Effect of Enrollment in the New Mexico Medical Cannabis Program on Prescription Opioid Use in Chronic Pain Patients

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Preventable Forms of Death

Deaths From Drug Overdoses, Car Accidents, and Gun Violence

From 1999 to 2014

Source: Centers for Disease Control and Prevention
Preventable Forms of Death

52,404 total deaths, or 144 drug overdose deaths per day.

Up 11.4% in just one year from 129 a day in 2014.
Prescription Opioids and Heroin

...died a day from opioids in 2015 (33,091, 63% of total overdose deaths)

Overdose Deaths From Opioids, 1999-2014

Source: Centers for Disease Control and Prevention
Modern Trends

- 94% of new heroin users being treated for opioid addiction report first becoming addicted to prescription painkillers, only to turn to street heroin as a cheaper alternative (Cicero et al., 2015; JAMA Psychiatry)
- Painkillers are creating U.S. heroin addicts

Local Trends (2014)

- 223 New Mexicans died from prescription painkillers (CDC)
- 139 people died of heroin overdoses, which increased 12.5% to 156 people in 2015
Who is most Affected?

Opioid Death Rate by Race

Deaths per 100,000 people

Source: Centers for Disease Control and Prevention
# Deaths from Prescription Painkillers

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>2014</th>
<th>2015</th>
<th>% change</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. (Rate)</td>
<td>No. (Rate)</td>
<td></td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>6,732 (4.2)</td>
<td>7,117 (4.4)</td>
<td>4.8%</td>
</tr>
<tr>
<td>Female</td>
<td>5,427 (3.3)</td>
<td>5,610 (3.4)</td>
<td>3.0%</td>
</tr>
<tr>
<td>Age group (yrs)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0–14</td>
<td>42 (0.1)</td>
<td>48 (0.1)</td>
<td>0.0%</td>
</tr>
<tr>
<td>15–24</td>
<td>726 (1.7)</td>
<td>715 (1.6)</td>
<td>-5.9%</td>
</tr>
<tr>
<td>25–34</td>
<td>2,115 (4.9)</td>
<td>2,327 (5.3)</td>
<td>8.2%</td>
</tr>
<tr>
<td>35–44</td>
<td>2,644 (6.5)</td>
<td>2,819 (6.9)</td>
<td>6.2%</td>
</tr>
<tr>
<td>45–54</td>
<td>3,488 (8.0)</td>
<td>3,479 (8.1)</td>
<td>1.3%</td>
</tr>
<tr>
<td>55–64</td>
<td>2,437 (6.1)</td>
<td>2,602 (6.4)</td>
<td>4.9%</td>
</tr>
<tr>
<td>≥65</td>
<td>706 (1.5)</td>
<td>736 (1.5)</td>
<td>0.0%</td>
</tr>
</tbody>
</table>
Most Common Prescriptions

- 300M painkillers are prescribed in the U.S. (>24B/yr. market)...unlike other countries
  - hydrocodone (119M Rxs, 99% U.S.)
  - oxycodone
Opioid Abuse Treatments

- Agonists: so called “first-line treatments” (replacement therapies)
  - methadone
  - buprenorphine-tapering
- Antagonists:
  - Naloxone
  - Naltrexon

What if we could prevent overdoses and reduce abuse by treating the medical conditions opioids are used to treat, i.e., chronic pain?
### Interesting Trends

**Deaths From Prescription Painkillers**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>2014 No. (Rate)</th>
<th>2015 No. (Rate)</th>
<th>% change</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maine</td>
<td>80 (6.1)</td>
<td>102 (7.7)</td>
<td>26.2</td>
</tr>
<tr>
<td>Maryland</td>
<td>388 (6.2)</td>
<td>398 (6.5)</td>
<td>4.8</td>
</tr>
<tr>
<td>Massachusetts</td>
<td>178 (2.6)</td>
<td>225 (3.3)</td>
<td>26.9**‡‡</td>
</tr>
<tr>
<td>Nevada</td>
<td>224 (7.4)</td>
<td>259 (8.6)</td>
<td>16.2</td>
</tr>
<tr>
<td>New Hampshire</td>
<td>81 (5.8)</td>
<td>63 (4.4)</td>
<td>-24.1</td>
</tr>
<tr>
<td><strong>New Mexico</strong></td>
<td><strong>223 (10.9)</strong></td>
<td><strong>160 (8.1)</strong></td>
<td><strong>-25.7</strong>**‡‡**</td>
</tr>
<tr>
<td>New York</td>
<td>608 (3.0)</td>
<td>705 (3.4)</td>
<td>13.3**‡‡**</td>
</tr>
<tr>
<td>North Carolina</td>
<td>462 (4.7)</td>
<td>554 (5.5)</td>
<td>17.0**‡‡**</td>
</tr>
</tbody>
</table>
Why do we know so little about the health effects of Cannabis sativa?

Federal Barriers to Cannabis Research

• Schedule 1 drug: no acceptable safety levels and no medical potential
• Cannabis intervention studies are rare and require:
  – investigational new drug approval from the FDA
  – approval from the DEA
  – approval and purchase of the cannabis through NIDA
• Federally-funded intervention studies are still rare and not externally valid (but very expensive)!!! (Stith & Vigil, 2016, Science)
Total financial cost of pain to society

Combining health care costs and productivity estimates in 2010 dollars:

Pain ($635B) > Heart Disease ($309B) > Cancer ($243B) > Diabetes ($188B)

(Gaskin & Richard, 2011)
MCP Research Studies

• Currently over 1 million patients
• MCPs are unique: patient-managed care, federally-illegal
• No randomized controlled trial (RCT) studies in the U.S.
• Current study: a pragmatic, pilot cohort study to compare prescription opioid consumption in MCP and non-MCP enrollees, and how enrollment has affected patient wellbeing.
The Lynn and Erin Compassionate Use Act was passed in New Mexico in 2007, enabling the medical-advised authorization and regulation of cannabis treatment for people with chronic, debilitating health conditions.

- MDs authorize use for self-medication, not prescribe
- There are 20 qualifying conditions for the NM MCP (severe chronic pain, painful peripheral neuropathy)
- There are approximately 40,000 patients enrolled in the NM MCP, and 28+ Programs in the U.S
Past Research (Spending)

- National overall reductions in Medicare program and enrollee spending when states implemented medical marijuana laws were estimated to be $165.2 million per year in 2013. (Bradford & Bradford, 2016; Health Affairs).

<table>
<thead>
<tr>
<th>Condition category</th>
<th>Annual number of daily doses prescribed per physician in states:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Without a medical marijuana law</td>
</tr>
<tr>
<td>Anxiety</td>
<td>11,220.29</td>
</tr>
<tr>
<td>Depression</td>
<td>9,576.73</td>
</tr>
<tr>
<td>Glaucoma</td>
<td>2,551.40</td>
</tr>
<tr>
<td>Nausea</td>
<td>10,067.92</td>
</tr>
<tr>
<td>Pain</td>
<td>31,810.07</td>
</tr>
<tr>
<td>Psychosis</td>
<td>11,421.46</td>
</tr>
<tr>
<td>Seizures</td>
<td>9,398.60</td>
</tr>
<tr>
<td>Sleep disorders</td>
<td>7,557.97</td>
</tr>
<tr>
<td>Spasticity</td>
<td>2,067.82</td>
</tr>
</tbody>
</table>
Past Research (Mortality)

- State-level studies: Implementation of medical cannabis laws reduces mortality rates in states where such Programs exist.

  - MCP friendly states have 33% lower opioid-related mortality rates (Bachhuber et al., 2014, *JAMA Intern. Med.*)

  - MCPs are associated with a 50% lower odds of fatal car accidents involving opioids in drivers 21-40 years (Kim et al., 2016, *Am. J Public Health*)
Past Research (Opioid Use)

- Israeli study: Physician-directed cannabis treatment improved functionality, reduced pain, and reduced prescription narcotics use by 44% in cannabis-naïve, chronic pain patients at a 6 month follow-up. (Haroutounian et al., 2016, Clin J. Pain)

  + only study to measure association between Cannabis use and changes in prescription opioid consumption on individual level.

  - No reliable baseline levels, no comparison group, short observation period (6 mos.)
Project Origins

- Perspicacious Collaborator: Dr. Anthony P. Reeve (Industrial Rehabilitation Clinics)
- Clinical observations
- Research Question: Are patients being truthful when they say that they are replacing their narcotic consumption with cannabis?
- Research tools: Patient surveys and Prescription Monitoring Program records
Research Approach

• Subjective: Document self-reported changes in pain, opioid use, and well-being
  – Patients surveyed one year post-enrollment (at renewal)

• Objective: Determine veracity of patient reports
  – Prescription Monitoring Program Records
    • All scheduled prescriptions must be reported by pharmacies to the PMP
Survey Data Summary

- 137 MCP patients
  - Initially referred by Dr. Reeve to the MCP one year prior
  - Surveyed at the time of referral for MCP license renewal (approx. one year after enrollment)
- All chronic pain patients
- Single physician/clinic in Albuquerque, NM
- Enrolled in the MCP between 4/1/2010 and 10/3/2015
  - 68% male, mean age = 49
PMP Data

• MCP Patient Records (N=137)
  – pre-enrollment, post-enrollment, post-renewal
• Comparison Group (N=53)
  – Selected based on common chronic pain diagnoses from the same physician at the same clinic
  – All patients declined referral to the MCP and confirmed that they were not using other sources of cannabis
  – Two year sample through 10/1/2016
Survey: Medical Cannabis Program Rating

On a scale of 0 to 10, how would you rate the Cannabis Program?

10 = very successful
0 = not successful

51% rated it 10
28% rated it 9
16% rated it 8
1% rated it 7
2% rated it 6
2% rated it 5
0% rated it 4
0% rated it 3
1% rated it 2
0% rated it 1
0% rated it 0
Survey: Effect of Cannabis on Pain

In general, has cannabis reduced your pain levels?

Yes = 99%
No = 1%

Pain Scale (0 = No Pain, 10 = Worst Pain)
Survey: Side Effects

- Two patients reported negative side effects {Yes, No}
- “Other” effects
  - 0% hallucinations
  - <1% paranoia
  - 1.5% impaired judgment
  - 1.5% anxiety
  - 7.5% increased libido
  - 15% euphoria
  - 23% drowsiness
Survey: Effect of Cannabis Use on Self-Reported Opioid Use

% of Patients

Pre-MCP Opioid Use | Opioid Use at Renewal

Yes | No

77% | 23% | 33% | 67%
Survey: Effect of MCP on Subjective Well-Being of Chronic Pain Patients

Quality of life:
- Great benefit: 65%
- Good benefit: 30%
- No effect: 0%
- Negative impact: 4%
- Extremely negative impact: 0%

Social life:
- Great benefit: 52%
- Good benefit: 30%
- No effect: 17%
- Negative impact: 0%
- Extremely negative impact: 0%

Activity:
- Great benefit: 61%
- Good benefit: 26%
- No effect: 9%
- Negative impact: 4%
- Extremely negative impact: 0%

Concentration:
- Great benefit: 41%
- Good benefit: 18%
- No effect: 32%
- Negative impact: 9%
- Extremely negative impact: 0%
Objective (PMP) Analysis of the Effect of MCP Enrollment

• Two Studies:

1. Effect on # of prescriptions, types of drugs prescribed, doctors prescribing, and dates prescriptions filled
   – Forthcoming in JAMDA (Journal of the American Medical Directors Association)

2. Effect on average milligrams of IV morphine prescribed per day
   – Under review
Study 1: Effect of MCP on Scheduled II-V Prescription Usage

• Background: Co-prescribing of scheduled drugs endemic in the United States
  – Increases health risks to patients
  – Burden on healthcare systems

• Study Design:
  – Sample: at least one prescription in first six months of sample period (pre-enrollment for MCP)
    • 83 chronic pain patients enrolled in NM MCP between 4/1/2010-10/3/2015
    • 42 non-enrolled patients between 10/01/2014 and 10/01/2016
  – Outcomes: pre- and post-enrollment monthly trends in prescription use patterns
  – Independent variables: MCP enrollment, month, age, gender, patient fixed effects
Study 1: Results

- No prescriptions filled during the last six months of observation \{0,1\}
  - MCP: 34\% (28/83)
  - Comparison Group: 2\% (1/42)

- Monthly trends in # of prescriptions, types of medications, doctors prescribing and dates prescriptions filled (counts)
  - MCP: -0.02 to -0.04 for all four measures (p-values from <0.001 to 0.017)
  - Comparison Group: no change
MCP Enrollment

Comparison Group

MCP
Study 2: Effect of MCP on Opioid Use

• **Background:** Opioid prescription use is a leading cause of death.
  – Surveyed chronic pain patients report reducing and quitting opioid use as a result of enrollment in the NM MCP
  – No existing studies can confirm or deny the patients’ claims

• **Sample:** Back pain patients filling opioid prescriptions in 2 of 3 months (pre-enrollment for MCP; first 3 months for Comparison)
  – 37 MCP patients (67% male, 49)
  – 29 Comparison Group patients (71% male, 59)

• **Outcomes:** Ceased opioid use, reduced opioid use, and average daily use (mg IV morphine)

• **Independent variables:** MCP enrollment, month, age, gender, patient fixed effects
Prescription Monitoring Program Analysis Patient-Level

Effect of Enrollment in the Program on Prescription Opioid Use

1. Complete cessation of opioid use: \{0,1\}
   - Did a patient fill any prescriptions in the last three months of observation?

2. Reduction in opioid use: \{0,1\}

<table>
<thead>
<tr>
<th>3-Month Group</th>
<th>Months 1 to 3</th>
<th>Months 4 to 6</th>
<th>Months 7 to 9</th>
<th>Months 10 to 12</th>
<th>Months 13 to 15</th>
<th>Months 16 to 18</th>
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<tr>
<td>MCP</td>
<td>Pre-Enrollment</td>
<td>First Year Post-Enrollment</td>
<td>Post-Renewal</td>
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<td>Comparison Group</td>
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</tbody>
</table>
## Descriptive Statistics

<table>
<thead>
<tr>
<th>Variable (N=66)</th>
<th>Comparison Group (N=29)</th>
<th>MCP (N=37)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ceased opioid use {0,1}</td>
<td>3.4% (1)</td>
<td>40.5% (15)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Reduced opioid use {0,1}</td>
<td>44.8% (13)</td>
<td>83.8% (31)</td>
<td>0.001</td>
</tr>
</tbody>
</table>
### Effect of MCP Enrollment on How Prescription Opioid Use Changes Over Time

- Establish differences in starting dosages of opioids
- Distinguish differences in how opioid use changed over time between the MCP group and the Comparison group

<table>
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<th>Months 16 to 18</th>
<th>Months 19 to 21</th>
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<td>First Year Post-Enrollment</td>
<td>Post-Renewal</td>
<td>Post-Renewal</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Comparison Group</td>
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</tbody>
</table>
Effect of MCP Enrollment in Mean Daily Dose: Raw Data

The University of New Mexico

Mean daily mg IV morphine

Month

MCP Enrollment

Comparison Group

MCP Group
Linear Changes in Prescription Opioid Use

Full Results Available Upon Publication

The University of New Mexico

MCP Enrollment

Comparison Group

MCP Group

Mean daily mg IV morphine

Month

1 3 5 7 9 11 13 15 17
Limitations of the Studies

• Selection issues:
  – Self-selected into program/not randomly assigned
  – Only includes patients who renewed their cannabis licenses
  – MCP patients might be fundamentally different from Comparison Group patients/other patient populations

• Measurement issues:
  – Actual cannabis consumption not measured
  – Diversion/illegal consumption of both opioids and cannabis

• Generalizability issues:
  – Small N, only New Mexicans, one doctor/one clinic
  – Cannabis may be dangerous for certain patient and non-patient populations
  – Cannabis can be addicting (relative risk important)
Medical Implications of Current Study

• Cannabis may be a safer and more effective substitute for prescription painkillers for patients with chronic pain.
  – Revealed Preference: Effective substitution may be due to the cannabis plant’s ability to treat patients’ underlying pain symptoms, without the adverse side-effects of synthetic opioids (e.g., GI discomfort).

• Results contrary to “Gateway Hypothesis”
  – Preliminary findings (e.g., cannabis may also have indirect reductions of sedatives)
Research Opportunities NOW

• Types of research:
  – RCTs (require federal approval)
  – Naturalistic studies on how MCP enrollees self-medicate and are affected by cannabis-based medications (products) for conditions X, Y, and Z.
  – Public Policy Issues, e.g., access to care, cost effectiveness, quality incentives, efficacy of “self-regulation,” information dissemination
  – Case studies, e.g., Baby Amylea
Thank You for Your Attention!

This research was supported in part by the Medical Cannabis Research Fund mcrf.unm.edu