



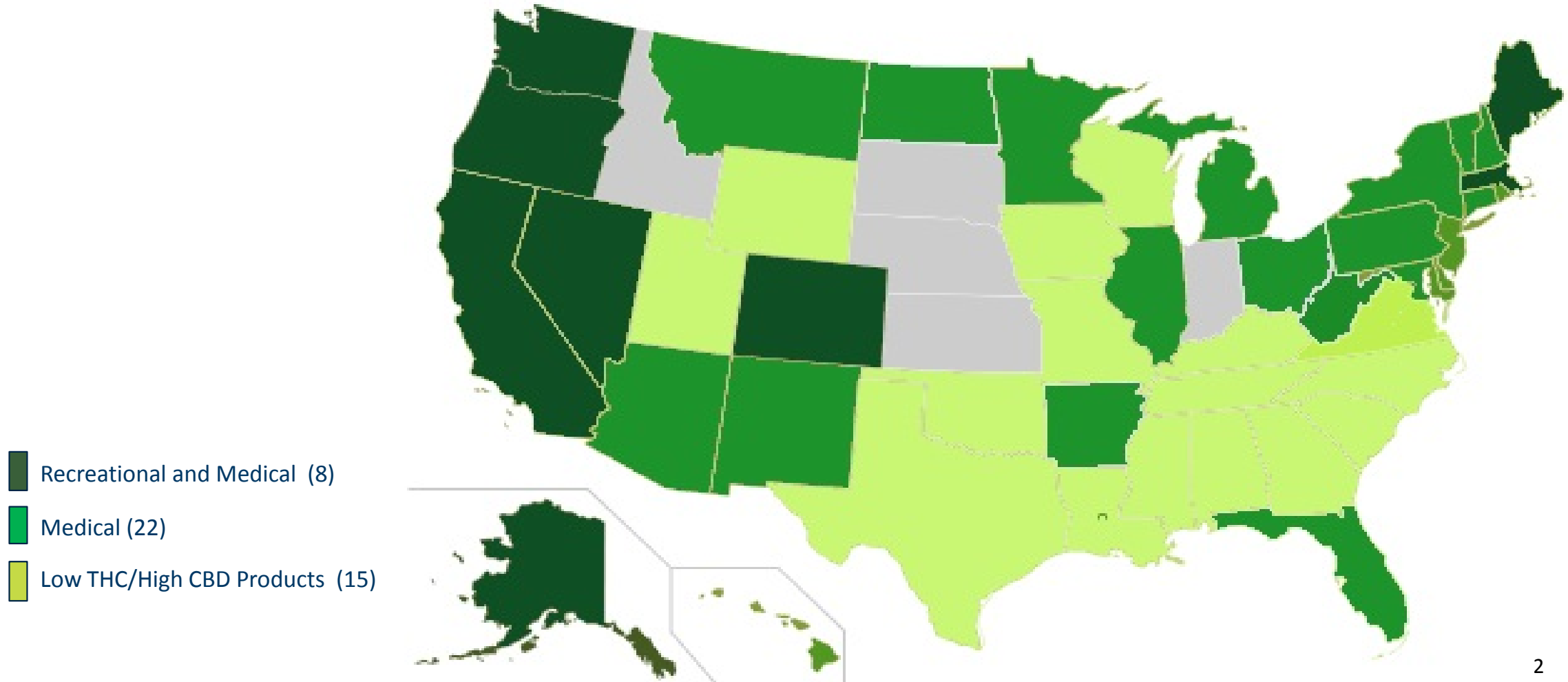
# Minnesota Medical Cannabis Program

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ECHO Program, St. Gabriel's Family Medical Center - January 16, 2019

# Office of Medical Cannabis

Most states have some variety of medical cannabis program



# However:

- State medical cannabis programs are illegal under current federal law

# Minnesota's program is different:

- No smokeable or plant form marijuana (only liquids and oils in capsule, tincture, or vaporized form. Topical preparations of oils allowed starting August, 2017)
- Commitment to learning from experience with the program (reports and observational studies on effectiveness, side effects, etc.)

# Qualifying Medical Conditions

- Cancer – with severe or chronic pain, or nausea, or cachexia
- Glaucoma
- HIV/AIDS
- Tourette's Syndrome
- Amyotrophic Lateral Sclerosis
- Seizures, including those characteristic of epilepsy
- Severe and persistent muscle spasms, including those characteristic of multiple sclerosis

# Qualifying Medical Conditions (continued)

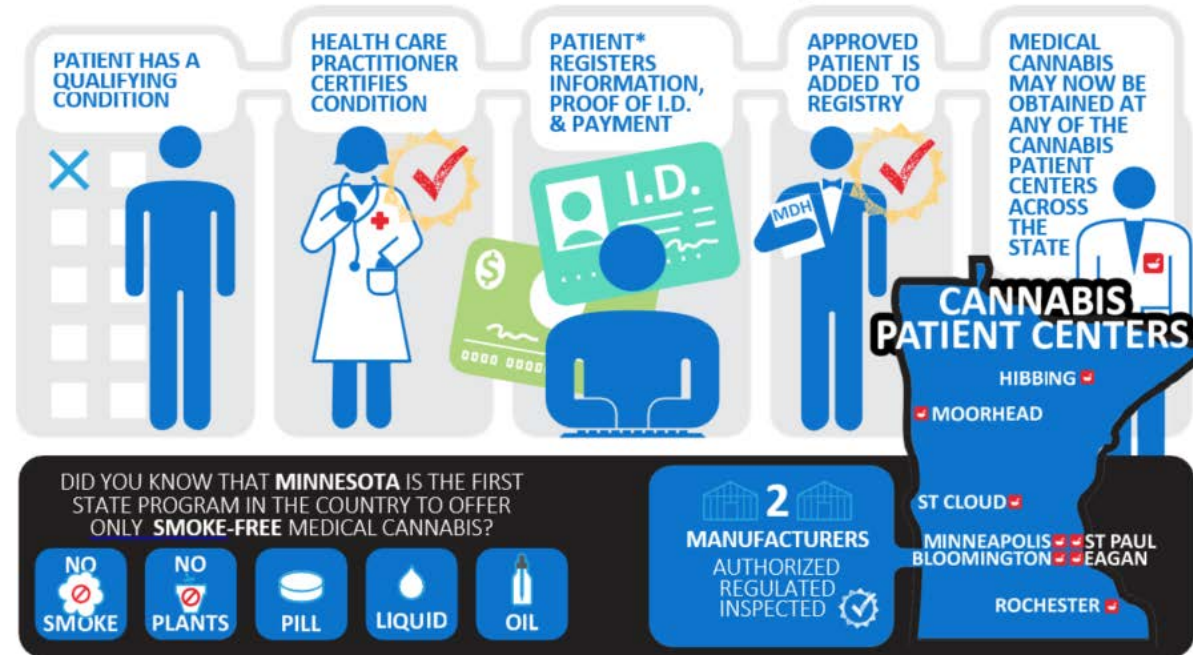
- Inflammatory Bowel Disease, including Crohn's Disease
- Terminal Illness with life-expectancy < 1 year – with severe or chronic pain, or N/V, or cachexia
- Intractable Pain (effective August 1, 2016)
- PTSD (effective August 1, 2017)
- Autism (effective August 1, 2018)
- Obstructive Sleep Apnea (effective August 1, 2018)
- Alzheimer's Disease (effective August 1, 2019)

# Patients

- Must be Minnesota resident (no reciprocity with other state medical cannabis programs)
- Must enroll in registry and agree that data in registry can be used for aggregate reports and research May line up designated caregiver(s), who must register, undergo background check, and be approved
- Annual enrollment fee of \$200 (reduced to \$50 for persons receiving state medical assistance)
- Cost of medical cannabis will be out of pocket; manufacturers may provide discounts for financial hardship

# Office of Medical Cannabis

## Overview of MN Medical Cannabis Program



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

**MDH** Minnesota Department of Health



# 14,467 Active Patients (as of Jan. 7, 2019)

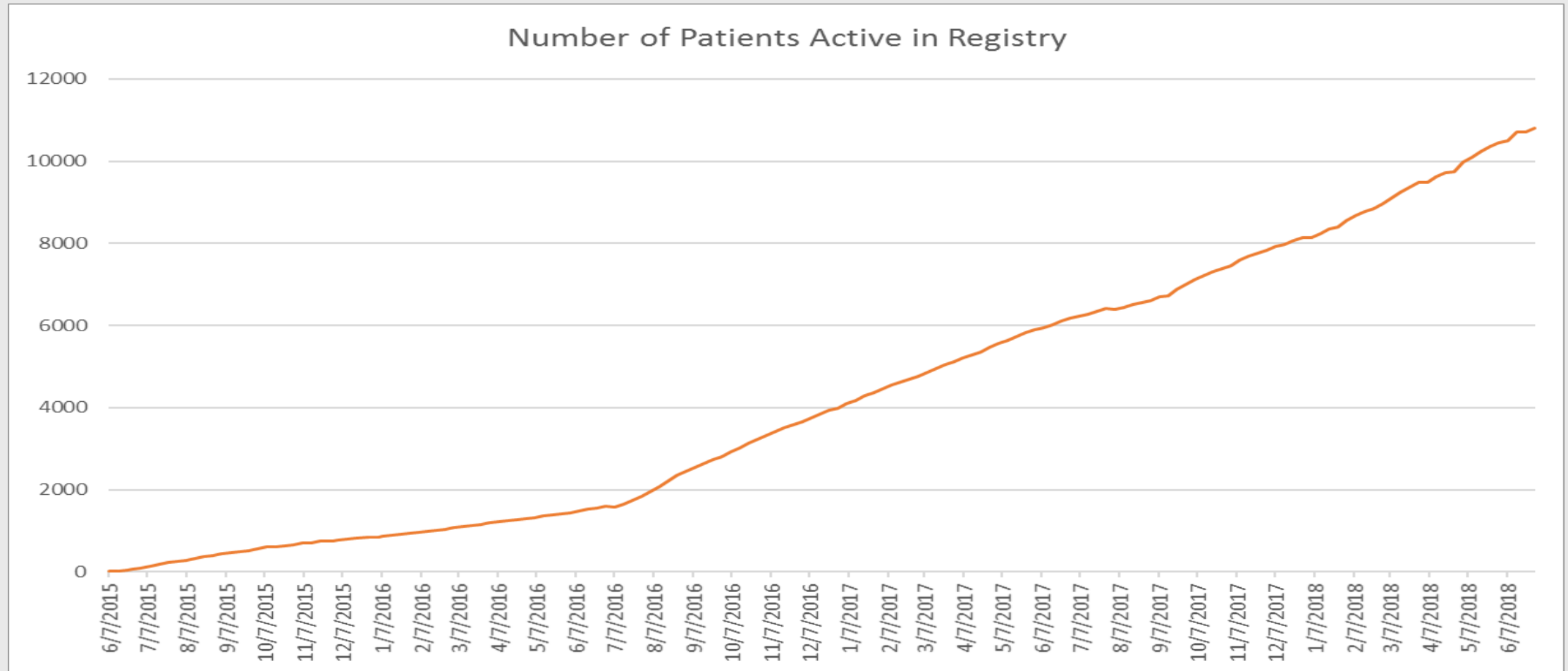
- 64% Intractable Pain
- 16% PTSD
- 13% Severe and persistent muscle spasms
- 9% Cancer
- 4% Seizures
- 3% Inflamm. Bowel Disease, Obstructive Sleep Apnea, Autism
- 1% Terminal illness, Tourette syndrome, HIV/AIDS, Glaucoma
- < 1% ALS

Note: 14% of patients >1 condition

# 14,467 Active Patients (as of Jan. 7, 2019)

Age distribution	0-4	(<1%)
	5-17	( 3%)
	18-24	( 4%)
	25-35	(15%)
	36-49	(27%)
	50-64	(32%)
	65+	(19%)
Gender: M/F	49%/51%	

# Weekly Number of Active Patients



# Registered Caregivers

- The Department of Health will only register a caregiver if a health care practitioner has certified the patient needs a caregiver
- Registered caregivers apply to and register with the Department of Health separately from the patient under their care
- Caregivers must be at least 21 years and must pass a background check. Persons who have been convicted of a state or federal felony violation of a controlled substances law are disqualified.
- Limit of one patient per caregiver, unless patients share same address.

# Certifying Health Care Practitioners

- Physicians, APRNs, or PAs
- Participation is voluntary; protection from disciplinary action by Medicine, Nursing, and Pharmacy Boards for participation
- Register in the program registry system (once)
- Certify patient has qualifying condition (and annual recertification)
- Indicate (when appropriate) patient has disability causing inability to access or administer medical cannabis (allows patient to line up caregiver)
- Acknowledge medical relationship with patient and sufficient knowledge of history, physical findings and testing results to certify diagnosis; treatment plan; available for ongoing care
- Agree to provide health record data at request of Commissioner
- Certifying practitioner able to view product purchases and use instructions, symptom scores, side effects

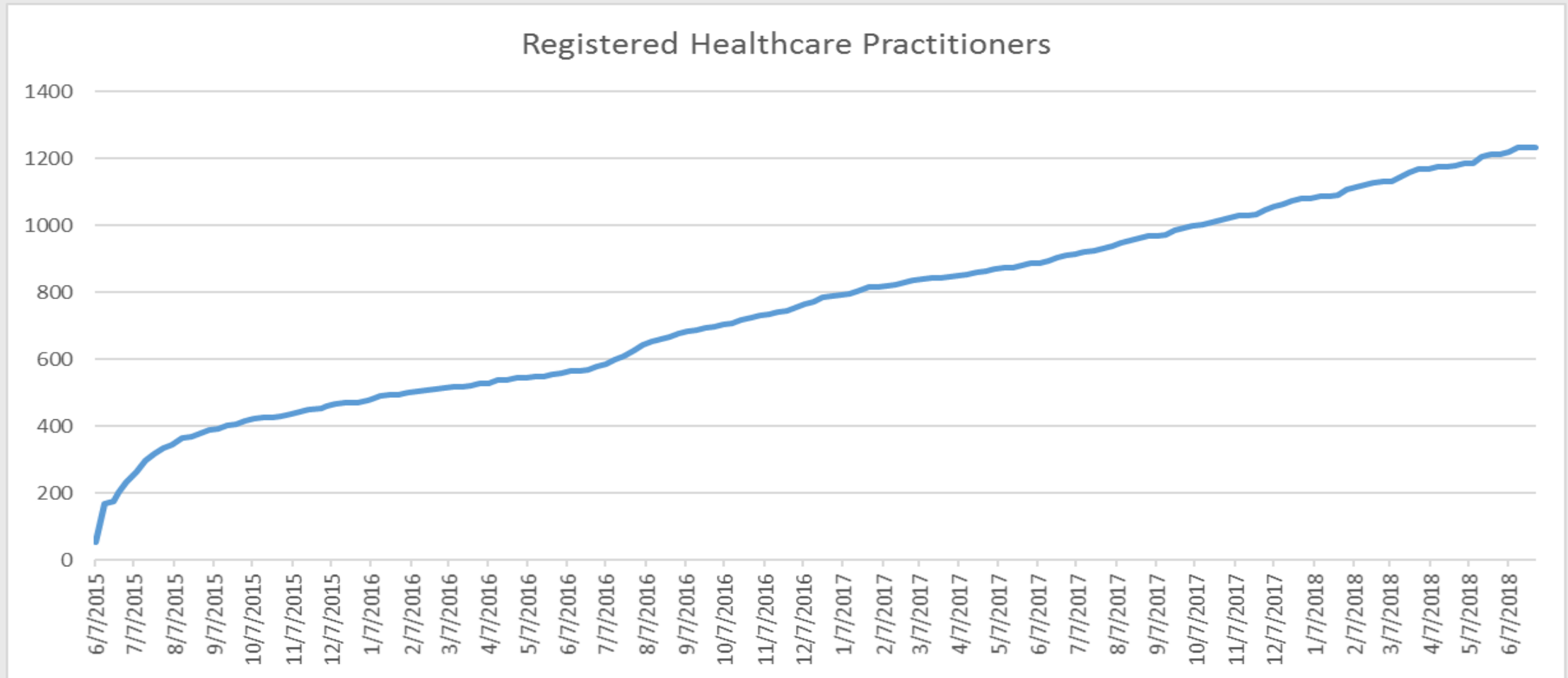
# Registered Health Care Practitioners

As of Jan. 7, 2019:

**1417 registered**

- 75% physicians
- 18% advanced practice registered nurses
- 7% physician assistants

# Cumulative Number of Registered HCPs



# Endocannabinoid System

- New knowledge over the past 30 years
- Complex systems of receptors and ligands modulating nerve discharge and immune system
- Endocannabinoids are molecules produced by the body that are similar to the phytocannabinoids found in the cannabis plant (e.g. THC, CBD).
- Best characterized endocannabinoids: anandamide and 2-AG (2-arachidonoyl glycerol)
- Cannabinoid receptors:
  - CB1 – mostly in central nervous system , especially brain (but few in brain stem), some in peripheral and GI nerve systems
  - CB2 – mostly on T-cells, also B-cells and macrophages
  - Additional receptors are being identified



# Manufacturing and Distribution

- Two grower/manufacturer/distributors, each with one growing/manufacturing site and 4 distribution centers. Patients not limited to which distribution centers they can visit.
  - <http://www.leaflineabs.com/>
  - <http://minnesotamedicalsolutions.com/>
- Pharmacist at distribution center consults with patient and recommends formulation and dose (max 30 day supply) Patient symptom measures and side effects captured at each visit to distribution center

# Extraction and Refining

- Harvesting
- Drying
- Cutting/shredding
- Supercritical CO2 extraction (high pressure liquid CO2)
- Separation (sometimes) – to isolate specific cannabinoids
- Mixing (sometimes) – to adjust THC:CBD ratio
  
- Note: Sativex – approved for use in Canada, UK, multiple European countries and elsewhere, is a cannabis extraction product.

# Extract Components

- Cannabinoids
  - >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
  - Pharmacologically active. Some evidence of synergistic action with cannabinoids, but much more study needed to define clinical role.
- Other (flavonoids, fats, more)

# Product Composition

- Different medical cannabis products in MN are characterized by different ratios of THC:CBD and mode of delivery (capsule/oral suspension, tincture, oil for vaporization, topical)
- The two manufacturers each determine their product line, which will evolve over time. But each specific product is to remain consistent as long as it is produced.
- Current products listed on the two companies' web sites (links on Office of Medical Cannabis web site).

# Laboratory Testing

- Content – cannabinoid profile
- Contamination:
  - Metals
  - Pesticides
  - Microbials
  - Residual solvents
- Consistency and stability

# Cannabinoid Pharmacokinetics

- Absorption
  - Vaporized: peak blood concentration at 5-10 min. Peak CNS effect delayed (around 15 min?) by blood/brain barrier crossing. Higher bioavailability than oral
  - Oral: peak blood concentration at 2-4 hours and more prolonged effect (4-6 hours) than with vaporized (3-4 hours)
  - Oromucosal: similar to oral
- Distribution
  - Highly lipophilic with much taken up by fatty tissues and released slowly. Plasma protein binding – 97% (11-hydroxyl THC metabolite strongly binds albumin)

Health Canada, *Cannabis and the cannabinoids: Information for health care professionals* 2013.

# Cannabinoid Pharmacokinetics (continued)

- Metabolism
  - Metabolized in liver through Cytochrome P450 system
  - Oral – higher blood levels of active metabolite 11-hydroxy THC due to first-pass metabolism. Part of reason for longer duration of effect (4-6 hours) with oral route
- Excretion
  - Feces (65%) and urine (20%)
  - After 5 days 80-90% of total dose excreted

Health Canada, *Cannabis and the cannabinoids: Information for health care professionals* 2013.

# Acute Intoxication Effects

- Vary based on:
  - Composition of product, route of administration, and dose
  - Patient experience with cannabis
  - (Likely) factors related to individual differences in endocannabinoid system and cannabinoid metabolism
- Common adverse effects – typically mild and resolve spontaneously
  - Dizziness, fatigue, dry mouth, lightheadedness, euphoria/dysphoria, (long list)



# More Serious Acute Intoxication Effects

- Psychotic episode
- Anxiety/panic attack
- Cognitive dysfunction
- Altered perception and reaction time

# Potential Long-Term Harm

**Caution:** much of the existing evidence is based on recreational use of street marijuana. Many studies are cross-sectional, where determining causality is problematic.

- Effect on brain development – esp. childhood/adolescence
  - Synapse formation, reduced functional connectivity
  - Cognition, memory, school performance
- Psychotic mental illness – exacerbation; earlier expression
- Addiction – cannabis use disorder develops in around 9% of recreational marijuana users; how this applies to the various products in the MN medical cannabis program is not known

Volkow et al. Adverse Health Effects of Marijuana Use. *NEJM* 2014;370:2219-2227.

# Learning from Participants' Experience

- Observational study from data reported by patient and their certifying health care practitioner
  - Patient-reported data at time of each medical cannabis purchase
  - Surveys
- Adverse event reporting

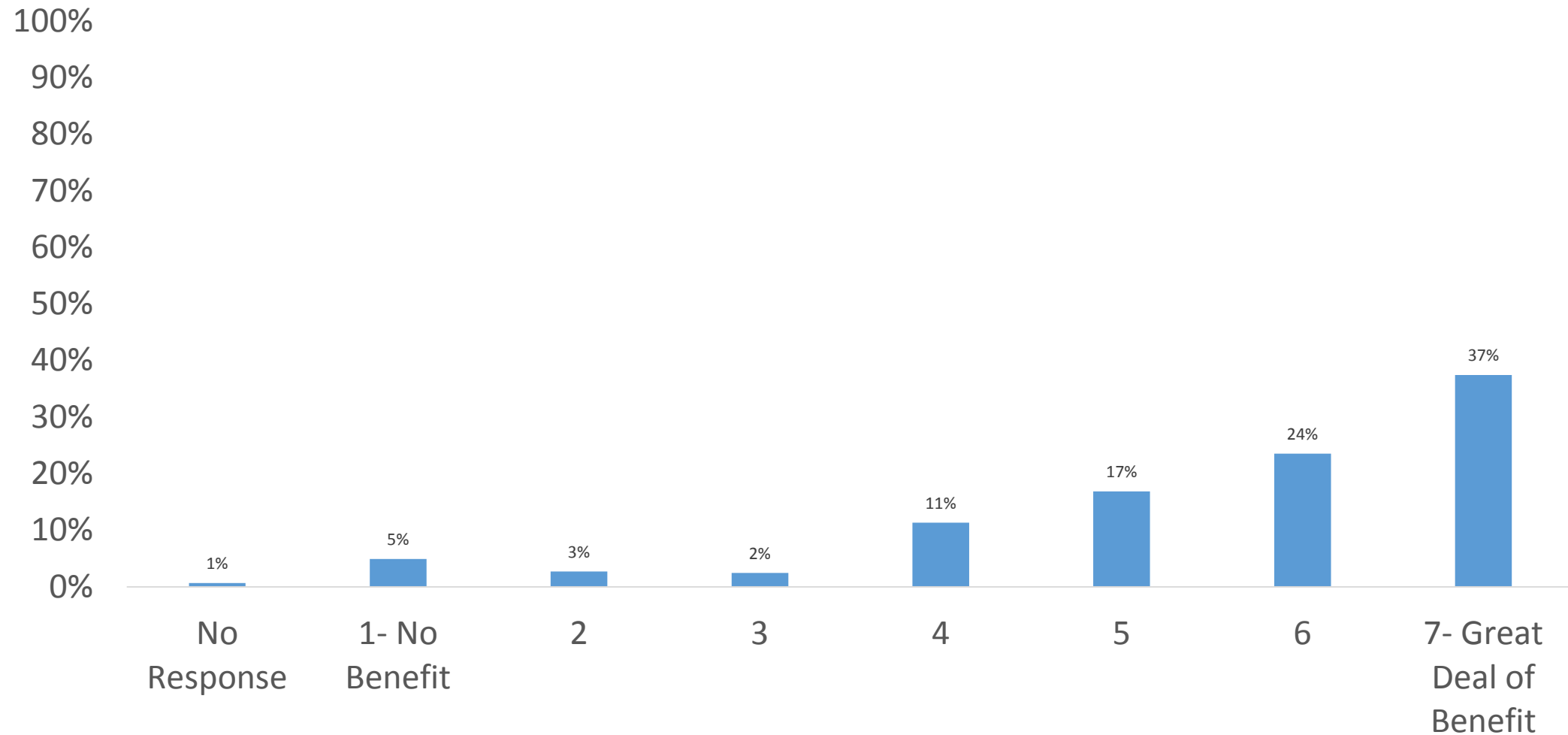
# Two Comprehensive Reports So Far

- Patients who enrolled during the first year (1660 patients)
  - Participation (counts, conditions, demographics, etc)
  - Purchasing and use patterns
  - Benefits
  - Adverse side effects
  - Affordability
- Intractable Pain patients who enrolled during the first five months after Intractable Pain became a qualifying condition (2245 patients)
  - Sections as above

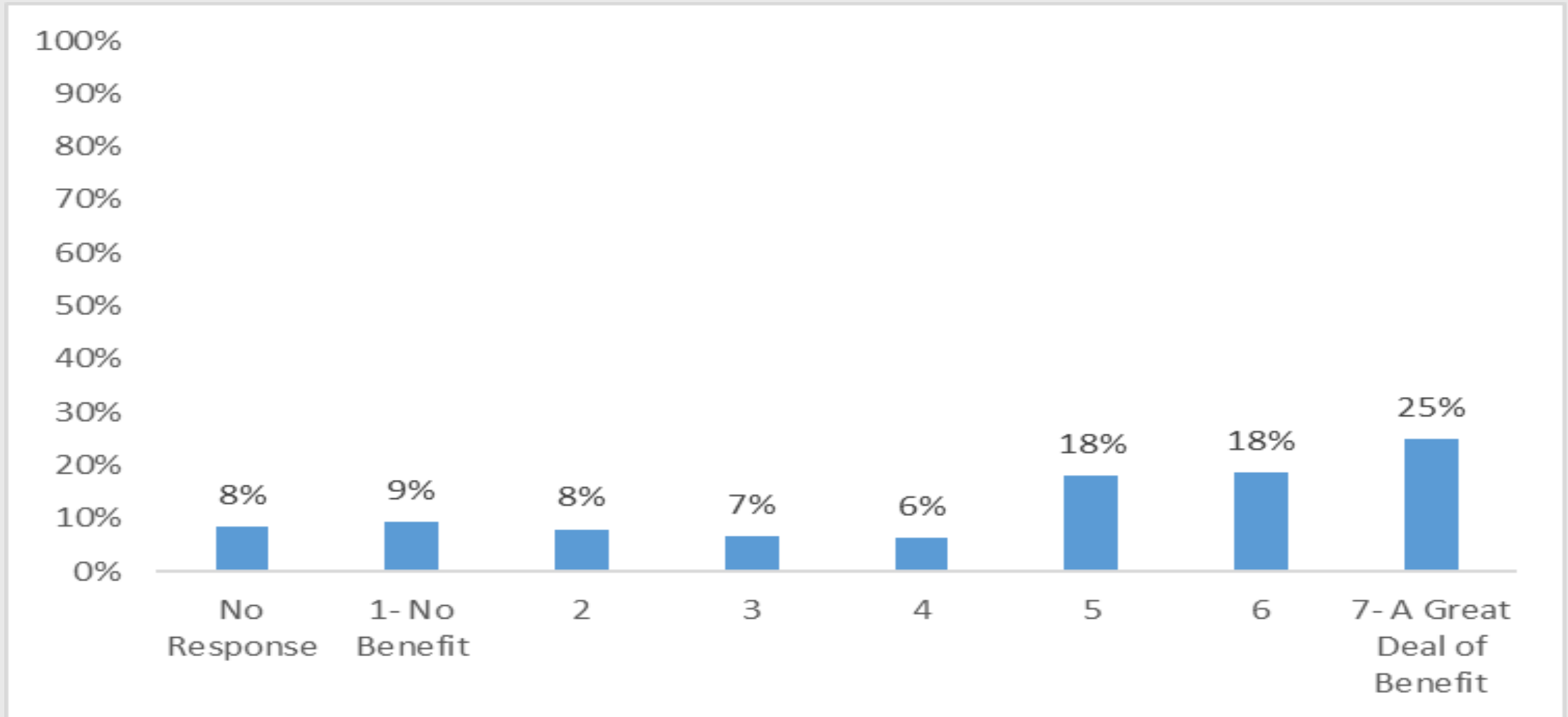
# Patients Certified for Intractable Pain (Aug-Dec, 2016)

- PEG Scale (patient-reported 3-item scale assessing pain intensity and interference with enjoyment of life and general activity):
  - 42% achieved  $\geq 30\%$  reduction; 22% both achieved and maintained  $\geq 30\%$  reduction, on average, over next four months
- Clinician pain scale assessment (six months):
  - 41% achieved  $\geq 30\%$  reduction
- Among patients using opioid medications when they started medical cannabis, 64% were able to reduce or eliminate opioid usage after six months (data from healthcare provider surveys)

# Intractable Pain Report: Patient-Perceived Benefit at 6-Month Survey (54% response rate)



# Intractable Pain Report: Clinician-Perceived Benefit at 6-Month Survey (40% response rate)



# Patient Survey Comments

- “After serving in the Marines from 2005-2009 my body has many ailments (arthritis, IBS, pinch nerve, fused disk, and others) and my PTSD was not always easy to handle. This program helps me a great deal in living a normal life that is comfortable and being able to continue my professional career. Before medical marijuana I was miss work too often and also miss out on life’s daily joys. Now I can do much more.”
- “At first it helped a lot but my seizures have returned.”
- “Within 1 week of use, my tics disappeared and have stayed gone even with occasional use. This has never happened previously in my life, so it is very effective”



# Adverse Effects

- 15% of patients reported  $\geq 1$  adverse effect (first year cohort)
- Of all reported adverse effects:
  - 47% mild (symptoms do not interfere with daily activities)
  - 44% moderate (symptoms may interfere with daily activities)
  - 9% severe (symptoms interrupt usual daily activities)
- As of January 10, 2019: four reports of serious adverse events – all four cannabinoid hyperemesis syndrome. Each patient recovered fully after discontinuing the high THC products they were using.

# Thank you!

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<http://www.health.state.mn.us/topics/cannabis/>