Outcomes, Transition from Chronic Pain, and Perspective from Practicing Physician on Medical Cannabis
Cannabis in the Treatment of Intractable Pain: A Minnesota Perspective

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Today’s Discussion

- Brief History of Medical Uses of Cannabis (Art)
- How the Minnesota Cannabis Certification Program works (Susan)
  - Current qualifying conditions
- Medical Use of cannabis (Art)
- Intractable pain – medical aspects (Art)
- Intractable pain – Minnesota experience to date (Susan)
- Step by step directions on how to certify patients (Susan)
- Other stuff (Art)

- Discussion (everyone)
History

• Therapeutic use of cannabis in India and China for thousands of years
• 1839 – Brought to England by William O’Shaughnessy after studying it in India
• 1892 – Sir William Osler included it in his textbook – “Best treatment for migraine”
• 1894 – Use of cannabis praised in first issue of Lancet by Queen Victoria’s physician

Source: Tom Arneson, M.D.
History

• c. 1900 – Recreational use in US started in SW
• 1920’s – US doctors wrote millions of Rx for cannabis each year
• 1937 – Marijuana Tax Act (opposed by AMA)
• 1970 – Controlled Substances Act – marijuana “temporarily” assigned to Schedule 1
• 1985 – Dronabinol (synthetic THC) approved for treating loss of appetite/weight loss in AIDS pt; subsequently extended to N/V

Source: Tom Arneson, M.D.
History

• 1988 – After two years of hearings, DEA Chief Administrative Law Judge recommended cannabis be rescheduled
  – “One of the safest therapeutic agents known to man”
  – Rejected by DEA
• 1996 – California Proposition 215, first state medical marijuana program
• 2014 – Minnesota becomes 22nd state with medical marijuana program

Source: Tom Arneson, M.D.
Minnesota Medical Cannabis Program

2014: Minnesota Medical Cannabis Therapeutic Research Act
Minnesota Medical Cannabis Program

2014: MN became 22nd state with full medical cannabis program

- Recreational and Medical (8)
- Medical (21)
- Low THC/High CBD Products (15)
However...

- State medical cannabis programs are illegal under current federal law
How is Minnesota’s Program Different from Most?

• No smokeable or plant form cannabis (only pill or liquid/oil forms)
  • Only pill or liquid/oil forms (topicals starting Aug. 1, 2017)

• Two vertically-integrated manufacturers (cultivation-production-distribution supply chain)

• Commitment to learning from experience with the program (reports and observational studies on effectiveness, side effects, etc.)
  • Patients agree to provide access to medical data
Overview of MN Medical Cannabis Program

DID YOU KNOW THAT MINNESOTA IS THE FIRST STATE PROGRAM IN THE COUNTRY TO OFFER ONLY SMOKE-FREE MEDICAL CANNABIS?

*Care-giver may represent a patient by applying and meeting conditions including a background check.

MDH Minnesota Department of Health

Program Overview
Qualifying Medical Conditions

• Cancer (or its treatment), with (a) Severe or chronic pain, (b) nausea or severe vomiting, (c) cachexia or severe wasting

• Glaucoma

• HIV/AIDS

• Tourette Syndrome

• Amyotrophic Lateral Sclerosis

• Seizures, incl. those characteristic of epilepsy

• Severe and persistent muscle spasms, incl. those characteristic of multiple sclerosis

• Inflammatory bowel disease, incl. Crohn’s disease

• Terminal illness with <1yr life expectancy, with (a) Severe or chronic pain, (b) nausea or severe vomiting, (c) cachexia or severe wasting

• Intractable Pain – Starting Aug. 1, 2016

• PTSD – Starting Aug. 1, 2017
Pharmacologically Active Constituents

- Cannabinoids – thought to be most important constituent for therapeutic use:
  - >80 types of these 21-carbon molecules
- Main cannabinoids:
  - THC (tetrahydrocannabinol) – psychoactive. Analgesic, anti-nausea/vomiting, more. Marinol is synthetic THC
  - CBD (cannabidiol) – not psychoactive. Anti-inflammatory, anti-epileptic, analgesic, more
- Terpenes: Aromatic compounds – give distinctive aromas
  - Some evidence of synergistic action with cannabinoids, but much more study needed to define clinical role
- Other (flavonoids, more)

Source: Tom Arneson, M.D.
Does it work?

Is it safe?
Benefits Are Unclear

- Few studies that show definite benefit
  - Schedule 1 – therapeutic trials not legal
- Anecdotal reports that show possible benefit for some patients who may not have responded to other treatment
- Its use is considered experimental
## Relevant Studies

<table>
<thead>
<tr>
<th>Qualifying Condition</th>
<th>Studies Reviewed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cancer, if the underlying condition or treatment produces one or more of the following:</td>
<td>4 clinic trials</td>
</tr>
<tr>
<td>Severe or chronic pain</td>
<td>1 observational study (extension of clinical trial)</td>
</tr>
<tr>
<td>Nausea or severe vomiting</td>
<td>5 clinical trials</td>
</tr>
<tr>
<td>Cachexia or severe wasting</td>
<td>1 systematic review and meta-analysis</td>
</tr>
<tr>
<td>Glaucoma</td>
<td>1 clinical trial</td>
</tr>
<tr>
<td></td>
<td>2 observational studies</td>
</tr>
<tr>
<td>HIV/AIDS</td>
<td>6 clinical trials</td>
</tr>
<tr>
<td></td>
<td>1 observational study (extension of clinical trial)</td>
</tr>
<tr>
<td>Tourette’s syndrome</td>
<td>3 clinical trials</td>
</tr>
<tr>
<td>Amyotrophic lateral sclerosis</td>
<td>1 clinical trial</td>
</tr>
<tr>
<td></td>
<td>1 observational study</td>
</tr>
</tbody>
</table>
Relevant Studies, continued

<table>
<thead>
<tr>
<th>QUALIFYING CONDITION</th>
<th>STUDIES REVIEWED</th>
</tr>
</thead>
<tbody>
<tr>
<td>Seizures, including those characteristic of epilepsy</td>
<td>3 clinical trials</td>
</tr>
<tr>
<td>Crohn’s disease</td>
<td>1 clinical trial (concluded, but results not yet reported)</td>
</tr>
</tbody>
</table>
| Severe and persistent muscle spasms, including those characteristic of multiple sclerosis | 10 clinical trials  
3 observational studies (extensions of clinical trials)  
4 additional observational studies (including 2 safety registries)                      |
| Terminal illness with probable life expectancy of less than one year if the illness or its treatment produces one or more of the following:  
  Severe or chronic pain ..............  
  Nausea or severe vomiting ...........  
  Cachexia or severe wasting ........... | Included in studies accounted for above                                           |

Other suggested uses

- Asthma
- Obesity
- Rheumatoid arthritis
- Preventing organ rejection after kidney Tx
- Hemorrhoids
- Dandruff
- Leprosy
Conclusions from MDH Review

• Mild and moderate side effects are common, but very few serious adverse events related to cannabis have been seen.

• There is a high degree of variation in how individuals respond to cannabis.
  – Start at low dose, increase slowly, titrating to symptom reduction or beginning of intolerable side effects.
Risks Are Relatively Low

• May “unmask” or exacerbate schizophrenia
• Documented deleterious effect on developing adolescent brain
• Can affect performance when driving or using heavy equipment
• Risk of addiction?
Possible side effects

- Dry mouth
- Nausea, vomiting
- Dry or red eyes
- Heart and blood pressure problems
- Impaired mental functioning
- Headache
- Dizziness
- Panic reactions, hallucinations, flashbacks, depression
- Sexual problems.
- Interaction with warfarin (can increase risk of bruising or bleeding)
Contraindications

- Pregnancy
- Schizophrenia
- Use caution if
  - Adolescent/young adult
  - Heart disease
  - Weakened immune system
  - Seizure disorder
  - Pending surgery (effect on anesthesia)
DEATHS FROM ALCOHOL

DEATHS FROM CIGARETTES

DEATHS FROM MARIJUANA
Compared to other drugs

- Opioids – 33,091 deaths (2015)
- Benzodiazepines – 6973 (2013)
- Cannabis – 0 deaths

- Think of warfarin, amiodarone, chemotherapeutic agents
MARIJUANA IS A BAD HOBBIT
Intractable Pain!

• MN legislature resisted initial efforts to add to certifying conditions
  – Required Commissioner of Health to investigate and decide by end of 2015
• Advisory panel of eight clinicians from across state
• Patient input: electronic, in writing, and at several public forums
Intractable Pain Definition

- **Definition of Intractable Pain**
- **Minnesota Statutes, section 152.125 INTRACTABLE PAIN.**
- § Subdivision 1. Definition. For purposes of this section, “intractable pain” means a pain state in which the cause of the pain cannot be removed or otherwise treated with the consent of the patient and which, in the generally accepted course of medical practice, no relief or cure of the cause of the pain is possible, or none has been found after reasonable efforts. Reasonable efforts for relieving or curing the cause of the pain may be determined on the basis of, but are not limited to, the following:
  - (1) When treating a non-terminally ill patient for intractable pain, evaluation by the attending physician and one or more physicians specializing in pain medicine or the treatment of the area, system, or organ of the body perceived as the source of the pain; or
  - (2) When treating a terminally ill patient, evaluation by the attending physician who does so in accordance with the level of care, skill, and treatment that would be recognized by a reasonably prudent physician under similar conditions and circumstances.
Working Definition from MDH

“Pain whose cause cannot be removed and, according to generally accepted medical practice, the full range of pain management modalities appropriate for this patient has been used without adequate result or with intolerable side effects.”

Second opinion is not required.
What’s the evidence?

• Minnesota Evidence Based Practice Center
  – Literature “sparse and patchy”
  – 19 articles, 21 studies

• Low strength evidence
  – No benefit for pts with MS and central neuropathic pain
  – Improvement for peripheral neuropathic pain
  – All other evidence of insufficient strength to guide decisions
Final decision

• Advisory Panel – final vote 3 – 5 against
• Patient input was overwhelmingly in favor
• The Commissioner of Health decided to add intractable pain to the list of qualifying conditions.
  – Certification started July 2016, patients can purchase cannabis for this purpose beginning in August 2016
Should You Participate?

- Decision is philosophic, not scientific
  - Evidence based: No evidence of benefit, clear evidence of harms – vote no
  - Pragmatic: No evidence that there is no benefit, harms are minimal, by definition other treatment doesn’t work for intractable pain – vote yes
Intractable Pain Patients: Demographics
Intractable Pain (IP) Patients: First 6 months

- **2631 enrollees** between 8/1/16 and 1/31/17
Other Qualifying Conditions

- 14.9% of IP patients certified for more than just IP

<table>
<thead>
<tr>
<th>Other Qualifying Conditions</th>
<th># of Patients</th>
<th>% of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Muscle Spasms</td>
<td>330</td>
<td>12.5</td>
</tr>
<tr>
<td>IBD</td>
<td>23</td>
<td>0.9</td>
</tr>
<tr>
<td>Cancer</td>
<td>22</td>
<td>0.8</td>
</tr>
<tr>
<td>Seizures</td>
<td>20</td>
<td>0.8</td>
</tr>
<tr>
<td>Glaucoma</td>
<td>9</td>
<td>0.3</td>
</tr>
<tr>
<td>Terminal Illness</td>
<td>6</td>
<td>0.2</td>
</tr>
<tr>
<td>HIV/AIDS</td>
<td>4</td>
<td>0.2</td>
</tr>
<tr>
<td>Tourette Syndrome</td>
<td>0</td>
<td>0.0</td>
</tr>
<tr>
<td>ALS</td>
<td>0</td>
<td>0.0</td>
</tr>
</tbody>
</table>
Gender and Age

<table>
<thead>
<tr>
<th>Gender</th>
<th>% of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female</td>
<td>52.3</td>
</tr>
<tr>
<td>Male</td>
<td>47.1</td>
</tr>
<tr>
<td>Prefer Not to Answer</td>
<td>0.5</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Age (yrs)</th>
<th>% of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 - 4</td>
<td>0.1</td>
</tr>
<tr>
<td>5 - 17</td>
<td>0.4</td>
</tr>
<tr>
<td>18 - 24</td>
<td>2.7</td>
</tr>
<tr>
<td>25 - 35</td>
<td>13.4</td>
</tr>
<tr>
<td>36 - 49</td>
<td>26.9</td>
</tr>
<tr>
<td>50 - 64</td>
<td>37.5</td>
</tr>
<tr>
<td>65+</td>
<td>19.0</td>
</tr>
</tbody>
</table>
Certifying HCPs

- 296 HCPs certified the first 6 months of IP enrollees

<table>
<thead>
<tr>
<th>PAIN ASSESSMENT TOOL USED AT CERTIFICATION</th>
<th>% of Patients (n)</th>
<th>Avg Score</th>
<th>StDev</th>
<th>Score Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>PEG 3 Scale (0-10 scale)</td>
<td>40.2 (1058)</td>
<td>7.5</td>
<td>1.6</td>
<td>0 - 10</td>
</tr>
<tr>
<td>Pain Intensity Numerical Rating Scale: past 24 hours/today (0-10 scale)</td>
<td>37.7 (991)</td>
<td>6.8</td>
<td>1.9</td>
<td>0 - 10</td>
</tr>
<tr>
<td>Brief Pain Inventory - short form: Pain severity composite score (0-10 scale)</td>
<td>10.6 (278)</td>
<td>8.3</td>
<td>1.9</td>
<td>3 - 10</td>
</tr>
<tr>
<td>Oswestry Low Back Disability Index - (0% to 100% [most] disabled)</td>
<td>5.3 (139)</td>
<td>36.4</td>
<td>19.8</td>
<td>5 - 90</td>
</tr>
<tr>
<td>Neuropathic Pain Scale: Pain intensity (0-10 scale)</td>
<td>2.1 (54)</td>
<td>7.6</td>
<td>1.4</td>
<td>4 - 10</td>
</tr>
<tr>
<td>Brief Pain Inventory - short form: Pain interference composite score (0-10 scale)</td>
<td>2.0 (53)</td>
<td>9.6</td>
<td>8.5</td>
<td>3 - 49</td>
</tr>
<tr>
<td>Rheumatology Modified Health Assessment Questionnaire and Pain Scale</td>
<td>2.0 (52)</td>
<td>1.9</td>
<td>0.5</td>
<td>1 - 3</td>
</tr>
<tr>
<td>Brief Pain Inventory - long form</td>
<td>0.1 (2)</td>
<td>9.0</td>
<td>0.0</td>
<td>9 - 9</td>
</tr>
<tr>
<td>Unspecified</td>
<td>0.0 (1)</td>
<td>5.0</td>
<td>--</td>
<td>5 - 5</td>
</tr>
<tr>
<td>Karnofsky Performance Status Scale</td>
<td>0.0 (1)</td>
<td>0.0</td>
<td>--</td>
<td>0 - 0</td>
</tr>
<tr>
<td>No scale used</td>
<td>0.0 (1)</td>
<td>10.0</td>
<td>--</td>
<td>10 - 10</td>
</tr>
<tr>
<td>Quality of Life scale</td>
<td>0.0 (1)</td>
<td>49.0</td>
<td>--</td>
<td>49 - 49</td>
</tr>
</tbody>
</table>
Data Collection

• Patient Experience Survey
  • Benefits and Harms

• HCP Survey on Patients
  • Benefits and Harms
  • Changes to other medications

• Symptom changes
  • Standard 8
  • Condition-specific
How do I Become a Certifying Health Care Practitioner (HCP)?

**HCP requirements:**

- Must be a MN-licensed:
  - Physician
  - Advanced Practice Registered Nurse (APRN)
  - Physician Assistant

- Must register with online medical cannabis registry to certify patients – *Participation is voluntary*
How do I Become a Certifying Health Care Practitioner?

• **HCP responsibilities:**
  - Certify diagnosis via online registry
  - Certify need for caregiver (if applicable)
  - Provide ongoing treatment
  - Allow MDH access to health records
  - Recertify annually
Where do I start the HCP Registration Process?

• Register online:

  Office of Medical Cannabis (OMC) website: mn.gov/medicalcannabis

  OMC Registry Login Page: https://apps.health.state.mn.us/cannabis/
Registration and Certification Information

- Intractable Pain Certification in the MN Medical Cannabis Program: A Primer for Health Care Practitioners (PDF)
  Presents detail on certifying patients for intractable pain and information resources on pain management and the potential for cannabis therapy as part of pain management.

- Health Care Practitioners for Medical Cannabis
  Three types of practitioners: doctors, physician assistants, and advanced practice registered nurse can certify that patients have a qualifying condition for medical cannabis. MDH will not maintain or publish a list of practitioners who are certifying these conditions.

- Serious health effect reporting

- Patient Information (PDF)
  Important information and warnings about using medical cannabis.

- Create Account
  Enroll in the Medical Cannabis Registry. You will need:
  - General information: name, address, email and phone.
  - Your medical license.
  - Your DEA license.
  - General information about the clinic(s) where you practice.

- Log in to Certify a Patient
  Once you have created your account, you can log in to the registry and certify a patient.

- Patient Annual Recertification and Enrollment
  Patients that are enrolled in the Minnesota Medical Cannabis Program must have their qualifying condition recertified by a Minnesota licensed physician, physician assistant (PA) or an advanced practice registered nurse (APRN) on
I’ve Submitted My Registration Application – Now What?

• Registration **PENDING email** and subsequent **phone follow-up** from OMC staff
OMC Approval of your Registration

(TTEST) MN Dept of Health: Change in Health Care Practitioner Registry Status - APPROVED

HealthDepartmentRegistry@state.mn.us

Dear Doctor Doktor:

OMC ID: H2218128

There has been an update to your Minnesota Medical Cannabis Patient Registry account. Your Health Care Practitioner status is now APPROVED. The Office of Medical Cannabis will now begin to review and change each of your certified patients' statuses to "Approved," provided they also have completed all the registration requirements.

When you certify a patient for the program, the patient is immediately sent an e-mail that gives them instruction for proceeding with enrollment and a document that contains important information and warnings about use of medical cannabis (see attachment). The e-mail encourages patients to consider information in the document before enrolling and while enrolled in the program. The document is also on the Office of Medical Cannabis website in the "For Patients" section.

If you need assistance, please contact the Minnesota Department of Health/Office of Medical Cannabis at health.cannabis@state.mn.us or 651-351-5568 (Metro) or 1-844-579-3381 (Non-Metro) if you have any questions.

[Signature]

http://mn.gov/medicalcannabis
Log Into Registry to Certify Patients

Medical Cannabis Registry Enrollment Process

Registration involves the following steps:

- Step 1: The patient visits his/her health care practitioner.
- Step 2: The patient's health care practitioner enrolls in the Medical Cannabis Registry and certifies that the patient has a qualifying medical condition.
- Step 3: The patient gets an email with a link to the enrollment application. If the patient has a caregiver, the caregiver will need to complete an application and pass a background check.
- Step 4: The patient (and caregiver, if applicable) will be notified by the Office of Medical Cannabis once the application is approved.
Certifying New Patients

To certify patients who have NEVER had their condition(s) certified previously by an HCP
Certifying New Patients

To certify new patients:

If this patient has NEVER been certified for the medical cannabis program, please enter in the patient's legal name and date of birth to start the certification process. These steps will prevent unnecessary duplication of patients in the registry.

If you've certified this patient before, please re-certify this patient from your "My Patients" list (click the re-certify link under the "Re-Certification" column).

If this patient has been certified before but never by you, please go to Re-Certification Search to re-certify this patient.

Patient Information

Patient First Name *

Patient Last Name *

Date of Birth *

mm/dd/yyyy

Submit
Certify Patient

Patient Information

Email Address *
LuuLee.LeeLaLa@gmail.com

Patient First Name *
Tywin

Patient Middle Initial

Patient Last Name *
Lannister

Date of Birth *
01/01/1901

Phone Number

Patient Clinic Site *
Casterly Rock Clinic

Certify Need for Caregiver
No

Patient Notes

Notes

Patient Medical Condition(s): (check all that apply)

Patient Medical Conditions *

☐ Intractable Pain

☐ Post-Traumatic Stress Disorder (PTSD) - Meeting DSM-5 Criteria

☐ Cancer - Severe or chronic pain

☐ Cancer - Nausea or severe vomiting

☐ Cancer - Cachexia or severe wasting

☐ Terminal Illness - Severe or chronic pain

☐ Terminal Illness - Nausea or severe vomiting

☐ Terminal Illness - Cachexia or severe wasting
- Glaucoma
- Human Immunodeficiency Virus (HIV) or Acquired Immune Deficiency Syndrome (AIDS)
- Tourette Syndrome
- Amyotrophic Lateral Sclerosis (ALS)
- Seizures, including those characteristic of Epilepsy
- Severe and persistent muscle spasms, including those characteristic of Multiple Sclerosis (MS)
- Inflammatory Bowel Disease, including Crohn's Disease

Please check this box to review and accept the legal acknowledgement, consent, and disclosure statements.
Certifying Patients Who Have PREVIOUSLY had their Conditions Certified (i.e., re-certification)

To certify patients who’ve previously been certified by an HCP
Certifying Patients Who Have PREVIOUSLY had their Conditions Certified (i.e., re-certification)

Re-Certification Search

If you are:
1) Re-certifying an existing patient for re-enrollment OR their 90-day certification has expired
   AND
2) You did not previously certify this patient yourself

Please have the patient supply the e-mail address tied to their Registry account or their Registry Patient ID, as well as their date of birth to be re-certified. Please enter patient’s information below to pull up their record.

If the patient does not remember their Patient ID or the e-mail address they used to register with the program, please have the patient contact OMC (651-201-5598 metro or 1-844-879-3381 non-metro).

Patient Information

Patient Email  

Patient ID  

Date of Birth *  
mm/dd/yyyy

[Search]
Other Stuff

• Electronic Medical Records
• Legal Issues
• Cannabis and Opioids

• Assume best intentions

• For more information
EMR Concerns

• Problem List
  – ICD-10: Z79.899
  – Long term (current) use of other medications
  – Shows up as “Medical Marijuana Use”

• Medication List
  – Will need to create a historical notation
  – Unsure if should put dose here or Problem List
Legal Issues

• Does “certification” put you at risk?
  – Not for criminal prosecution
  – Cole memorandum

• Malpractice risk – low but present
  – Remember HCP role: for questions about taking the cannabis, refer pt to dispensing pharmacist
  – Still need to provide care for condition

• For patient
  – Random drug tests
  – Worker’s compensation
  – ADA
Cannabis and Opioids

• States with medical cannabis laws have a 25% lower average opioid death rate compared to others.

• Among 274 chronic pain patients who were given medical cannabis, opioid consumption at follow-up decreased by 44 percent.
  – Clin J Pain. 2016 Feb 17
Assume Best Intentions

• Of each other
  – We all want what is best for the patient
• Of patients
  – They’re not all (or even mostly) “drug-seekers”
• Government
  – Minnesota Department of Health was (and is) gratifyingly responsive and practical
For More Information

Go to the Minnesota Department of Health web site: Google “MDH cannabis”.

For good evidence review, click of “For Health Care Practitioners.”

For intractable pain in, “About the Minnesota Medical Cannabis Program” then “Intractable Pain.”