOD

Effective Doses of Low-Dose Naltrexone for Chronic Pain – An Observational Study

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Purpose: Despite the availability of a wide variety of analgesics, many patients with chronic pain often experience suboptimal pain relief in part related to the absence of any medication to address the nociplastic component of common pain syndromes. Low-dose naltrexone has been used for the treatment of chronic pain, typically at 4.5 mg per day, even though it is also noted that effective doses of naltrexone for chronic pain presentations range from 0.1 to 4.5 mg per day. We performed an observational analysis to determine the range of effective naltrexone daily dosing in 41 patients with chronic musculoskeletal pain.

Methods: Charts of 385 patients, 115 males, 270 females, ages 18–92, were reviewed. Two hundred and sixty patients with chronic diffuse, symmetrical pain were prescribed a titrating dose of naltrexone to determine a maximally effective dose established by self-report of 1) reduction of diffuse/generalized and/or severity level of pain and/or 2) positive effects on mood, energy, and mental clarity. Brief Pain Inventory and PROMIS scales were given pre- and post-determining a maximally effective naltrexone dose.

Results: Forty-one patients met all criteria for inclusion, successfully attained a maximally effective dose, and completed a pre- and post-outcome questionnaire. Hormesis was demonstrated during the determination of the maximally effective dosing, which varied over a wide range, with statistically significant improvement in BPI.

Conclusion: The maximally effective dose of low-dose naltrexone for the treatment of chronic pain is idiosyncratic, suggesting the need for 1) dosage titration to establish a maximally effective dose and 2) the possibility of re-introduction of low-dose naltrexone to patients who had failed initial trials on a fixed dose of naltrexone.

Plain language summary: Low-dose naltrexone (LDN) has been used to treat chronic pain. There is, however, no agreed on effective dose, leaving clinicians without guidelines on initiating treatment with naltrexone. It appears that the dose of LDN for any patient is idiosyncratic, and in a small study, ranges from 0.1 to 6.0 mg/day. Understanding the various possible mechanisms of action of LDN may help the clinician to understand how and why it can effectively reduce chronic pain. A titration schedule to establish the maximally effective dose for chronic myofascial pain is presented.

Keywords: myalgia, low-dose naltrexone, chronic pain, hypermobile Ehlers Danlos syndrome, nociplastic pain, musculoskeletal pain

pharmacies across the country, these pharmacies have unique access to a large number of patients taking the medication. These pharmacists could potentially contribute significantly to the literature if they were able to design a study examining the efficacy of LDN using these data.

Conclusion

While some animal and in vitro studies support the use of LDN, its clinical efficacy as an analgesic and antiinflammatory has been tested only in a small number of chronic conditions such as MS, fibromyalgia, Crohn's disease, and CMT. Additionally, the efficacy of LDN for disease modification in various chronic conditions is not well established. As a result, the overall quality of the evidence thus far is insufficient to allow any definitive conclusions as to the efficacy of LDN for analgesia, antiinflammation, or disease modification. This means it currently may be premature to recommend LDN as an effective medication due to a lack of high-quality evidence.

Despite this limited evidence, LDN prescriptions are still compounded extensively for a variety of off-label indications such as chronic pain, inflammation, and pruritus. The large off-label use of LDN may be driven by patients looking to relieve symptoms, for alternatives to chronic opioid use in those diseases where opioids are indicated, or to improve quality of life.7 Patients with refractory diseases may look for treatments that are safe and are outside the usually prescribed therapies. While LDN has the potential to be a useful medication, health care providers should be aware of how limited the evidence of efficacy is at present. This allows providers to assist their patients in filtering out misinformation. While LDN has a history of being safe and well tolerated, if it is not efficacious, then it would be affecting patients financially without any benefit. As 86% of health care spending is in patients with chronic conditions, this is especially problematic for patients who may already have a high financial burden due to the cost of their illness.60 Perhaps with future clinical research, LDN may be shown to be not just safe but also effective for use as an immunomodulator, non-opioid analgesic, or novel antiinflammatory in a variety of chronic disease states that are currently challenging to treat.

References

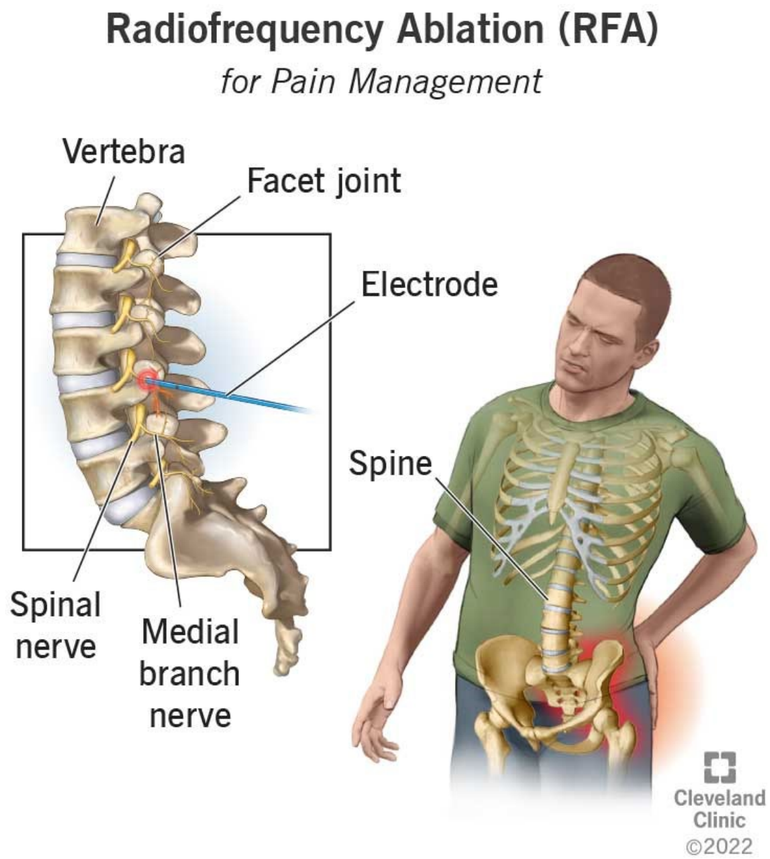
Botox for pain

- Migraine
- Peripheral neuropathy
- Back pain
- Spastic disorders
- Entrapment neuropathies

NERVE BLOCKS-PERIPHERAL

- LATERAL FEMORAL CUTANEOUS
- OBTURATOR
- PUDENDAL
- SUPRASCAPULAR
- Ganglion impar for rectal/pelvic
- Occipital block with ultrasound

RADIOFREQUENCY ABLATION



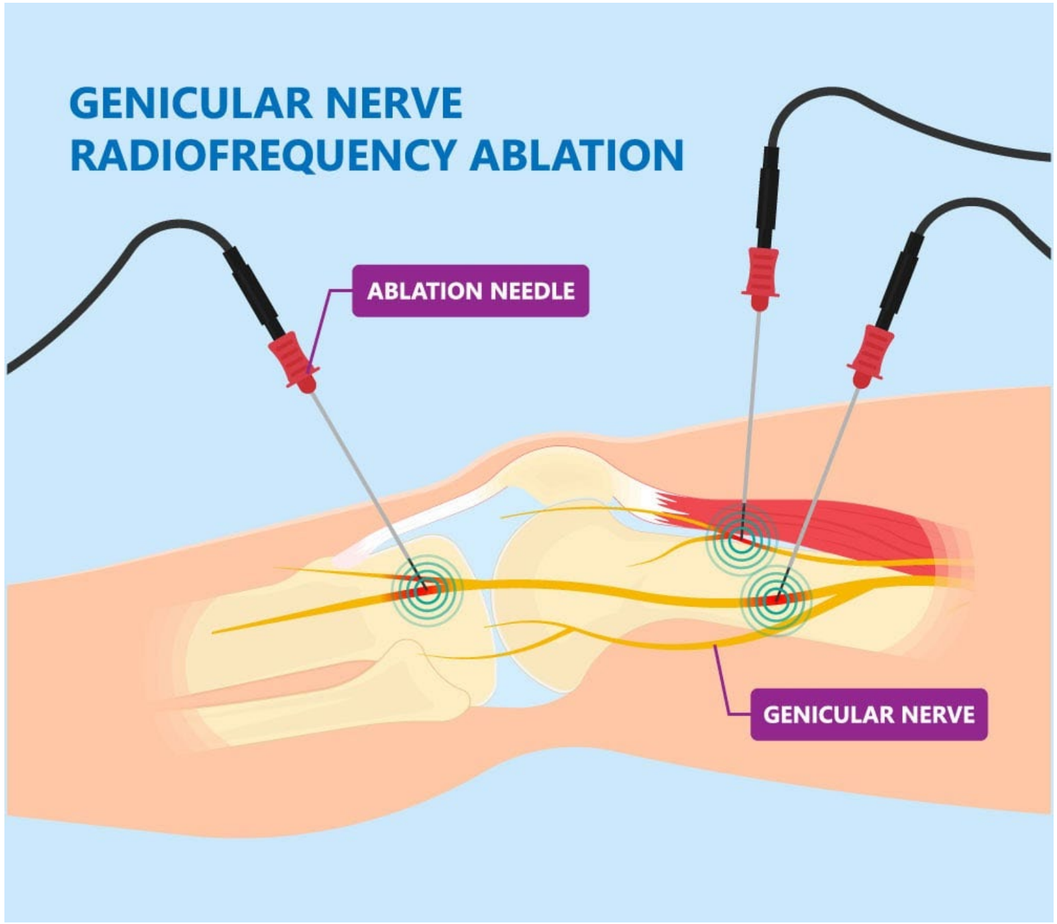
KETAMINE INFUSION

- UNRESPONSIVE NEUROPATHIC PAIN OR CENTRAL PAIN
- SEVERE CONCOMITANT DEPRESSION AND MULTI SITE PAIN
- MONTHLY DOSING AT PRESENT

LIDOCAINE INFUSION

- SIMILAR TO KETAMINE
- HOPE TO MOVE THIS TO OFFICE

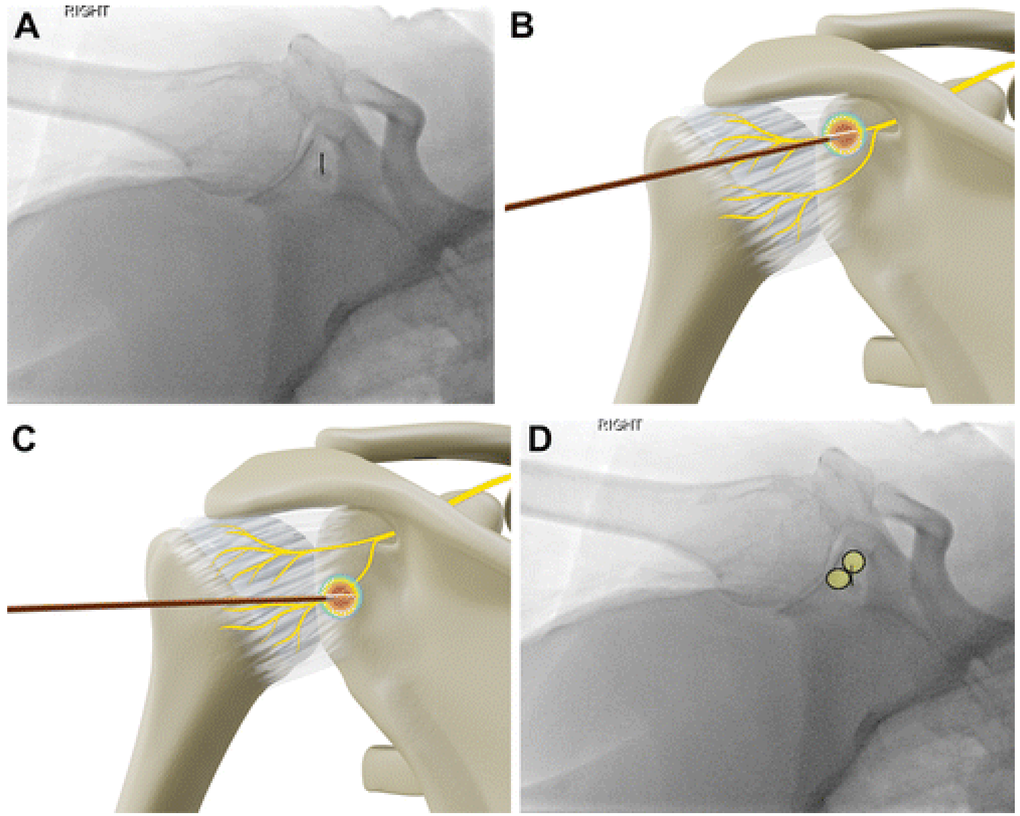
NEW OPTIONS FOR MSK PAIN



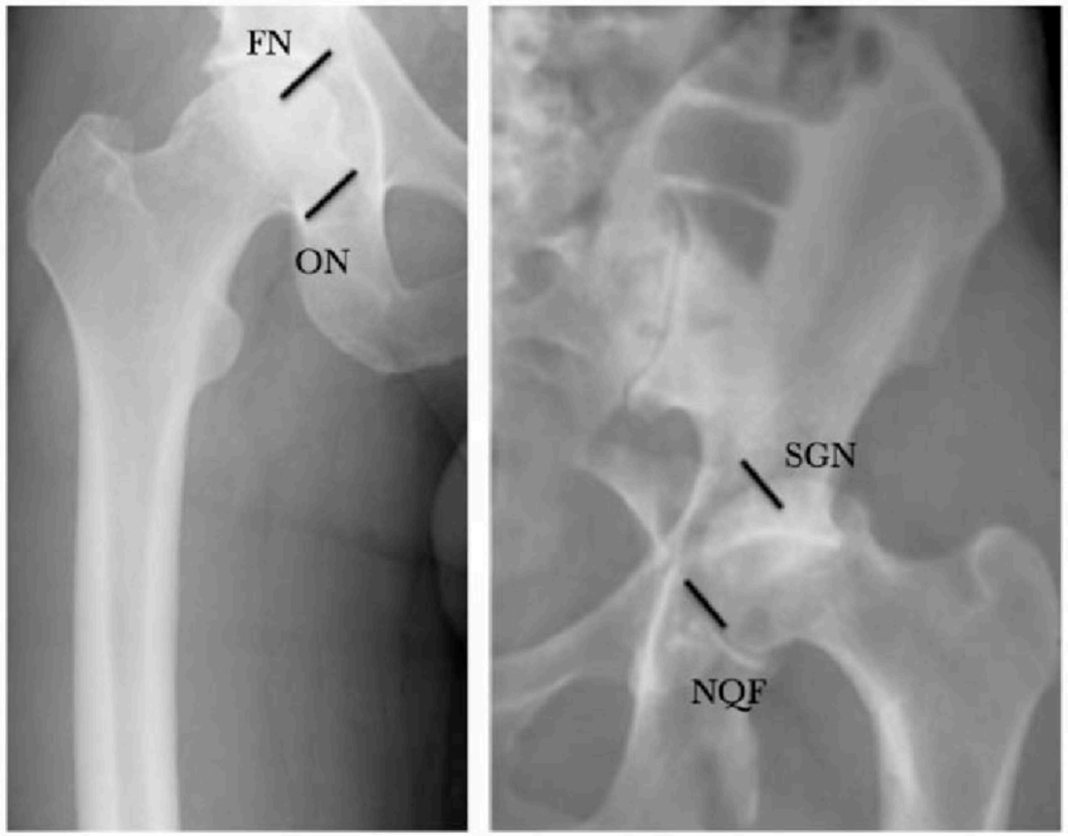
Are there better things than steroids for joint?

- Platelet rich plasma
- Stem cells
- Prolotherapy

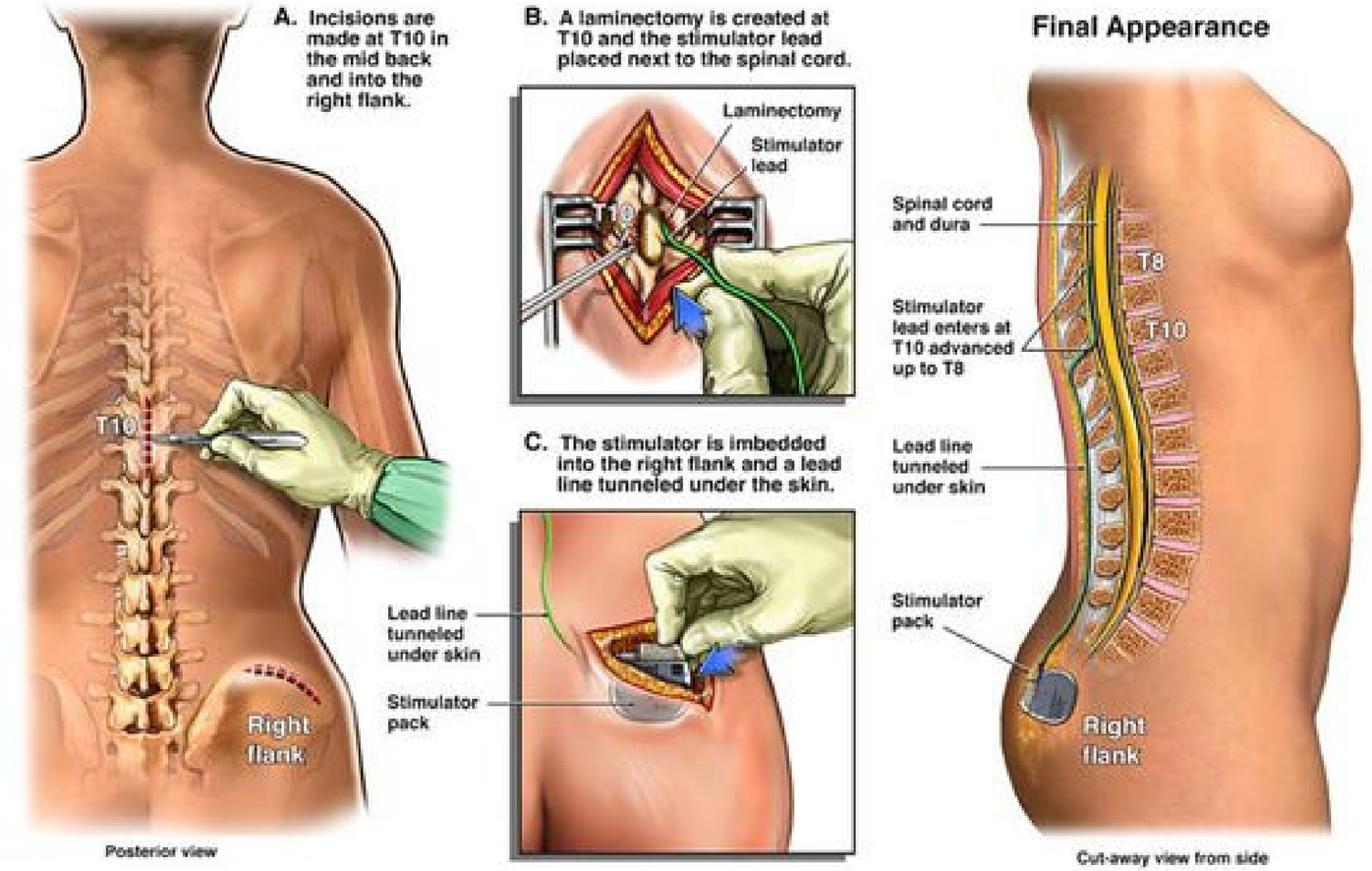
SHOULDER



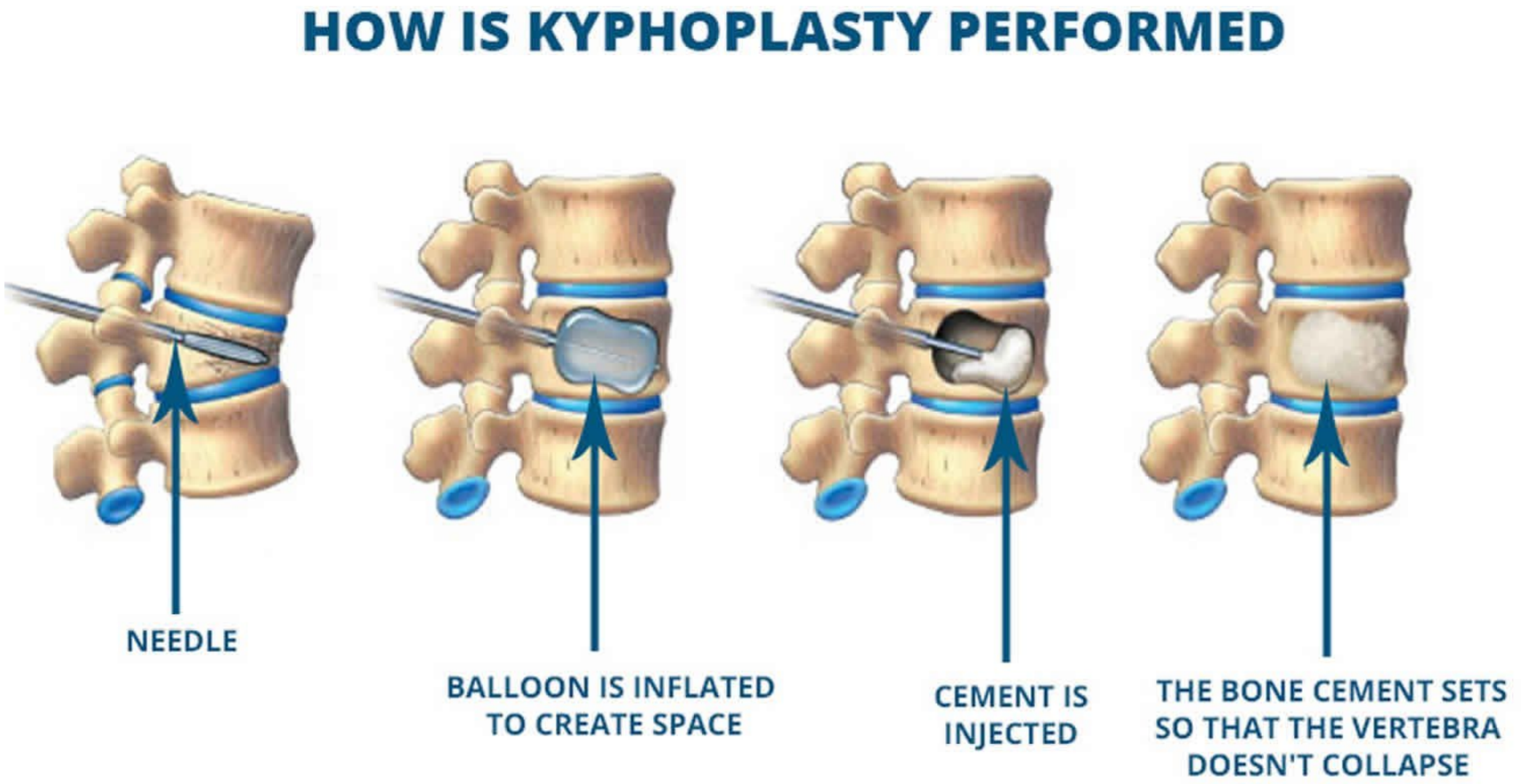
HIP



SPINAL CORD STIMULATION



KYPHOPLASTY



Mail - Tim Fitzpatrick - Outlook

AMN-PEI

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Relaunch to update

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AMN-PEI 1 / 1 100%

1

Atlantic Mentorship Network
Prince Edward Island

PRACTICAL LEARNING -- SAFE & SUPPORTIVE SPACE

COMMUNITY OF PRACTICE -- CLINICAL RESOURCES & TOOLS

The Atlantic Mentorship Network (AMN) is designed to provide an ongoing clinical resource for health care professionals in developing core knowledge, skills, and confidence to deliver high-quality, compassionate care in the community to individuals with chronic pain, addictions, and mental illness.

What is Adaptive Mentorship?

Adaptive mentorship is a safe, non-judgmental experience providing opportunities for clinical conversations tailored to Mentees' evolving needs.

One-to-One Mentoring

Mentors provide one-to-one clinical, as well as core knowledge and skill development support to Mentees.

Small Group Mentoring

Regional groups connect in-person or virtually to increase core knowledge and skill through case discussions and/or topic-specific presentations.

Large Group Mentoring

Members share knowledge and experience of peers in focused learning opportunities such as monthly virtual webinars, workshops, and online forums.

Continued Professional Development Offerings

Health care professionals connect and build capacity through multi-modal learning opportunities such as conferences and courses.

Benefits of a Mentorship Program

See what people are saying about the AMN-P&A

"The inter-disciplinary discussions are invaluable."

HOW MENTORSHIP HAS HELPED MY PATIENTS

- TIES WITH DALHOUSIE PAIN AND NEUROSURGERY
- AMN WEBINARS
- AMN CONTACTS EX COMMUNITY PSYCHOLOGY
- BARRIERS OF PRIVATE/PUBLIC ACCESS
- VIRTUAL HALLWAY

Pelvic and abdominal pain

- Visceral very complex
- Co morbidities abundant
- Interventions more complex- celiac/hypogastric plexus blocks
- Lidocaine/ketamine somewhat useful

Other supports

- AMN!!!!
- POWER OVER PAIN ONTARIO SITE
- CANADIAN PAIN SOCIETY

OTHER ISSUES TO CONSIDER

- PELVIC PAIN /WOMEN'S HEALTH
- PAIN AND ADDICTIONS
- PRIMARY MENTAL HEALTH DISORDERS

SUMMARY

- WE ARE UNDER THE AVALANCHE NOW
- PRIORITIES INCLUDE SUICIDE PREVENTION, AVOIDANCE OF HOSPITAL VISITS
- SELF MANAGEMENT AND VIRTUAL TOOLS WILL BE ESSENTIAL
- LIMITS OF MEDICATIONS/PHYSICAL THERAPY/INTERVENTIONS ARE CLEAR AS STAND-ALONE APPROACH
- SIGNIFICANT POTENTIAL FOR POSITIVE IMPACT WITH HUB/SPOKE AND COMMUNITY INVOLVEMENT

THANK YOU

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- STU
- JOE DESREUX
- DR PAT MCREA
- PCH OR NURSES AND JULIE CHAISSON
- MEDICAL AFFAIRS JULIE/KATHIE/EILEEN LARKIN

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- tjfitzpatrick@ihis.org

Access to Means...
To What?...
End??

Lessons about Suicidality from the Intersection of Medical Toxicology and Psychiatry

AMN - PEI Education Day

April 19, 2024 Charlottetown, PE, Canada

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Penn State University College of Medicine

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Disclosure / Disclaimer:
J.J. Rasimas, Ph.D., M.D.

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The views presented herein are my own and do not reflect the positions or policies of the National Institutes of Health, the U.S. Public Health Service, or its Department of Health and Human Services.

NIMH
National Institute of Mental Health

Language of Suicide

- Thoughts of or preoccupation with death
- Suicidal ideation (“active” and “passive”)
- Self-destructive behaviour
- Self-injurious behaviour
- Self-harm
- Suicidal “gesture”
- Suicide attempt
- Highly lethal attempt
- Completed (“successful”) suicide
- **Suicidality** = any thoughts or actions related to volitionally ending one’s own life.

The Working Definition

- **For the purpose of understanding psychiatric research since about 2009…**

  “Thoughts and / or actions that if fully carried out may lead to serious self-injury or death.”

- **Adopted as the standard for assessment of the medication question**

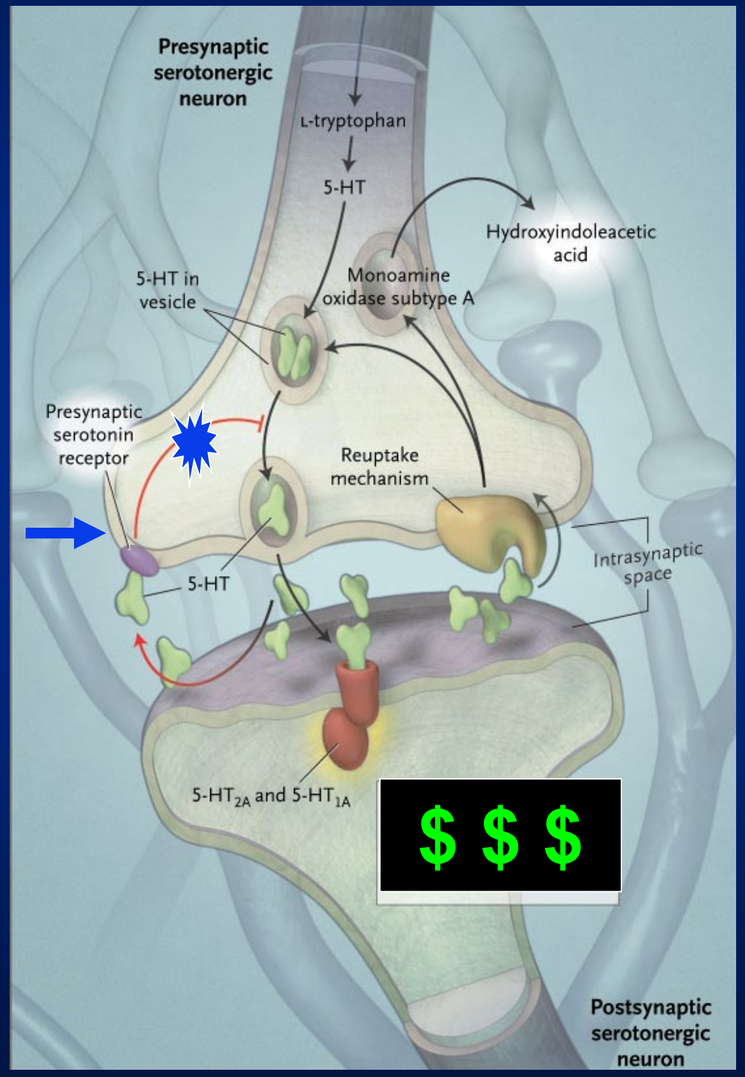
Access

- IV Ketamine remains a labour-intensive, narrowly available treatment in psychiatry
  - IN delivery may not impact suicidality
- "Traditional" Antidepressants (reuptake inhibitors)
  - Increase "risk" early in treatment / titration
  - Perhaps directly related to serotonin physiology
    - PRX, FLV, VLFX >> CIT, SRT, FLX
- SSRI prescriptions correlate with lower rates of suicide in children and adolescents
  - For what?... Unipolar depression and anxiety d/o

Clinical Background

- Patients in the deepest neurovegetative states of depression rarely suicide
- Antidepressants are not “happy pills”
  - Focus and motivation return early
  - Elevation of mood comes late
- Early stages of recovery are a high-risk period for suicide
  - Energy to act in a state of despair is dangerous
  - Akathisia is subjectively
- The brain is in the body…

“Toxic” Pathophysiology



Boyer & Shannon, *NEJM* 2005

- **5-HT reuptake inhibition**
  - Convenient and obvious
  - Initially potent, but wanes
  - Little impact of drug t ½
- **5-HT1A autoreceptor**
  - Presynaptic
  - Dampens further release
  - Hyperactive in depression
  - SSRIs bind and inhibit
  - Greater impact of drug t ½
- **Potential for harm is tied – mechanistically – to the potential for benefit**

NPDS Data on Means

- In past, OTC analgesics were the most common class of agents involved in both attempts & deaths

- More recently, psychotropic overdoses have increased
  - Antidepressants have seen largest increase
  - Atypical antipsychotic overdoses also much more frequent
  - Psychotropic polypharmacy prescribing is (more) common
    - Sedative/Hypnotics & Antipsychotics are involved in a large number of suicide deaths

Gummin, et al. Clin Tox 2021, 59(12);1282–1501

Further Access

- Clozapine
  - RCTs in severely ill patients, and those with recognized risk of violence toward self & others
  - Better data are primarily in psychotic disorders – limited studies and case series in severe bipolar disorder, TBI, and other impulse control disorder conditions
    - Reduction in suicide deaths not consistently shown
    - Somatic toxicity / side effect burden is heavy

Fontaine, et al. (2001), using mathematical modeling, estimated that over a 10-year period, 492 suicide deaths per 100,000 schizophrenia patients are prevented with clozapine and that 416 additional deaths are caused due to metabolic toxicity.

Further Access

- Lithium
  - Small / Medium sized intervention trials
    - Some results limited by attrition rates
  - Large pharmacy registry data
    - Adherence? Other effects?
  - Narrow therapeutic index, but overdoses are rarely lethal

Prescription rates are quite low over recent decades, with newer agents replacing lithium in “diagnosis-focused” treatment.

Am J Prev Med 2014, 47(3S2);S195–S203

Means

	Cases	% of Total	Most Common Compounds
Total	655	100	
OTC Analgesics	167	25.5	Acetaminophen (148)
Antidepressants	144	22.0	Amit, Bupro, Cital, Sert, Mirtaz
Sedative Hypnotics	130	19.8	Clonaz, Alpraz, Loraz, Traz
Antipsychotics	123	18.8	Quetiapine, Olanzapine
Anticholinergics / Antihistamines	110	16.8	Diphenhydramine
Opioids	89	13.6	Hydrocod, Oxycod, Tramadol
Muscle Relaxants	72	11	Cyclobenzaprine, Carisoprodol
Anticonvulsants	56	8.5	LTG, VPA, TOP, CBZ, PHB
Sympathomimetics	46	5.0	Psychostimulants, cocaine
Cardiovascular Drugs	42	7.0	Metoprol, Clonid, Lisin, Amlodip
Lithium	35	5.3	Lithium carbonate IR
Other – Pharmaceutical	19	2.9	Dextromethorphan, warfarin
Diabetic Medications	11	1.7	Insulin, Glipizide
Gases / Vapers / Irritants / Dusts	11	1.7	CO, Chlorine gas, Hydrocarbons
Caustics	6	0.9	
Herbals / Dietary Supps / Vitamins	4	0.6	
Pesticides	4	0.6	
Plants and Fungi	4	0.6	
Chemotherapeutic / Immune	3	0.5	
Psychoactives	3	0.5	

- 655 purposeful exposures
- 291 (44.4 %) polydrug
- Rx drugs more common
- Typically, but not always the patient's own

Restriction ???

Psych Res 2017, 255; 304–313

Overdose Cohort Psychology

- 203 (31.0%) had available both CNS-acting and non-CNS acting substances
  - 34 (16.7%) took medications of both types
  - 157 (77.3%) took only CNS-acting agents
  - 12 (5.9%) took only non-CNS-acting drugs
- 583 (89.0%) patients experienced delirium, profound sedation, and/or coma as a result of their ingestions
  - 4 of these 583 continued to have active suicidal ideation after inpatient medical hospitalization
- 49 (7.5%) had normal or near-normal sensorium
  - 29 of these 49 continued to have active suicidal ideation after inpatient medical hospitalization

Psych Res 2017, 255; 304–313

Purposeful Lithium Overdoses

	Total Lithium Ingestions	Lithium Monoingestions
Preserved Mentation	17	13
Remaining suicidal	13	10
Altered Mentation	18	8
Remaining suicidal	1	1

35 Total Cases Involving Purposeful Lithium Ingestion

Psych Res 2017, 255; 304–313

Themes and Realities

- Even profoundly suicidal patients are conflicted about their decisions
- Not all self-poisonings have death as the goal

Main goal often may not be death *per se*, but rather obliteration of consciousness

“They’ll just find another way”

- Majority of attempts are not extensively planned
  - Barriers to means for such attempts make a difference
  - Physical, material, and chemical
- “Nature abhors a vacuum”
  - A “suicidal” act serves a purpose
  - Without a replacement strategy, cannot expect health to follow
    - Means are needed to cope differently
- Harm reduction ?
  - Access to substances that transiently relieve crises even if they come with risk… ketamine ???

Summary

- Access to Means
  - For Intentional Toxic Exposure AND For Treatment and Care
- Clinical judgment trumps the notion of prescriptions as property
  - Supplies can be gathered up and curtailed
- Psychotropic prescribing could and should involve return of pills no longer prescribed before new ones are acquired
- Prescriptions are part of a care relationship
  - Risk / benefit balance parallels the quality / utility of relationship
  - Always inform prescribers and non-prescribing clinicians about self-poisoning events
- Removing means necessitates replacing means

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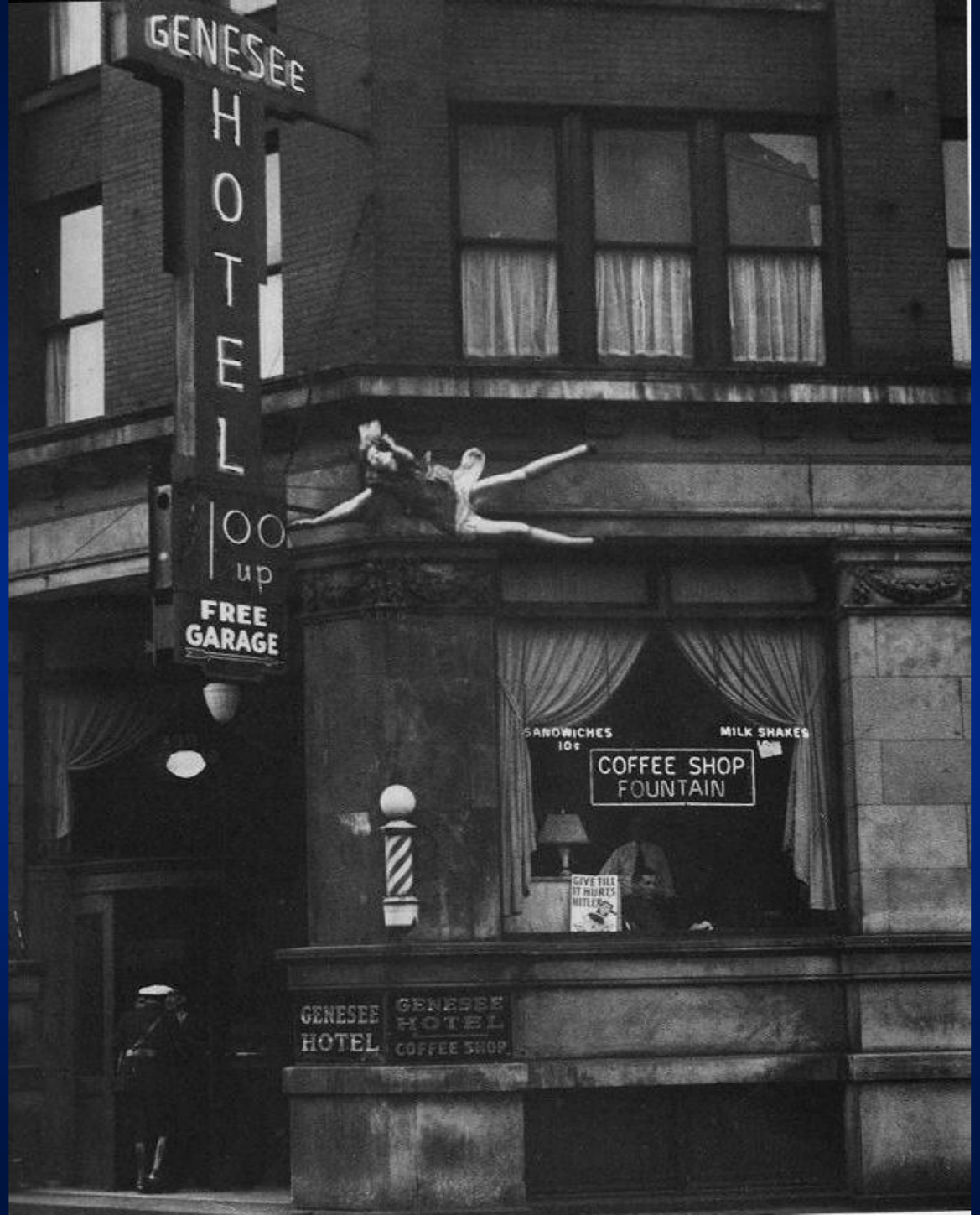
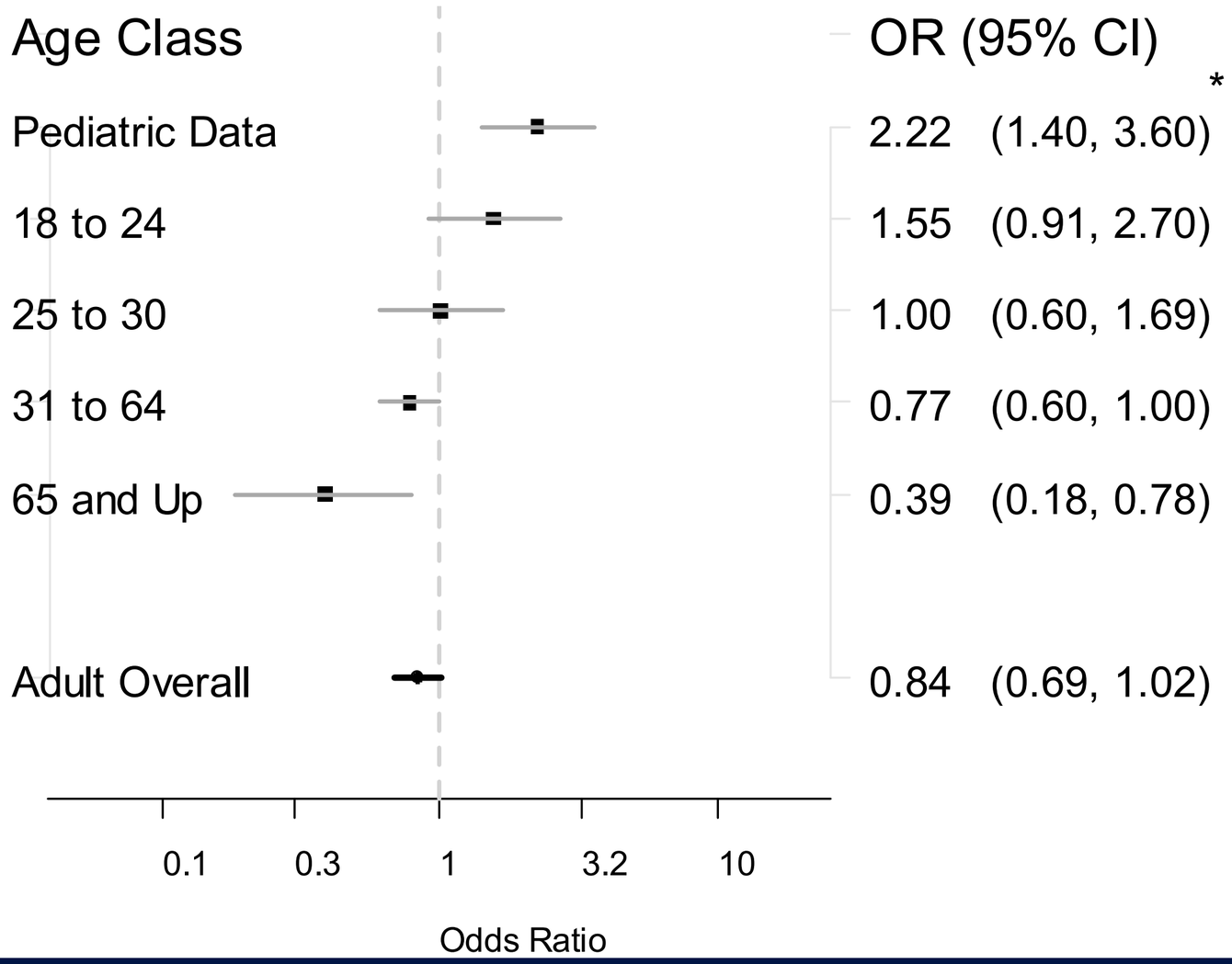
SUPPLEMENTAL MATERIALS



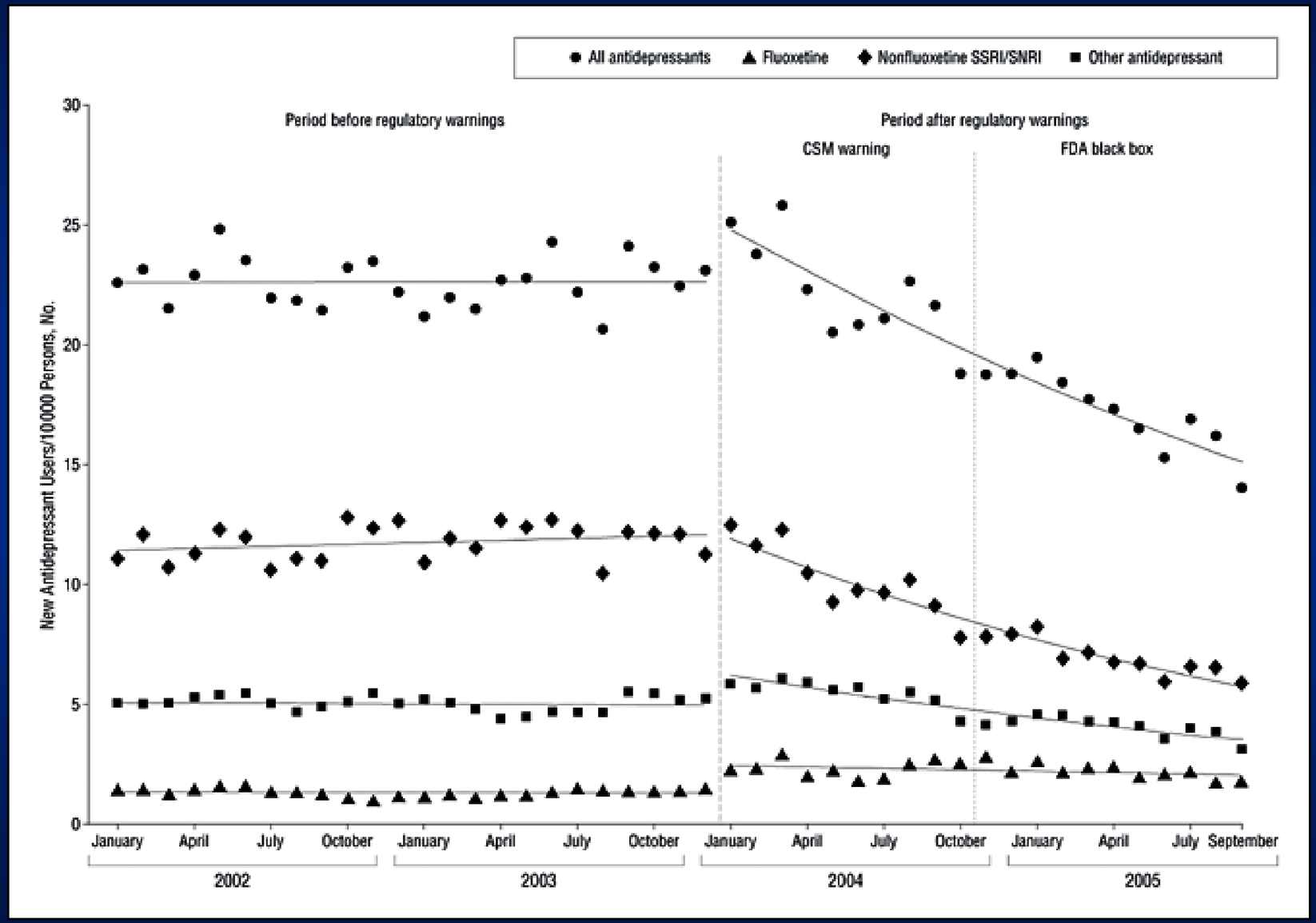
Suicide
I. Russell Sorgi
1942

Suicidal Behavior and Ide
Psychiatric Indications
Odds Ratio



* Reanalysis of FDA data / Hammad, et al., 2004

Antidepressant Prescriptions



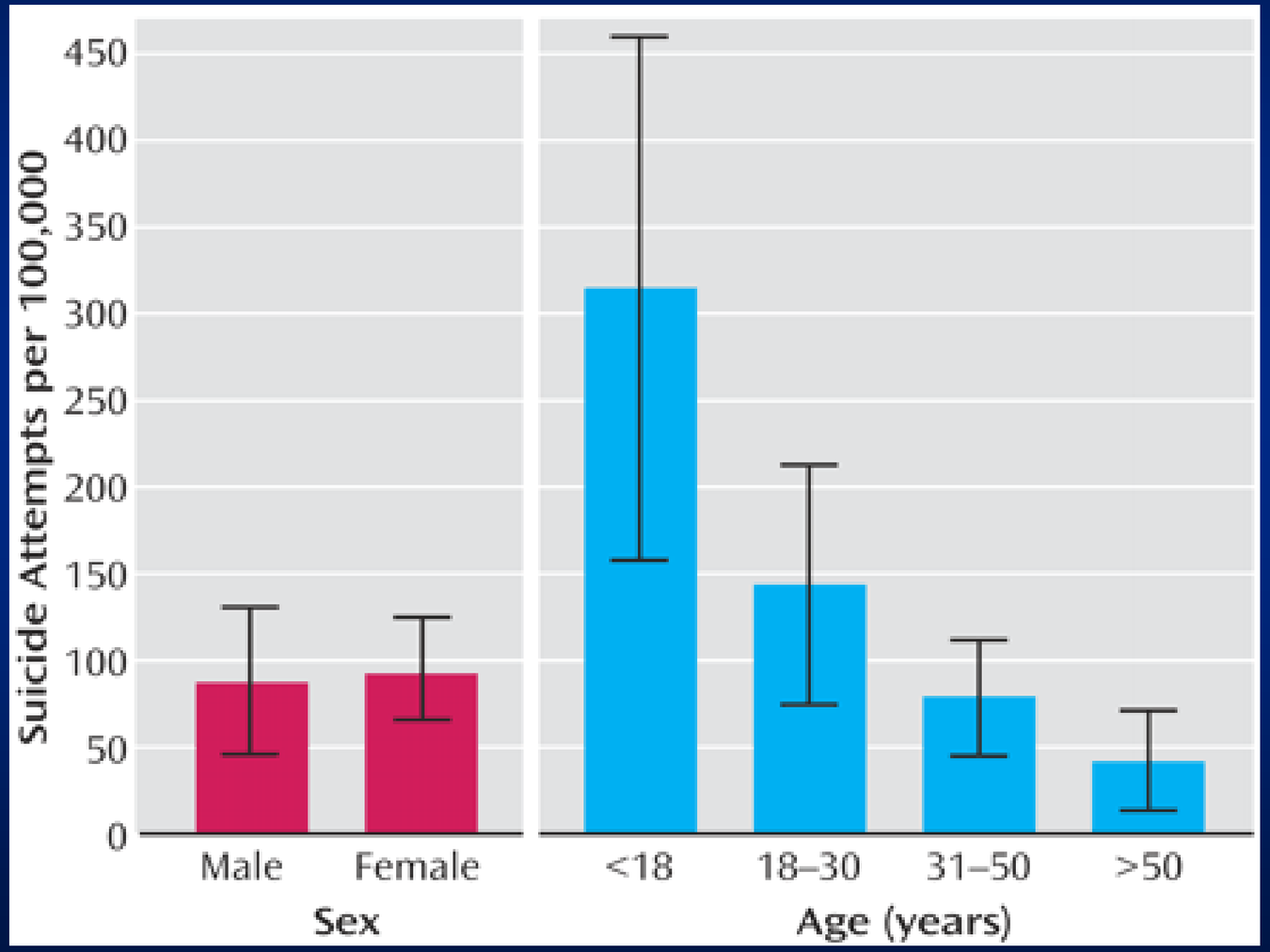
Kurian, et al., Arch Pediatr Adolesc Med, 2007

Suicide Rates

- Suicide rate increased from 2.8 to 3.3 per 100,000 per year in U.S. children (5-19) in the following year
- Suicide rate increased from 0.8 to 1.3 per 100,000 per year in Dutch children (5-19) in 2 years following
- Retrospective population data from the 1990s indicate that more SSRI prescriptions correlate with lower rates of suicide in children and adolescents
- Adults: Suicide attempt rates in depressed VA patients are higher in those not prescribed SSRIs, and fewer received SSRIs in 2004

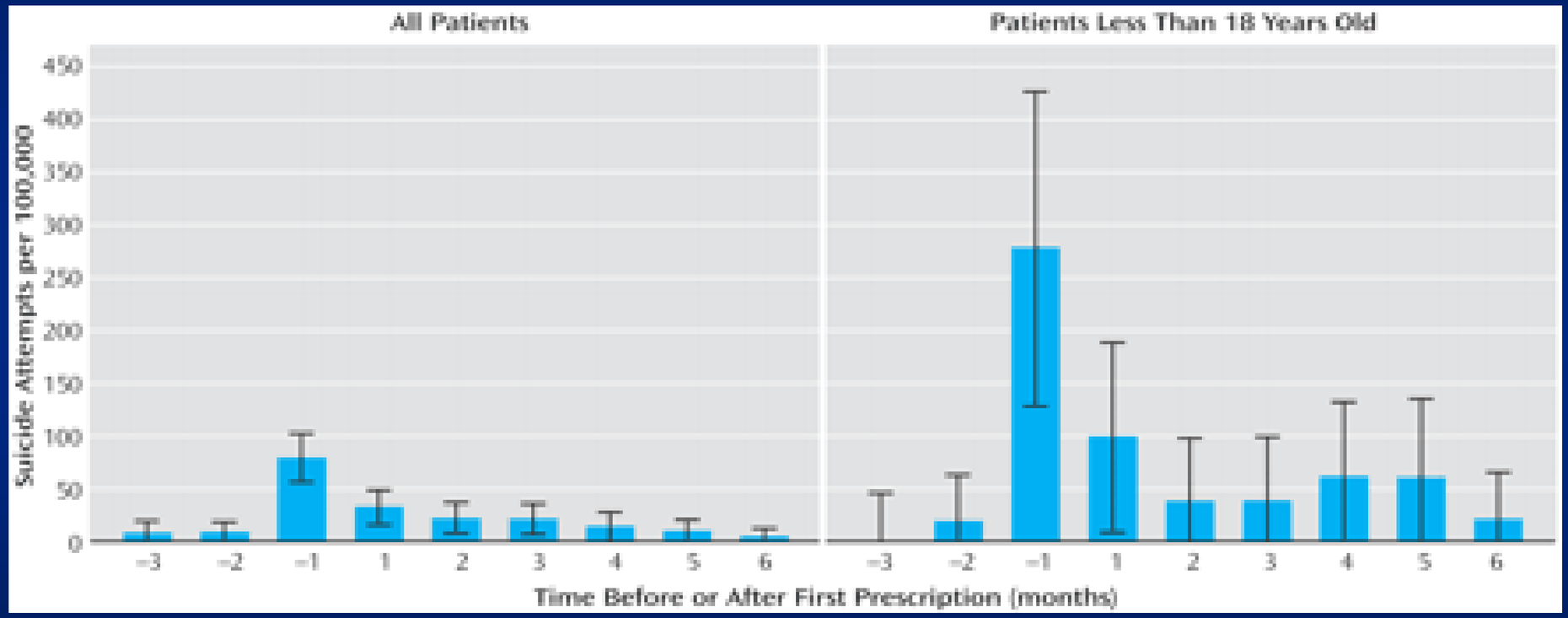
Gibbons, et al., Am J Psych, 2006 and 2007 (3 papers)

Suicide Attempts During First 6 Months After Initial Antidepressant Rx



Simon, et al., Am J Psych, 2006

Suicide Attempts by month Before and After Initial Antidepressant Rx



Simon, et al., Am J Psych, 2006

The Pendulum Swings

- Medication treatments for psychiatric disorders have increased slightly in recent years
- The message in favor of more careful prescribing and even more careful early clinical follow-up may stick…
- With the help of the Columbia group, methods for prospective, focused monitoring are in place
  - Systematic, standardized assessments
  - Clarity of language involving thoughts, urges, intent, and behaviour
- Support for clinical trials involving real-world populations is growing

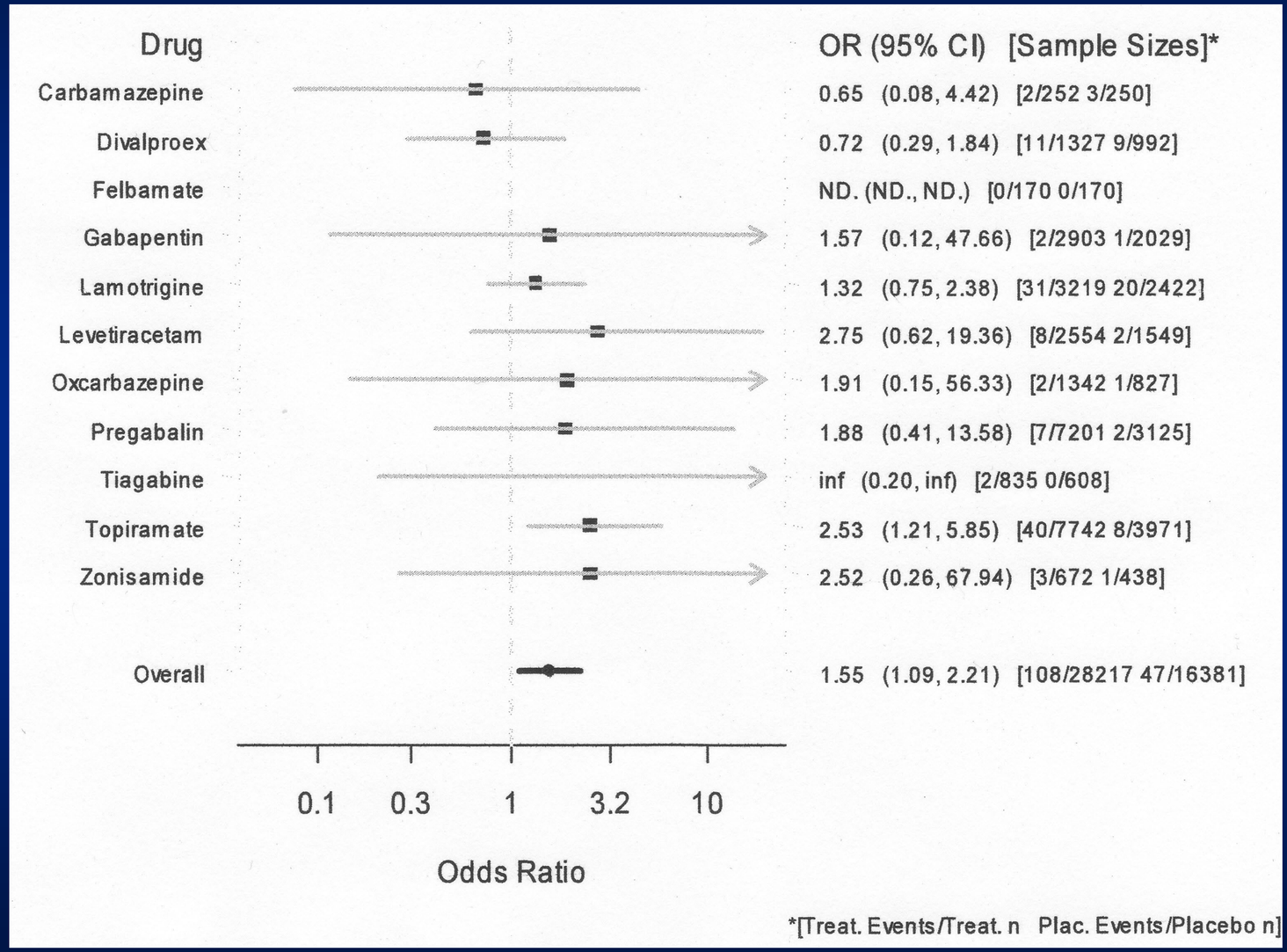
Meyer, et al., J Clin Psychiatry, 2010

Antiepileptic Drugs (AEDs)

- Variety of pharmacologic mechanisms involving ion channel modulation and ↑↑ GABA activity
- Prescribed for epilepsy as well as mood disorders
- In epileptics, "suicidality" is exceedingly more common than in the general population
  - Completed suicide rates 5 to 25 times greater
  - "Suicidality" exceeds many psychiatric samples
- Data reviewed by end of 2007, alert in Jan 2008, hearings spring 2008, non-boxed alert May 2009
  - Phenytoin and phenobarbital privileged

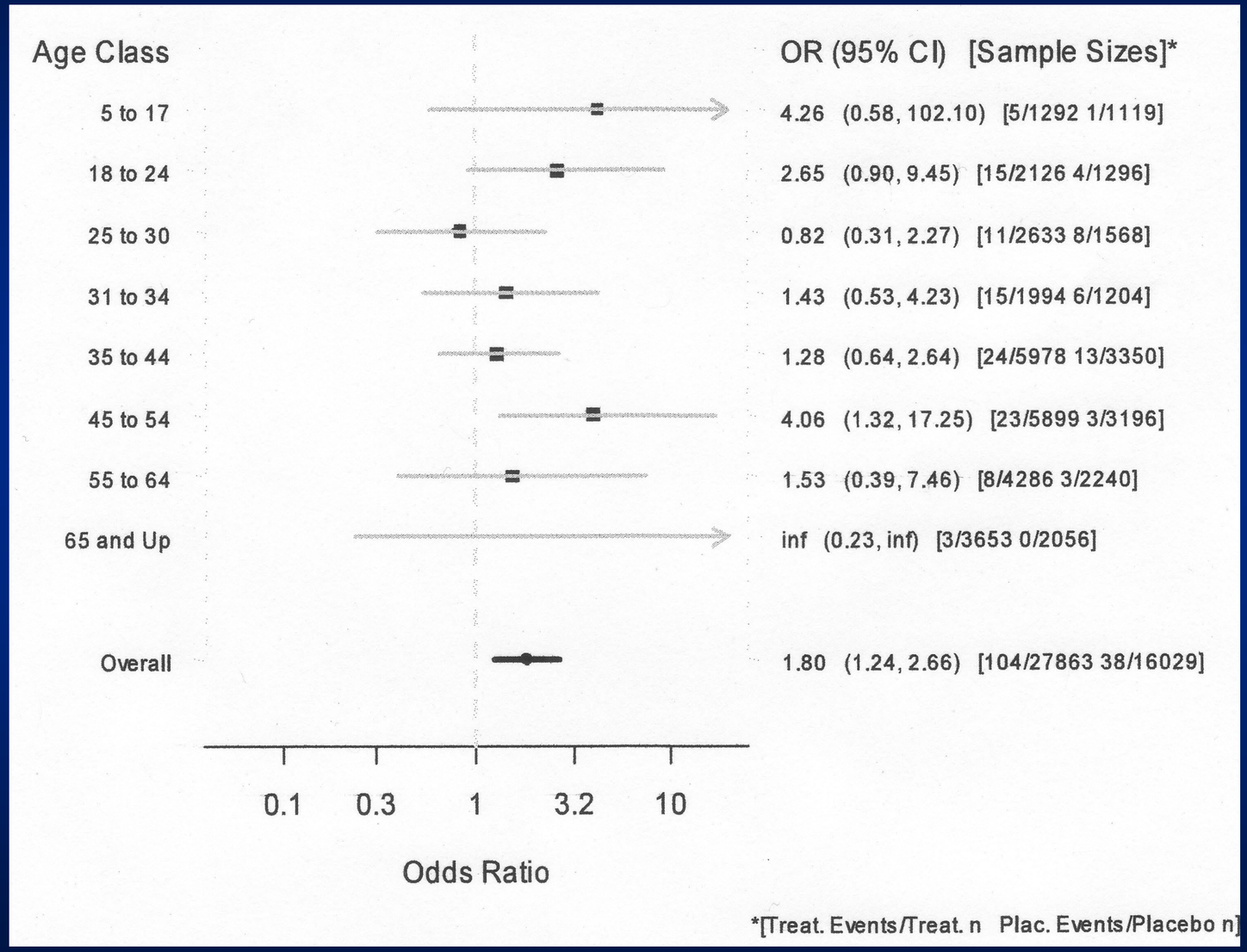
Kalinin, Drug Safety, 2007

“Suicidality” and AEDs



FDA, 2009

“Suicidality” by Age with AEDs



FDA, 2009

Since the AED Alert

- Subsequent studies have shown mixed results
  - More "suicide-related events" in patients without epilepsy, but with depression or with no other illness
  - More attempts / completions with gabapentin, lamotrigine, oxcarbazepine, and tiagabine
  - Fewer attempts in bipolar patients with AEDs
- Critiques of FDA methodology
- Concerns regarding under-treatment of epilepsy
- Recommendations for careful prescribing and closer monitoring

Arana et al., 2010; Patorno, et al., 2010; Gibbons, et al., 2009

Other Psychotropics

- Psychostimulants (for ADHD) have not demonstrated concern leading to greater review
  - Stimulants for weight loss have raised some concerns, considering population vulnerability
- Antipsychotic medications do not appear to increase "suicidality"
  - Frequently used to augment Rx of resistant psych d/o
  - "Suicidality" appears to be diminished in depressed patients taking atypical antipsychotics
    - Retrospective data review of 2 aripiprazole trials
    - One prospective risperidone study
    - Consistent with 5-HT activity mechanism proposed above

Weisler, et al., J Clin Psychiatry, 2010; Reeves, et al., J Clin Psychiatry, 2008

Get In Touch With Us

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