Evan Schwarz MD, FACEP, FACMT
Associate Professor of Emergency Medicine
Washington University School of Medicine
Disclosures

Physician Consultant for the State Targeted Response
Barnes Jewish Hospital Foundation Grant for Addiction Management
ACEP Opioid Task Force Member

Thanks to Dr. Eric Ketcham and Dr. Kate Hawk for Use of Some Slides
So We Have 90 Minutes...And That Is A Long Time!

Statistics

Pathophysiology

Treatments

Opioid Alternatives

Opioid Prescribing

Harm Reduction
58,000 Died in Vietnam War
51,000 Died from AIDS in ’95
> 70,000 Died in 2017

Life Expectancy Decreases For 3rd Year in a Row
So What Changed?

What caused the death rate to increase 29% in one year?
What contributed to average life expectancy falling 3 years in a row?

Rhode Island 2013-14: 32% of 165 unintentional deaths were fentanyl related
Not The First Time...
What Happens When We Do Things Poorly
Preliminary 2017 Data:

Opioid overdose deaths increase to ~134 Americans per day.

Source: National Center for Health Statistics, CDC Wonder

www.drugabuse.gov/related-topics/trends-statistics/overdose-death-rates
Preliminary 2017 Data:

Fentanyl and fentanyl analogues related overdoses are the most rapidly growing type of opioid overdose deaths.
MO Dept of Health and Human Services

Heroin
Non Heroin
Opioids

Year 2001-2016

# Deaths

MO Dept of Health and Human Services
Criminal Chemistry

Traffickers manufacturing fentanyl often purchase the key ingredient from China, which doesn’t regulate its sale. Here’s how the chemical building blocks become a highly profitable street drug.

The key ingredient is NPP, 25 grams of which can be bought from China for about $87.

NPP can be combined with about $720 of other chemicals† to produce fentanyl.

The resulting 25 grams of fentanyl cost about $810 to produce... and are equivalent to up to $800,000 of pills on the black market.

†Average current price from Chinese suppliers
‡Prices from U.S. suppliers

Sources: NES Inc.; Drug Enforcement Administration; Calgary Police

THE WALL STREET JOURNAL
Criminal Chemistry
Traffickers manufacturing fentanyl often purchase the key ingredient from China, which doesn’t regulate its sale. Here’s how the chemical building blocks become a highly profitable street drug.

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...and are equivalent to up to $800,000 of pills on the black market.

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...and are equivalent to up to $800,000 of pills on the black market.

Sources: NES Inc.; Drug Enforcement Administration; Calgary Police

THE WALL STREET JOURNAL.
ADDICTION

A MEDICAL DISEASE

Drug seeking is compulsive. Difficult to control.

Addiction > consequence.

Relapsing & remitting.

Patient’s suffering with O.U.D. Use to:

- Get high
- Normal
- Not feel sick

Chemical Receptor Imbalance – an organic brain disease

Endorphins
Dynorphins
Dopamine
Reward system
Malfunction
Voluntary Action \[\rightarrow\] Behavioral Change \[\rightarrow\] Impulsive Action

Neuroadaptations

NEJM 2016;374:363.
net·fli·xing
/ˈnetflɪks-ing/ v

1. The act of watching an entire season of a show in one sitting.

A totally valid excuse for avoiding social obligations.

“Sorry I can’t make it to the party tonight. I am netflixing.” — CalumCJL
Typically, dopamine increases in response to natural rewards such as food. When cocaine is taken, dopamine increases are exaggerated, and communication is altered.
Opioid Agonist Therapy is Much More Effective than Drug Counseling!!

Swedish Study:
- 40 patients randomized
- Daily supervised medication administration for the first 6 months

Retention at 1 year:
- 75% in the bup group
- 0% in the placebo group

1 year Mortality:
- 0% in the bup group
- 20% in the taper group

Medication for Addiction Treatment

- Methadone
- Buprenorphine
- Naltrexone
Medication for Addiction Treatment

Methadone

Buprenorphine

Naltrexone
Medication for Addiction Treatment

Methadone

Buprenorphine

Naltrexone

Abstinence Based Care: About 5%
Methadone

Adverse Events

Tough To Start
Delirium/Precipitated Withdrawal

Naltrexone
DEPENDENCE ≠ ADDICTION

Every 19 minutes, an opioid addicted baby is born in the United States.
In **1996**, France responded to its heroin overdose epidemic by training GP’s to prescribe bup.

Over 8 years....

- 3x increase methadone treated patients (~15K pts)
- + 4.5x increase in bupe tx pts (~90K pts)

90% reduction in heroin overdoses!!

Heroin overdose deaths and opioid agonist treatment: Baltimore, MD, 1995–2009

- Rate of heroin overdose deaths drops in half.

- Despite a substantial increase in local heroin purity

MEDICATION FIRST MODEL

BUPRENORPHINE:
Suboxone and Subutex For Opiate Addiction Treatment
ED Initiated Suboxone Treatment for Opioid Dependence

Non medical prescription use or heroin use in last 30 days
+UDS
MINI score ≥ 3
Patients: 53% IVDA; 25% prescription drugs only
> 50% with psychiatric d/o
ETOH and cocaine abuse
329 Randomized

104 Randomized to receive a referral
   104 Received referral as randomized

   102 Included in the primary analysis
      2 Lost to follow-up

   69 Completed 30-d follow-up interviews for assessment of secondary outcomes
      24 Unable to contact
         16 Inpatient treatment
         5 Incarcerated
         3 Lost to follow-up
      11 Refused

111 Randomized to receive a brief intervention
   111 Received brief intervention as randomized

   111 Included in the primary analysis

   82 Completed 30-d follow-up interviews for assessment of secondary outcomes
      19 Unable to contact
         9 Inpatient treatment
         3 Incarcerated
         7 Lost to follow-up
      10 Refused

114 Randomized to receive brief intervention and buprenorphine
   114 Received a brief intervention and buprenorphine as randomized

   114 Included in the primary analysis

   93 Completed 30-d follow-up interviews for assessment of secondary outcomes
      13 Unable to contact
         7 Inpatient treatment
         2 Incarcerated
         4 Lost to follow-up
      8 Refused
At 30 Days

<table>
<thead>
<tr>
<th>Referral</th>
<th>BI</th>
<th>Suboxone</th>
</tr>
</thead>
<tbody>
<tr>
<td>38/102 (37% CI 28-47)</td>
<td>50/111 (45% CI 36-54)</td>
<td>89/114 (78% CI 70-85)</td>
</tr>
<tr>
<td>Inpatient: 37%</td>
<td>Inpatient: 35%</td>
<td>Inpatient: 11%</td>
</tr>
</tbody>
</table>

Buprenorphine group also had larger reduction in mean days of illicit use.
What It Is Already Like Working in the ED

We Can’t Handle Anything Else!
<table>
<thead>
<tr>
<th>Myth</th>
<th>Reality</th>
<th>Possible Policy Response</th>
</tr>
</thead>
<tbody>
<tr>
<td>Buprenorphine treatment is more dangerous than other chronic disease management.</td>
<td>Buprenorphine treatment is simpler than many other routine treatments in primary care, such as titrating insulin or starting anticoagulation. But physicians receive little training in it.</td>
<td>Amend federal buprenorphine-treatment eligibility requirements to include training during medical school and competency prerequisites during medical school and residency programs. As with past provider education about opioid use disorder, common myths.</td>
</tr>
<tr>
<td>Use of buprenorphine is simply a “replacement” addiction.</td>
<td>Addiction is defined as compulsively using a drug despite harm. Taking a prescribed medication to manage a chronic condition does not meet that definition.</td>
<td>Provide education to patients on the potential for misuse of prescription medication and that buprenorphine can be safely taken.</td>
</tr>
<tr>
<td>Detoxification for opioid use disorder is effective.</td>
<td>There are no robust data showing that inpatient detoxification reduces the risk of relapse, discontinuing treatment, and developing tolerance.</td>
<td>Develop and disseminate protocols for primary care settings that emphasize out-of-office induction and treatment.</td>
</tr>
<tr>
<td>Prescribing buprenorphine can reduce overdose deaths.</td>
<td>Despite decreasing opioid prescribing, overdose mortality has increased. Patients with opioid use disorder may shift to the illicit drug market, where the risk of overdose is higher.</td>
<td>Develop a national system of virtual consultation for physicians to reach addiction and pain specialists who can support treatment of patients with suspected opioid use disorder.</td>
</tr>
</tbody>
</table>

NEJM 2018;379:1-4
Unfortunately Nearly 80% Don’t Receive Treatment!!

NEJM 2018;379:1-4
Did Any Of This Really Make A Difference?

Figure 2 Engagement in formal addiction treatment.

Patients in treatment/compliant with Meds

Journal of the American Medical Association
What It Is Already Like Working in the ED

We Can’t Handle Anything Else!

This is Outside of What We Do

We Don’t Have the Resources

It’s Too Hard

Someone Else Will Do It
The Benefits

Ondansetron
Haldol
Promethazine
Prochlorperazine

45 minutes to place an IV

And Nothing Really Works

OR…

Maybe an IM or SL dose of Ondansetron

Start Buprenorphine
Titrate if Needed

Discharged within an hour

Addictionpolicy.org
The Paradox of Diverted Buprenorphine
April 18, 2019

Written by Mark Gold, MD
Dr. Mark S. Gold is a teacher of the year, translational researcher, author, mentor and inventor best known for his work on the brain systems underlying the effects of opiate drugs, cocaine and food.
Read more about Dr. Mark Gold
<table>
<thead>
<tr>
<th>Concern</th>
<th>Reality</th>
<th>Solution</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients will return repeatedly for redosing.</td>
<td>Repeated visits for redosing have not been demonstrated at sites that consistently offer buprenorphine.</td>
<td></td>
</tr>
<tr>
<td>Patients will flock to the ED for treatment.</td>
<td>Patients with OUD are already in the ED. Sites with ED-initiated buprenorphine do not report an uptake of patients seeking treatment.</td>
<td>Initiate treatment protocols at triage to promote rapid assessment, treatment, and referral.</td>
</tr>
<tr>
<td>Many patients don’t want treatment anyway.</td>
<td>Some patients, often after an overdose, are not ready for treatment after a brief psychosocial intervention, but discussion may lead to a change in motivation in the future. The ED visit is often a missed opportunity to engage patients who may be contemplating a positive change but need guidance and support.</td>
<td>Introduce harm-reduction strategies such as overdose prevention and naloxone distribution. Establish rapport to facilitate improved outcomes.</td>
</tr>
<tr>
<td>Obtaining a waiver to prescribe buprenorphine is too burdensome.</td>
<td>The training required to obtain a waiver can be done all online or as half-day courses coupled with half-day online services. Most training is free and similar to other required learning and counts toward CME requirements for specialty certification, recertification, and licensing in many states.</td>
<td>Identify resources online and at institutions using the SAMHSA and ASAM websites. Offer faculty development days or group learning events.</td>
</tr>
</tbody>
</table>

* ASAM denotes the American Society of Addiction Medicine, CME continuing medical education, and SAMHSA the Substance Abuse and Mental Health Services Administration.
So How Do You Give Buprenorphine?

• SL Formulation with poor bioavailability
• Either film or tabs take approximately 5 minutes to absorb
• The combo product is only there for misuse
• Should get effects within 15-20 minutes
• Dose 12-24 mg/day
BUPRENORPHINE (BUP) ALGORITHM

MODERATE TO SEVERE OPIOID WITHDRAWAL?

YES

COMPPLICATING FACTORS?

YES

ADMINISTER
8 mg SL BUP

1 HOUR

SYMPTOMS IMPROVED
AFTER 1ST DOSE?

YES

GIVE 2ND DOSE
8-24 mg SL BUP

1 HOUR

SYMPTOMATIC TREATMENT

HALOXYNE KIT
(Optional)
PRESCRIBE BUP
IF WAVERED

NO

MODERATE TO SEVERE OPIOID WITHDRAWAL?

NO

ADDRESS
COMPPLICATING
FACTORS BEFORE
PROCEEDING

NO

YES

COMPLICATING FACTORS

Identify and manage complicating factors prior to proceeding.
The only absolute contraindication is allergy to buprenorphine.

Refer to Buprenorphine Guide before dosing buprenorphine for:

- Unlikely to precipitate withdrawal
- 20 weeks pregnant
- Intoxicated or altered
- Withdrawal precipitated by naloxone
- Taking methadone or long acting opioid
- Chronic pain patients taking prescribed opioids
- Withdrawal symptoms are inconsistent or borderline (COWS 6-8)
- Or opioid use within 12 hours; consider beginning with a low dose (2-4 mg SL) and titrating every 1-2 hours

PARENTERAL DOSING

- Use if unable to take sublingual (SL)
- Start with 0.3 mg IV/IM buprenorphine; may repeat as needed; switch to SL when tolerated

PRECIPITATED WITHDRAWAL

- Buprenorphine can cause precipitated withdrawal if too large a dose is given too soon after the last opioid use
- The longer the time since last opioid use (> 24 hours) and the more severe the withdrawal symptoms (COWS ≥ 13) the better the response to initial dosing
- Only patients with objective improvement in withdrawal after the 1st dose should receive subsequent dosing
- Worsening after buprenorphine is likely precipitated withdrawal; no further buprenorphine should be administered in the ED; switch to symptomatic treatment

SYMPTOMATIC TREATMENT

- Supportive medications such as clonidine, gabapentin, metoclopramide, low-dose ketamine, acetaminophen, NSAIDs

LOWER TOTAL DOSE OPTION (16 mg)

- Possible lower risk of sedation or precipitated withdrawal
- Patients may go back into withdrawal in less than 12 hours increasing risk of early dropout
- Buprenorphine prescription or next day follow-up should be available

HIGHER TOTAL DOSE OPTION (24-32 mg)

- Increased magnitude and duration of opioid blockade
- More complete treatment of withdrawal in heavy users
ED-Initiated Buprenorphine

Diagnosis of Moderate to Severe Opioid Use Disorder

Assess for opioid type and last use
Patients taking methadone may have withdrawal reactions to buprenorphine up to 72 hours after last use
Consider consultation before starting buprenorphine in these patients

COWS

(0-7) none - mild withdrawal
(≥8) mild - severe withdrawal

Dosing:
None in ED

Waivered provider able to prescribe buprenorphine?

YES
Unobserved buprenorphine induction and referral for ongoing treatment

NO
Referral for ongoing treatment

Dosing:
4-8mg SL*

Observe for 45-60 min
No adverse reaction
If initial dose 4mg SL, repeat 4mg SL for total 8mg

Waivered provider able to prescribe buprenorphine?

YES
Prescription
16mg dosing for each day until appointment for ongoing treatment

NO
Consider return to the ED for 2 days of 16mg dosing (72-hour rule)
Referral for ongoing treatment

Notes:
*Clinical Opioid Withdrawal Scale (COWS) ≥ 13 (Moderate-Severe) consider starting with 8 mg buprenorphine or buprenorphine/naloxone SL
**Patient remains in moderate withdrawal may consider adding additional 4mg and observation for 60 minutes
Warm hand-offs with specific time & date to opioid treatment providers/programs within 24-72 hours whenever possible
All patients should be educated regarding dangers of benzodiazepine and alcohol co-use
Ancillary medication treatments with buprenorphine induction are not needed

https://medicine.yale.edu/edbup/treatment/
Some More Considerations

- An X-waiver is not required (72 hour rule)
- Don’t feel like you need to start with everyone
  - Can be difficult to combine with sedatives (benzo or alcohol dependent)
  - Start with the easy patients!
- No issue with renal impairment
- What about hepatic issues?
- Aside from HCG, no labs are required
  - They can be obtained at follow up
What About Poor Follow up: High Dose Bup Loading?

Some Thought That A Single Dose is Beneficial Smartphrase for documentation
What Is Precipitated Withdrawal?
Treatment = More Buprenorphine

Using COWS Can Help
Many Patients Actually Are Familiar with This
ED: Calls Central Agency

Behavioral Health Network of Greater St. Louis

5 Treatment Centers in St. Louis Receiving State Funds
Recovery Coach In the ED

• Meets with patient. Gets additional ‘buy-in’
• Sets up follow up and arranges them getting there
  • Normally in 0-3 days
• Gives them naloxone
• Each patient receives a phone number to call
• Fills buprenorphine prescription
  • Between 20-30 waived ED physicians

PATIENTS HAVE BEEN VERY RECEPTIVE TO THIS!
If you have good insurance or financial resources?

ED Calls → Treatment Center Follow up Obtained → Bup in the ED/ Naloxone prescription

Treatment Programs Contacted Us Once they Saw We Had This Interest They Actually Want Our Referrals and Are Willing to Work With Us
Pts with an ID consult requiring at least 2 weeks of IV antibiotics
Pt had an OUD
Addiction consults at primary team’s discretion
Included 38 pts with a consult and 87 without
ICU Total Re-Admit Days: 9 days vs 88 days
ED-BRIDGE supports emergency departments throughout California to develop and implement plans for 24/7 access to buprenorphine for patients with opioid use disorder.

THE TREATMENT GAP

This E.R. Treats Opioid Addiction on Demand. That’s Very Rare.

Some hospital emergency departments are giving people medicine for withdrawal, plugging a hole in a system that too often fails to provide immediate treatment.
Providing clinical leaders with the tools necessary to start and maintain patients on effective treatment for opioid use disorder

Patients with opioid use disorder are frequently hospitalized with complications from the condition, yet don’t receive treatment for their underlying disease. This is a missed opportunity that leaves patients at high risk of future overdose. These hospitalizations are an ideal opportunity to start effective medication treatment for addiction and connect patients to ongoing outpatient services.

Two key treatments for opioid use disorder — buprenorphine and methadone — have been proven to cut overdose rates by two-thirds, lower HIV infections, and reduce criminal behavior. As many as 70% of patients are still in treatment after one year, compared to 6% of patients receiving medication-free treatment. However, when patients being treated with buprenorphine or methadone are hospitalized, these medications are often discontinued, increasing their risk of relapse.

This program provides clinical leaders with the tools they need to start and maintain patients on buprenorphine or methadone during hospitalizations for any condition, be it medical, surgical, or obstetric. Specialists from the University of California, San Francisco (UCSF) provide a suite of supports: coaching, toolkits, protocols, monographs for pharmacy and therapeutics committees, webinars, and onsite presentations.
Overview of Medication Assisted Treatment
HARM REDUCTION WORKS FOR PEOPLE WHO USE DRUGS.

HARM REDUCTION

HEALTH ALERT:
Fentanyl is killing Missourians.
Fentanyl is a dangerous opioid that is showing up in heroin, cocaine, methamphetamine, & other drugs.
ANYONE USING DRUGS IS AT RISK.

SAFETY TIPS:

Never use alone.
If you overdose, it is important to have someone around to help.

Stagger your use.
Use about 30 minutes apart so someone is alert enough to give naloxone or call 911.

Go slow and notice change.
Start with a little and beware of any change. Your supply may be mixed with other drugs you don’t know about. You never know how strong a new supply is.

Always carry naloxone.
It can reverse overdoses from heroin, fentanyl, and other opioids.
For more information on where to get naloxone visit: MissouriOpioidSTR.org

Missouri Institute of Mental Health
In an opioid emergency...

SECONDS COUNT

REACH FOR VOICE GUIDANCE

The first and only intelligent 2 mg take-home auto-injection system with voice and audio.

Ask your healthcare provider if EVZIO® is right for you.
I, Surgeon General of the United States Public Health Service, VADM Jerome Adams, am emphasizing the importance of the overdose-reversing drug naloxone. For patients currently taking high doses of opioids as prescribed for pain, individuals misusing prescription opioids, individuals using illicit opioids such as heroin or fentanyl, health care practitioners, family and friends of people who have an opioid use disorder, and community members who come into contact with people at risk for opioid overdose, knowing how to use naloxone and keeping it within reach can save a life.

April 5, 2018

BE PREPARED. GET NALOXONE. SAVE A LIFE.
Students Push for Narcan Availability on Harvard's Campus to Combat Overdoses


12,000 dosages administered from 2013-2015

93.5% survived overdose

84.3% alive at 1 year
Addiction & Overdose: Deadlier than STEMI @ 1 Year

Of discharged patients who survived after 3 days:

• **7.5% Mortality Rate @ 1 Year**

• OUD – a disease primarily of age 20 - 50

Of all patients (including patients not surviving to d/c):

• **7.3% Mortality Rate @ 1 Year**

• CAD – a disease primarily of age 60+
Other Harm Reduction Efforts

Syringe-exchange laws across the nation

- Green: Explicitly authorizes exchanges
- Light yellow: No laws prohibiting exchanges
- Dark yellow: Explicitly prohibits exchanges

SOURCE: The Pew Charitable Tru
The Opioid Crisis Is Not A War Against Pain Relief
Physician concerns are: side effects

Concerns about dependency

Patient fears are: side effects

Inadequate pain assessment

Sociocultural barriers

Fear of obscuring diagnosis

www.AccessAnesthesiology.com
Copyright © McGraw-Hill Education. All rights reserved.
So What Do We Know?

1. We still don’t have a great way to predict who will go on to develop a substance use disorder and who will not

2. Opioids are not always the best treatment for pain

So When Possible

Keep Opioid Naïve patients Naïve
And Our Prescribing Does Have Long Term Consequences

Opioid-Prescribing Patterns of Emergency Physicians and Risk of Long-Term Use

Michael L. Barnett, M.D., Andrew R. Olenski, B.S.,
and Anupam B. Jena, M.D., Ph.D.


http://epmonthly.com/article/unpacking-opioid-blame-game/
Results

• Returns to ED similar in both groups
• Results similar when review by prescription number or median dose or other stratifications
• Opioid related hospitalizations in the next 12 months
  • 9.96 vs 9.73%; OR 1.03 (1-1.05)
• Doesn’t answer appropriateness or why
Characteristics of Initial Prescription Episodes and Likelihood of Long-Term Opioid Use — United States, 2006–2015

Anuj Shah¹; Corey J. Hayes, PharmD¹,²; Bradley C. Martin, PharmD, PhD¹
ED Prescription Opioids as an Initial Exposure Preceding Addiction

Time to Type of Non-Medical use, by Substance Use Disorder

13% of opioid naïve patients continue to fill prescriptions 90-180 days later
10% continued to fill opioid prescriptions beyond 3 months after surgery.
# Post op opioid prescribing

## New Persistent Opioid Use

<table>
<thead>
<tr>
<th>Condition</th>
<th>Percentage</th>
<th>Study Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intestinal</td>
<td>6%</td>
<td>Brummett CM et al. <em>JAMA Surg.</em> 2017; 152(6).</td>
</tr>
<tr>
<td>Musculoskeletal</td>
<td>13%</td>
<td>Johnson SP et al. <em>JHS.</em> 2016;41(10).</td>
</tr>
<tr>
<td>Breast</td>
<td>10%</td>
<td>Lee JS et al. <em>JCO.</em> 2017. Epub</td>
</tr>
<tr>
<td>Breast</td>
<td>19%</td>
<td>Marcusa D et al. <em>PRS.</em> 2017;140(6).</td>
</tr>
</tbody>
</table>

*Courtesy of Dr. Jeanmarie Perrone*
But Sometimes You Do Need An Opioid
“Oral oxycodone has a substantially elevated abuse liability compared to oral morphine or hydrocodone”
Key Findings

- Evidence from randomized controlled trials of HAT in Canada and Europe indicates that supervised injectable HAT — with optional oral methadone — can offer benefits over oral methadone alone for treating OUD among individuals who have tried traditional treatment modalities, including methadone, multiple times but are still injecting heroin.

- Although heroin cannot be prescribed in the United States because it is a Schedule I drug, it would be legal to conduct a human research trial on HAT.

- The literature on treating OUD with hydromorphone (e.g., Dilaudid) is less extensive than the literature on HAT; however, the existing results are encouraging. Hydromorphone trials in the United States would face fewer barriers than HAT trials.
Oxycodone Ingestion Patterns in Acute Fracture Pain with Digital Pills

Peter R Chai, MD, MMSa, Stephanie Carreiro, MDb, Brendan J Innes, BSb, Brittany Chapmanb, Kristin L Schreiber, MD, PhDb, Robert R Edwards, PhDb, Adam W Carrico, PhDb, and Edward W Boyer, MD, PhDb

Median of 6 (3-9.5) digital pills over 7 days

<table>
<thead>
<tr>
<th></th>
<th>Operative repair participants (N=7)</th>
<th>Non-operative repair participants (N=8)</th>
<th>Total (N=15)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median ingestion events</td>
<td>8 (6, 11)</td>
<td>5 (1.5, 7)</td>
<td>6 (3, 9)</td>
</tr>
<tr>
<td>days during study period</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Participants remaining</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>on opioids after 1 week</td>
<td>6/7 = 86%</td>
<td>0/8 = 0%</td>
<td>6/15 = 40%</td>
</tr>
<tr>
<td>Pills, % of weekly dose</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ingested by day 3</td>
<td>7.0 pills, 84%</td>
<td>4.4 pills, 80%</td>
<td>5.6 pills, 82%</td>
</tr>
</tbody>
</table>

Anesth Analg 2017;125(6):2105-2112
**Key Points**

**Question** What factors are associated with opioid consumption after surgery?

**Findings** In this population-based study of patients undergoing surgery in Michigan, 2392 patients used only 27% of the opioids prescribed to them. Prescription size had the strongest association with opioid consumption after surgery, with patients using an additional 5 pills for every 10 extra pills prescribed.

**Meaning** Excessive opioid prescribing is associated with higher opioid consumption after surgery. Using patient-reported opioid consumption will improve postoperative opioid prescribing to better match patient opioid requirements.
Reduce Opioid Duration and Quantity to Limit Use, Avoid Addiction

By Evan Schwarz, MD, FACEP, FACMT; and R. Corey Waller, MD, MS, FACEP, DFASAM | on March 19, 2019 | 0 Comment

So
What About Keeping them Opioid Naive When Possible???
Ketamine for Analgesia in the ED

Case
A 47-year-old construction worker without past medical history presents to your emergency department after falling off of scaffolding; he complains of left lower leg pain. On presentation he is well appearing but distressed in pain. Exam is notable for an open fracture of the tibia and fibula. The foot is warm and well perfused. You initiate appropriate radiology and call orthopedics, order pre-operative labs and 8 mg IV morphine. Several minutes later the nurse approaches you and tells you that the patient refused the morphine. On further questioning, the patient reports that he is a recovered heroin addict, clean for 10 years, and cannot touch opiates. Is there anything else you can give him to relieve his pain?

Ketamine for Analgesia
Ketamine was developed in the 1860s in a successful effort to synthesize a dissociative anesthetic that didn’t make people as...
<table>
<thead>
<tr>
<th>Study</th>
<th>ID</th>
<th>ES (95% CI)</th>
<th>Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Motov (2015)</td>
<td></td>
<td>1.20 (-0.05, 2.45)</td>
<td>31.54</td>
</tr>
<tr>
<td>Miller (2014)</td>
<td></td>
<td>0.82 (-0.64, 2.28)</td>
<td>27.57</td>
</tr>
<tr>
<td>Majidinejad (2014)</td>
<td></td>
<td>-0.45 (-1.26, 0.36)</td>
<td>40.89</td>
</tr>
<tr>
<td>Overall (I-squared = 64.3%, p = 0.061)</td>
<td></td>
<td>0.42 (-0.70, 1.54)</td>
<td>100.00</td>
</tr>
</tbody>
</table>

NOTE:Weights are from random effects analysis.

Mean Difference in NRS Score
Ketamine

Dose 0.1-0.3 mg/kg.....but generally 10-30 mg IV
Issues with Ketamine
Significantly less psych issues when placed in 100 ml and administered over 15 minutes
Another oldie but a goodie: Lidocaine

4% Much Cheaper Than 5%
Lidocaine
Lidocaine for Renal Colic

- A few prior trials from the Middle East evaluating this (3 trials)
- Retrospective chart review of adults with nephrolithiasis
- Included 44 patients
  - 45% lidocaine only, 45% with ketorolac, 10% with morphine
- Weight base dose of 1% lidocaine @ 1.5 mg/kg IV

<table>
<thead>
<tr>
<th>Pain scores</th>
<th>Lidocaine given as first line</th>
<th>Lidocaine given as rescue</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>Initial pain</td>
<td>Post pain</td>
</tr>
<tr>
<td>Initial pain</td>
<td>8.29</td>
<td>2</td>
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<tr>
<td>p-Val</td>
<td>&lt;0.0001</td>
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<tr>
<td>95% CI</td>
<td>4.93–7.58</td>
<td></td>
</tr>
<tr>
<td>MeanDiff</td>
<td>6.26</td>
<td></td>
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</tbody>
</table>

Motov et al. Am J of EM 2018;36:1862-64
Safety and Efficacy of Intravenous Lidocaine for Pain Management in the Emergency Department: A Systematic Review

• Systematic review that included 8 trials and 536 patients
• 6 RCTs and 2 case series
• Dosing different between studies
• What was reported was very different between studies
• Positive results in renal colic and limb ischemia
• Not found to be effective for migraine headaches
• 20 adverse events in 225 pts
• Only 1 severe (error in dosing)

Ann Emerg Med 2018;72:135-144
<table>
<thead>
<tr>
<th>Outcome</th>
<th>Effect</th>
<th>No. of Studies</th>
<th>Certainty in the Evidence*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reduction in pain scores</td>
<td>Only 2 trials found significant reduction, and most trials, especially for renal colic pain, failed to compare with standard of care and typical medications.</td>
<td>6 randomized controlled trials and 2 case series</td>
<td>Very low ☹☹☹☹ (because of methodological limitations, imprecision, and inconsistency)*</td>
</tr>
<tr>
<td>Need for rescue analgesia</td>
<td>Most studies did not describe in detail which agent or doses were used after the use of IV lidocaine and controls.</td>
<td>5 randomized controlled trials and 2 case series</td>
<td>Very low ☹☹☹☹ (because of methodological limitations, imprecision, and inconsistency)*</td>
</tr>
<tr>
<td>Incidence of adverse events</td>
<td>20 adverse events reported across the studies, 19 nonserious and 1 serious</td>
<td>4 randomized controlled trials and 2 case series</td>
<td>Very low ☹☹☹☹ (because of methodological limitations, imprecision, inconsistency, and potential publication bias)**</td>
</tr>
</tbody>
</table>
Nerve Blocks

Fig 1. Sphenopalatine Ganglion

(Wikipedia)
Trigger Points

• Trigger point: focal areas of hyperirritable muscle spasm
• Reproducible and painful on palpation
• Goal is direct mechanical inactivation of the trigger point
Topical Medications

- For patients with contraindications to oral medications
- Neuropathic pain, musculoskeletal pain
- Be careful over areas of non intact skin

NNT of 5.7-8.1 (for 50% pain reduction)
Gabapentin and Pregabalin

• In addition to being antiepileptics also work for neuropathic pain

• Used by many to decrease opioid use
Same Song, Different Lyrica - Pregabalin and Risk of Opiate Overdose

Pain/Sedation/Procedure, Pharmacy/Pharmacology, Retail/U Care

Written by Clay Smith

Spoon Feed
Use of pregabalin in addition to opioids vs opioids alone was associated with an increased risk of death by opioid overdose.

Louisville, KY—The nonopioid painkiller gabapentin is increasingly being misused, according to a new study, which urges pharmacists and other healthcare professionals to recognize its abuse potential.

The nerve-pain medication and anticonvulsant is marketed as Neurontin and available in generic forms. The report, in the journal Psychology of Addictive Behaviors, warns that the drug is typically combined with opioids, marijuana, cocaine, and opioid-addiction treatment medication, compounding side effects to the central nervous system that include euphoria and sedation.

The University of Louisville School of Nursing–led study points out that opioid abusers have turned to gabapentin when crackdowns made their drugs of choice difficult to obtain.

“People are looking for other drugs to substitute for opioids, and gabapentin has filled
Nonpharmacologics for Pain in the ED

- Osteopathic manipulation (physical)
- Chiropractic treatment (physical)
- Physical therapy (physical)
- Acupuncture (direct)
- TENS (direct)
- Music therapy (indirect)
- CBT (education)
- Aroma therapy (indirect)

Based on our analysis, we feel that these interventions have potential to improve acute pain management & pt satisfaction & improve pt outcomes, while reducing overall ED utilization and LOS

<table>
<thead>
<tr>
<th>Study</th>
<th>Experimental Total</th>
<th>Mean</th>
<th>SD Total</th>
<th>Mean</th>
<th>SD</th>
<th>Standardised Mean Difference</th>
<th>SMD</th>
<th>95%–CI</th>
<th>Weight</th>
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<td><strong>Physical</strong></td>
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<td>Lau et al. (2008)</td>
<td>55</td>
<td>5.60</td>
<td>1.80</td>
<td>55</td>
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<td>-0.93 [-1.33; -0.54]</td>
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<td>Mealy et al. (1986)</td>
<td>26</td>
<td>2.85</td>
<td>2.91</td>
<td>25</td>
<td>5.08</td>
<td>-0.82 [-1.40; -0.25]</td>
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<td>Schnabel et al. (2004)</td>
<td>88</td>
<td>1.04</td>
<td>1.81</td>
<td>62</td>
<td>1.60</td>
<td>-0.28 [-0.61; 0.04]</td>
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<td>McReynolds and Sheridan (2005)</td>
<td>29</td>
<td>3.30</td>
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<td>-0.25 [-0.77; 0.26]</td>
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<td>Bleakley et al. (2010)</td>
<td>39</td>
<td>2.89</td>
<td>2.35</td>
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<td>Eisenhart et al. (2003)</td>
<td>20</td>
<td>3.15</td>
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<td>Stockkendahl et al. (2012)</td>
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<td>2.75</td>
<td>3.82</td>
<td>44</td>
<td>3.06</td>
<td>-0.09 [-0.48; 0.31]</td>
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<td>312</td>
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<td>Goertz et al. (2006)</td>
<td>41</td>
<td>4.65</td>
<td>2.60</td>
<td>43</td>
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<td>-1.29 [-1.76; -0.82]</td>
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<td>Oncel et al. (2002)</td>
<td>25</td>
<td>3.90</td>
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<td>Bigdeli Shamloo et al. (2015)</td>
<td>63</td>
<td>4.95</td>
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<td>Hasegawa et al. (2014)</td>
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<td>Ozkurt et al. (2012)</td>
<td>102</td>
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<td>2.00</td>
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<td>Grissa et al. (2016)</td>
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<td>Harkin and Parker (2007)</td>
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<td>3.85</td>
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<td>3.28</td>
<td>0.24 [-0.41; 0.89]</td>
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<td>496</td>
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<td>Heterogeneity: ( \hat{\tau}^2 = 0.116 ), ( p &lt; 0.01 )</td>
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<td>Ayan et al. (2013)</td>
<td>40</td>
<td>1.08</td>
<td>1.07</td>
<td>40</td>
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<td>-1.60 [-2.11; -1.09]</td>
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<td>Ginandes and Rosenthal (1999)</td>
<td>5</td>
<td>0.60</td>
<td>0.89</td>
<td>0</td>
<td>3.17</td>
<td>-1.17 [-2.51; 0.16]</td>
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<td>Parlar Klic et al. (2015)</td>
<td>100</td>
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<td>-0.71 [-1.00; -0.43]</td>
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<td>Albert (2002)</td>
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<td>1.70</td>
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<td><strong>Random effects model</strong></td>
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<td><strong>Random effects model</strong></td>
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</tbody>
</table>
Of course it can’t be that easy...
QUESTIONS

schwarze@wustl.edu
@TheSchwarziee
Other References

• Title slide: https://www.sciencenews.org/article/opioid-epidemic-spurs-search-new-safer-painkillers
• Heroin: https://heroin.palmbeachpost.com/history-of-heroin/
• NAS: https://www.bhpalmbeach.com/blog/tragedy-opioid-addicted-babies/
• Harvard students: https://www.thecrimson.com/article/2018/12/7/students-push-for-narcan/
• Methadone: https://www.thefix.com/content/take-home-methadone-doses-sold-streets91255
• Naltrexone: http://fmntx.com/services/vivitol/
• Line: https://strother.wordpress.com/2012/10/26/communist-russia-milk-bread-and-meijer-are-no-match-for-family-bonds/
• Sublingual: http://blog.hannasherbshop.com/2013/07/22/sublingual-supplements/
• Time for a break: http://afterschoolcentre.org/why-you-should-take-a-break-after-working-for-a-while/