“This house believes that cannabis is an efficacious and safe analgesic for neuropathic pain”

Dr Mark A Ware
Argument principles

• Scientific plausibility
• Clinical need
• Evidence base
  – Quality
  – Safety
  – Efficacy
• Patient-centered care
Cannabinoids as ‘synaptic circuit-breakers’

Nat Med 2008;14(9):923-30
Cannabinoid agonists are effective in all peripheral neuropathic pain models

Nerve injury
- Chronic constriction injury
- Sciatic nerve ligation
- Brachial plexus avulsion
- Trigeminal neuralgia

Diabetes
- Streptozotocin

Chemotherapy
- Paclitaxel
- Cisplatin
- Vincristine

HIV neuropathy
...and in other pain models

- Spinal cord injury
- Multiple sclerosis
- Cancer pain
- Osteoarthritis
- Visceral pain
- Inflammatory, nociceptive pain
- Muscle pain
## Epidemiology of medical cannabis use

<table>
<thead>
<tr>
<th>Disease</th>
<th>Prevalence</th>
<th>Author(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Epilepsy</td>
<td>21%</td>
<td>Gross 2004</td>
</tr>
<tr>
<td>Chronic noncancer pain (CNCP)</td>
<td>15%</td>
<td>Ware 2003</td>
</tr>
<tr>
<td>Multiple sclerosis (MS)</td>
<td>10-12%</td>
<td>Page 2005, Clark 2006, Chong 2006</td>
</tr>
</tbody>
</table>
Dronabinol
Nabilone
Nabiximols

dronabinol

cannabidiol
# Recent randomized controlled trials

<table>
<thead>
<tr>
<th><strong>Nabilone</strong></th>
<th><strong>Nabiximols (2.5mg THC + 2.5mg CBD)</strong></th>
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</thead>
<tbody>
<tr>
<td>Neuropathic pain (Frank 2008)</td>
<td>Brachial plexus avulsion (Berman 2004)</td>
</tr>
<tr>
<td>Fibromyalgia pain (Skrabek 2008) and sleep (Ware 2010)</td>
<td>Rheumatoid arthritis (Blake 2005)</td>
</tr>
<tr>
<td>Spinal cord injury (Pooyania 2010)</td>
<td>MS neuropathic pain (Rog 2007)</td>
</tr>
<tr>
<td><strong>Dronabinol</strong></td>
<td>MS Spasticity (Novotna 2011)</td>
</tr>
<tr>
<td>MS spasticity (Svensen 2004)</td>
<td>Cancer pain (Portnoy 2012)</td>
</tr>
<tr>
<td>Chronic pain + opioids (Narang 2008)</td>
<td><strong>Herbal cannabis (1.8-9.4%THC)</strong></td>
</tr>
<tr>
<td><strong>Cannador (2.5mg THC + 1.2mg CBD)</strong></td>
<td>Neuropathic pain (Wilsey 2009, 2013, Eisenberg 2014)</td>
</tr>
<tr>
<td></td>
<td>MS spasticity (Corey-Bloom 2012)</td>
</tr>
<tr>
<td></td>
<td>Crohn’s disease (Naftall 2013)</td>
</tr>
</tbody>
</table>
This systematic review found that RCT evidence of analgesic efficacy superior to placebo in the context of HIV-SN exists only for smoked cannabis, rhNGF and high dose (8%) topical capsaicin.

...legal and mental health issues preclude routine recommendation of long term smoked cannabis for pain management.

...the efficacy of cannabis in HIV-SN would suggest that cannabinoids with an appropriate therapeutic index when delivered by a mechanism other than smoking might be worthy of investigation.
Vaporization as a Smokeless Cannabis Delivery System: A Pilot Study

Dl Abrams¹,²,³, HP Vizoso¹,³, SB Shade¹,³, C Jay⁴,⁵, ME Kelly¹,²,³ and NL Benowitz³,⁶
The Pharmacokinetics, Efficacy, Safety, and Ease of Use of a Novel Portable Metered-Dose Cannabis Inhaler in Patients With Chronic Neuropathic Pain: A Phase 1a Study

15 mg herbal cannabis; 19% THC
Single inhalation using Syqe® inhaler
N=10 neuropathic pain patients
Amygdala activity contributes to the dissociative effect of cannabis on pain perception

Michael C. Lee\textsuperscript{a,d,\,*}, Markus Ploner\textsuperscript{a,b}, Katja Wiech\textsuperscript{a}, Ulrike Bingel\textsuperscript{a,c}, Vishvarani Wanigasekera\textsuperscript{a}, Jonathan Brooks\textsuperscript{a}, David K. Menon\textsuperscript{d}, Irene Tracey\textsuperscript{a}
Adverse effects of medical cannabis

• General population considerations:
  – Comorbidities (medical and psychiatric)
  – Concomitant use of other medications
  – Substance abuse issues

• General drug considerations:
  – Very low toxicity/lethality
  – Most effects short-term
  – Experienced users report fewer AEs
  – Most common: dizziness, dry mouth, drowsiness

• Overall:
  – Poorly studied in medical use
  – Mostly addressed from population studies in recreational use

Wang et al CMAJ 2008
Other AE concerns

- Driving
- Psychosis
- Sedation
- Anxiety
- Tolerance
- Dependence
- Cognitive function
- Cardiovascular effects

- Pregnancy
- Nausea
- Arteritis
- Koro
Original Investigation

Medical Cannabis Laws and Opioid Analgesic Overdose Mortality in the United States, 1999-2010

Marcus A. Bachhuber, MD; Brendan Saloner, PhD; Chinazo O. Cunningham, MD, MS; Colleen L. Barry, PhD, MPP

Table. Association Between Medical Cannabis Laws and State-Level Opioid Analgesic Overdose Mortality Rates in the United States, 1999-2010

<table>
<thead>
<tr>
<th>Independent Variable</th>
<th>Primary Analysis</th>
<th>Secondary Analyses</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Estimate (95% CI)</td>
<td>Estimate (95% CI)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Medical cannabis law</td>
<td>$-24.8 (-37.5$ to $-9.5)^e$</td>
<td>$-31.0 (-42.2$ to $-17.6)^f$</td>
</tr>
<tr>
<td>Prescription drug monitoring program</td>
<td>$3.7 (-12.7$ to $23.3)$</td>
<td>$3.5 (-13.4$ to $23.7)$</td>
</tr>
<tr>
<td>Law requiring or allowing pharmacists to request patient identification</td>
<td>$5.0 (-10.4$ to $23.1)$</td>
<td>$4.1 (-11.4$ to $22.5)$</td>
</tr>
<tr>
<td>Increased state oversight of pain management clinics</td>
<td>$-7.6 (-19.1$ to $5.6)$</td>
<td>$-11.7 (-20.7$ to $-1.7)^e$</td>
</tr>
<tr>
<td>Annual state unemployment rate$^g$</td>
<td>$4.4 (-0.3$ to $9.3)$</td>
<td>$5.2 (0.1$ to $10.6)^e$</td>
</tr>
</tbody>
</table>

$^a$ All models adjusted for state and year (fixed effects).
$^b$ $R^2 = 0.876.$
$^c$ All intentional (suicide) overdose deaths were excluded from the dependent variable; opioid analgesic overdose mortality is therefore deaths that are unintentional or of undetermined intent. All covariates were the same as in the primary analysis; $R^2 = 0.873.$
$^d$ Findings include all heroin overdose deaths, even if no opioid analgesic was involved. All covariates were the same as in the primary analysis. $R^2 = 0.842.$
$^e$ $P \leq .05.$
$^f$ $P \leq .001.$
$^g$ An association was calculated for a 1-percentage-point increase in the state unemployment rate.
Cannabis and neuropathic pain

- Scientific plausibility
- Clinical need
- Evidence base
  - Quality
  - Safety
  - Efficacy
- Patient-centered care
This house believes that cannabis is an efficacious and safe analgesic for neuropathic pain