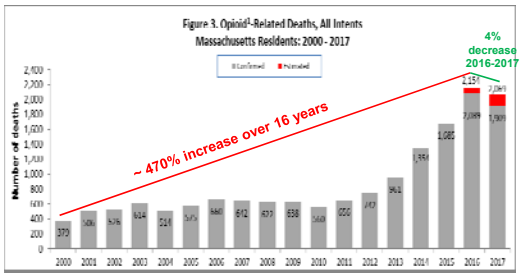
MASSACHUSETTS PAIN INITIATIVE

Monica Bharel, MD MPH
Commissioner of Public Health

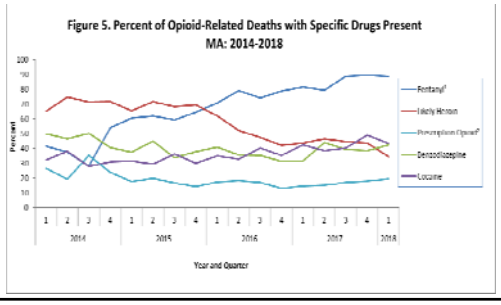
MASSACHUSETTS RESPONDS TO THE OPIOID EPIDEMIC

Monica Bharel, MD, MPH
Commissioner, Massachusetts Department of Public Health

Opioid-related overdose deaths declined in 2017 for the first time in 7 years – estimated 4 percent decrease from 2016



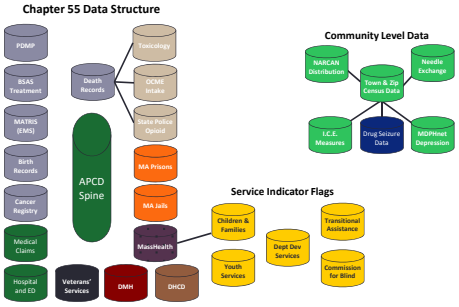
The proportion of fentanyl present in the toxicology of opioid-related overdose deaths rose to nearly **90 percent** in the first three months of 2018, while cocaine now surpassed heroin



Chapter 55 of the Acts of 2015

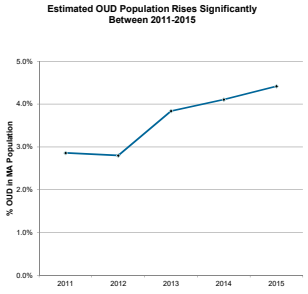
- Signed into law in August 2015
- Required a comprehensive report to the state legislature and cross-agency collaboration to address 7 specific questions about opioid-related deaths
- Specified major data sets across government
- Overcame legal barriers for use of some data

Chapter 55 Data Mapping

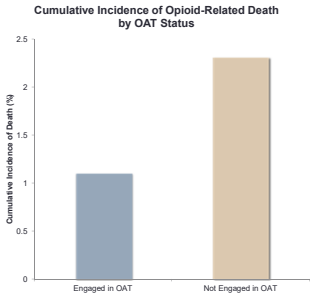


Chapter 55 – Key Finding

- Approximately 4% of individuals age 11 and older have OUD in Massachusetts.
- There was a sharp increase in 2013.
- This estimate is more than double previously reported figures.

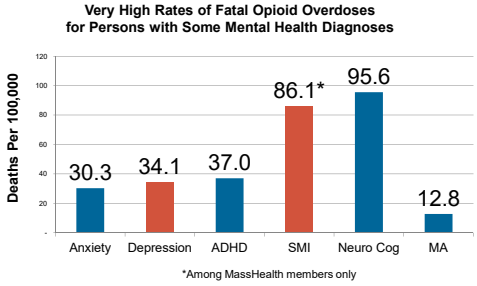


Chapter 55 Phase 1 Report – Key Finding

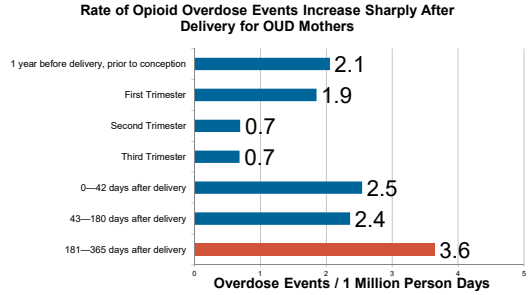


Following a non-fatal overdose, patients treated with methadone and/or buprenorphine (Opioid Agonist Treatment or "OAT" that block the effect of opioids) were significantly less likely to die; however, very few patients (~5%) engage in OAT following a non-fatal overdose.

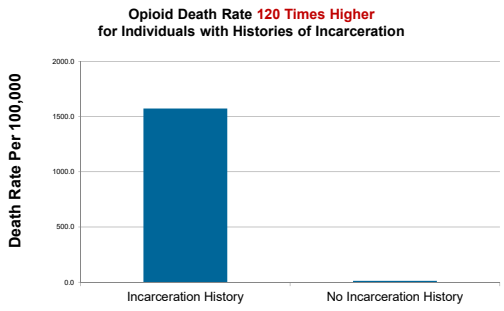
Individuals with Serious Mental Illness



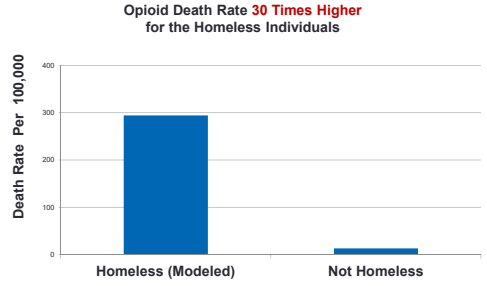
Pregnant and Postpartum Risk



Persons with Histories of Incarceration



Persons Experiencing Homelessness

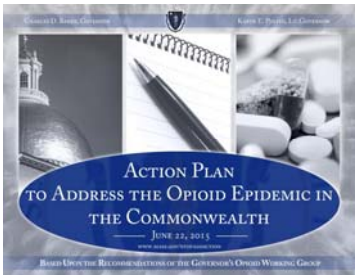


Data visualization of findings from Chapter 55 Report

http://www.mass.gov/chapter55/

Governor Baker's Opioid Working Group

Prevention Intervention Treatment Recovery



SURVEY: REASON FOR PRESCRIPTION PAINKILLER MISUSE

Source: Boston Globe and Harvard T.H. Chan School of Public Health, Prescription Painkiller Abuse: Attitudes among Adults in Massachusetts and the United States

Medical and Dental Education Core Competencies for the Prevention and Management of Prescription Drug Misuse

Working Groups: A Voluntary Approach

- **Four working groups – medical, dental, APRN, and PA – composed of over 60 national experts** representing all of the Commonwealth's prescriber programs voluntarily met over the course of 6 months and 9 in-person meetings.
  - Expertise in medical, dental, and nursing education, addiction medicine, oral and maxillofacial surgery, psychiatry, public health, restorative dentistry, neurology, pediatrics, family medicine, community health, emergency medicine, toxicology, anesthesia, pharmacology, and biomedical and biomaterial sciences.
- **The working groups conducted a review of nearly 50 academic journal articles** related to prescription drug misuse, substance use disorders, safe prescribing, and pain management.
- **This research highlighted a need for documented education standards for prevention and management of prescription drug misuse** (despite a strong presence of pain management and safe prescribing documentation). Given these findings, we chose to direct our focus on this highlighted educational need.
- *"What we found is that **less than 10 percent of American medical schools have a course in addiction.** Ditto nursing, ditto pharmacy schools. So, contemporary*

Framing Core Competencies

- **The core competencies are framed from the perspective of an encounter with a person** experiencing pain and/or other symptoms for which a prescription medication with the potential for misuse may be indicated.
- **The goal of these competencies is to support our workforce** with the skills and foundational knowledge needed to care for those suffering from substance use disorders during their education and training – the period during which they are developing their lifelong habits and routines. These core competencies are designed to serve as a vital bridge between education/training and their on-the-ground work.
- While the core competencies were initially developed for prescribers, you will see that most of the **competencies are not about safe prescribing, but about how to best screen for, interact with, refer, and care for individuals suffering from, or at risk for, substance use disorders**.

Developing Core Competencies for the Prevention and Management of Prescription Drug Misuse: A Medical Education Collaboration in Massachusetts

Karen H. Antman, MD, Harris A. Berman, MD, Terence R. Flotte, MD, Jeffrey Flier, MD, Dennis M. Dimitri, MD, and Monica Bharel, MD, MPH

Adopted by all 4 medical schools, 3 dental schools and all PA and APRN programs in MA

Medical Core Competencies: Primary Prevention Domain

- **Preventing Prescription Drug Misuse:**
  Screening, Evaluation, and Prevention

1. **Evaluate a patient's pain** using age, gender, and culturally appropriate evidence-based methodologies.
2. **Evaluate a patient's risk for substance use disorders** by utilizing age, gender, and culturally appropriate evidence-based communication skills and assessment methodologies, supplemented with relevant available patient information, including but not limited to health records, family history, prescription dispensing records (e.g. the Prescription Drug Monitoring Program or "PMP"), drug urine screenings, and screenings for commonly co-occurring psychiatric disorders (especially depression, anxiety disorders, and PTSD).
3. Identify and describe potential **pharmacological and non-pharmacological treatment** options including opioid and non-opioid pharmacological treatments for acute and chronic pain management, along with patient communication and education regarding the risks and benefits associated with each of these available treatment options.

Medical Core Competencies: Secondary Prevention Domain

- **Treating Patients At-Risk for Substance Use Disorder:**
  Engage Patients in Safe, Informed, and Patient-Centered Treatment Planning

4. **Describe substance use disorder treatment options**, including medication-assisted treatment, as well as demonstrate the ability to appropriately refer patients to addiction medicine specialists and treatment programs for both relapse prevention and co-occurring psychiatric disorders.
5. **Prepare evidence-based and patient-centered pain management and substance use disorder treatment plans** for patients with acute and chronic pain with special attention to safe prescribing and recognizing patients displaying signs of aberrant prescription use behaviors.
6. **Demonstrate the foundational skills in patient-centered counselling and behavior change** in the context of a patient encounter, consistent with evidence-based techniques.

Medical Core Competencies: Tertiary Prevention Domain

- **Managing Substance Use Disorder as a Chronic Disease:**
  Eliminate Stigma and Build Awareness of Social Determinants

7. **Recognize the risk factors for, and signs of, opioid overdose** and demonstrate the correct use of naloxone rescue.
8. **Recognize substance use disorders as a chronic disease** by effectively applying a chronic disease model in the ongoing assessment and management of the patient.
9. **Recognize their own and societal stigmatization and biases against individuals with substance use disorders** and associated evidence-based medication-assisted treatment.
10. **Identify and incorporate relevant data regarding social determinants of health** into treatment planning for substance use disorders.

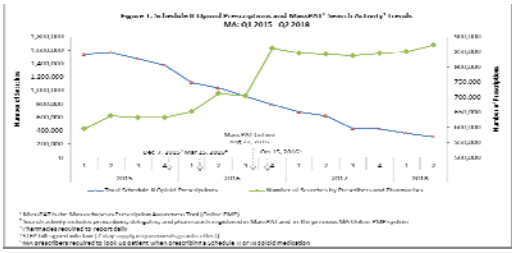
Further expansion of opioid education

- Core Competencies adopted by:
  - All 4 Medical Schools in MA
  - All 3 Dental Schools in MA
  - All PA programs in MA
  - All APRN programs in MA
  - All Schools of Social Work in MA
  - Some Massachusetts Medical Residency Programs
  - Massachusetts Community Health Centers
  - Pennsylvania state medical schools
- In Progress:
  - Pharmacy Schools in MA
  - Veterinary Schools in MA

New MassPAT Campaign

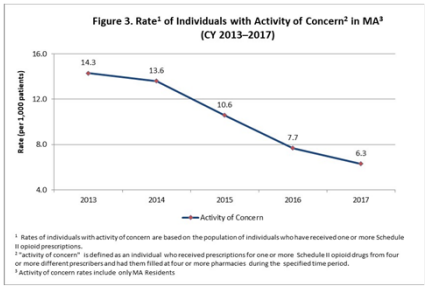
- Building awareness and promoting the use of the Massachusetts Prescription Awareness Tool

Prescription Monitoring Program – Data Trends



- Registered MassPAT providers conducted an **additional 100,000 searches** in the second quarter of 2018 compared to the previous quarter, which is the largest increase in a single quarter
- Approximately 258,000 people in Massachusetts received prescriptions for Schedule II opioids in the second quarter of 2018, which is more than **30 percent decrease** compared with Q1 2015, when there were 390,532 individuals receiving Schedule II opioids

The rate of individuals with activity of concern decreased by 56 percent from 14.3 to 6.3 per 1,000 individuals between 2013 and 2017



WHAT IS STIGMA? | TAKE THE PLEDGE
TAKE THE QUIZ | SHOW YOUR SUPPORT
FOR HELP: 1-800-327-5050 (tty: 1-800-439-2370)

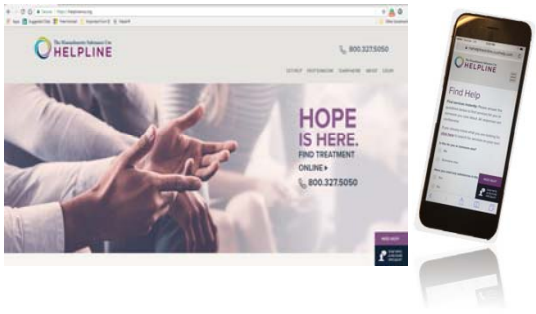
Access to Naloxone (Narcan®)

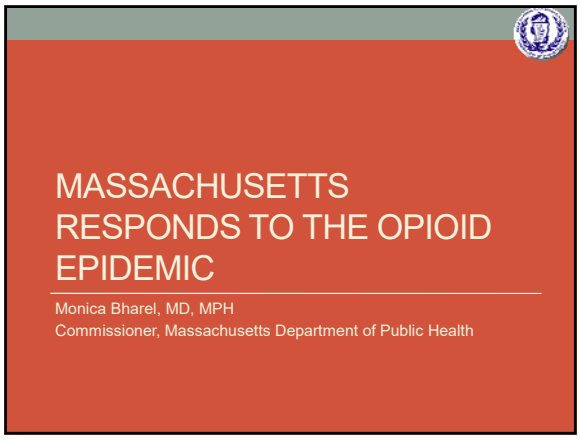
- First Responders
- Bystanders
- Pharmacies
- Community Bulk Purchasing Program

Treatment

- 800+ more Tx beds since 2015
- Ended use of prison for women with SUD
- Expanded Office Based Treatment
- Treatment for High-Risk Populations

Revamped Helpline




MASSACHUSETTS RESPONDS TO THE OPIOID EPIDEMIC
Monica Bharel, MD, MPH
Commissioner, Massachusetts Department of Public Health

Department of Public Health

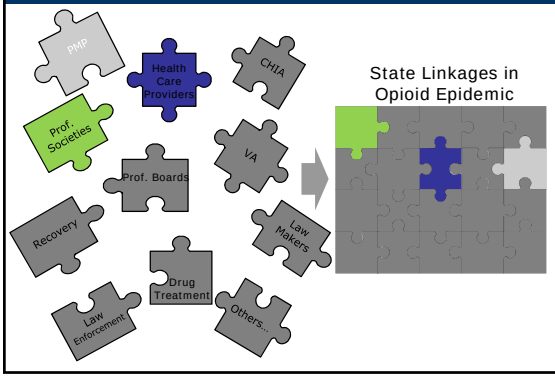
Prescription Monitoring Program
David Johnson, Director

The Massachusetts Pain Initiative's Fall 2018 Educational Program

October 25, 2018

Commonwealth of Massachusetts Department of Public Health

PMP is a Component in the Larger Opioid Effort



2

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Background

- The MA PMP was originally established by joint regulation of the Drug Control Program and Board of Registration in Pharmacy in 1992.
- Monthly reporting of only CII narcotics.
- No online access
- Program reviewed the data and notified law enforcement of potentially unlawful activity.

3

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PMP Maven

- The first online system went live in Jan. of 2011.
- Schedules III-V added
- Pharmacy data submission - weekly

4

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Opioid Working Group

Improve the Prescription Monitoring Program (PMP):

- Increase utilization by improving ease of use and expanding abuse alerts from the PMP to prescribers
- Ensure data compatibility of the PMP with other states & interface the PMP with electronic health records
- Enforce mandatory use of the PMP
- Require PMP data to be submitted within 24 hours by pharmacies

5

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MassPAT

The Prescription Monitoring Program's online tool, the Massachusetts Prescription Awareness Tool (MassPAT) is utilized by prescribers and pharmacists to help inform clinical decisions and thereby support the safe prescribing and dispensing of controlled substances.

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Department of Public Health

MassPAT

- MassPAT (MA Prescription Awareness Tool) provides a patient's prescription history (1 year) for Schedules II – V and Gabapentin to authorized end users (prescribers, pharmacists, and regulatory board investigators).
- Approximately 13 million prescription records per year.

7

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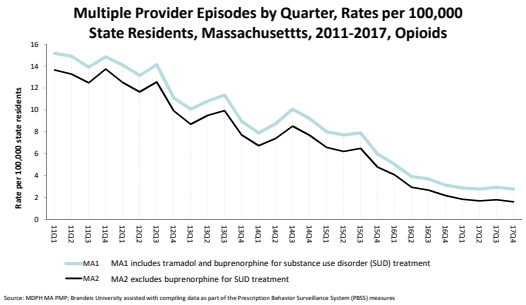
Department of Public Health

Multiple Provider Episodes



Source: MDPH MA PMP; Brandeis University assisted with compiling data as part of the Prescription Behavior Surveillance System (PBSS) measures

8

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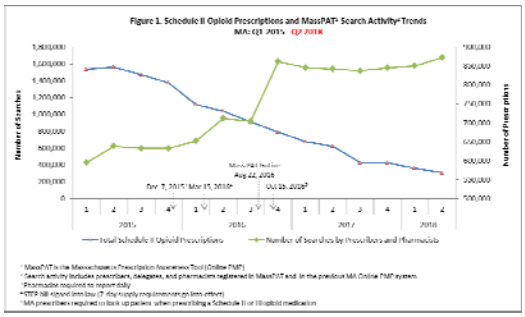
Department of Public Health



Source: MDPH MA PMP

9

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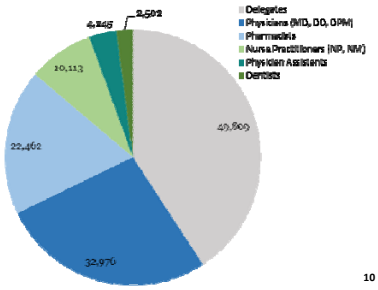
Department of Public Health

MassPAT Weekly Searches

122,107 Patient Searches Conducted in MassPAT from 12-04-2017 to 12-10-2017



Source: MDPH MA PMP

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Commonwealth of Massachusetts
Department of Public Health

The Law

MGL Ch. 94C, Sec. 24A requires a practitioner to utilize the Prescription Monitoring Program:

- Each time prior to issuing a prescription to a patient for a narcotic drug in Schedule II or III
- Prior to prescribing to a benzodiazepine to a patient for the first time

Chapter 208 of the Acts of 2018

- Check each time before prescribing a benzodiazepine (requires the promulgation of regulations)

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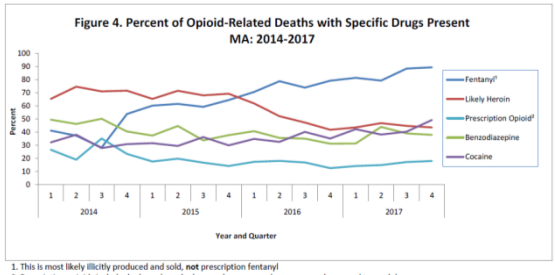

https://www.mass.gov/lists/current-opioid-statistics

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Changes to the Law

- The department may enter into agreements to permit health care facilities to integrate secure software or information systems into their electronic medical records for the purpose of using prescription monitoring program data to perform data analysis, compilation, or visualization, for purposes of diagnosis, treatment or coordinating care of the practitioner's patient.

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Law Enforcement Access

For Local, state and federal law enforcement, personnel of the United States attorney, office of the attorney general, a district attorney or prosecutorial officials working with the executive office of public safety and security, access to PMP data requires that the data request is in connection with a bona fide specific controlled substance or additional drug-related investigation and accompanied by a probable cause warrant issued pursuant to chapter 276.

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PMP Data

The MA PMP collects dispensing information on Massachusetts Schedule II - V controlled substances dispensed pursuant to a prescription. **As of August 1, 2017 Gabapentin, a Schedule VI is also collected.**

- The Department analyzes PMP data to:
  - Determine prescribing and dispensing trends;
  - Provide patient prescription history information to prescribers and dispensers;
  - Provide educational information to health care providers and the public;
  - Provide case information to regulatory and law enforcement agencies concerning drug distribution and diversion.

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General Practice Prescribing

Prescribing of Schedule II and III Opioid Medications
Among General Practice Providers
(CY 2015 Q1 compared with CY 2018 Q1)

General Medicine[1]	CY 2015 Quarter 1	CY 2018 Quarter 1	Percent Decrease
Prescription Count	386,271	290,352	-24.8
Solid Quantity	27,497,738	19,969,056	-27.4
Total MME	486,472,698	342,965,400	-29.5
Days Supply per Patient	43.3	47.8	10.4
Number of Patients	173,284	120,460	-30.5
Number of Prescribers[2]	6,106	6,761	10.7

[1] Includes the following specialties (Internal Medicine, Family Medicine, Family Health, Adult Health, Adult Medicine, Primary Care, General Practice)

[2] Based on self reported specialty in MassPAT
Notes: Analysis excludes out of state prescribers; Excludes all buprenorphine medications

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Dental Prescribing

Dentists General Practice[1]	CY 2015 Quarter 1	CY 2018 Quarter 1	Percent Decrease
Prescription Count	45,801	24,420	-46.7
Solid Quantity	693,907	314,644	-54.7
Total MME	4,594,274	1,951,536	-57.5
Days Supply per Patient	3.8	3.2	-15.8
Number of Prescribers[2]	2,817	2,255	-20.0

[1] Includes both DDS and DMD (General Dentists)

[2] Based on a combination of prof degree specified in the DEA file and self reported specialty in MassPAT

Source: MDPH MA PMP

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Dental Prescribing

Dentists General Practice[1]	CY 2015 Quarter 1	CY 2018 Quarter 1	CY 2015 Quarter 1	CY 2018 Quarter 1	
Days Supply Range	Number of Prescriptions	Number of Prescriptions	Percent Prescriptions	Percent Prescriptions	Percent Change
3 days or less	30,826	19,179	67.3%	78.6%	16.8%
4-7 days	14,283	5,008	31.2%	20.5%	34.3%
8-10 days	394	94	0.9%	0.4%	55.6%
11-15 days	86	37	0.2%	0.2%	0.0%
> 15 days (Max = 30)	212	94	0.5%	0.4%	20.0%

[1] Includes both DDS and DMD (General Dentists)

Source: MDPH MA PMP

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Commonwealth of Massachusetts Department of Public Health — Helping People Lead Healthy Lives in Healthy Communities

Chapter 55: Linking Data

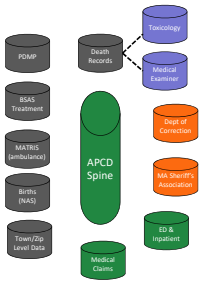
Data Sources

- DPH
- CHIA (MassHealth)
- EOPSS
- Jails & Prisons

System Attributes

- Data **encrypted** in transit & at rest
- Limited data sets **unlinked** at rest
- Simplified structure using **summarized** data
- No residual files after query completed
- Analysts can't see data
- Automatic cell suppression

Chapter 55 Data Structure



All Doors Opening

- Significant coordination within DPH
- Financial and technical support from MassIT's Data Office
- Coordination across agencies (legal & evaluation)
- High end machines for staff
- "Volunteer" analytic support from academia and industry

APCD = All Payer Claims Database

Commonwealth of Massachusetts Department of Public Health

Chapter 55 Collaboration

Chapter 55 – Key Findings from PMP Linkage

- Compared to the general population, those who received three months of prescribed opioids are four times as likely to die from an opioid-related overdose within one year, and 30 times as likely to die of an opioid-related overdose within five years.
- 58% of those who died of an opioid-related overdose had an active Rx opioid in the previous 12 months.
- The use of 3 or more prescribers within a 3 month period is associated with a 7-fold increase in risk of fatal opioid overdose
- Having a concurrent prescription for opioids and benzodiazepines results in a four-fold increased risk of opioid-related death.

Commonwealth of Massachusetts Department of Public Health

Data Submission Dispenser Guide

PMP AWARE™ PRESCRIPTION MONITORING PROGRAM

Data Submission Dispenser Guide
Massachusetts Prescription Monitoring Program (MA PMP)
Version 3.0
Published May 10, 2017

- The Data Submission Guide provides the guidelines, specifications, and instructions for submitting controlled substance prescription data to the MA PMP.
- Recent Changes to Data Submission Dispenser Guide:
  I. Customer ID must be collected at pick-up only.
  II. Customer ID must be collected for refills.
  III. Prescriber NPI must be submitted in each record.

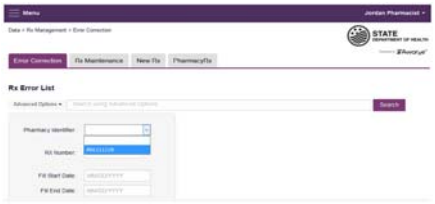
Commonwealth of Massachusetts Department of Public Health

Error Correction on MassPAT

Prescription Records with Errors are rejected and do not appear in MassPAT

Error Correction:

- Pharmacy staff who have been selected by the pharmacy and given privileges by the PMP will be able to view and correct errors for prescriptions submitted via sFTP, file upload, or Real-time to MassPAT that did not pass validation.



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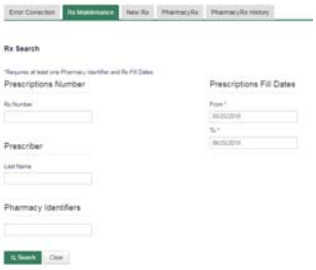
Rx Maintenance

For accepted files in need of correction, the Rx Maintenance feature on MassPAT can be utilized by Pharmacies.



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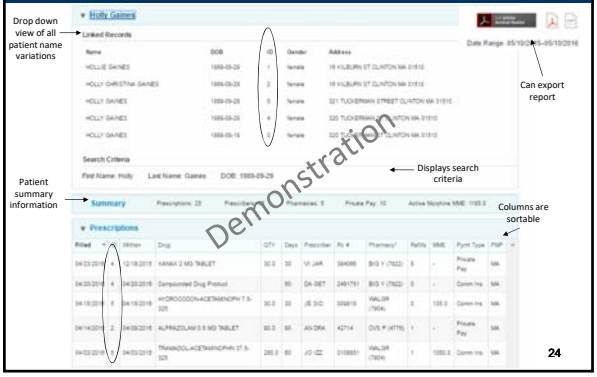
Example of MassPAT: Patient Report Data Matching



Workflow Improvements to MassPAT

Passwords no longer need to be changed every 90 days – it is now annual reset.

// forward slashes are auto-populated in patient date of birth

Integration of PMP data into EHR Systems

Delegates – helps with workflow and efficiency.

Compliance Report coming to MyRx

NarxCare Pilot

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EHR/EMR System Integration Overview

- The goal of integration is to provide a streamlined workflow to access MassPAT data through the providers Electronic Health Record (EHR).
  - Eliminating the need to log into a separate system and manually search for a patient.
- With integration, the a query to the PMP Gateway can be initiated directly from the patient's EHR to pull a patient's PMP record into the EHR.
- A one-time use HTML report will be returned for successful searches that find a patient match.
  - The report will appear similar to the MassPAT report providers are already familiar with.
- Practitioners will be required to have an active MassPAT account to perform searches.

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Integration Overview


TESTPATIENT, ALICE

Age: 118 Data as of: 3/27/2018

Demographics

Summary

Summary	Narcotics* (excluding buprenorphine):	Sedatives*	Buprenorphine*
Total Prescriptions: 2	Current Qty: 0	Current Qty: 0	Current Qty: 0
Total Prescribers: 1	Current MME/day: 0.00	Current LME/day: 0.00	Current mg/day: 0.00
Total Pharmacies: 1	30 Day Avg MME/day: 3.00	30 Day Avg LME/day: 0.00	30 Day Avg mg/day: 0.00

Prescriptions

Prescriptions Total Prescriptions: 2 Private Pay: 2

Fill Date	ID	Written	Drug	Qty	Days	Rx #	Prescriber	Pharmacy	Refill	Daily Dose *	Pymt Type	PMP
01/31/2018	1	01/31/2018	ACETAMINOPHEN-COD #3 TABLET	120	30	A00001	AL TES	ALICE	0	15.00 MME Private Pay		MA
10/17/2017	1	10/17/2017	ACETAMINOPHEN-COD #3 TABLET	120	30	A00001	AL TES	ALICE	0	15.00 MME Private Pay		MA

Providers Total Providers: 1

Name	Address	City	State	Zipcode	DEA
TESTPRESCRIBER, ALICE					BR1111111

Pharmacies Total Pharmacies: 1

Name	Address	City	State	Zipcode	DEA
ALICE'S PHARMACY	1111 FAKE ST	WICHITA			221234567

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Integration Request Process

- Massachusetts will cover all Appriss-related integration costs.
  - EHR vendors may have their own implementation fees which MA PMP will not cover.
- An online EHR System Integration Request Form has been created.
- The Provider will be required to complete:
  - Integration Request Form
  - Terms and Conditions
  - PMP Gateway Questionnaire
- Once submitted Appriss Health will contact the identified point of contact to discuss next steps within 7 business days.

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Massachusetts PMP EHR Integration Request Form

MA PMP STATEWIDE INTEGRATION

Please note, only authorized decision makers at the healthcare entity should complete the following forms.

Integration Process

1. Follow the instructions and complete ALL of the following:
   - Integration Request Form (located on the right of this page)
   - Terms and Conditions (Emailed to you within 24 hours)
   - PMP Gateway Licensee Questionnaire (Opens in a new window)
2. Once completed, your forms will be sent to MA PMP for review.
3. Once approved, MA PMP will submit your request to Appriss Health, the MA PMP software vendor, to begin the integration.
4. Appriss Health will contact you and/or your EHR/pharmacy management system vendor with next steps. Please allow up to 7 business days for this process to complete.

For more detailed information about this important initiative, please review the MA PMP EHR Integration Welcome Packet.

Please direct general questions regarding integration to the MA PMP at mapmp.dph@MassMail.State.MA.US.

Primary Point of Contact

First Name* Last Name*

Primary Point of Contact Email Address*

Job Title

Phone Number

Organization Information

Organization Name*

Organization Type*

- Please Select -

Organization Phone Number*

Integration Process

- Appriss Health will assign a Project Manager for every integration.
- Pre-production (test) credentials, test patients, and test provider information will be provided for every integration.
- The Provider will work with Appriss and the PMS vendor to deploy this to a pre-production environment.
  - A HCE can not begin implementation until their EHR vendor has completed the development work with Appriss Health.
- The Provider will be required to complete testing and submit an 'Integration Readiness Doc' prior to production approval.
  - This will be available on the MassPAT EHR Integration website.
- Once approved for production, the Provider will work with their vendor to determine a final roll-out schedule to go live.

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EHR Integration Limitations

- No delegate access
- Cannot return multiple patient reports
- Interstate Data Sharing is an issue.

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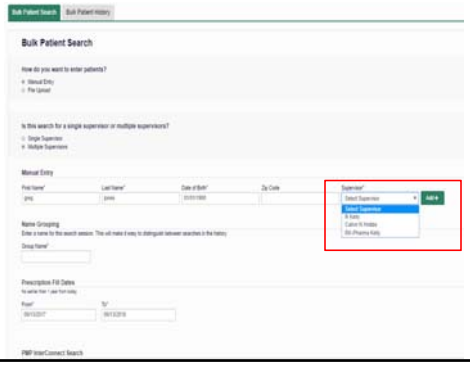
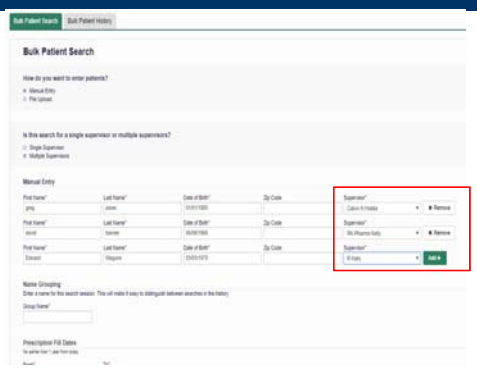
Commonwealth of Massachusetts Department of Public Health

Delegate Bulk Search



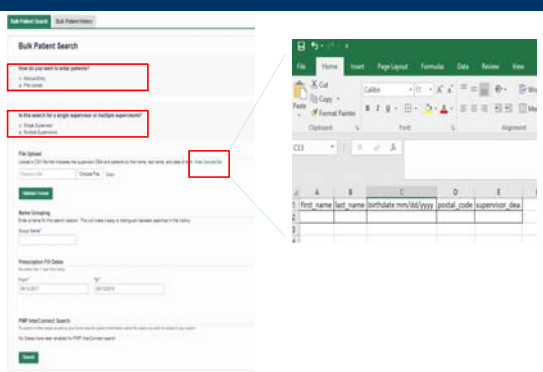
Commonwealth of Massachusetts Department of Public Health

Delegate Bulk Search



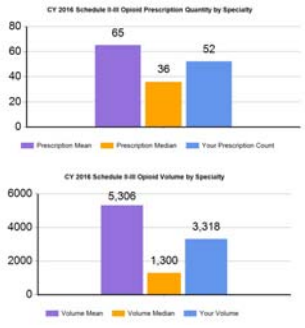
Commonwealth of Massachusetts Department of Public Health

Delegate Bulk Search



Commonwealth of Massachusetts Department of Public Health

Provider Trend Notification



- The STEP law requires DPH to annually provide information on how an individual provider is prescribing Schedule II and III opioids in comparison to other prescribers within their self-reported specialty.
- DPH calculated the mean and median prescribing quantity and volume (solid dosage units) of all prescribers who prescribed at least one Schedule II and III opioid in CY 2016 by self-reported specialty category.
- The first report was distributed on March 1, 2017.
- It is a confidential notification. It is not available for distribution by the Department and is only being shared with the individual provider.

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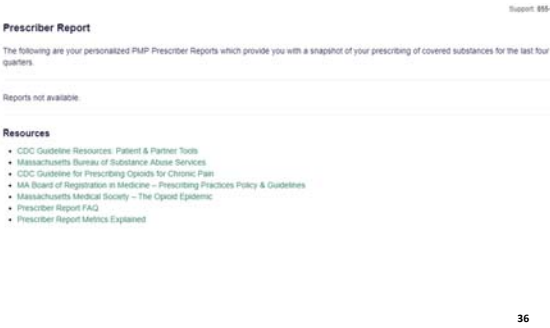
Commonwealth of Massachusetts Department of Public Health

Prescriber Reports



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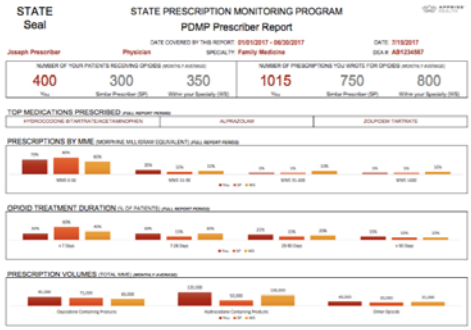
Commonwealth of Massachusetts
Department of Public Health

New Quarterly Provider Trend Notification Report Template



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Commonwealth of Massachusetts
Department of Public Health

Provider Trend Notification Report (Page 2)

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Commonwealth of Massachusetts
Department of Public Health

Prescriber Reports

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Commonwealth of Massachusetts
Department of Public Health

Prescriptions by Daily MME (Morphine Milligram Equivalent) (Full Report Period)
This metric categorizes all opioid prescriptions written by you into four groups based on their Daily Morphine Milligram Equivalent (MME) range. Each Daily MME range includes a comparison to your peers.

The Centers for Disease Control and Prevention (CDC) recommends that prescribers should reassess evidence of the benefits and risks to the patient when increasing dosage to ≥ 50 MME/day (e.g., ≥ 50 mg hydrocodone; ≥ 33 mg oxycodone) and avoid increasing to ≥ 90 MME/day (≥ 90 mg hydrocodone; ≥ 60 mg oxycodone) when possible due to an increased risk of complications.

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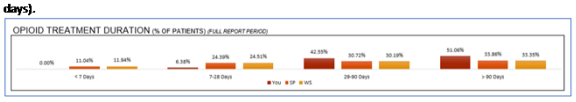
Opioid Treatment Duration (% Of Patients) (Full Report Period)
This metric categorizes your patients into four groups based on the duration of their opioid treatment. Each range includes a comparison to your peers. The ranges are based on the cumulative days' supply of a patient's prescriptions during the reporting period. The days' supply in the reporting period is not necessarily consecutive (e.g., two 5-day opioid prescriptions written a month apart would count as 10 days).



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MassPAT Alerts

PMP Clinical Alerts

Alert Name	Description
Prescriber & Dispenser Thresholds	Generates an alert when a specified number of Prescribers and Dispensers is met or exceeded within a set time period.
Daily Active MME Threshold	Generates an alert when the daily active MME (morphine milligram equivalent) is greater than or equal to a specified value.
Opioid & Benzodiazepine Threshold	Generates an alert when Opioids and Benzodiazepines are prescribed within a set time period.
Daily Active Methadone Threshold	Generates an alert when the daily active MME (morphine milligram equivalent) for Methadone is greater than or equal to specified value.
Opioid Consecutive Days Threshold	Generates an alert when Opioids have been received daily for longer than a set time period.

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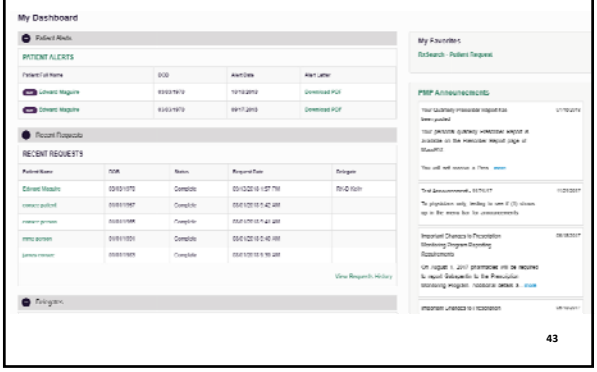
Patient Alerts



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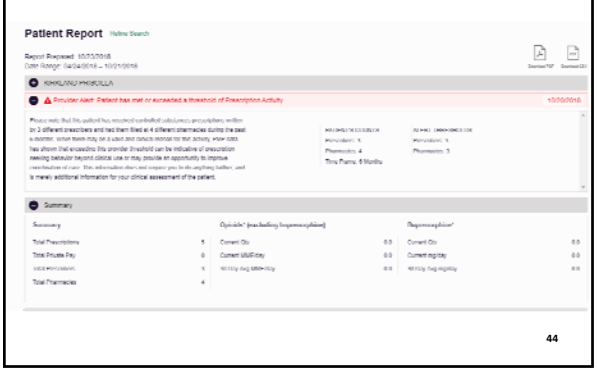
Provider Threshold Alert



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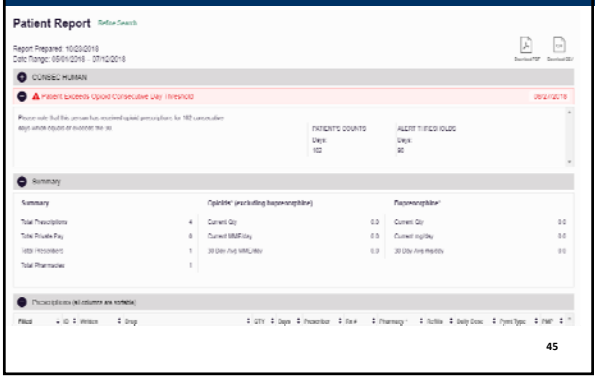
Opioid Consecutive Day Alert



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Reducing the Incidence of Addiction

You can be of the **Part of the Solution** by utilizing MassPAT in accordance with the law.

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Reefer Madness: Taking the Insanity out of Medical Cannabinoids

Michael E. Schatman, Ph.D.
Department of Public Health and Community Medicine
Tufts University School of Medicine

Disclosure

- Dr. Schatman is a consultant with Kaleo
- Dr. Schatman has no other conflicts of interest, although he is a veteran of 31 Grateful Dead/Dead and Company concerts

What the Heck is "Medical Marijuana"?!?!?!

- Lots of questions to be asked…
- Lengthy history in the US
  - ❖California became the first state to legalize MM in 1996
- Currently there are MM laws in 30 states plus DC

FindLaw. Medical marijuana laws by state. Available at: http://healthcare.findlaw.com/patient-rights/medical-marijuana-laws-by-state.html

- Individual states' medical marijuana laws are incredibly heterogeneous – varying widely in terms of process of obtaining, limits on possession, rules regulating dispensaries, allowable medical conditions, and every other parameter

What is Medical Marijuana?

- In the eyes of the pro-marijuana zealots, ALL marijuana is "medical"
- In the eyes of the FDA, NO marijuana is "medical"
- Perhaps the truth falls somewhere in between….
- CSA (1970) made cannabis a Schedule I drug – "drugs with no currently accepted medical use and a high potential for abuse"

US Drug Enforcement Administration. Drug Scheduling. Available at: http://www.justice.gov/dea/druginfo/ds.shtml

- Remains federally "illegal"

What is Medical Marijuana?

- Is it legal or illegal?
- Should it be legal?
- Is it safe?
- Is there an evidence basis for efficacy?
- If it's sold in a dispensary, should it therefore be considered "medical"?
- If it's "medical", can it be abused?

So Let's Complicate Things Even More….

- What constitutes "recreational marijuana"?
- Again, to the FDA, legal recreational marijuana doesn't exist
- However, tell this to the good citizens of:
  - ❖Washington
  - ❖Colorado
  - ❖Alaska
  - ❖Oregon
  - ❖California
  - ❖Nevada
  - ❖DC
  - ❖Massachusetts
  - ❖Maine
  - ❖Vermont

The Future of Recreational Pot?

- Predictions for legalization in:
  - ❖Arizona
  - ❖Arkansas
  - ❖Connecticut
  - ❖Delaware
  - ❖Florida
  - ❖Illinois
  - ❖Maryland
  - ❖Michigan
  - ❖Minnesota
  - ❖Montana
  - ❖New Hampshire
  - ❖New York
  - ❖Ohio
  - ❖Rhode Island
  - ❖Vermont

Stebbins S, et al. USA Today, updated January 5, 2018.

Politics

- Only add to the craziness around medical marijuana
- Obama administration: AG Holder, 2009: "[t]he policy is to go after those people who violate both federal and state law"

Associated Press, "Attorney General Signals Marijuana Policy Shift," NBC News, March 18, 2009.

- 2011 – Policy reversal, and the Justice Department began to raid dispensaries in selected states, blaming them for letting the industry get out of control

Onishi N. "Cities Balk as Federal Law on Marijuana Is Enforced," New York Times, June 30, 2012.

Politics

- 2012 – President Obama announced that cannabis use in states in which it is legal was not a priority for DOJ

Garvey T, Yeh BT. State legalization of recreational marijuana: Selected legal issues. Washington, DC: Congressional Research Service;2014.

- December, 2012 – WA and CO pass recreational MJ laws, Obama administration supported states' rights

Kamin S. Publius J Federalism 2015;45:427-451.

- 2014 – Congress passes the Rohrabacher–Blumenauer amendment, defunding the DOJ from enforcement of federal law in MM states

Lopez G. Vox, May 30, 2014.

Politics

- Must be renewed every fiscal year to stay in effect

Sullum J. Reason, January 4, 2016.

- Has been successfully renewed each year – attached to the federal budget bill
- Every time a budget agreement can't be reached, federal protection of states' laws is threatened
- And the DOJ can theoretically run wild….

Cannabinoids

- Marijuana contains over 100 cannabinoids

National Institute on Drug Abuse. Drug Facts: Is Marijuana Medicine? Revised April, 2014.

- Δ9-tetrahydrocannabinol (THC) – the principle psychoactive constituent of cannabis
- Gets all of the press – good and bad
- Recreational marijuana – goal is to maximize THC
- Seems to be the goal of "medical marijuana" as well…….
- Higher THC fetches a higher price in dispensaries

THC:CBD Ratio

- What kinds of ratios do we see in medical vs. non-medical cannabis?
- Study of over 5000 samples of cannabis seized in CA between 1996-2008:
  - ❖THC levels increased from 4.56% to 11.75%
  - ❖CBD levels decreased from 0.24% to 0.08%

Burgdorf JR, et al. Drug Alcohol Depend. 2011;117:59–61.

- THC:CBD ratio – 14:1 in 2001, 80:1 in 2014
  - ❖Increases in THC thought to be due to shift from traditional strains to sinsemilla

ElSohly MA, et al. Biol Psychiatry 2016;79:613-619.

THC:CBD Ratio

- Currently, measurable levels of CBD are rarely found in herbal cannabis

Niesink RJ, van Laar MW. Front Psychiatry 2013;4:130.

- The THC:CBD ratio is not examined in most studies
  - ❖Most current data come from toxicology following seizures

Vindenes V, Morland J. Increasing plant concentrations of THC and implications on health related disorders. In: Handbook of Cannabis and Related Pathologies: Biology, Pharmacology, Diagnosis, and Treatment. Academic Press, 2017. pp. 24-32.

- Ability to understand the THC:CBD ratio and the impact of breeding the CBD out of cannabis is essential to understanding its health risks

Synthetic THC

- Available as a Schedule III drug (dronabinol/Marinol) since 1985
- Nabilone/Cesamet (Schedule II) –A synthetic THC analogue – also FDA-approved in 1985
- Common side effects include drowsiness, unsteady gait, dizziness, inability to focus thoughts, confusion, mood changes, delusions, and hallucinations

WebMD. Drugs and medications: Marinol oral. http://www.webmd.com/drugs/drug-9308-Marinol+Oral.aspx?drugid=9308&drugname=Marinol+Oral&pagenumber=6.

- Tolerability is dubious
- Consequently, so is clinical utility for pain

Issa MA, et al. Clin J Pain 2014;30:472-478.

Safety Issues Associated with Marijuana

- The myriad safety concerns identified are thought to be due primarily to THC; more THC means more risks

Rehm J, et al. Int J Health Policy Manag. 2016;5:1–4.

- Can we assume that as the THC levels continue to rise, that safety risks will do the same?
- Smoking remains the most common route of administration

Russell C, et al. Int J Drug Policy. 2018;52:87-96.

- Recent review – pulmonary effects are even worse than we'd thought – "Marijuana Lung"

Leb JS, et al. Chronic Obstr Pulm Dis. 2018;5:81-83.

- Tars from smoked marijuana contain more carcinogens than do those from tobacco

Wu TC, et al. N Engl J Med. 1988;318:347-351.

Physical Safety Issues

- Insufficient data on safety of vaporization – "Preliminary findings do support the idea that vapourization is an improvement over smoking"

Loflin M, Earleywine M. Can J Respir Ther. 2015;51:7–9.

- Increases rates of acute myocardial infarction and cardiovascular mortality – doubles rate of MI

Hall W. Addiction 2015;110:19-35.

Franz CA, Frishman WH. Cardiol Rev. 2016;24:158-162.

- Predicts heart failure and CVA – whether recreational or medical

Kalla A, et al. J Cardiovasc Med (Hagerstown). 2018;19:480-484.

Physical Safety Issues

- Associated with higher rates of acute ischemic stroke

Rumalla K, et al. J Neurol Sci. 2016;364:191-196.

- Increased duration of marijuana use is associated with increased risk of death from hypertension

Yankey BA, et al. Eur J Prev Cardiol. 2017;24(17):1833-1840.

- Sexual functioning - THC impairs gonadal function by blocking gonadotropin-releasing hormone (GnRH) release

Harclerode J. NIDA Res Monograph 1984;44:46-64.

- Immunosuppressive – Reduces T-Cell activation

Henriquez JE, et al. J Pharmacol Exp Ther. 2018[Epub ahead of print].

Physical Safety Issues

- Cannabinoid Hyperemesis Syndrome
  - ❖Characterized by a syndrome of cyclic vomiting, abdominal pain and compulsive showering in some habitual users
  - ❖Symptoms improve with cessation utilization
  - ❖The prevalence of cannabinoid hyperemesis syndrome seen in EDs has doubled since the liberalization of marijuana laws in Colorado

Kim HS, et al. Acad Emerg Med. 2015;22:694-699.

  - ❖Can masquerade as an eating disorder

Brewerton TD, Anderson O. Int J Eat Disord. 2016;49:826-829.

  - ❖Estimated 2.75 million cases in the US annually

Habboushe J, et al. Basic Clin Pharmacol Toxicol. 2018;122:660-662.

  - ❖Fatal cases now being reported

Nourbakhsh M, et al. J Forensic Sci. 2018[Epub ahead of print].

Physical Safety Issues

- Cannabis use is associated with higher rates of occupational injuries, injury severity, and prolonged lost workdays among construction workers

Khashaba E, et al. Toxicol Ind Health 2018;34:83-90.

- Drugged driving – 96% of cases involve cannabis

Bonar EE, et al. Addict Behav. 2018;78:80-84.

- Drugged driving continues to increase, with increases associated with more traffic fatalities

Rogeberg O, Elvik R. Addiction 2016;111:1348-1359.

Robertson RD, et al. Accid Anal Prev. 2017;99(Pt A):236-241.

Physical Safety Issues

- French study: One in two drivers in fatal accidents under the influence of ETOH were also under the influence of cannabis

Martin JL, et al. PLoS One 2017 8;12(11):e0187320.

- High-risk drinking behavior recently found to be related to medical cannabis utilization

Davis AK, et al. Addict Behav. 2018;77:166-171.

- Older adults – Cannabis use associated with greater physical injury risk and ED visits

Choi NG, et al. Am J Drug Alcohol Abuse. 2018;44:215-223.

- Increases the likelihood of fatal two-vehicle crashes

Li G, et al. Ann Epidemiol. 2017;27(5):342-347.

Physical Safety Issues

- Perhaps the issue is that users of MJ have been found to have greater <u>perceived</u> safety than those who don't

Sartor CE, et al. Addict Behav. 2017;66:114-117.

- Pregnancy – Use of marijuana among pregnant women increased by 69% between 2009 and 2016

Young-Wolf KC, et al. JAMA 2017;318(24):2490-2491.

- Currently at 22%

Oga EA, et al. Matern Child Health J. 2018[Epub ahead of print].

- Cannabis use associated with preterm birth

Prunet C, et al. J Gynecol Obstet Hum Reprod. 2017;46(1):19-28.

- Likelihood of stillbirth or miscarriage 12 times higher among women using MJ during pregnancy

Coleman-Cowger VH, et al. Neurotoxicol Teratol. 2018;68:84-90.

Physical Safety Issues

- Addiction
  - ❖Not as severe as opioid or benzo addiction
  - ❖Abrupt cessation results in irritability, insomnia, anorexia

Haney M, et al. Neuropsychopharmacology 2013;38:1557-1565.

- Perceived barrier to quitting MJ – fear of severe withdrawal symptoms

Zvolensky MJ, et al. Addict Behav. 2018;76:45-51.

- When used hs, withdrawal's impact on sleep is particularly problematic

Cranford JA, et al. Drug Alcohol Depend. 2017;180:227-233.

- Reduced MJ use associate with improved sleep quality

Hser YI, et al. J Subst Abuse Treat. 2017;81:53-58.

Cognitive Safety Issues

- We've known about chronic MJ use and its impact on diminution of grey matter in the brain for years

Block RI, et al. Neuroreport 2000;11:491-496.

- Of particular concern in the developing brain
- Executive functioning deficits associated with MJ use

Clark DB, et al. Front Behav Neurosci. 2017;11:223.

- Myriad studies and review indicate that chronic MJ use results in cognitive deficits
  - ❖Long-term and short-term

Cognitive Safety Issues

- Long-term deficits ("residual cannabis effect") include (from a meta-analysis):
  - ❖Learning
  - ❖Forgetting/Retrieval
  - ❖Abstraction/Executive Functioning
  - ❖Attention
  - ❖Motor Skills
  - ❖Verbal/Language

Schreiner AM, Dunn ME. Exp Clin Psychopharmacol. 2012;20(5):420-429.

Mental Health Risks

- Clearly are going to overlap with cognitive risk data, although no consensus regarding the extent of such
- Most studied issue has been early-onset psychosis and recovery from it in marijuana users
- MJ-Psychosis association recognized back to the 1950s

Ames F. J Ment Sci. 1958;104(437):972-999.

- High THC cannabis increases the risk of psychosis 3-fold compared to non-users, and 5-fold among daily users

Di Forti M, et al. Lancet Psychiatry 2015;2(3):233-238.

❖Particularly problematic in patients using ultra-high-THC wax dabs

Pierre JM, et al. Schizophr Res. 2016;172(1-3):211-212.

Mental Health Risks – Psychosis

- Cannabis use in first episode psychosis is associated with failure of anti-psychotic medications

Patel R, et al. BMJ Open. 2016;6(3):e009888.

❖As well as is adherence to anti-psychotic medications

Schoeler T, et al. Lancet Psychiatry 2017;4(8):627-633.

- Extended abstinence from MJ doesn't seem to reverse symptoms in cannabis-dependent schizophrenics

Rabin RA, et al. Schizophr Res. 2018;194:55-61.

- A risk factor for violent behavior in early phase psychosis

Moulin V, et al. Front Psychiatry. 2018;9:294.

Mental Health Risks – Bipolar Disorder

- Cannabis using patients with bipolar disease demonstrate poorer treatment adherence

Van Rossum I, et al. J Nerv Ment Dis. 2009;197(1):35-40.

- Cannabis predicts earlier age of bipolar disorder onset

De Hert M, et al. Schizophr Res. 2011;126(1-3):270-276.

❖The heavier the use, the earlier the onset

Lagerberg TV, et al. Eur Arch Psychiatry Clin Neurosci. 2011;261(6):397-405.

- Continued MJ use following diagnosis is associated with higher risk of recurrence and poorer functioning

Zorrilla I, et al. Acta Psychiatr Scand. 2015;131(2):100-110.

Mental Health Risks – Bipolar Disorder

- MJ use has been associated with lower remission rates in patients with Bipolar Disorders

Kim SW, et al. Psychiatry Investig. 2015;12(3):349-355.

- A significant correlation between MJ use and suicide attempts in patients with bipolar disorders

Carrà G, et al. Bipolar Disord. 2015;17(1):113-114.

- Cannabinoid hyperemesis syndrome is associated with manic episodes due to lowering of serum mood stabilizer levels

Gregoire P, et al. BMJ Case Rep. 2016;pii: bcr2016215129.

Mental Health Risks - Anxiety

- The acute induction of anxiety associated with THC cannot be ignored
- Early studies found an anti-anxiety effect of MJ

Sethi BB, et al. Biol Psychiatry 1986;21:3-10.

- Recent meta-analysis concludes that THC's impact on anxiety is not necessarily impressive

Turna J, et al. Depress Anxiety. 2017;34:1006-1017.

❖However, that may have much to do with Indica vs. Sativa strain

- Recent study found that longitudinally, reduction of MJ use was associated with decreased anxiety

Hser YI, et al. J Subst Abuse Treat. 2017;81:53-58.

Mental Health Risks - Anxiety

- PTSD – Once thought to be "treatable" with cannabis
- However chronic MJ use has been found to impair fear extinction

Papini S, et al. J Abnorm Psychol. 2017;126:117-124.

- MJ use after initiating tx associated with worse PTSD symptoms, more violent behavior, and alcohol use

Wilkinson ST, et al. Curr Addict Rep. 2014;1:115-128.

- Indicas may be helpful, activating sativas likely to exacerbate
- Good news: Dispensary employees found to be more likely to recommend an indica or a hybrid for PTDS than a sativa

Haug NA, et al. Cannabis Cannabinoid Res. 2016;1:244-251.

Cannabidiol (CBD)

- Contrary to popular belief, THC is not the most relevant cannabinoid for medical application

Campos AC, et al. Philos Trans R Soc Lond B Biol Sci. 2012;367:3364–3378.

- CBD was first isolated in 1934

Robson P. Br J Psychiatry 2001;178:107-115.

- First synthesized in 1967, first easily useable form in 1985

Baek SH, et al. Tetrahedron Lett. 1985;26:1083-1086.

- Ignored for many years
- Seen as something limiting the amount of THC marijuana could potentially contain

CBD

- Of no interest to recreational users….and tragically, for many medical users
- Initially described as "nonpsychotropic"
- However, produces anxiolysis through increasing serotonergic transmission

Espejo-Porras F, et al. Neuropharmacology 2013;75:155-163.

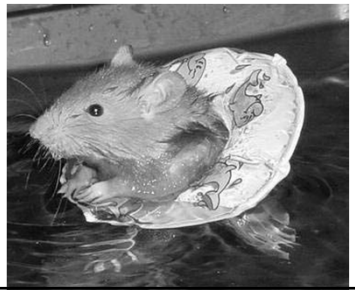
- Appears to have a mild antidepressant effect with those with low levels of serotonin

Sales AJ, et al. Prog Neuropsychopharmacol Biol Psychiatry. 2018;86:255-261.

- More appropriately called "noneuphoriant"

Russo EB. Ther Clin Risk Manag. 2008;4:245-259.

Rat Cheating on a Forced-Swim Test



CBD Safety Profile

- Safety has been well-established

Cunha JM, et al. Pharmacol. 1980;21:175-185.
Consroe P, et al. Pharmacol Biochem Behav. 1991;40:701-708.
Zuardi AW, et al. J Psychopharmacol. 2006;20:683-686.
Zuardi AW, et al. J Psychopharmacol. 2009;23:979-983.
Zuardi AW, et al. J Psychopharmacol. 2010;24:135-137.
Bergamaschi MM, et al. Curr Drug Saf. 2011;6:237-239.
Devinsky O, et al. Lancet Neurol. 2016;15:270–278.
McGuire P, et al. Am J Psychiatry 2018;175:225-231.

- Attenuates the "high" caused by THC at 8:1 CBD:THC ratio

Kim PS, Fishman M. Curr Pain Headache Rep. 2017;21(4):19.

- The Director of NIDA wrote, "CBD appears to be a safe drug"

Volkow N. Huffington Post July 23, 2015.

CBD Availability

- Despite its safety profile and the impossibility of abusing it, CBD from whole plant MJ is still considered a Schedule I drug
- Other than recently FDA-approved Epidiolex

Traynor K. Am J Health Syst Pharm. 2018;75:1088-1089.

- Has been available in all medical marijuana states
- 13 states had the wisdom to legalize it without MM legalization
- New changes in the law allow for CBD from the hemp plant

Knight R. DEA clarifies marijuana extract rule and CBD legality. Available at: http://kightoncannabis.com/dea-clarifies-marijuana-extract-rule-and-cbd-legality/

CBD Legal Status

- Hemp plant is in the same genus as MJ, but contains, by definition and law, <0.3% THC content

Yang Y, et al. Cannabis Cannabinoid Res. 2017;2:274-281.

- THC will not show up in standard UDT immunoassays
- Now most commonly used for pain, anxiety, depression, and sleep disorders

Corroon J, Phillips JA. Cannabis Cannabinoid Res. 2018;3:152-161.

- Due to lack of regulation, CBD products online are often mislabeled regarding constituents

Freedman DA, Patel AD. Pediatr Neurol Briefs. 2018;32:3.

CBD and Pain

- Much of the existing supportive data is preclinical
- CBD is anti-inflammatory

Thapa D, et al. FASEB J. 2017;31(Suppl 1):Abstract 811.7.

- Anti-inflammatory, analgesic in arthritis

Hammell DC, et al. Eur J Pain 2016;20:936-938.

- Attenuation of early phase inflammation by cannabidiol prevents pain and nerve damage in osteoarthritis

Philpott HT, et al. Pain 2017; 158:2442-2451.

CBD and Pain

- Found to be anti-inflammatory in human cell lines

Petrosino S, et al. J Pharmacol Exp Ther. 2018;365:652-663.

- Relevance for back pain: CBD has anti-inflammatory effects on rat nucleus pulposus cells

Chen J, et al. Mol Med Rep. 2016;14:2321-2327.

- Reduces chemotherapy-related peripheral neuropathy without diminishing nervous system function or chemotherapy efficacy

Ward SJ, et al. Br J Pharmacol. 2014;171:636-645.

- High-dose CBD appears to be hypnotic – increasing sleep, while low-dose CBD has been associated with increased wakefulness

Babson KA, et al. Curr Psychiatry Rep. 2017;19:23.

More Recent CBD Research

- Safety established when co-administered with fentanyl

Manini AF, et al. J Addict Med. 2015;9:204-210.

- Enhances fracture healing

Kogan NM, et al. J Bone Miner Res. 2015;30:1905-1913.

- Animal model - Protective effects on lesion-induced intervertebral disc degeneration

Silveira JW, et al. PLoS One 2014;9:e113161.

- Animal model – synergistic with morphine for certain pain conditions

Neelakantan H, et al. Behav Pharmacol. 2015;26:304-314.

- Clinical research – Effective for reducing chronic pain in kidney transplant patients (small study)

Cuñetti L, et al. Transplant Proc. 2018;50:461-464.

Marijuana and Pain Research

- Extremely difficult to do in the US
- All federally-funded MM research currently must use low-grade MJ grown at the U of Mississippi for NIDA
- 3 dose strengths available
  - ❖Low potency (1.29% THC)
  - ❖Moderate potency (3.53%)
  - ❖High potency (7%)

Wilsey B, et al. J Pain 2013;14:136-148.

- Why is this a problem?

Marijuana and Pain Research

- Oil or wax dabs available at some dispensaries have THC contents as high as 90%!!!!

Loflin M, Earleywine M. Addict Behav. 2014;39:1430–1433.

  - ❖Now being used regularly by 36.5% of cannabis users

Sagar KA, et al. Drug Alcohol Depend. 2018;190:133-142.

- Medical marijuana sold in dispensaries is higher in THC than that sold on the streets

Sevigny EL, et al. Int J Drug Pol. 2014;25:308-319.

- Recent breakthrough – NIDA has approved a 13.4% THC MJ for research

Edibles

- THC dosing in edibles has been described as “insane” by toxicologists

Gussow L. Emerg Med News 2014;36:24.

- Edibles are infused with almost pure THC
- They typically take 30-90 minutes to take effect, reach their peak in 2-3 hours, and can last for 4-12 hours

Grotenhermen F. Clin Pharmacokinet. 2003;42:327-360.

- Thus, they don’t allow for titration due to a lack of immediate effect
- Labeling of constituents’ content is often inaccurate

Vandrey R, et al. JAMA 2015;313:2491-2493.

Edibles

- This inability to titrate effectively has led to increases in ER visits due to THC intoxication

Kim HS, Monte AA. Ann Emerg Med. 2016;68:71-75.

Vo KT, et al. Ann Emerg Med. 2018;71:306-313.

- And multiple deaths

Hancock-Allen JB, et al. MMWR Morbidity and Mortality Weekly Report 2015; 64: pp. 771-772.

Science vs. "Religion"

- Medical marijuana advocates tend not to let the data get in the way of their opinions
- Try discussing potential harms of MM on Twitter….
- "There is none so blind as those who will not see…"

MM and Pain Research – What DO We Know?

- Is it effective for chronic pain?
- Depends on the properties of the marijuana being used and one's definition of "effective"
- It also depends upon goals of treatment
  - ❖Is analgesia sufficient, even if it incapacitates the patient?
- It also depends on the medical indication
- E.g., opioids are effective for many types of pain, but not for neuropathic pain

MM and Pain Research

- Neuropathic pain – first methodologically-robust study conducted in 2008 – found efficacy
  - ❖Higher doses (7% THC) resulted in cognitive deficits

Wilsey B, et al. J Pain 2008;9:506–521.

- Similar findings in a 2009 study on neuropathic pain in HIV

Ellis RJ, et al. Neuropsychopharmacology 2009;34:672-680.

- 2010 Canadian study using 9.4% THC MJ – efficacy for neuropathic pain

Ware MA, et al. CMAJ 2010;182:E694-701.

MM and Pain Research

- 2013 study using low-dose (1.29% THC) MJ – efficacy for neuropathic pain, without significant cognitive effects

Wilsey B, et al. J Pain 2013;14:136-148.

- 2015 study on MJ for pain diabetic neuropathy – higher dose (7% THC) more effective than lower dose (1.29%)…but with more cognitive effects

Wallace MS, et al. J Pain 2015;16:616-627.

- Similar findings in 2016 study on neuropathic pain due to spinal cord injury or disease

Wilsey B, et al. J Pain 2016;17:982-1000.

MM and Pain Research

- Conclusions of MJ for neuropathic pain:
  - ❖Weak evidence as effective in terms of analgesia at higher doses

Murff HJ. Ann Intern Med. 2017;167:JC62.

  - ❖Cognitive side effects are dose-related
  - ❖Never studied head-to-head against gabapentinoids
  - ❖Gabapentinoids also have dose-related cognitive side effects
  - ❖Research needed on MM with significant CBD content as well
  - ❖Research needed on the types of MJ actually carried in dispensaries (25%+ THC)
- Recommendation: Consider as a last option for neuropathic pain
- Recent Australian review suggests that CBD may be better

Casey SL, Vaughan CW. Medicines (Basel). 20185(3). pii: E67.

MM and Pain Research

- Musculoskeletal pain and arthritis – "Evidence is Needed"

Perrot S, Trouvin AP. Joint Bone Spine. 2018[Epub ahead of print].

- Rheumatic conditions – no evidence for efficacy
- Experts recommend against it until more research is available

Häuser W, et al. Dtsch Arztebl Int. 2017;114:627-634.

- Fibromyalgia – No empirical evidence for efficacy

Fitzcharles MA, et al. Schmerz 2016;30:47-61.

- Headache – very limited evidence for efficacy

Lochte BC, et al. Cannabis Cannabinoid Res. 2017;2:61-71.

- Cancer pain – May have "potential use" – although human studies are of poor quality, limited size, and outdated

Wilkie G, et al. JAMA Oncol. 2016;2:670-675.

MM and Opioids

- The most compelling evidence basis for MJ in treating chronic pain was for its opioid-sparing effect

Boehnke KF, et al. J Pain 2016;17:739-744.

Vigil JM, et al. PLoS One. 2017;12:e0187795.

- Medical cannabis laws were associated with lower opioid overdose mortality rates

Bachhuber MA, et al. JAMA Intern Med. 2014;174:1668-1673.

- Less so, however, as laws on dispensaries have become tougher

Powell D, et al. J Health Econ. 2018;58:29-42.

- Synergistic with opioids? Likely urban myth…
- Not associated with lower prescription rates and dosages of Schedule II opioids

Liang D, et al. Addiction. 2018[Epub ahead of print].

MM and Opioids

- Perioperative opioid use is significantly higher in MJ-users despite lower subjective pain scores

Bauer FL, et al. Perm J. 2018 Jul 19;22.

- MJ use recently found to be predictive of opioid dependence

Butelman ER, et al. Front Psychiatry. 2018;9:283.

- Predictive of a 2.5 fold increase in the rate of opioid aberrancy

DiBenedetto DJ,…Schatman ME, et al. Pain Med. 2017[Epub ahead of print].

- Medical marijuana users more likely to use prescription drugs – including opioids – non-medically

Caputi TL, Humphreys K. J Addict Med. 2018[Epub ahead of print].

"Watcha Smoking, Dude?"

- To talk about "medical marijuana" as a single entity is ridiculous
- We need to be discussing "medical **marijuanas**"
- Indica or sativa? – 2 separate species, usually in a hybrid form
- Indicas empirically established as preferable for pain management, but cause more sedation than sativas

Cohen NL, et al. J Stud Alcohol Drugs 2016;77(3):515-520.

"Watcha Smoking, Dude?"

- Sativas are more of a euphoriant, but also more likely to cause anxiety and paranoia

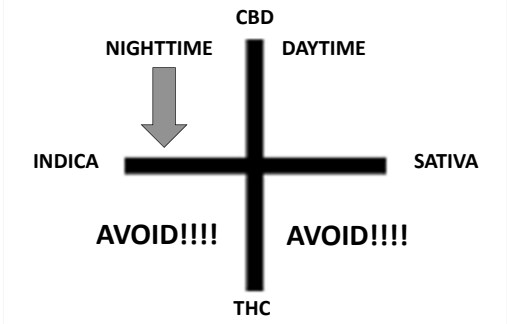
Baconi DL, et al. J Mind Med Sci. 2014;1:28-39.

- Do we know which strain is more effective for pain management?
- Head-to-head research is needed

Indica vs. Sativa – Street Reputations

- Indicas
  - ❖Relaxing and calming
  - ❖Body buzz or 'couch lock'
  - ❖Best suited for night use
- Sativas
  - ❖Uplifting and energetic
  - ❖Cerebral, spacey or hallucinogenic
  - ❖Best suited for day use

Leaf Science, 2014. *Indica vs. Sativa: Understanding The Differences.* Available at: *http://www.leafscience.com/2014/06/19/indica-vs-sativa-understanding-differences/.*



Treatment Recommendation

- "The Medicinal Cannabis Treatment Agreement: Providing Information to Chronic Pain Patients via a Written Document"

B Wilsey, et al. Clin J Pain 2015;31:1087-1096.

- Absolutely brilliant!!!!
- "Medical marijuana" is heavily abused

Wen H, et al. J Health Econ. 2015;42:64-80.

- "….physicians would seem to have an obligation to understand and inform their patients on key issues of the evidence base on cannabinoid therapeutics"

Medical Cannabis Agreement

- Covers reduction of diversion – particularly to vulnerable children and adolescents
- Addresses inappropriate utilization by the authorized patient
  - ❖We must not lose sight of the data indicating that marijuana is indeed addictive
- Discusses the risks of marijuana generally and to specific populations
- Recommends vaporization over smoking

Medical Cannabis Agreement

- Warns against driving a car or operating machinery
- Emphasizes "start low, go slow" when dosing – particularly with new strains
- Covers potential benefits of FDA-approved cannabinoids over smoked marijuana
  - ❖Based on empirical evidence…and clinical experience, I disagree
- Recommends withdrawing slowly if a patient wants to stop
- Addresses the need to evaluate the efficacy and appropriateness of therapy on an ongoing basis
- Covers not using MM in public places

Medical Cannabis Agreement

- Warns that medical authorization will NOT protect a patient's job
- Gives the physician the right to discontinue MM treatment
- Respect for patient autonomy is contingent upon the doctrine of informed consent

Dalla-Vorgia P, et al. J Med Ethics 2001;27:59-61.

- This is exactly what these agreements are providing
- Thus – they constitute ethical pain medicine practice
- And perhaps even protect the physician as well as the patient

Closing Thoughts

- The future of medical cannabinoids in the US is uncertain
- To assume that marijuana is safe because it's "natural" is neuromysticism
- As is assuming that anecdotal evidence of efficacy provides us with "the truth"
- Improving the quality and quantity of MM research is imperative if MJ is ever to become "medicine"
- CBD, not THC, promises to be the most medically-relevant cannabinoid

Closing Thoughts

- If you're going to use MM in your practice, educate yourself and your patient – and do it right
- Take marijuana as a drug seriously – irrespective of what you smoked as a youth
- If you use an opioid agreement, consider using a medical cannabis agreement
- Practicing cannabinoid medicine is challenging when we know so little
- Better data are hopefully just around the corner

THANK YOU