Pain Management and Opioid Therapy 2019:
A Responsibility to Protect

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Objectives:

- Develop an understanding of the multiple national position statements and their emphasis on balancing management of pain with risks associated with opioids
- Gain knowledge in the risk assessment of the chronic pain patient and the appropriate management of those patients in a multi-modal treatment plan
- Understand the implications of SB 1446 and 848 in the management of the acute and chronic pain patient and how it impacts your practice

Recent Actions

- Presidents Commission on Combating Drug Addiction and the Opioid Crisis 2018
- HHS Pain Management Best Practices Final Report 2019
- CDC Guidelines for Opioid Prescribing 2016
- SB 1446 and SB 848
- All agree there is a role for opioids in carefully selected and monitored patients
- All agree on identifying abuse and addiction

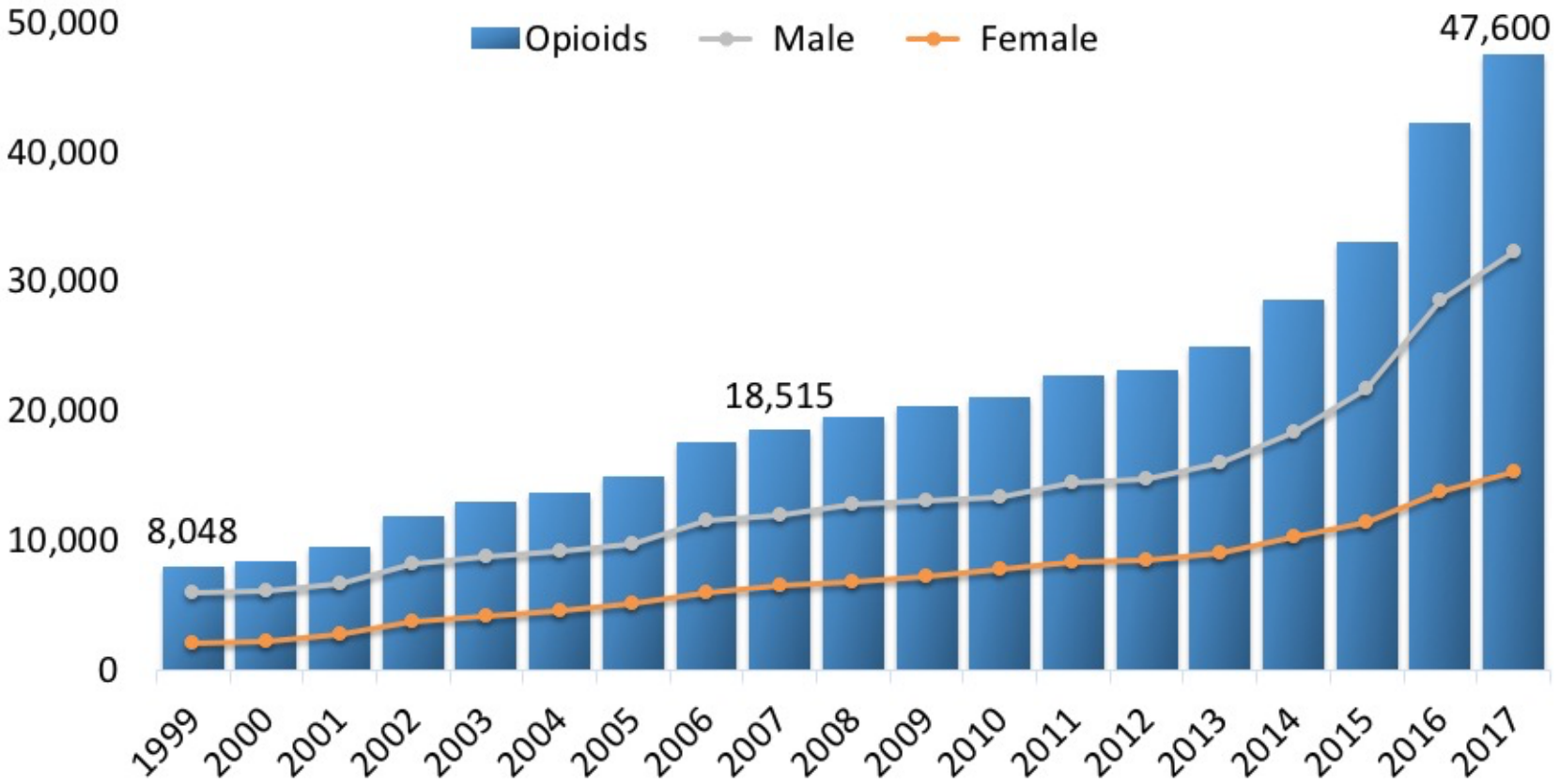
Consensus

- Much emphasis placed on addiction and abuse
- Emphasis on training physicians and providers
- Focus on alternatives to opioids
- Risk reduction
- The need for further research
- Attempts to decrease acute pain episodes leading to chronic opioid therapy

Opioid Deaths

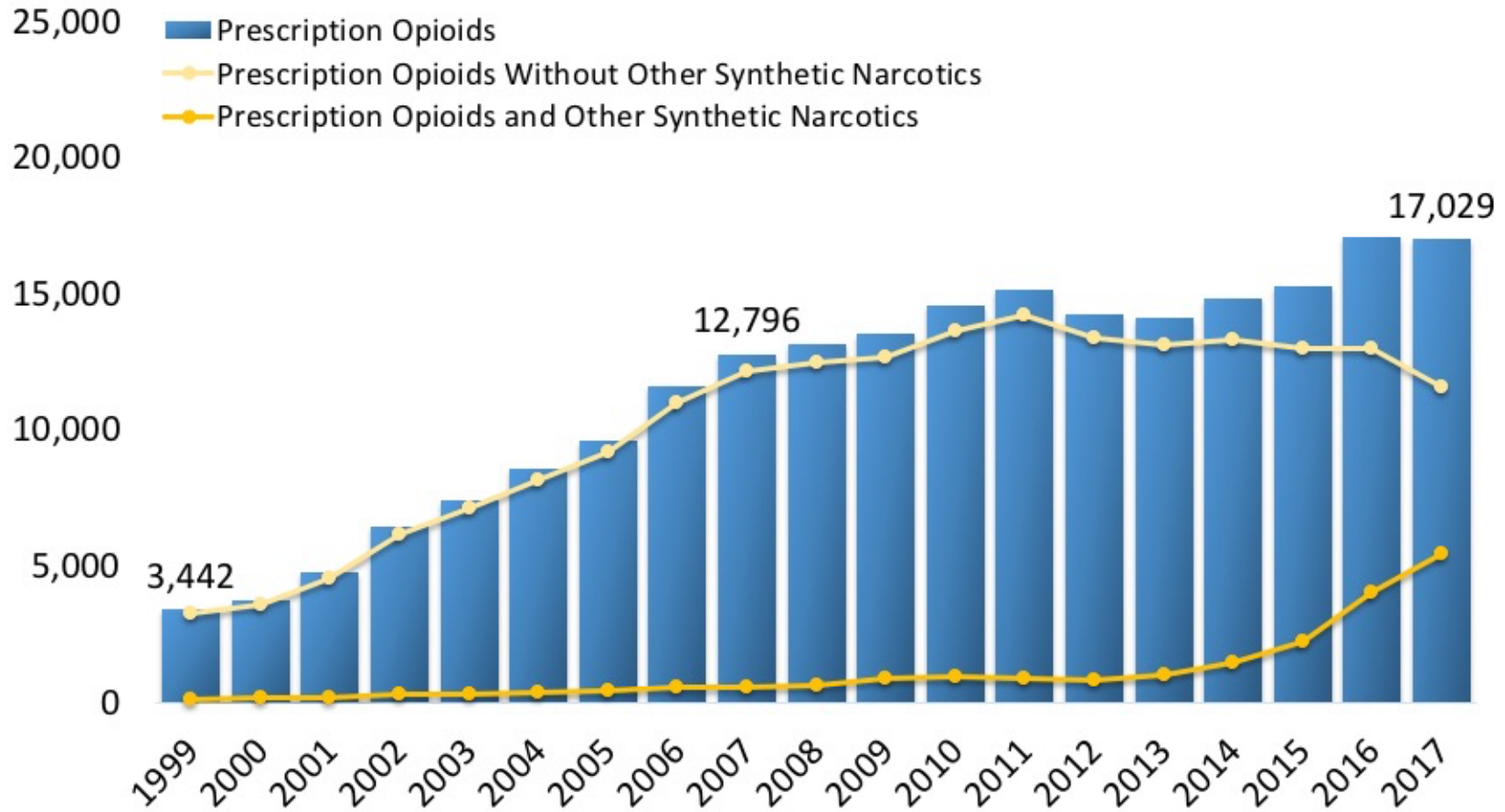
- Major reason for CDC, national and state legislative involvement
- 47,600 deaths involving all opioids in 2017
- Significant escalation in illicit opioids
- Diversion: most deaths are from “non-prescribed” opioids
- Lethal combinations especially with benzodiazepines
- Illegal opioids outpacing prescribed opioids
- We are now in the midst of a fentanyl crisis

Figure 3. **National Drug Overdose Deaths Involving Any Opioid,** Number Among All Ages, by Gender, 1999-2017



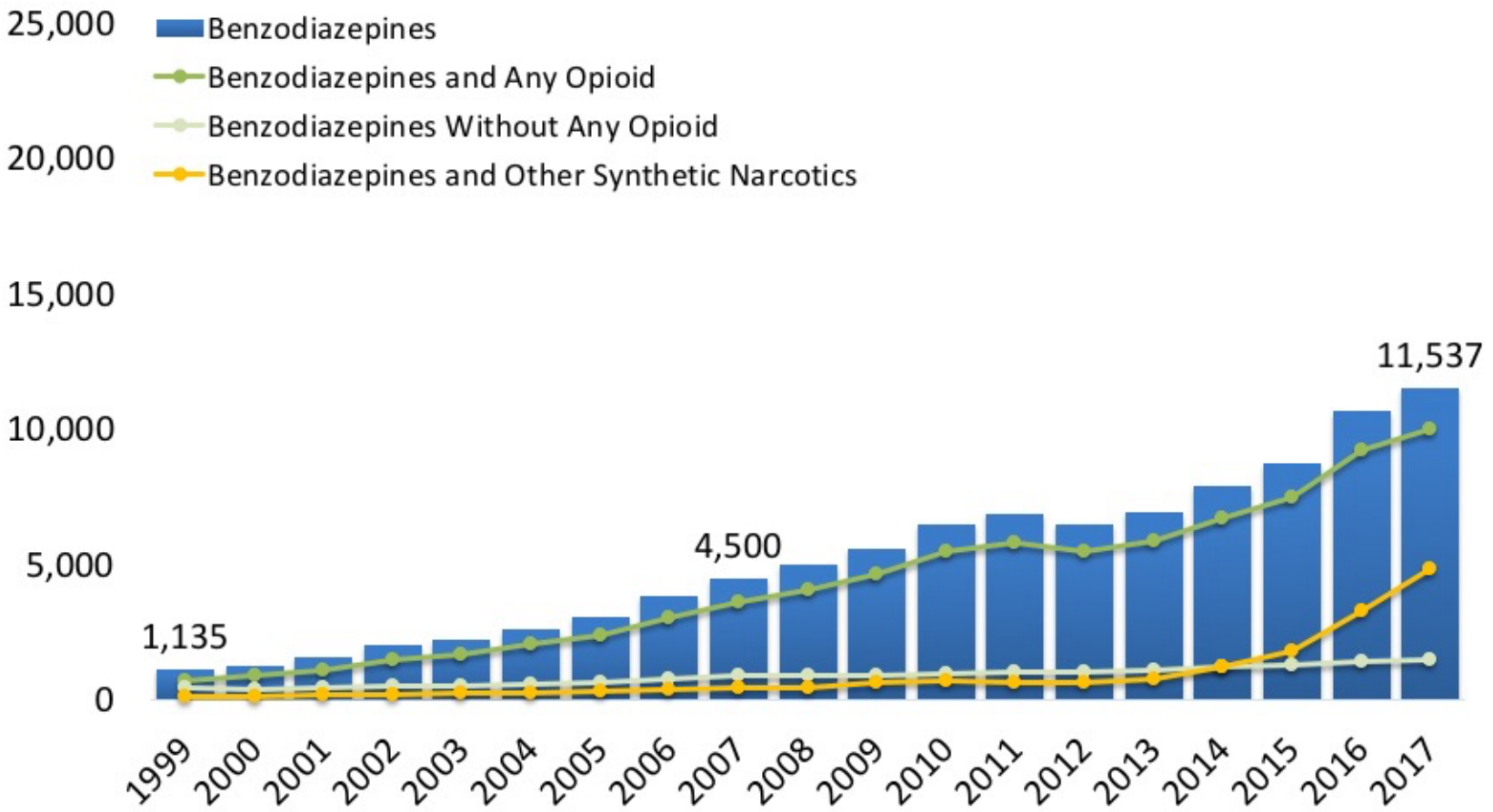
Source: : Centers for Disease Control and Prevention, National Center for Health Statistics. Multiple Cause of Death 1999-2017 on CDC WONDER Online Database, released December, 2018

Figure 4. **National Drug Overdose Deaths Involving Prescription Opioids,** Number Among All Ages, 1999-2017

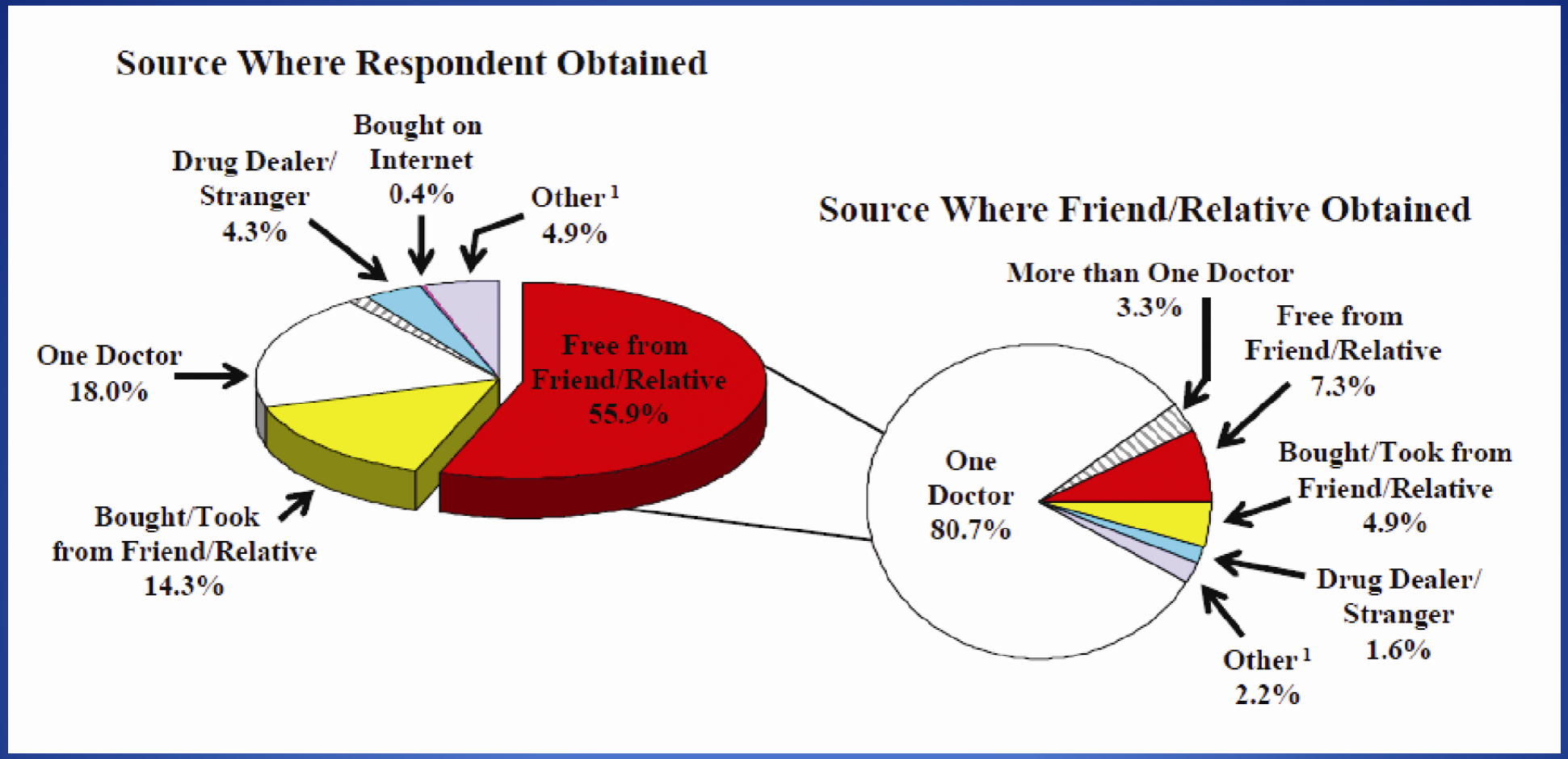


Source: : Centers for Disease Control and Prevention, National Center for Health Statistics. Multiple Cause of Death 1999-2017 on CDC WONDER Online Database, released December, 2018

Figure 8. **National Drug Overdose Deaths Involving Benzodiazepines, by Opioid Involvement,** Number Among All Ages, 1999-2017



Source: : Centers for Disease Control and Prevention, National Center for Health Statistics. Multiple Cause of Death 1999-2017 on CDC WONDER Online Database, released December, 2018


Source Where Respondent Obtained
Drug Dealer/ Stranger 4.3%
Bought on Internet 0.4%
Other 1 4.9%
One Doctor 18.0%
Free from Friend/Relative 55.9%
Bought/Took from Friend/Relative 14.3%
Source Where Friend/Relative Obtained
More than One Doctor 3.3%
Free from Friend/Relative 7.3%
One Doctor 80.7%
Bought/Took from Friend/Relative 4.9%
Drug Dealer/ Stranger 1.6%
Other 1 2.2%

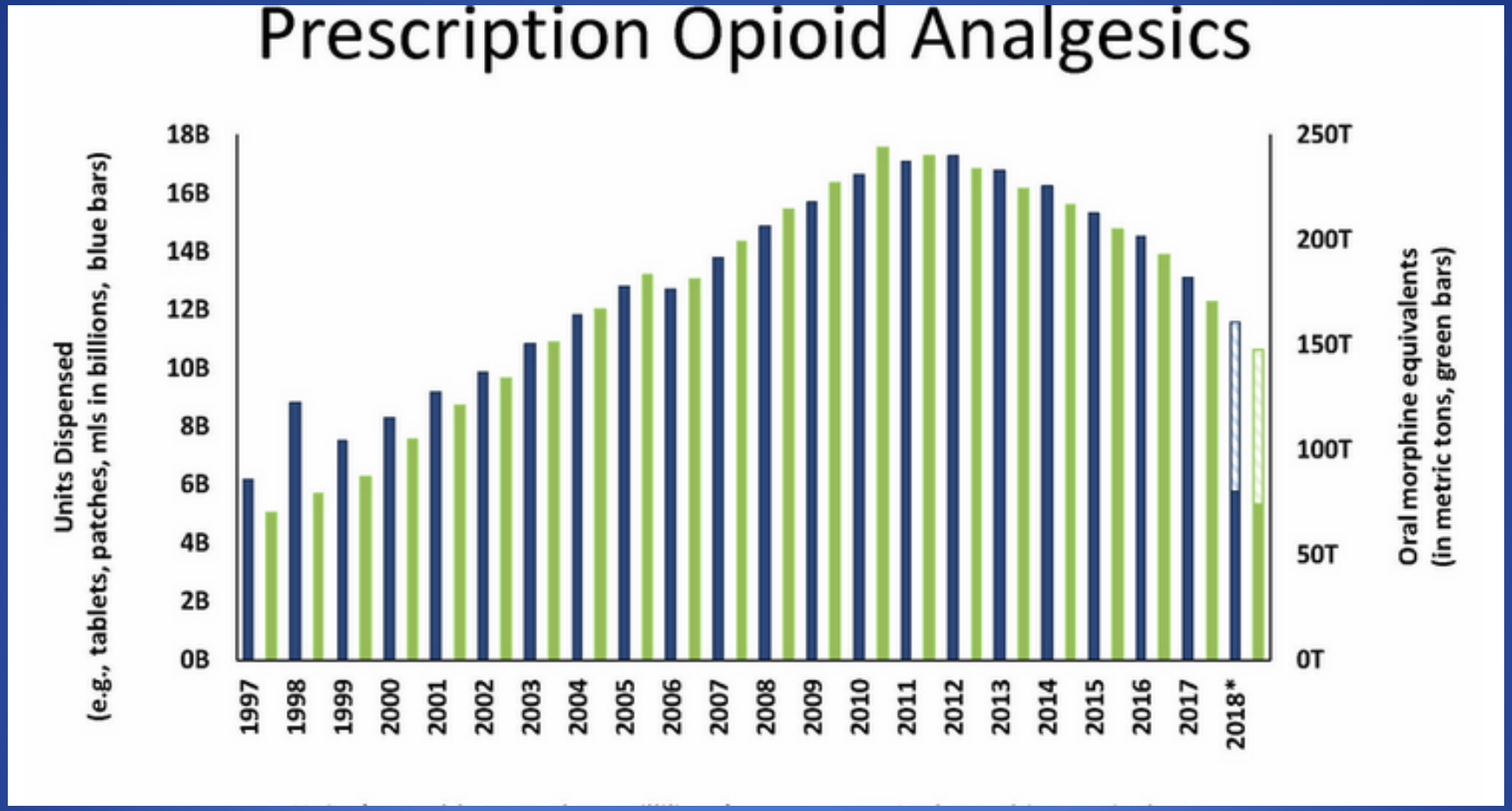
CDC Enhanced Opioid Overdose Surveillance 2017

- 11 states participated including Oklahoma
- 59% of deaths due to illicit opioids
- 18.5% combined prescription and illicit opioids
- 18% positive for only prescription opioids
  - 50% of these deaths also positive for benzodiazepine
  - "Findings indicate that illicit opioids were a major driver of deaths… and were detected in approximately three of four deaths"

The Origin of the Crisis

- NEJM article 1980
- Big pharma and opioid sales
- Provider education
- Patient education
- 5th vital sign
- Pain scores
- Pill mills
- FDA inaction

Prescription Opioid Reduction



Contributing Factors to Opioid Reduction

- Awareness and education
- Regulatory oversight
- Fear
- Increased vigilance
- Targeting of misuse
- Better awareness of misuse and addiction
- Tightening of availability of opioids

Competing Views

- "The ongoing opioid crisis lies at the intersection of two substantial public health challenges… reducing the burden of suffering from pain and containing the rising toll of the harms that can result from the use of opioid medications." *HHS 2019*
- We are faced with two separate populations of patients who are vulnerable and suffering
- "Life saving therapy" or "legalized heroin"

Unintended Consequences

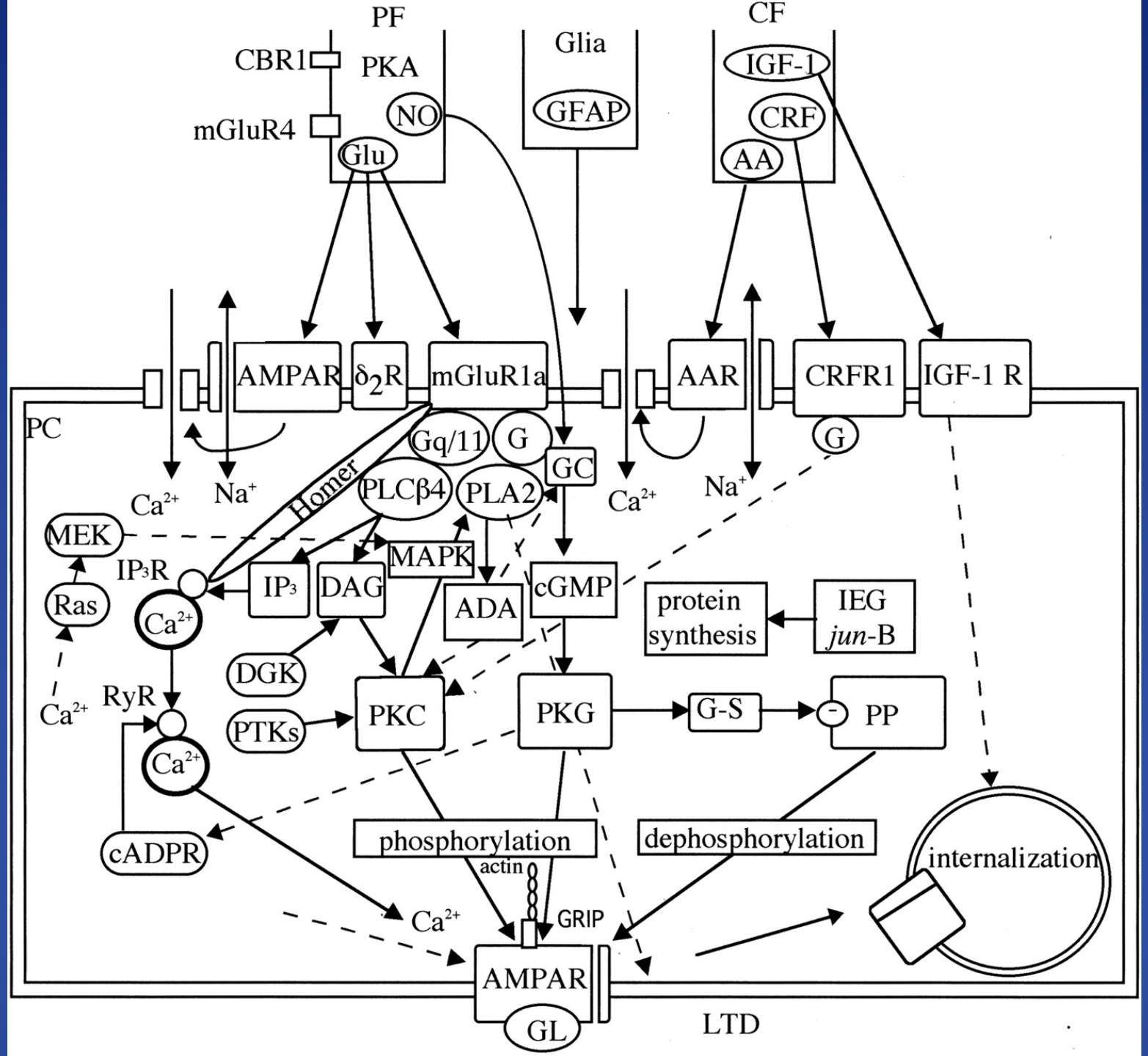
- Forced opioid tapering
- FDA warning: “Serious harm”
- Patient abandonment
- Increase in “over” referrals
- Reduction in physicians willing to prescribe
- Stigma associated with opioids
  - Patient and physician
- Suffering, suicide and disability

“Forced” Dose Reductions

- There is really no evidence for this approach
- A vulnerable population of patients
- The “legacy” patient
- Does this lead to more harm?
- Rupture of patient-physician relationship
- Increased disability, suffering and suicide
- Risk of illicit drug use
- Attempted Oregon initiative

CDC Letter: April 2019

- CDC committed to addressing needs of patients
- Does not endorse mandated or abrupt dose reduction
- Taper or reduce ***only*** when harm outweighs benefit
- The recommendation of high dose opioids focuses on initiation
- Different recommendations for patients on higher doses of opioids
- Emphasizes patient collaboration


PF
CF
Glia
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NO
Glu
GFAP
IGF-1
CRF
AA
AMPAR
δ2R
mGluR1a
AAR
CRFR1
IGF-1 R
PC
Gq/11
G
GC
Homer
PLCβ4
PLA2
Ca2+
Na+
MEK
MAPK
IP3R
IP3
DAG
ADA
cGMP
protein synthesis
IEG jun-B
Ras
Ca2+
DGK
RyR
PKC
PKG
G-S
PP
PTKs
cADPR
phosphorylation
dephosphorylation
actin
internalization
GRIP
AMPAR
GL
LTD

Opioid Prescribing:

- Chronic pain is highly complex
- Opioids alone are often inadequate
  - 25-50% improvement in pain scales
- Opioid therapy can be beneficial in select patients who demonstrate compliance and function
- Often the only remaining option for some patients
- Best outcomes are in a multi-model setting

Contributing Factors to Inadequate Treatment and Prescribing

- Physician lack of knowledge in best clinical practice
- Inadequate research
- Poor understanding of risk mitigation
- Poor utilization of PMP and UDS
- Lack of multi-model treatment
- Physician misunderstanding of dependence/addiction
- Complete relief may not be an attainable goal

Are Opioids Efficacious for Chronic Pain?

- Long term outcome studies are lacking but also lacking for most all pain therapies
- Insight based on available evidence
  - Opioid use may be the most important factor impeding recovery of function
  - Opioids may not consistently and reliably relieve pain and can decrease quality of life
  - The routine use of opioids cannot be recommended
- Appropriate only for selected patients with moderate-severe pain that significantly affects quality of life

CDC Summary Comments

- Recommendations are based on the best available evidence
- The scientific evidence is low in quality
- Much left to be learned about opioid therapy
- Need research leading to safer and more effective care
- Strong evidence for many pain therapies is lacking
- Does the potential benefits outweigh the risks

Future Research is Needed

- A good example… “are opioids effective in musculoskeletal pain?”
- There is absence of data on long term opioid effectiveness which has been interpreted as lack of evidence
- Research on the risks of long term opioids and addiction
- Updating CDC guidelines with ongoing research
- Recent FDA comments on the need for more research regarding opioid therapy

We Lack Knowledge

- Support studies to determine the long-term efficacy of opioids in the treatment of chronic pain
  - Supported by CDC and HHS
- Conduct clinical trials on specific disease entities
- Research that takes into account patient variability and co-morbidities
- Research conducted in the real world setting of multi-modal treatment
- Research on outcomes of opioid reduction

High Dose Opioids

- SB1446: Key issue
- Providers should prescribe lowest possible dose
- Additional precautions at > 50 MME's
- Should avoid > 90 MED's
- Risks of fatal and non-fatal overdoses increase
- Demands documented increase in function and no adverse side effects
- Recommend consultation over 90 MME's
  - Closer follow-up and assessment of other risk factors

High Dose Opioid Therapy

- Data is proving more reliable
- Defined typically as >90 MME's
- Strong evidence linked with poor outcome
- Higher risk of OUD
- Overdose risk doubles at >50 MME
- 9x increase in deaths with 100mg or higher MME
- Remember, existence of persisting pain does NOT constitute evidence of undertreatment

First Line Approach

- Important issue in SB1446
- Non-pharmacological approach
- Non-opioid approach
- Emphasis on
  - Behavioral therapies
  - Functional therapies
  - Adjunctive medications
  - Interventional therapies

Patient Selection and Risk Stratification

- History, physical examination and diagnostic testing
- Psychosocial risk assessment
- Expectations: physician and patient
- Risk assessment is an underdeveloped skill for most clinicians
- SB1446/SB 848 requires vigilant monitoring of abuse and addiction
- SB1446/SB 848 emphasizes documentation of the progress of the patient to the treatment objectives

Chronic Opioid Therapy (COT)

- Consensus agreement that it can be useful in carefully selected patients with moderate to severe pain
- Absolutely demands:
  - Compliance: As with any medical problem
  - Documentation
  - Vigilant monitoring for SUD and OUD
  - Assessment of opioid related side effects
  - Understanding of opioid use in chronic pain

Appropriate Initiation of COT

- Informed consent and discussion of risk vs. benefit
- Therapeutic trial of 4-6 weeks
- Exhaustion of other modalities
- Insufficient data on starting dose
  - Start low-go slow
- Ongoing monitoring and assessment of benefit vs. risk, expectations and alternative modalities
- Consider a taper or wean even in functional patients

Opioid Prescribing Caveats:

- IR vs. ER/LA opioid therapies
- Lowest effective dose
- Shortest possible time
- Benzodiazepine use with opioids
  - Significant increase in deaths and ER visits
- Acute pain leading to chronic therapy
- Combine with other modalities
- Offering naloxone to patients at risk (50 MME's)
- Ongoing assessment of psychological risks

Characteristics of Ideal Patient

- Well defined pathology
- Good insight and desire to improve
- Willing to “work hard” to improve
- Interested in other modalities and work-up
- Not focused on opioids but desire to improve
- Good understanding that opioids will provide “some” relief to help them improve
- Examples

The Worrisome Patient

- Diffuse and poorly localized pain
- No interest in work-up or other modalities
- Focus is on opioids alone
- Poor insight and unrealistic expectations
- Poorly motivated with no desire to “work hard”
- Poor functionality
- Examples

Patients at Risk

- Psychosocial issues
- History of Substance Use Disorder (SUD)
- Adverse Childhood Experience (ACE)
  - Abuse, neglect, household dysfunction and traumatic stressors
- Poor motivation and lack of insight
- No firm cause of pain delineated
- Disability, Medicaid and even prior criminal activity
- Prior overdose

Substance Use Disorder (SUD)

- “The catalyst of the opioid crisis was a denial of the addictive potential of prescription opioids”
- History of alcohol, nicotine, THC, sedatives
- SUD increases risk of developing OUD
- Screening helps identify and reduce risk
- Screening tools for SUD should be incorporated prior to and during opioid therapy
- Beware: flashing light for potential OUD

Opioid Use Disorder

- 3-26% incidence
- Significant impairment or distress
- Poor insight and social support
- Inability to reduce opioids
- Inability to control use
- Often of younger age
- Social function reduced
- Failure to fulfill work, home or school obligations
- Commonly referred to as “abuse” in the literature

Common Pathways to OUD

- Poor pain control (often opioids alone)
- Prior history of SUD
- Initial exposure to opioids at a younger age
- Ongoing emotional distress
- Higher opioid doses
- Long term use of opioids
- Type of opioid
- Misuse of opioids for psychoactive purposes and for unrelieved pain

Medication Assisted Treatment

- Emphasized with patients who display OUD
- Buprenorphine: Partial agonist
- Methadone
- Behavioral therapies
  - Help maintain retention
  - Help reduce relapse rate
- Consensus concerns:
  - Availability
  - Cost

Opioid Induced Hyperalgesia

- Increased sensitivity to noxious or non-noxious stimuli
- Sensitization of pro-nociceptive mechanisms
- Glial cell inflammation at the mu-receptor
- Hypersensitivity and allodynia
- Confused with tolerance
- Caused with rapid escalation and high dose therapy?
- Activity at the NMDA receptor in dorsal horn
- Novel medications now and future

Future Novel Agents

- NKTR-181: slow entry to CNS reduces high, addiction
- VX-150: peripheral acting sodium channel blocker
- AT-121: binds mu-receptor and blocks FQ peptide
- Tanezumab: monoclonal antibody/blocks NGF
- Blue 181: synthetic opioid only acts on spinal receptor
- Low dose naltrexone: action on glial inflammation

Common Errors

- Continued escalation of opioids despite no evidence of improvement in pain or function
- Opioids used in pain syndromes know to be poorly responsive
- Failure to document (emphasized in SB1446)
- Not addressing psychosocial issues and OUD
- Not using medication assisted treatment options
- Lenient with abuse behaviors
- Failure to use monitoring systems

Addressing Worsening Pain

- Evaluate prior to dose increase for OUD
- Common scenarios patient request for opioids or opioid increase
  - Progression of disease
  - New painful diagnosis
  - Psychological issues
  - Poor understanding of pain and opioids
  - Failure to use adjunctives or other therapies
  - OUD or diversion

Risk Mitigation

- Pay attention to a pattern of activity that suggests abuse and address
- Monitor closely through follow up and documentation
- Use available tools:
  - PMP database
  - UDS and pill counts
  - Opioid risk tools
- Obligated to protect yourself, your patient and society from opioid abuse and diversion

Prescription Monitoring Program

- Powerful tool
- Physician and staff friendly
- Crosses state lines
- Helpful to determine other scheduled drugs like benzodiazepines
- Good “teaching moment” with the patient
- “Best Practices” are confusing as to checking PMP
- Unfortunately a high percentage of overdoses are from non-prescribed opioids

Enhancements to the PMP

- Required utilization in the ER
- Adding medical marijuana
- Naloxone administration
- Overdose information
- Coding the prescriptions should be mandatory
  - Chronic pain
  - Acute pain
  - Palliative care
  - Cancer pain

SB 848: Changes to 1446

- “Clean up bill” signed by Governor Stitt
- “Emergency bill” enacted with signature in June 2019
- Must state on prescription for “acute” or “chronic”
- After 1 year of compliance with PPA the physician may assess patient and review treatment plan every 6 months
- ALL opioids fall under the prescribing requirements
- Best Practices Guidelines provided by OOA/OSMA

SB1446 and 848: Major Points of Emphasis

- Addiction and abuse
- Dose reduction and cessation
- Emphasis on lower MME's
- Alternative therapies
- Strong focus decreasing the risks of acute pain leading to chronic opioid therapy
- ***Strong language for assessing, documenting and specifying your care of the opioid patient***

Prior to Issuing an Initial or Chronic Prescription

- Practitioner shall discuss and ***document*** with a note in medical record of the risks not limited to
  - Risks of addiction and overdose and risks of combining alcohol and or benzodiazepines
  - The reasons why the prescription is necessary
  - Alternative treatments that may be available
  - Risks associated with the drug being prescribed such as physical and psychological dependence, that “opioids are highly addictive” and overutilization can lead to death

Patient-Provider Agreement

- Provides informed consent
- Essentially an opioid “contract”
- Needed before the 3rd prescription and for chronic pain treatment
- Needed at initial prescription for under 18 and pregnancy
- The Boards have provided an approved agreement for use

Patient-Provider Agreement

- Explain the possible risks
- Document the understanding of patient and physician
- Establish the rights and obligations of the patient
- Storage of opioids
- Establish specific medications and other treatments
- Specify the measures used by the physician to monitor the patient
- Delineate the process for termination of agreement
- Compliance shall constitute valid informed consent

Chronic Utilization of Opioids

- Review at a minimum every 3 months (first year) or every 6 months if compliant with PPA
  - The course of treatment
  - Any new information about the etiology of the pain
  - Progress of the patient toward treatment objectives
  - Monitor the compliance with the pain management agreement and any recommendations that the patient seek a referral
  - Check PMP (not required BUT encouraged)
  - ***Document the results***

Chronic Utilization of Opioids

- Periodically make reasonable efforts, unless clinically contraindicated, to
  - Stop use of controlled substance
  - Decrease the dosage
  - Try other medications and treatment modalities in an effort to reduce the potential for abuse or development of physical or psychological dependence
  - DOCUMENT and SPECIFY the efforts undertaken

Qualifying Opioid Therapy Patient

- ***A patient requiring opioid treatment for more than 3 months***
  - Does it matter if low dose or high dose? NO
- ***A patient who is prescribed a benzodiazepine and opioid together***
  - What about different doctors prescribing each?
  - Psychiatrist and PCP
- ***A patient prescribed a dose of opioids over 100 MME's***

Conclusions

- Carefully weigh the benefits vs. the harms of opioid therapy
- Ongoing risk assessment is mandatory
- Ongoing balance of opioids with adjunctive therapy
- The real need for further research in this field
- Stakeholders need to work together for the protection of the patients with chronic pain and/or addiction