The Pain Conundrum: It’s Time For a Redesign

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Objectives

1. Describe the FDA's concern and request for a new risk evaluation and mitigation strategy (REMS) for prescribing opioid medications.
2. Discuss the recent articles and concerns about the increase in mortality associated with opioid prescribing.
3. Discuss the new CDC guidelines concerning opioid therapy.
4. Discuss measures to reduce deaths from opioid overdose and prescription drug abuse (i.e., inappropriate prescribing, adequate counseling, patient monitoring, patient misuse or abuse).
5. Discuss the difference between pain and suffering.
“Pain is a metaphor for a dying world”
C.S Lewis

Death Rate per 100,000


0 1 2 3 4 5 6 7 8 9 10
Chronic Pain is Complex

**Patient “A”** Pain 8/10
- Physical Injury
- Functional Disability
- Cultural Background
- Environmental Stressors
- Depression & Anxiety
- Cognitive Dysfunction

**Patient “B”** Pain 8/10
- Physical Injury
- Genetics
- Social Disability
- Subject Use
- Depression & Anxiety
- Cultural Background
- Environmental Stressors

With permission, SCOPE of Pain, 2015

Psychiatric Co-Morbidities

<table>
<thead>
<tr>
<th>Condition</th>
<th>Prevalence Chronic Pain Patients</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Depression</td>
<td>33 - 54%</td>
<td>Cheatle M, Gallagher R, 2006</td>
</tr>
<tr>
<td></td>
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<td>Dersh J, et al., 2002</td>
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<tr>
<td>Anxiety Disorders</td>
<td>16.5 - 50%</td>
<td>Knaster P, et al., 2012</td>
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<td></td>
<td></td>
<td>Cheatle M, Gallagher R, 2006</td>
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<tr>
<td>Personality Disorders</td>
<td>31 - 81%</td>
<td>Polatin PB, et al. 1992</td>
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<td></td>
<td></td>
<td>Fischer-Kern M, et al., 2011</td>
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<tr>
<td>PTSD</td>
<td>49% veterans 2% civilians</td>
<td>Otis, J, et al., 2010</td>
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<td>Knaster P, et al., 2012</td>
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<tr>
<td>Substance Use Disorders</td>
<td>15 - 28%</td>
<td>Polatin PB, et al. 1992</td>
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<td></td>
<td>Cheatle M, Gallagher R, 2006</td>
</tr>
</tbody>
</table>

With permission, SCOPE of Pain, 2015
Multidimensional Care

- **Cultivate Well-being**
  - Exercise
  - Manual therapies
  - Orthotics
  - TENS
  - Other modalities *(heat, cold, stretch)*

- **Reduce Pain**
  - CBT/ACT
  - Tx mood/trauma issues
  - Address substances
  - Meditation

- **Improve Quality of Life**
  - Nerve blocks
  - Steroid injections
  - Trigger point injections
  - Stimulators
  - Pumps

- **Restore Function**
  - Physical
  - Psycho-behavioral

**SELF CARE**

With permission, SCOPE of Pain, 2015
The path of pain management is changing

Conundrum

Prescribe Safely

Status quo

Limit use and/or discontinue therapy
Question?

□ What kills more American’s per year than homicides, suicides, gunshots and in some state automobile accidents?

A. Marijuana overdose?
B. Crystal meth overdose?
C. Crack overdose?
D. Cocaine overdose?
E. Answer is not here!
Question?

☐ What kills more American’s per year than homicides, suicides, gunshots and in some state automobile accidents?

A. Marijuana overdose?
B. Crystal meth overdose?
C. Crack overdose?
D. Cocaine overdose?
E. Prescription Drug Abuse
Drug-Induced Deaths Second Only to Motor Vehicle Fatalities, 1999–2007

West Virginia Data

Total Number of Motor Vehicle, Gun, and Drug Related Fatalities by Year of Death, 2007-2017
(Data for 2017 is a Predicted Total for the Entire Year)

Number of Fatalities

<table>
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<tr>
<th>Year</th>
<th>Motor Vehicle Related</th>
<th>Gun Related</th>
<th>Fatal Drug Overdose</th>
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<td>2007</td>
<td>1124</td>
<td>836</td>
<td>721</td>
</tr>
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<td>2008</td>
<td>928</td>
<td>818</td>
<td>735</td>
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<td>2009</td>
<td>841</td>
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<td>2010</td>
<td>823</td>
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<td>2011</td>
<td>878</td>
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<td>690</td>
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<tr>
<td>2012</td>
<td>877</td>
<td>835</td>
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<td>2013</td>
<td>832</td>
<td>852</td>
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<td>2014</td>
<td>808</td>
<td>901</td>
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<tr>
<td>2015</td>
<td>879</td>
<td>940</td>
<td>994</td>
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<tr>
<td>2016</td>
<td>890</td>
<td>1057</td>
<td>1028</td>
</tr>
<tr>
<td>2017*</td>
<td>836</td>
<td>985</td>
<td>1459</td>
</tr>
</tbody>
</table>

1 Top 3 methods of death (motor vehicles, guns, and drugs) include all manners of death (accident, homicide, suicide, and undetermined)
Prescription Drug Abuse

- Things we know about deaths from unintentional drug overdose:
  - Opioid overdoses has risen above heroin and cocaine
    - Prescription drug abuse deaths/100,000 are 4 times higher than cocaine and heroin deaths.
  - 7 to 9 people a day die in Florida from Rx drug overdoses.
  - In some states, drug abuse death is higher than traffic accident deaths.
  - Visits to ED has doubled from 2004 to 2008
  - Increase entrance to substance-abuse programs by 400% over the last 10 years
  - Sales of oxycodone and methadone have quadrupled from 1997-2002

SC Rx Drug Abuse Summit, Columbia, SC, 11/16/2011
Facts About the Opioid Crisis

- Roughly 21 to 29 percent of patients prescribed opioids for chronic pain misuse them.
- Between 8 and 12 percent develop an opioid use disorder.
- An estimated 4 to 6 percent who misuse prescription opioids transition to heroin.
- About 80 percent of people who use heroin first misused prescription opioids.
- Opioid overdoses increased 30 percent from July 2016 through September 2017 in 52 areas in 45 states.
- The Midwestern region saw opioid overdoses increase 70 percent from July 2016 through September 2017.
- Opioid overdoses in large cities increase by 54 percent in 16 states.

National Institute on Drug Abuse, March 2018 Report
Overdose By Region
Question?

The rate of opioid use in the United States is:

A. 10 daily doses/million/day
B. 4,000 daily doses/million/day
C. 10,000 daily doses/million/day
D. 45,000 daily doses/million/day
Question?

The rate of opioid use in the United States is:

A. 10 daily doses/million/day
B. 4,000 daily doses/million/day
C. 10,000 daily doses/million/day
D. 45,000 daily doses/million/day
FDA and FDA advisory boards urge that training in appropriate use of opioids be mandatory for all physicians who prescribe them.

REMS: Risk Evaluation and Mitigation Strategy

REMS example - www.nucyntaerrems.com

Tension

undertreatment vs harmful access

Our rate of narcotic use is 45,000 daily doses/million/day (2007-2009). It is the highest in the world (Canada 25,000; Germany 22,000)
Prescription Drug Abuse

- South Carolina data, 2008
  - 12.6 deaths/100,000 (#25 ranking of all states)
  - NC is ranked #24 (13 deaths/100,000)
- Assuming 4 million people – 520 deaths/year
  - Highest drug overdose death is New Mexico 27/100,000
  - West Virginia at 26/100,000, then Nevada
  - Lowest is Nebraska 5/100,000
- 7 kg /10,000 sold in SC in morphine equivalents
  - Similar to the national rate
  - Practical meaning - “ Enough opioids were prescribed last year to medicate every American adult with 5 mg hydrocodone every 4 hours for a month.”

MMWR November 4, 2011:1487-92
“Enough opioids were prescribed last year to medicate every American adult with 5 mg hydrocodone every 4 hours for a month.”

MMWR November 4, 2011:1487-92
Five Priorities of HHS and NIH

1. improving access to treatment and recovery services
2. promoting use of overdose-reversing drugs
3. strengthening our understanding of the epidemic through better public health surveillance
4. providing support for cutting-edge research on pain and addiction
5. advancing better practices for pain management

National Institute on Drug Abuse, March 2018 Report
Surgeon General’s Report 10/2/18

- Kills 70,000 people in 2017
- 48,000 were related to opioids (66%)
- HHS is funding $1 billion to states
- $930 million grants to SAMHSA to support prevention and recovery services
Death Rate

- Premature Mortality from Drug Overdoses from 2001 to 2015 in 13 Countries with high quality death certificate data
- Includes accidental and intentional deaths
- 2016 - 63,632 deaths
  - assuming 66% as opioid deaths = ~42,000
- New data on rates from 2016
  - 35 deaths / 100,000 in males
  - 20 deaths / 100,000 in females
  - Total of 55 deaths/100,000 [36 opioid deaths/100,000]
- World rates - highest rate in USA, next is Norway (16/100,000 males); then England (Wales) at 15

Annals Intern Med, Letter November 13, 2018
Death Rates in USA - 2016

- 165/100,000 for heart disease
- 158/100,000 for cancer
- 48/100,000 for COPD and other respiratory
- 45/100,000 for accidental deaths
- 38/100,000 for stroke
- Assuming 36/100,000 for opioid related deaths
- 29/100,000 for Alzheimers Disease
- 21/100,000 for diabetes
- 15/100,000 for pneumonia and influenza
- 13.5/100,000 kidney death
- 13/100,000 for suicide
- 8/100,000 for hypertension and related

Many faces of pain

- Pain and Suffering
  - Physical
    - Pain sensation, nausea,
    - breathlessness, itching
  - Mental
    - Anxiety, grief, hatred, anger, boredom

- “Pain is a metaphor for a dying world”
  
  C.S. Lewis

- Suffering is wanting what you do not get and getting what you do not want!
  
  David McIntosh, Pastor
  
  - Illness, disease, unemployment, shattered dreams, lost longing
Humanistic approach to suffering

- **Hedonism**
  - Good and bad consist ultimately in pleasure and pain.
  - Many hedonists emphasize avoiding suffering over pursuing pleasure.
  - They find that the greatest happiness lies in a tranquil state free from pain and from the worrisome pursuit or unwelcome consequences of pleasure.

- **Buddhism**
  - Considers liberation from suffering as basic for leading a holy life and attaining nirvana.
Christian approach to suffering

- The better name for Easter is Pascha
  - Passion week - The suffering Christ
  - Pascha means: Passover feast, Paschal Supper, Paschal Lamb or Christ Himself

- Arthur Pink
  - “As we turn to the Holy Scriptures for light upon this subject of Trouble, Suffering, Affliction, Tribulation, Persecution etc., we must through much tribulation enter into the kingdom of God.”
By MARTIN SCHONGAUER, 1475
Is suffering all bad?

..., but we also rejoice in our sufferings, because we know that suffering produces perseverance; perseverance, character; and character, hope. Romans 5:3-4
If pain is all bad then why do women have more than one child?

Dajung Yun, USA, 2010
Said to be Bipolar Artist

Edvard Munch (December 12, 1863 – January 23, 1944)

“My fear of life is necessary to me, as is my illness. Without anxiety and illness, I am a ship without a rudder. My art is grounded in reflections over being different from others. My sufferings are part of my self and my art. They are indistinguishable from me, and their destruction would destroy my art. I want to keep those sufferings”

Norwegian Painter
Father of German Expressionism and Symbolism
CDC Opioid Guidelines for Chronic Pain

- Chronic pain - US prevalence 11.2% of all adults
  - People with pain lasting longer than 3 mths
- 3-4% are on long-term opioid therapy
- Over 15 years, 165,000 have died from opioid misuse
- ~ 40 people per day die
- Guidelines are for primary care
  - Family, internist, APRN, PA
- These guidelines exclude active cancer, palliative care, end-of-life care
- Intended to improve communication
- Clinical judgment trumps the guideline

Guideline Grading System

**Recommendation Categories**
Recommendation categories are based on evidence type, balance between desirable and undesirable effects, values and preferences, and resource allocation (cost).

**Category A recommendation:** Applies to all persons; most patients should receive the recommended course of action.

**Category B recommendation:** Individual decision making needed; different choices will be appropriate for different patients. Clinicians help patients arrive at a decision consistent with patient values and preferences and specific clinical situations.
Evidence Type
Evidence type is based on study design as well as a function of limitations in study design or implementation, imprecision of estimates, variability in findings, indirectness of evidence, publication bias, magnitude of treatment effects, dose-response gradient, and constellation of plausible biases that could change effects.

**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.
Select Recommendations

- Nonpharmacologic therapy and nonopioid pharmacologic therapy are preferred for chronic pain
  - Use of CBT and exercise therapy should be used to reduce pain and improve function
- Non-opioid therapy
  - See next slide
- Establish realistic treatment goals- discontinued if benefits do not outweigh risks
- When starting opioid therapy for chronic pain, clinicians should prescribe immediate-release opioids instead of extended-release/long-acting (ER/LA) opioids
- Clinicians should prescribe the lowest effective dosage, doses of ≥50 morphine milligram equivalents increase risk of death
Multipurpose Adjuvant Analgesics

- Tricyclic antidepressant drugs
- Corticosteroids
- Anticonvulsants
- Calcitonin – increase in melanoma?
- Bisphosphonates
- Lidoderm®
- Capsaicin
  - Qutenza® topical Rx patch for postherpetic neuralgia
Select Recommendations

- Avoid increasing dosage to ≥90 MME/day or carefully justify a decision to titrate dosage to ≥90 MME/day
- Methadone and fentanyl are not a first choice long-acting
  - They recommend clinicians use it only if they have experience with the drug
# Table 1. Morphine Equivalent Dose (MED) Calculations

<table>
<thead>
<tr>
<th>Opioid</th>
<th>Multiplier (Opioid dose x multiplier = MED)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morphine (reference)</td>
<td>1</td>
</tr>
<tr>
<td>Codeine</td>
<td>0.15</td>
</tr>
<tr>
<td>Fentanyl transdermal (mcg/hr)</td>
<td>4</td>
</tr>
<tr>
<td>Hydrocodone</td>
<td>1</td>
</tr>
<tr>
<td>Hydromorphone</td>
<td>4</td>
</tr>
<tr>
<td>Methadone</td>
<td>4-12(^{a})</td>
</tr>
<tr>
<td>Oxycodone</td>
<td>1.5</td>
</tr>
<tr>
<td>Oxymorphone</td>
<td>3</td>
</tr>
<tr>
<td>Tramadol</td>
<td>0.10</td>
</tr>
</tbody>
</table>

Abbreviation: MED = morphine equivalent dose

\(^{a}\)Do not use this table to determine doses when switching from one opioid to another, especially for fentanyl and methadone. The table is intended only for calculating a patient’s daily MED. An online calculator is available at: [http://www.agencymeddirectors.wa.gov/Calculator/DoseCalculator.htm](http://www.agencymeddirectors.wa.gov/Calculator/DoseCalculator.htm)

\(^{a}\)Varies greatly depending on duration and dose.
Real Case!

- Patient is 62 years old with chronic lumbar sacral or back pain
- His regimen includes
  - Oxycodone 30 mg - 1 every 6 hours as needed
  - Fentanyl 100 mcg - change every 3 days
  - Alprazolam 2 mg - 1 twice a day

How many MME’s or MED’s?
Real Case!

- Patient is 62 years old with chronic lumbar sacral or back pain
- His regimen includes
  - Oxycodone 30 mg - 1 every 6 hours as needed
    - x 1.5 factor, so 30 mg x 4 = 120 mg
    - Morphine mg Equivalent = 120 x 1.5 = 180 mg
  - Fentanyl 100 mcg - change every 3 days
    - x 4 factor, so 100 mcg x 4 = 400 morphine per day
  - Alprazolam 2 mg - 1 twice a day
Select Recommendations

- When opioids are used for acute pain, clinicians should prescribe the lowest effective dose of immediate-release opioids. Three days or less will often be sufficient; more than seven days will rarely be needed.

- Considering offering naloxone when factors that increase risk for opioid overdose, such as history of overdose, history of substance use disorder, higher opioid dosages (≥50 MME/day), or concurrent benzodiazepine use, are present.

- Review PMP data.

- Consider urine drug testing at least annually.

- Clinicians should avoid prescribing opioid pain medication and benzodiazepines concurrently whenever possible.
UNIVERSAL PAIN ASSESSMENT TOOL

This pain assessment tool is intended to help patient care providers assess pain according to individual patient needs. Explain and use 0-10 Scale for patient self-assessment. Use the faces or behavioral observations to interpret expressed pain when patient cannot communicate his/her pain intensity.

**MODERATE**

<table>
<thead>
<tr>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
<th>10</th>
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<tbody>
<tr>
<td><strong>Verbal Descriptor Scale</strong></td>
<td>NO PAIN</td>
<td>MILD PAIN</td>
<td>MODERATE PAIN</td>
<td>MODERATE PAIN</td>
<td>SEVERE PAIN</td>
<td>WORST PAIN POSSIBLE</td>
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<tr>
<td><strong>Wong-Baker Facial Grimace Scale</strong></td>
<td>Alert Smiling</td>
<td>No humor serious flat</td>
<td>Furrowed brow pursed lips breath holding</td>
<td>Wrinkled nose raised upper lips rapid breathing</td>
<td>Slow blink open mouth</td>
<td>Eyes closed moaning crying</td>
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<tr>
<td><strong>Activity Tolerance Scale</strong></td>
<td>NO PAIN</td>
<td>CAN BE IGNORED</td>
<td>INTERFERES WITH TASKS</td>
<td>INTERFERES WITH CONCENTRATION</td>
<td>INTERFERES WITH BASIC NEEDS</td>
<td>BEDREST REQUIRED</td>
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<td><strong>Spanish</strong></td>
<td>NADA DE DOLOR</td>
<td>UNPOQUITO DE DOLOR</td>
<td>UN DOLOR LEVE</td>
<td>DOLOR FUERTE</td>
<td>DOLOR DEMASIADO FUERTE</td>
<td>UN DOLOR INSOPORTABLE</td>
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<td>Konting Sakit</td>
<td>Katamtamang Sakit</td>
<td>Matinding Sakit</td>
<td>Pinaka-Matinding Sakit</td>
<td>Pinaka-Malalang Sakit</td>
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<td><strong>Chinese</strong></td>
<td>不痛</td>
<td>輕微</td>
<td>中度</td>
<td>嚴重</td>
<td>非常嚴重</td>
<td>最嚴重</td>
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<td>보통 통증</td>
<td>심한 통증</td>
<td>아주 심한 통증</td>
<td>최악의 통증</td>
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<td><strong>Persian (Farsi)</strong></td>
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<td>درد ملایم</td>
<td>درد معتدل</td>
<td>درد شدید</td>
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<td>Đau Vừa Phải</td>
<td>Đau Nắng</td>
<td>Đau Thót Nắng</td>
<td>Đau Đơn Tận Cứng</td>
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<tr>
<td><strong>Japanese</strong></td>
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<td>ものすごく痛い</td>
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</table>
What is happening in South Carolina?
SC DHEC Stats

• Prescription Opioid Overdose Deaths

• In 2016, 550 deaths occurred in South Carolina from a drug overdose with prescription opioid drugs listed on the death certificate
  • up 7% from 512 in 2015
  • up 18% from 464 in 2014

• Opioid Overdose Deaths Surpass Homicides: In 2015, the number of deaths from heroin and opioid overdoses in South Carolina surpassed the number of homicides.

• EMS Naloxone Administration by County: South Carolina EMS personnel...
Opioid-Related Overdose Deaths:

- In 2015, there were 594 opioid-related overdose deaths in South Carolina vs. 311 homicides.
  - 508 overdose deaths occurred in 2014
  - 594 occurred in 2015 (16.9% increase)
- 616 in 2016 - report by Governor’s office

- In April 2017, DAODAS was awarded a $6,575,623 grant for State Targeted Response to the Opioid Crisis. With 17 initiatives and more than 60 partners, DAODAS will use these funds to achieve a comprehensive response to opioid issues in South Carolina.
Impact of Opioids

- Overdose deaths are the leading injury death in the United States.
- The CDC has reported 52,404 total overdose deaths in 2015, an average of over 144 drug overdose deaths per day. This is up 11.4% in just one year – from 129 a day in 2014.
- Last year, the mortality rate from synthetic opioids other than methadone (including illicitly-manufactured fentanyl) increased by 72.2%, and deaths related to heroin increased by 20.6%. Increases have occurred across all demographic groups, regions and in numerous states.

In South Carolina

- 5,702 patients were discharged from emergency departments (EDs) with issues related to opiate abuse/dependence in 2015.
- 2,398 patients were discharged from EDs with issues related to opiate overdose/poisoning in 2015.
- There has been a 135% increase in service utilization at state-funded substance use disorder treatment programs for individuals looking for help with an opiate use disorder – from CY 2006 (2,469) to 2016 (5,803).
- There has been a 67% increase in the number of attempts to reverse opioid overdose conducted by EMS personnel throughout South Carolina from 2013 through 2016.
  - 3,847 attempts in 2013
  - 4,187 attempts in 2014
  - 4,610 attempts in 2015
  - 6,427 attempts in 2016
Opioid-Involved Overdose Deaths by County of Occurrence, 2016

Deaths due to opioid overdose in SC by county of occurrence, 2016

Number of deaths due to opioid overdose by county of occurrence, 2016

- 0 - 1
- 2 - 4
- 5 - 20
- 21 - 101

Bold number: Number of deaths due to opioid overdose by county of occurrence, 2016

NOTE: Breaks on map are by quartile
Source: Division of Biostatistics, DHEC
Created 08/22/17
Naloxone

- Formal recommendation of Surgeon General’s advisory, April 5, 2018
- Why? 77% of overdose deaths occur outside of a medical setting, with ~65% of these at home
- Competitive opioid receptor antagonist
- 3 ways to give
  - Nasal spray
  - Autoinjector (Evzio®)
  - Injection (vial and bristojet)
  - Use injection with atomizer
Opiate Overdose

Intranasal naloxone literature

- IN naloxone is at least 80-90% effective at reversing opiate overdose
- When compared directly it is equivalent in efficacy to IV or IM therapy
- IN naloxone results in less agitation upon arousal
- Elimination of needle eliminates needle stick risk
- They awaken more gently than with IV naloxone
- Simple to give
Narcan Nasal Spray by Adapt Pharma

- November 18, 2015 the FDA granted fast-track designation and priority review for Narcan nasal spray

- Administering the drug in one nostril delivered approximately the same levels or higher of naloxone as a single dose of an FDA-approved naloxone intramuscular injection, and achieved these levels in approximately the same time frame.

- Cost: ~$57.50/dose
Very Unique Medication Autoinjector

- Evzio® - naloxone auto-injector for opioid overdose
  - Comes with electronic voice instructions and a trainer kit
  - Device is used even when you are not sure of the exact problem
  - Use device, then call 911
  - $$$
He called it our “silent hurricane”
He created the Opioid Emergency Response Team
This team meets monthly
Limits initial opioid pain medication to 5 days when patient leaves hospital or after surgery
Many insurance companies follow suit
Does not affect those with chronic pain at this time
  The concern is the gateway effect of acute meds
Does not include cancer patients or those with serious illness
No budget at this time

December 2017 Statement
Opioid prescribing limits to be imposed in South Carolina

By Alexis Simmons | March 8, 2018 at 11:16 PM EST - Updated August 15 at 2:02 PM

CHARLESTON, SC (WCSC) - The South Carolina Medicaid Agency and BlueCross BlueShield of South Carolina will limit how many opioids doctors can prescribe to patients in some cases.

This comes after Gov. Henry McMaster issued an executive order in December establishing an emergency response team to battle the opioid crisis in South Carolina.

BlueCross BlueShield of South Carolina will enact what it's calling a Opioid Management Program on April 1 where it will limit short-acting opioid prescriptions to seven days.

On May 1, the South Carolina Medicaid Agency is limiting opioid prescriptions to a five-day supply for acute or post surgery pains.
Nine Bills Passed in SC to Fight Opioids

**H.3819: Prescriptions to minors:** Requires that doctors speak with minors in educating them and their families on opioids before prescribing said opioids and to assess whether the minor may have a mental health or substance use disorder issue. It also requires a consent form known as “Start Talking” to be signed by a minor’s parent/guardian after the doctor discusses the opioids that are being prescribed.

**H.3822: Controlled substance schedules:** DHEC must report any changes made to the schedules listing controlled substances and the addition, deletion, or rescheduling of a substance to the Code Commissioner.

**H.3826: Prescriptions:** Requires DHEC to develop the form and content for a counterfeit-resistant prescription blank, which must be used by practitioners for the purpose of prescribing a controlled substance. This bill is aimed at combating prescription fraud.
Nine Bills Passed in SC to Fight Opioids

**H.4117**: *Confidentiality exceptions*: Allows DHEC to release data from the Prescription Monitoring Program (PMP) to a drug court official seeking information related to a specific case involving a designated person.

**H.4487**: *Controlled substances, scheduling*: Clarifies that DHEC can continue to amend the list of controlled substances to conform to scheduling changes by the DEA, but must forward copies of the change to the Chairmen of the Medical Affairs Committee and the Judiciary Committee of the Senate, the Chairman of the Medical, Military, Public and Municipal Affairs Committee, and the Chairman of the Judiciary Committee of the House of Representatives, and to the Clerks of the Senate and House, and the Code Commissioner, and shall post the schedules on the department's website indicating the change and specifying the effective date of the change.

**H.4488**: *Confidentiality exceptions*: Authorizes DHEC to provide data in the Prescription Monitoring Program to a coroner, deputy coroner, medical examiner, or deputy medical examiner who is involved in a specific inquiry into the cause and manner of death of a designated person.
Nine Bills Passed in SC to Fight Opioids

**H.4600:** *Opioid antidote, prescriptions to community organizations:* This bill adds a section to the South Carolina Opioid Prevention Act (Chapter 130, Title 44). This section states that a prescriber may directly or by standing order prescribe an opioid antidote (such as Naloxone) to a community distributor for the purpose of distributing the antidote to caregivers of people who are at risk of overdosing and to people who know that they have the potential to overdose.

**H.4601:** *Addiction counselors:* Requires anyone representing himself as an addiction counselor to be licensed by LLR and establishes requirements for licensure. There are approximately 400 addiction counselors that will be getting licensed in the state. This bill will help ensure that people who are receiving care for opioid addictions, are receiving that care from qualified addiction counselors.

**S.918:** *Opioid prescriptions, limits, prescription report cards:* The bill establishes a seven-day limit on the initial prescription of opioids for acute pain management or post-operative pain management, except when clinically indicated for cancer pain, chronic pain, hospice care, palliative care, major trauma, major surgery, treatment of sickle cell disease, treatment of neonatal abstinence syndrome, or medication-assisted treatment for substance use disorder. The bill also tasks DHEC to develop and maintain as part of the prescription monitoring program, a system to provide prescription report cards to practitioners to inform the practitioner about certain prescribing trends.
Resolved, that the ADA supports mandatory continuing education (CE) in prescribing opioids and other controlled substances, with an emphasis on preventing drug overdoses, chemical dependency, and diversion. Any such mandatory CE requirements should:

1. Provide for continuing education credit that will be acceptable for both DEA registration and state dental board requirements,
2. Provide for coursework tailored to the specific needs of dentists and dental practice,
3. Include a phase-in period to allow affected dentists a reasonable period of time to reach compliance, and be it further

Resolved, that the ADA supports statutory limits on opioid dosage and duration of no more than seven days for the treatment of acute pain, consistent with Centers for Disease Control and Prevention (CDC) evidence-based guidelines, and be it further

Resolved, that the ADA supports improving the quality, integrity, and interoperability of state prescription drug monitoring programs.

American Dental Association
October 2018
ADA Statement on NSAIDs

An overview of systematic reviews published in the April 2018 edition of the Journal of the American Dental Association (JADA) found that combinations of ibuprofen and acetaminophen were more effective at relieving acute dental pain with fewer acute adverse events. The authors concluded that the use of non-steroidal medications (NSAIDs), with or without acetaminophen, offered the most favorable balance between benefits and harms, optimizing efficacy while minimizing acute adverse events. The ADA recommends that dentists consider non-steroidal anti-inflammatory analgesics as the first-line therapy for acute pain management.
# Suggested Therapy (Expert Panel)

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Start with this*</th>
<th>If needed, maximum Oxycodone 5 mg pills recommended</th>
</tr>
</thead>
<tbody>
<tr>
<td>Routine Tooth Extractions</td>
<td>Acetaminophen and/or Ibuprofen (NSAIDs)</td>
<td>0</td>
</tr>
<tr>
<td>Extractions of impacted teeth including 3rd molars</td>
<td>Acetaminophen and/or Ibuprofen (NSAIDs)</td>
<td>15</td>
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<tr>
<td>Surgical extractions</td>
<td>Acetaminophen and/or Ibuprofen (NSAIDs)</td>
<td>12</td>
</tr>
<tr>
<td>Alveoloplasty</td>
<td>Acetaminophen and/or Ibuprofen (NSAIDs)</td>
<td>12</td>
</tr>
<tr>
<td>Bone grafting procedures</td>
<td>Acetaminophen and/or Ibuprofen (NSAIDs)</td>
<td>12</td>
</tr>
<tr>
<td>Soft tissue procedures</td>
<td>Acetaminophen and/or Ibuprofen (NSAIDs)</td>
<td>0</td>
</tr>
<tr>
<td>Gingivectomy</td>
<td>Acetaminophen and/or Ibuprofen (NSAIDs)</td>
<td>0</td>
</tr>
<tr>
<td>Flap procedures</td>
<td>Acetaminophen and/or Ibuprofen (NSAIDs)</td>
<td>0</td>
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</tbody>
</table>
## Suggested Therapy (Expert Panel)

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Suggested Therapy</th>
<th>Rating</th>
</tr>
</thead>
<tbody>
<tr>
<td>Periodontal bone grafting and regeneration procedures</td>
<td>Acetaminophen and/or Ibuprofen (NSAIDs)</td>
<td>6</td>
</tr>
<tr>
<td>Soft tissue grafting procedures</td>
<td>Acetaminophen and/or Ibuprofen (NSAIDs)</td>
<td>10</td>
</tr>
<tr>
<td>Implant surgery</td>
<td>Acetaminophen and/or Ibuprofen (NSAIDs)</td>
<td>10</td>
</tr>
<tr>
<td>Peri-radicular surgery</td>
<td>Acetaminophen and/or Ibuprofen (NSAIDs)</td>
<td>4</td>
</tr>
<tr>
<td>Tooth resection/root amputation</td>
<td>Acetaminophen and/or Ibuprofen (NSAIDs)</td>
<td>0</td>
</tr>
</tbody>
</table>
Pain Ladder

Nonpharmacologic Approaches

Acetaminophen or nonacetylated salicylates

NSAIDs

Tylenol #3 or Tramadol or buprenorphine

Tylenol #3 + NSAID

NSAID + Acetaminophen

Oxycodone or Oxymorphone

Hydrocodone or combo

Morphine
Traditional NSAIDs

- Ibuprofen (Motrin®, Advil®)
- Diclofenac sodium (Voltaren®)
- Naproxen (Naprosyn® and EC Naprosyn®)
- Naproxen sodium (Anaprox®)
- Flurbiprofen (Ansaid®)
- Etodolac (Lodine®)
- Nalbumeetone (Relafen®)
- Oxaprozin (Daypro®)
- Indomethacin (Indocin®)
More to consider!

- Presupposition
  - Drugs in solution get faster peaks in the serum and therefore faster analgesic activity.
- Gelcap products might have more efficacy in patients
- OTC ibuprofen all come in liquid gelcap formulations
- New Advil® Film-coated (ibuprofen sodium, 256 mg)
  - Uses an ion core technology that increase the speed of dissolution
  - Marketed in a white box (others are blue and red)
**Pain Ladder**

- Acetaminophen or nonacetylated salicylates
- NSAIDs
- Tylenol #3 or Tramadol or buprenorphine
- Tylenol #3 + NSAID
- Oxycodone or Oxymorphone
- Hydrocodone or combo
- Morphine

**Nonpharmacologic Approaches**
Pain Ladder

Fentanyl

Hydromorphone

Ladder Extension

160
Some Recent Facts in the Literature
The Conundrum is Real

- There is concern that prescribers will stop prescribing opioids
- Insurance drug plans are adopting complicated and confusing opiate-prescribing rules
- Getting a patient off therapy requires patience and sometime confrontational meetings
- Will there be a transition to illegal meds like heroin
- Many insurance companies penalize those on buprenorphine - it has pain relieving properties and safer in overdose situations
- REMS (UDS, documentation, PMP, naloxone)
The Science is being addressed

- NIH is finally asking questions
- Taking a science viewpoint to address:
  - Better overdose-reversal
  - Prevention intervention to reduce mortality
  - New medications and technologies to treat addiction
  - Nonaddictive medications and technologies to treat chronic pain

NEJM 2017;377:391-4
Litigation is Here!

- "Somebody has got to go to jail" (National Treasure)
- If you can’t throw them in jail, then sue ‘em
- Somebody has to pay!
- May law suits against the pharmaceutical industry as tobacco industry - lots of money to be raised!
- Purdue settled a $600 million dollar federal settlement for misleading physicians about product addiction and for misbranding abuse-resistant
- There have been 11 or 12 settlements thus far with state and federal agencies

NEJM 2017;377:2301-5
Is it FAKE?

- Class-action suits are now being considered
- Law suits will redistribute wealth for federal programs
- It will build public awareness
- It will build the case for regulation and oversight
- However, there is nothing said about:
  - personal responsibility of patients
  - appropriate medication education on pain management
  - prescriber responsibility
  - illegal networks
  - spiritual issues - filling the void!

NEJM 2017;377:2301-5
A Gateway to Heroin?

- Nonmedical use of Rx opioids is a strong risk factor for heroin use
  - Heroin users often have use nonmedical Rx opioids in the past but those who currently use heroin rarely use the Rx opiates
  - They rarely use both

- The transition is consider low

- It is more likely a progression of addiction

- These authors state that policy driven reduction in opioid use and increases in heroin use is a causal link

- Most studies show that the increase heroin rates precede the changes in opioid policy

- A more likely association is the lower price, high purity, accessibility

- The idea of viewing each in a unified way is justified

NEJM 2016;374:154-63
Figure 1. Age-Adjusted Rates of Death Related to Prescription Opioids and Heroin Drug Poisoning in the United States, 2000–2014. Data are from the Centers for Disease Control and Prevention.\(^5\)
A Gateway to Heroin?
More than just Rx opioids

- Problem is ALL other substances correlate with heroin use

<table>
<thead>
<tr>
<th>Substance abuse or dependence in previous year</th>
<th>Risk Ratio (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td>Alcohol</td>
<td>1.8 (1.2–2.9)</td>
<td>0.009</td>
</tr>
<tr>
<td>Marijuana</td>
<td>2.6 (1.5–4.6)</td>
<td>0.002</td>
</tr>
<tr>
<td>Cocaine</td>
<td>14.7 (7.4–29.2)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Prescription opioid</td>
<td>40.0 (24.6–65.3)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Other psychotherapeutic agent†</td>
<td>1.6 (0.8–3.2)</td>
<td>0.22</td>
</tr>
</tbody>
</table>
Is There Evidence?

☐ Systematic Review

☐ Evaluate the evidence on the effectiveness and harms of opioid therapy for chronic pain

☐ They evaluated 39 studies out of 4209 potentially relevant articles

☐ “No study of opioid therapy versus placebo, no opioid therapy, or nonopioid therapy evaluated long-term (>1 year) outcomes related to pain, function or quality of life.”

☐ “No RCT evaluated opioid abuse, addiction, or related outcomes with long-term opioid therapy versus placebo or no opioid therapy.”

Ann Intern Med 2015;162(4):276-86
Included studies
(n = 39 [40 publications])

Effectiveness: 0 studies
Harms: 19 studies
Dosing strategies: 17 studies
Risk mitigation strategies
  Accuracy of risk mitigation instruments: 4 studies
  Benefits and harms: 0 studies
Their conclusion

- “Evidence is insufficient to determine the effectiveness of long-term opioid therapy for improving chronic pain and function. Evidence supports a dose-dependent risk for serious harms.”

Serious harms (findings in single trials)

- Increase risk of overdose event in patients prescribed opioids
- Higher doses increase risk
- Fracture risk – OR 1.27
- 180 days of opioids over 3 yrs = OR 1.28 for MI
- Opioid use is associated with increase use of ED meds and testosterone
- Higher rate of motor vehicle accidents – OR 1.21 to 1.42
New Outcome Trial - SPACE TRIAL

240 Veterans with chronic low back pain or hip/knee arthritis pain

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Opioid medications

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Non-opioid medications

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12 months

Function Pain Side effects

ClinicalTrials.gov: NCT01583985
Funded by VA Health Services Research & Development IIR 11-125
Krebs EE, et al. JAMA. 2018;319(9):872-882
Interventions

- All medications in both arms on VA formulary
- Each arm included 3 medication steps

Table: Example medications within arms

<table>
<thead>
<tr>
<th>Opioid arm</th>
<th>Non-opioid arm</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Step 1</strong></td>
<td></td>
</tr>
<tr>
<td>Morphine IR*</td>
<td>Acetaminophen*</td>
</tr>
<tr>
<td>Hydrocodone/APAP</td>
<td>Naproxen</td>
</tr>
<tr>
<td><strong>Step 2</strong></td>
<td></td>
</tr>
<tr>
<td>Morphine SR</td>
<td>Nortriptyline</td>
</tr>
<tr>
<td>Oxycodone SA</td>
<td>Capsaicin topical</td>
</tr>
<tr>
<td><strong>Step 3</strong></td>
<td></td>
</tr>
<tr>
<td>Fentanyl transdermal</td>
<td>Tramadol</td>
</tr>
</tbody>
</table>

* Preferred initial medication selection
## Results

Table 2. Patient-Reported Primary and Secondary Outcomes Among Patients With Chronic Back Pain or Hip or Knee Osteoarthritis Pain Randomized to Opioid vs Nonopioid Medication

| Outcome                                | Opioid Group, Mean (SD) (n = 119) | Nonopioid Group, Mean (SD) (n = 119) | Between-Group Difference (95% CI)$^d$ | Overall P Value$^b$
|----------------------------------------|-----------------------------------|--------------------------------------|---------------------------------------|------------------
| Pain-Related Function (Primary Outcome) |                                   |                                      |                                       |                  |
| BPI interference scale                 |                                   |                                      |                                       |                  |
| (range, 0-10; higher score = worse)$^c$|                                   |                                      |                                       |                  |
| Baseline                               | 5.4 (1.8)                         | 5.5 (2.0)                            | -0.1 (-0.6 to 0.4)                   | .58              |
| 3 mo                                   | 3.7 (2.1)                         | 3.7 (2.2)                            | 0.0 (-0.6 to 0.6)                    |                  |
| 6 mo                                   | 3.4 (2.1)                         | 3.6 (2.4)                            | -0.2 (-0.8 to 0.4)                   |                  |
| 9 mo                                   | 3.6 (2.2)                         | 3.3 (2.4)                            | 0.4 (-0.2 to 1.0)                    |                  |
| 12 mo                                  | 3.4 (2.5)                         | 3.3 (2.6)                            | 0.1 (-0.5 to 0.7)                    |                  |

Nice improvement in both trial arms

| Pain Intensity (Secondary Outcome)     |                                   |                                      |                                       |                  |
| BPI severity scale                    |                                   |                                      |                                       |                  |
| (range, 0-10; higher score = worse)$^d$|                                   |                                      |                                       | .03              |
| Baseline                               | 5.4 (1.5)                         | 5.4 (1.2)                            | 0.0 (-0.4 to 0.3)                    |                  |
| 3 mo                                   | 4.3 (1.8)                         | 4.0 (1.7)                            | 0.3 (-0.2 to 0.7)                    |                  |
| 6 mo                                   | 4.1 (1.8)                         | 4.1 (1.9)                            | 0.0 (-0.5 to 0.5)                    |                  |
| 9 mo                                   | 4.2 (1.7)                         | 3.6 (1.7)                            | 0.7 (0.2 to 1.2)                     |                  |
| 12 mo                                  | 4.0 (2.0)                         | 3.5 (1.9)                            | 0.5 (0.0 to 1.0)                     |                  |

Looked at many scales in this trial - all others - p= = NS
A Number of Outcome Scales

Abbreviations: ASEX, Arizona Sexual Experience Scale; BPI, Brief Pain Inventory; GAD-7, 7-Item Generalized Anxiety Disorder Questionnaire; MFI, Multidimensional Fatigue Inventory; MIDAS, Migraine Disability Assessment Scale; PHQ-8, 8-Item Patient Health Questionnaire; PROMIS, Patient Reported Outcomes Measurement Information System; RMDQ-11, 11-Item Roland-Morris Disability Questionnaire; VR-12, Veterans RAND 12-item Health Survey.
No Benefit but More Harm

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Opioid Group</th>
<th>Nonopioid Group</th>
<th>Between-Group Difference (95% CI)a</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary Adverse Outcome</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Medication-related symptom checklist (0-19; higher score = worse), mean (SD)b</td>
<td>1.2 (1.9)</td>
<td>1.2 (1.9)</td>
<td>0.0 (−0.5 to 0.5)</td>
<td>.03c</td>
</tr>
<tr>
<td>Baseline</td>
<td>2.3 (2.5)</td>
<td>1.3 (1.8)</td>
<td>1.0 (0.5 to 1.6)</td>
<td></td>
</tr>
<tr>
<td>3 mo</td>
<td>2.1 (2.7)</td>
<td>1.3 (2.3)</td>
<td>0.7 (0.1 to 1.4)</td>
<td></td>
</tr>
<tr>
<td>6 mo</td>
<td>1.9 (2.8)</td>
<td>0.9 (1.9)</td>
<td>1.0 (0.4 to 1.6)</td>
<td></td>
</tr>
<tr>
<td>9 mo</td>
<td>1.8 (2.6)</td>
<td>0.9 (1.8)</td>
<td>0.9 (0.3 to 1.5)</td>
<td></td>
</tr>
<tr>
<td>12 mo</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Secondary Adverse Outcomes</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All-cause hospitalization, No. (%)d</td>
<td>99 (83)</td>
<td>99 (83)</td>
<td>0 (−10 to 10)</td>
<td>.94a</td>
</tr>
<tr>
<td>0</td>
<td>15 (13)</td>
<td>16 (13)</td>
<td>1 (−9 to 8)</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>6 (5)</td>
<td>5 (4)</td>
<td>1 (−5 to 6)</td>
<td></td>
</tr>
<tr>
<td>≥2</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All-cause ED visit, No. (%)d</td>
<td>60 (50)</td>
<td>73 (61)</td>
<td>−11 (−24 to 2)</td>
<td>.18a</td>
</tr>
<tr>
<td>0</td>
<td>34 (28)</td>
<td>30 (25)</td>
<td>3 (−8 to 15)</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>26 (22)</td>
<td>17 (14)</td>
<td>8 (−2 to 17)</td>
<td></td>
</tr>
<tr>
<td>≥2</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of falls in 12 mo after enrollment, No. (%)f</td>
<td>63 (53)</td>
<td>63 (53)</td>
<td>0 (−13 to 13)</td>
<td>.19a</td>
</tr>
<tr>
<td>0</td>
<td>26 (22)</td>
<td>17 (14)</td>
<td>8 (−2 to 17)</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>29 (25)</td>
<td>39 (33)</td>
<td>−8 (−20 to 3)</td>
<td></td>
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<tr>
<td>≥2</td>
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</table>
Question?

Which part of Obama’s 4-step program will have the most implication for the prescriber?
A. Law enforcement
B. Prescriber education
C. Take back programs
D. State prescription drug monitoring programs
Question?

Which part of Obama’s 4-step program will have the most implication for the prescriber?

A. Law enforcement
B. Prescriber education
C. Take back programs
D. State prescription drug monitoring programs
Prescription Drug Abuse

Doctor shopper had 425 scripts

By RYAN EMERY and DAVE HANKINSON
AUSTRALIA’S worst doctor shopper is a WA man who was prescribed 1,135 medications in just five months.

He received narcotic and non-narcotic based prescription drugs worth thousands under the auspices of his wife, who reviews all his prescriptions.

In June, 2006, the man, who had been prescribed over 1,135 medications, was charged with theft and deception.

Spokesman John Traboulay said: “This guy is definitely No. 1 on the hit parade.”

The man called doctors across borders to Victoria and South Australia.

“Despite the limitations of the Health Insurance Commission, no one is under any illusions about the potential of the drug shopper phenomenon,” he said.

Doctors who have been charged with prescribing excessive amounts of medication have been referred to the police.

Dr Capodanno said the man’s actions were not motivated by personal gain, but were aimed at obtaining drugs for others.

The NSW police are working with the Australian Federal Police to keep up with the demand for prescription drugs.

Lossing our perspective between pain and suffering!
First New Generation Marijuana

- Cannabidiol (Epidiolex®)
- Indication

- Party on Friday night - NO!
- Arthritis - NO!
- Chronic Pain - NO!
- Cancer management - NO!
- Weight loss in elderly - NO!

- Indication is for seizures associated with Lennon-Gastaut syndrome or Dravet’s syndrome in those > 2 years old

- Specialty med - ~$32,000 per year
CBD is in the news

- CBD = cannabidiol (a cannabinoid)
- Comes from 2 varieties of plant - marijuana and hemp
- This is NOT THC (tetrahydrocannabinol) which is what makes one high
- The classic dronabinol (Marinol®) is a synthetic THC
- CBD comes in oral tabs, caps, SL spray, and topical oils and creams
- They are not tested for safety, efficacy or quality
- There is concern with THC contaminants
  - Have to be < 0.3% to sale
- Data is lacking for common situations that CBD is being used for: pain, nausea, anxiety, Parkinson’s, multiple sclerosis, depression
CBD May have beneficial effects

CBD may have the following beneficial effects:
• Analgesia
• Anticonvulsant
• Anti-oxidant
• Anxiolytic and antipsychotic effects
• Muscle relaxant
• Neuroprotective
• May reduce undesirable effects of THC when used together or in a combination product (e.g., sedation, paranoia)
The Combination of CBD + THC is the future - nabiximols

- Evidence for use may be slightly stronger for nabiximols (combination of CBD and THC) than nabilone (synthetic THC) in patients with refractory pain or spasticity due to multiple sclerosis
- Limited evidence supports use to reduce the number of voids per day in patients with urinary frequency (evidence is primarily with nabiximols)
- There is limited evidence to support improving short-term sleep in patients suffering from obstructive sleep apnea, fibromyalgia, chronic pain, and multiple sclerosis (evidence is primarily with nabiximols)
CBD Negative Effects

CBD may have the following negative effects:

• Decreased appetite and weight loss
• Diarrhea
• Dizziness, drowsiness, and fatigue
• Liver injury (especially with higher doses or when combined with clobazam or valproate)

• There are potential drug interactions as CBD can be an inhibitor of liver enzymes - CYP3A4, CYP2C19
Other CBD Issues to Consider

- Risk of Dependence
- Use of **pure CBD** is unlikely to lead to dependence
- Be aware that unregulated products promoted to only contain CBD may also contain some THC and therefore could lead to dependence due to THC content
- This impurity situation could lead to a + urine drug screen (UDS) - CBD does not show a positive UDS

- High fat foods can increase absorption
- CNS depressants (alcohol, opioids) can bring out CBD side effects like dizziness, drowsiness
FARM TO PHARMACY

CREATED BY PHARMACISTS FOR PHARMACISTS

ANANDA PROFESSIONAL

PROPRIETARY GENETICS
We are the exclusive source of everything we grow, harvest and sell.

LEGALLY COMPLIANT
We are 100% compliant and proudly operate under the 2018 Farm Bill.

HIGHEST QUALITY
We continuously test our extracts to ensure quality and consistency.
Pain Pharmacotherapy
Case Study
Mary Williams

PEG Scale Assessment
In the past week:

**Pain on average?**
- 0: No pain
- 8 to 10: As bad as you can imagine
- 7: Completely interferes
- 6: Completely interferes
- 5: Completely interferes
- 4: Completely interferes
- 3: Completely interferes
- 2: Completely interferes
- 1: Completely interferes
- 0: Completely interferes

**Pain interfered with Enjoyment of life?**
- 0: Does not interfere
- 8 to 10: Completely interferes
- 7: Completely interferes
- 6: Completely interferes
- 5: Completely interferes
- 4: Completely interferes
- 3: Completely interferes
- 2: Completely interferes
- 1: Completely interferes
- 0: Completely interferes

**Pain interfered with General activity?**
- 0: Does not interfere
- 8 to 10: Completely interferes
- 7: Completely interferes
- 6: Completely interferes
- 5: Completely interferes
- 4: Completely interferes
- 3: Completely interferes
- 2: Completely interferes
- 1: Completely interferes
- 0: Completely interferes
# Universal Pain Assessment Tool

This pain assessment tool is intended to help patient care providers assess pain according to individual patient needs. Explain and use 0-10 Scale for patient self-assessment. Use the faces or behavioral observations to interpret expressed pain when patient cannot communicate his/her pain intensity.

<table>
<thead>
<tr>
<th>Scale</th>
<th>Verbal Descriptor Scale</th>
<th>Wong-Baker Facial Grimace Scale</th>
<th>Activity Tolerance Scale</th>
<th>Spanish</th>
<th>Tagalog</th>
<th>Chinese</th>
<th>Korean</th>
<th>Persian (Farsi)</th>
<th>Vietnamese</th>
<th>Japanese</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>NO PAIN</td>
<td>Alert Smiling</td>
<td>NO PAIN</td>
<td>NADA DE DOLOR</td>
<td>Walang Sakit</td>
<td>不痛</td>
<td>통증 없음</td>
<td>بدون درد</td>
<td>Không đau</td>
<td>痛みがない</td>
</tr>
<tr>
<td>1</td>
<td>MILD PAIN</td>
<td>No humor serious flat</td>
<td>CAN BE IGNORED</td>
<td>UNPOQUITO DE DOLOR</td>
<td>Konting Sakit</td>
<td>輕微</td>
<td>악한 통종</td>
<td>드른다음</td>
<td>Dau Nhẹ</td>
<td>少し痛み</td>
</tr>
<tr>
<td>2</td>
<td>MODERATE PAIN</td>
<td>Furrowed brow pursed lips breath holding</td>
<td>INTERFERES WITH TASKS</td>
<td>UN DOLOR LEVE</td>
<td>Katamtamang Sakit</td>
<td>中度</td>
<td>보통 통종</td>
<td>드른다음</td>
<td>Dau Viết Phải</td>
<td>いくらか痛み</td>
</tr>
<tr>
<td>3</td>
<td>MODERATE PAIN</td>
<td>Wrinkled nose raised upper lips rapid breathing</td>
<td>INTERFERES WITH CONCENTRATION</td>
<td>DOLOR FUERTE</td>
<td>Matinding Sakit</td>
<td>嚴重</td>
<td>심한 통종</td>
<td>드른다음</td>
<td>Dau Năng</td>
<td>かなり痛み</td>
</tr>
<tr>
<td>4</td>
<td>MODERATE PAIN</td>
<td>Slow blink open mouth</td>
<td>INTERFERS WITH BASIC NEEDS</td>
<td>DOLOR DEMASIADO FUERTE</td>
<td>Pinaka-Matinding Sakit</td>
<td>非常嚴重</td>
<td>아주 심한 통종</td>
<td>드른다음</td>
<td>Dau Thất Nặng</td>
<td>ひどく痛い</td>
</tr>
<tr>
<td>5</td>
<td>SEVERE PAIN</td>
<td>Eyes closed moaning crying</td>
<td>BEDREST REQUIRED</td>
<td>UN DOLOR INSOPORTABLE</td>
<td>Pinaka-Malalang Sakit</td>
<td>最嚴重</td>
<td>최악의 통종</td>
<td>드른다음</td>
<td>Dau Ôn Tận Căng</td>
<td>ものすごく痛い</td>
</tr>
<tr>
<td>6</td>
<td>WORST PAIN POSSIBLE</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Opioids are not all the same

Natural (Opiates) and Semisynthetic Opioids are not all the same

Synthetic
Activation of Mu-Opioid Receptors

Opioid Pharmacodynamics

- Turn on descending inhibitory systems in the midbrain
- Prevent ascending transmission of pain signal
- Inhibit terminals of C-fibers in the spinal cord
- Inhibit activation of peripheral nociceptors
- Activate opioid receptors in midbrain ("reward pathway")


*Image source:* www.mayo.edu/proceedings
# Opioid Choice*

<table>
<thead>
<tr>
<th>Immediate Release (IR/SA)</th>
<th>Extended Release / Long-acting (ER/LA)</th>
</tr>
</thead>
<tbody>
<tr>
<td>▪ Morphine</td>
<td>▪ Morphine</td>
</tr>
<tr>
<td>▪ Hydrocodone</td>
<td>▪ Hydrocodone</td>
</tr>
<tr>
<td>▪ Hydromorphone</td>
<td>▪ Hydromorphone</td>
</tr>
<tr>
<td>▪ Oxycodone</td>
<td>▪ Oxycodone</td>
</tr>
<tr>
<td>▪ Oxymorphone</td>
<td>▪ Oxymorphone</td>
</tr>
<tr>
<td>▪ Tramadol</td>
<td>▪ Tramadol</td>
</tr>
<tr>
<td>▪ Tapentadol</td>
<td>▪ Tapentadol</td>
</tr>
<tr>
<td>▪ Codeine</td>
<td>▪ Methadone</td>
</tr>
<tr>
<td></td>
<td>▪ Fentanyl transdermal</td>
</tr>
<tr>
<td></td>
<td>▪ Buprenorphine transdermal</td>
</tr>
</tbody>
</table>

*Product-specific information at
- [http://dailymed.nlm.nih.gov/dailymed](http://dailymed.nlm.nih.gov/dailymed);
- pharmacy medication guide;
Opioid Choice

IR/SA Opioids

- No opioid tolerance/opioid naïve
- Intermittent or occasional pain
- Incident or breakthrough pain with ER/LA opioids

ER/LA Opioids

- Opioid tolerance exits
- Constant, severe, around-the-clock pain
- To stabilize pain relief when patient using multiple doses of IR/SA opioids
- MUST NOT be broken, chewed or crushed
Pain Ladder

- Nonpharmacologic Approaches
- Acetaminophen or nonacetylated salicylates
- NSAIDs
- Tylenol #3 or Tramadol or buprenorphine
- Tylenol #3 + NSAID
- NSAID + Acetaminophen
- Oxycodone or Oxymorphone
- Hydrocodone or combo
- Morphine
Pain Ladder

Ladder Extension

Hydromorphone

Fentanyl
Deterring Abuse

**Novel Approaches to Deterring Drug Abuse**

<table>
<thead>
<tr>
<th>Coating</th>
<th>Unable to dissolve</th>
<th>Antagonist</th>
<th>Punishment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hard coating</td>
<td>Gummy pill becomes gooey in solvents including water and alcohol.</td>
<td>Inactive drug within counteracts the effects of active drug if tampered with.</td>
<td>Take too much or tamper with it and you will feel sick instead of high.</td>
</tr>
</tbody>
</table>

**OxyContin:** Purdue Pharma

**Remoxy:** Pain Therapeutics, King Pharmaceuticals

**Embeda:** King Pharmaceuticals

**Acurox:** King Pharmaceuticals, Acura Pharmaceuticals
Aversion Technology

AVERSION® Technology
Unique Composition of Safe and Effective Ingredients

Gelling Ingredients

Ingredient(s)

Intended Action

Induce Irritation Effects

Impede Opioid Extraction

Common Abuse Methods

Nasal Snorting

Intravenous
Abuse Deterrent Technologies

- Hot topic, especially if more people died of prescription drug overdose that car accidents per day in most states.
- Nexafed (IMPEDE technology)
  - Polymer matrix technology that disrupts pseudoephedrine extraction – it forms a thick gel
References

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http://www.dhec.sc.gov/Health/Opioids/OpioidStatistics/