Chronic Opioid Therapy and Return to Work

Robert Lavin, MD, MS
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I have NO RELEVANT financial disclosures

Robert Lavin, M.D.
Why look at opioids?


% Total Pharmacy Spending.

- Antidepressants: 6.3%
- Skeletal Muscle Relaxants: 6.4%
- Dermatologicals: 7.4%
- Anti-Inflammatories: 8.8%
- Anticonvulsants: 14.8%
- Opioid Analgesics: 30.3%

[Graph showing percentage distribution of pharmacy spending on different types of medications]
Sobering Statistics

NY Times, Sunday Sept. 3, 2016

CDC provisional data for 2016

• 2016 Drug-related deaths 64,000
• 2015 Drug-related deaths 52,404 (22% increase)
• Majority of deaths (83%) in 2016 involved an opioid
  • prescript. opioids 14,400
  • fentanyl/analogues 20,100
  • heroin 15,400
  • methadone 3,300
• 2010 vs. 2016 opioid OD deaths > 6,000 vs. 53,000
Drug OD deaths / 100,000 (21 states with high quality data)

• Three states with greatest 1-year increases in 2016:
  - Maryland  21 → 36
  - Florida    16 → 25
  - Delaware  21 → 32

NJ and Penn not mentioned
Perspective – General Population

• Large national pharmacy database found that among more than 10 million incident opioid recipients - Quinn et al., 2017

Hazard Rates (95% CI)

- Prior nonopioid SUD diagnoses 3.15 (3.06-3.24)
- Depressive disorder 1.94 (1.91-1.96)
- Anxiety disorder 1.92 (1.89-1.95)
- Suicide/self-injury 2.55 (2.21-2.94)
- MVA 1.99 (1.85-2.14) – Quinn et al., 2017

• In 2015, 91.8 million (37.8%) U.S. adults used prescription opioids; 11.5 million (4.7%) misused them; and 1.9 million (0.8%) had a use disorder
  - Han, et al., Ann Intern Med. 2017
Recent reductions in opioids prescribed for injured workers in most states

Large variations between states and amounts of opioids prescribed

Thumula, et al., 2017
Opioid Therapy and Ability to Return to Work

Presentation Outline

• Pharmacologic Considerations
• CDC Guidelines
• ACOEM Guidelines
• Summary of Evidence for ACOEM Guidelines
• Summary of Other Studies
  ▪ Epidemiologic
  ▪ Psychomotor
  ▪ Cognitive
  ▪ Driving / Simulation
Acute vs. Chronic Opioid Use

- Acute adverse drug effects of opioids: sedation & confusion
- Associated with:
  - New medication
  - Increase in dose
- Resolves within 5 to 7 days (Tolerance) with chronic exposure
- Prescription opioids often blamed for effects of other substances: TCAs, muscle relaxants, sedative-hypnotics, anxiolytics, THC, cocaine, alcohol, and acute (illicit) exposure to opioids (snorting, IV)
Short-acting vs. Long-acting Opiates

**Short-acting opioid**

- Lower dose, faster uptake*, shorter duration

**Long-acting opioid**

- Higher dose*, slower uptake, longer duration

*Associated with psychogenic effects (euphoria, sedation, abuse)
Summary of CDC Guidelines
Basic Principles of Chronic Non-cancer Pain Treatment

• Non-opioid treatments are preferred or used in combination with opioids
• When indicated opioids are prescribed at the lowest effective dose for the shortest reasonable time; avoid increasing dosage to ≥ 90 MME/day or carefully justify decision to do so.
• Clinicians should exercise caution when prescribing opioids and should monitor all patients closely (PDMP, UDT)
• Continue opioids only if there is clinically meaningful improvement in pain and function that outweighs risks to patient safety.
CDC Guidelines

• Type 1 evidence: Randomized clinical trials or overwhelming evidence from observational studies.

• Type 2 evidence: Randomized clinical trials with important limitations or exceptionally strong evidence from observational studies.

• Type 3 evidence: Observational studies or randomized clinical trials with notable limitations.

• Type 4 evidence: Clinical experience and observations, observational studies with important limitations, or randomized clinical trials with several major limitations.
ACOEM Guidelines

• “Quality evidence consistently demonstrates increased risk of vehicle crashes and is recommended as the surrogate for other safety sensitive work tasks.”

• “Acute or chronic opioid use is not recommended for patients who perform safety sensitive jobs. By analogy, this recommendation is extended beyond operation of motor vehicles to include other modes of transportation, forklift driving, overhead crane operation, heavy equipment operation, work with sharps, work with risk of injury (eg, heights) and tasks involving high levels of cognitive function.”
We found an increased standardized incidence ratio of MVAs that resulted in injury and involved drivers exposed to codeine.

<table>
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<th>Conclusions (Table 1) – Bachs 2009</th>
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<td>“We found an increased standardized incidence ratio of MVAs that resulted in injury and involved drivers exposed to codeine.”</td>
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<td>65 of 83 high consuming codeine subjects involved in MVAs were prescribed other impairing drugs in the days prior to filling codeine prescription. The remaining 18 patients analyzed separately did not reveal increased risk for MVA.</td>
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Conclusions (Table 1) – Engeland 2007

Increased risk for MVA with injury for users of:
- opioids (2.0)
- benzos (2.9)
- hypnotics (3.3)

• No relationship between when drug was prescribed; cannot distinguish drug risk from risky behavior of person taking the drug.
• Subjects involved in MVAs may have different risk for MVAs than general population.
• Was MVA related to drug or medical condition?
• Retrospective study
• Does not address polypharmacy or toxicology screening
Conclusions (Table 1) – Bramness 2012

“Men exposed to methadone appear to have an increased risk of being involved in motor vehicle accidents involving personal injuries.”

- Opioid Maintenance Treatment pts
- Many prescribed benzos; those not using benzos had higher risk of MVA
- Use of other controlled substances and alcohol were not assessed
- “Patients were considered to be exposed even if they did not collect prescriptions regularly”
- Unknown whether new OMT patients or had recent changes in dosing
“Among drivers prescribed opioids, a significant relationship exists between drug dose and risk of road trauma.”

• OR ranged from 1.21 – 1.42 depending on dose.
• More relevant population (methadone Rx excluded)

• Ontario Provincial Public Drug Program eligibility criteria: “unemployed, disability, high Rx drug costs relative to net income, or receipt of home care services.”
• Excluded methadone Rx, but unknown: how prescription drugs were used, diversion, illicit use, or private payment for drugs (double dipping).
• Controlled for psychotropics present in association opioids.
“[T]he risk of [MVA] is increased by the use of benzodiazepines, [and] opioids ... for the duration of their usage, the risk decreasing once the medication is discontinued.”

- Looks at **acute opioid use**, not chronic use. **Duration of prescriptions was unknown.**
- **Was MVA due to effects of disease vs. prescribed opioid medications?**
- Comorbid substance use/misuse was not assessed
### Conclusions (Table 1) – Morland 2011

**“[I]n Northern European countries, alcohol and impairing non-alcohol drugs are frequently detected in killed vehicle drivers, and very frequently in younger drivers killed in single vehicle accidents.”**

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<th>Of fatalities:</th>
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<td>• 522 drugs +/- alcohol; 225 drugs only</td>
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<td>• Only 17 non-SA opioids + 26 Methadone + &amp; Buprenorphine +</td>
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<td>• Unclear how many opioids were legal Rx or used with other psychoactive drugs and alcohol.</td>
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<td>• 40% of single vehicle crashes w/o alcohol had illicit drugs (THC, amphetamines); Benzos &gt; opioids.</td>
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<td>• 67 had antidepressants + 11 antipsych.</td>
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Conclusions (Table 1) – Majdzadeh 2009

“These results suggest a heightened risk of traffic injuries after opium consumption in regular users.”

- “75 regular opium users”
- Included inhalation of opium
- No evidence of controlled use or stable serum levels
Conclusions (Table 1) – Corsenac 2012

“196 drivers exposed to buprenorphine or methadone on the day of crash were young, essentially males, with an important co-consumption of other substances (alcohol and benzodiazepines).”

• Subjects with SA hx (methadone and buprenorphine) plus alcohol and other psychoactive substances
• “The increased risk could be explained by the combined effect of risky behaviors and treatments.”
“[T]he results of our study suggest that opioids negatively affect safe driving.”

- Odds Ratio of unsafe driving action controlling for age, sex, other medications, and driving record. OR for females + for opioids from ages 25 (OR: 1.35) to 55 (OR: 1.30). For males ages 25 (OR: 1.66) to 65 (OR: 1.39). OR for older drivers on opioids were not elevated.

- Unclear whether opioids were prescription or illicit
- Approximately 60% of those drivers taking opioid analgesics were also taking at least one other medication compared to only 16% of those drivers testing negative for opioids.
- Drivers taking opioids had worse driving records.
French drivers in MVAs OR + for morphine = 8.2 was highly significant, but opioids represented 2.7% of 900 injured drivers (n=24).

- Measurement of morphine introduces a bias to include heroin and exclude other legitimate synthetic prescription opioids.
- Unclear how many drivers were using morphine in combination with other psychoactive and illicit substances.
Conclusions (Table 1) – Movig 2004

“Increased [2-fold] risks, although not statistically significantly, were assessed for drivers using amphetamines, cocaine, or opiates.”

- Study noted significant increased risk for MVAs for benzodiazepines, alcohol, combinations of drugs, and combinations of drugs and alcohol.
- **Of the 9 out of 110 drivers + for opioids it is unclear how many were + for other psychoactive drugs and alcohol.**
• Study examined risks related to sleepiness, sleep apnea, and meds. “There was an increased accident risk with narcotic analgesic use (OR 2.40, p 0.01) and antihistamine use (OR 3.44, p 0.04).”

• Acute or chronic opioid use?
• Prescription or illicit opioids?
• Related to pain vs. opioid medication?
Critique of ACOEM Guidelines

- Epidemiologic studies show an association; do not determine cause and effect
- Do not account for presence of other drugs of abuse, acute or chronic opioid use, opioids used for SA vs. pain vs. illicit use.
- Studies of driving statistics are used as surrogates for studies on working populations
- Are these populations suitable proxies for working populations?
Other Epidemiologic Driving Studies NOT referenced by ACOEM Practice Guidelines

• Bernard et al., 2008 – 635 individuals using methadone suspected of drugged driving. Only 10 had methadone w/o any other substances. “Cases of driving impairment involving methadone alone were very rare. No correlation between methadone concentration and impairment.”

• Orriols, et al., 2010 - Unable to relate opioids used for pain to responsibility for MVAs in large French epidemiologic study. Did not distinguish licit from illicit use of opioids, but distinguished difference between opioids used to treat pain (OR = 1.04) vs. opioid dependence (OR=1.46).
Association ≠ Relationship

• Ice cream consumption is associated with wearing swimsuits.

• Penicillin prescriptions are associated with treatments for STDs. *What about five year-olds with strep throat?*

• Opioid prescriptions are associated with OUD & SA.

• Are we measuring drug effects or the population attracted to the drugs? (Willingness to engage in risky behavior and SA)
Psychometric Testing

• Haythornthwaite et al., 1998 – Compared to chronic pain group not receiving opioids, “group receiving long-acting opioid medications showed significant improvement [in] psychomotor speed and sustained attention.”

• Dagtekin et al., 2007 – “Long-term use of transdermal buprenorphine for chronic noncancer pain does not impair driving ability, but because of the individual variability of test results, an individual assessment is recommended.”

• Jamison, et al., 2003 - psychomotor effects of long-term opioid use in 144 LBP patients. All subjects were administered two neuropsychological tests at 90 and 180 days pre and post prescription opioids. “Test scores significantly improved while subjects were taking opioids for pain”
Psychomotor Testing continued

• Sabatowski et al., 2003 – “stable doses of transdermal fentanyl for the treatment of chronic non-cancer pain are **not associated** with significant impairments in psychomotor and cognitive performance.” (9/30 patients disqualified because additional drugs were present)

• Mintzer, et al., 2002 – Methadone maintenance subjects were **impaired** on psychomotor testing. “subjects had years of polysubstance abuse, and personality type and frontal lobe dysfunction may play a role in abnormal psychomotor testing. (Problem: Participants using heroin or cocaine only abstained for 24 h prior to performance testing.)

• Pluck et al., 2012 - Opioid abusers may have frontal lobe behaviors that preceded SA.

• Comparing opioid abusers to carefully monitored chronic pain patients who use their opioids as prescribed may not be appropriate.
Cognitive Testing

• Darke, et al., 2012 “The [opioid maintenance] group exhibited poorer performance” (Problem: The opioid maintenance group was using multiple psychotropic meds within 48 hours prior to testing, based on subject report.)

• Loeber, et al., 2011 - [In SA patients] “the duration of opiate dependence and maintenance treatment [and] substance consumption (alcohol, amphetamines, and cocaine) are the main variables contributing to cognitive impairment ... Comorbid depressive symptoms negatively affected reaction times”
Cognitive Testing continued

• Shmygalev, et al., 2011 – 30 Patients on stable dose of SL buprenorphine showed no significant impairment of complex psychomotor or cognitive performance as compared to healthy controls. However, intake of illicit drugs [19/30 excluded from study] as well as the lack of social reliability are major problems...Despite of the absence of a relevant impact of the drug on driving ability, those patients do not seem to be qualified for getting their driving license.”

• Tassain, et al., 2003 - 12 months treatment with oral morphine does not disrupt cognitive functioning [and] results in moderate improvement of some aspects of cognitive functioning, as a consequence of the pain relief and concomitant improvement of well-being and mood. [only 18 chronic pain patients in test group and 10 chronic pain patients in control group]
Driving / Simulation

• Byas-Smith, et al., 2005 – Byas-Smith et al., 2005 – “Many patients with chronic pain, even if treated with potent analgesics such as morphine and hydromorphone, show comparable driving ability as normals.”

• Gaertner et al., 2006 – “The use of Controlled Release Oxycodone does not prohibit driving, but individual assessment is necessary.”

• Gaertner et al., 2008 – “increasing the daily dosage of opioids ...had no effect on functions relevant to driving ability, as assessed 7 days later.”

• Galski et al., 2000 – chronic opioid therapy (N=16)] patients outperformed the cerebrally compromised controls on driving tests... Participants using opioids demonstrated rapid completion times on tasks [but] made significantly more errors compared to the cerebrally compromised control group”
Driving Simulation continued

- Linnoila and Hakkinen, 1974 – slightly more collisions in driver simulations among the codeine-treated group
- Lenné et al., 2003 – There was no difference in driving ability between the placebo group and [former heroin addicts] treated with either Buprenorphine or Methadone
- Leung et al., 2013; Nilsen et al., 2011 – no differences between codeine group and controls in driver simulations
- Menefee, et al., 2004 – “addition of transdermal fentanyl ... for patients with chronic nonmalignant pain did not negatively affect their driving performances, reaction times, cognition, or balance.”
Problems: Psychomotor, Cognitive, Driving Studies

- Small numbers of subjects in studies
- No UDS
- Do not control for co-prescribed substances (TCAs, sedative-hypnotics, benzos, muscle relaxants, etc.)
- Use of SA patients not comparable
  - Recent use of illicit drugs
  - Premorbid behavioral differences (brain scan and behavioral studies)
- Unclear whether pain or pain medication affects performance
- Did not assess for co-morbid conditions (depression) that affect responses
- Different test instruments may not be comparable between studies
- Subjects’ test responses under less than ideal situations not evaluated
Summaries: Fishbain, et al., 2003 – Evidence-based review according to AHCPR guidelines and a quantitative method

(1) Moderate evidence for no psychomotor impairment of opioid maintained patients
(2) Inconclusive evidence for no cognitive impairment of opioid- maintained patients
(3) Strong evidence on multiple studies for no psychomotor impairment immediately after being given opioids
(4) Strong evidence for no greater incidence in motor vehicle violations/motor vehicle accidents vs. comparable controls of opioid-maintained patients.
(5) Consistent evidence for no impairment in driving simulation and off/on road driving of opioid-maintained patients.

“it can be concluded that the majority of the reviewed studies appeared to indicate that opioids do not impair driving-related skills in opioid dependent/tolerant patients.”
Summaries: Borgeat, 2010 Optimizing Driving Safety

• Functional status and side effects of medications should be reassessed continuously.

• The patient should be asked repeatedly how they feel their medications are affecting their driving ability. A discussion dealing with the realities and responsibilities of driving should be undertaken with the patient.

• Patient examination should include mental status, proprioception, and analysis of walking.

• Any drug adjustment (increase) requires no driving for at least 5 to 7 days.

• Alcohol consumption is prohibited. The addition of a new drug acting on the CNS requires no driving for at least 5 to 7 days before a new medical examination can be performed.

• According to disease worsening or development of comorbidity, some driving restrictions should be considered (no night driving, no driving in the rain or snow, and so on).
“it is important to consider whether LOT [Long-term Opioid Therapy] will result in clinically meaningful improvements in function such as readiness to return to work/duty and/or measurable improvement in other areas of function, such that the benefits outweigh the potential harms.”
Clinically Meaningful Improvement in Function
Guideline for Prescribing Opioids to Treat Pain in Injured Workers


• “Effective use of opioids must result in **clinically meaningful improvement in function**”

• “Continuing to prescribe opioids in the absence of clinically meaningful improvement in function or after the development of a severe adverse outcome is not considered proper and necessary care in the workers’ compensation system.”
Our Research with LWCC database

Ed Bernacki, Grant Tao, Larry Yuspeh, & others

Negative outcomes with regard to claim costs and duration of disability are associated with:

- Prescription opioids and other controlled substances
- Increasing doses of prescription opioids
- Early post injury prescription of opioids

These findings have been corroborated by other researchers.
Timing is Everything

• Early opioid prescribing
If opioids were prescribed within initial 60 days post injury, then OR of claim \( \geq 100,000 \) = 1.88 (compared to claims with no opioids).

Tao, et al., JOEM 2015

• Early opioid discontinuation
If opioids were prescribed during initial 30 days and discontinued after initial 30 days, the OR of claim \( \geq 100,000 \) = 1.08 (which is comparable to claims with no opioids).

Lavin, et al., JOEM 2016
New Data – Do Opioids Prevent Injured Workers from being Released to RTW?

Opioids – prescribed as part of a comprehensive Occupational Injury Program (case management, surgery, med management, rehabilitation, ergonomics, job placement) for injured workers who show functional benefits and use responsibly.

Methodology – Divide Injured Workers at JHMI who received
• No Opioids
• Acute Opioids (< 3 months opioids)
• Chronic Opioids (≥ 3 consecutive months opioids)
• Temporary Total Days (TTD)
• Number of Days Opioids Prescribed
• RTW (Released to Return to Work)
Chronic Opioid Therapy and Released to RTW

Lavin, et al., JOEM 2017

- Opioids < 3 consecutive months
  419 claimants  99.8% RTW
- Opioids ≥ 3 consecutive months
  112 claimants  98.2% RTW
  66.8 Ave. MED/Day
  (CDC Guidelines < 90 MED/Day)
- 64 claimants released to RTW while on opioids
- Average opioid cost = 3.61% of total claim cost
Fig 2. Supply Days-TTD: A Surrogate for Days Working while taking Opioid

Consecutive Months of Opioid

% of Workers

Supply Days-TTD

# Workers

Supply Days-TTD
Conclusions
Considerations for continuing to prescribe opioids

• Is individual at risk for aberrant drug use?
• Is there evidence of clinically meaningful improvement in function that justifies risk?
• Does daily opioid dose stabilize?
• Can the individual be closely monitored?
• Are opioids being used as one part of a comprehensive work rehabilitation program?
Co-authors

• Edward Bernacki
• Xuguang (Grant) Tao
• Nimisha Kalia
• Larry Yuspeh
• Jill Barry
Questions?