Disclosure Statement

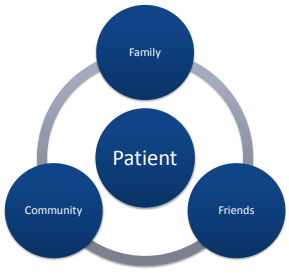
I have no financial relationships or potential conflict of interest relevant to this activity.

Objectives

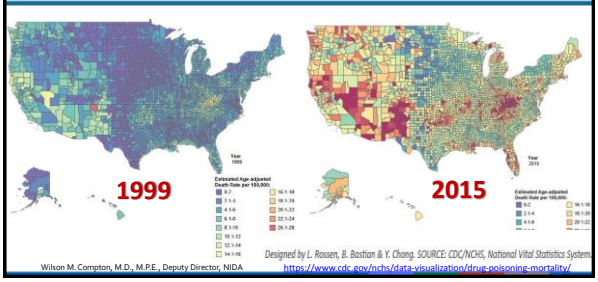
Upon conclusion of this presentation, participants will be able to:

1. Discuss current issues with opioid prescribing practices in today's healthcare landscape for pediatrics
2. Recognize the utility of North Carolina Controlled Substance Reporting System and how to enhance interprofessional communication among healthcare providers
3. Describe pharmacological approaches to acute dental pain and patient considerations

Opioid Prescribing Practices And The Abuse Epidemic

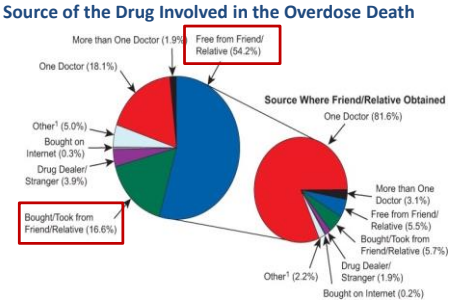


Marked Geographic and Temporal Variation in Overdose Deaths :
Estimated Age-adjusted Death Rates for Drug Poisoning by County



Wilson M. Compton, M.D., M.P.E., Deputy Director, NIDA
https://www.cdc.gov/nchs/data-visualization/drug-poisoning-mortality/

Source of the Drug Involved in the Overdose Death



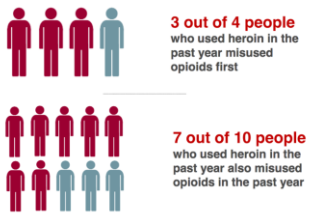
National Survey on Drug Use and Health, Substance Abuse and Mental Health Services Administration, 2012

Dependence Risk from Excess Opioids

- Excess supply of prescription opioids after surgical procedures
- Approximately 5-15% of opioid-naïve patients who undergo "successful" surgery develop dependence
  - New persistent opioid use one of the most common postoperative complications.
- 40-70% of opioid pills prescribed postoperatively remain unconsumed, providing a massive reservoir for diversion into the community.
- Post-surgical patients receiving opiates for pain control are particularly vulnerable to dependence due to
  - Excessive post-procedural prescribing of opioids
  - Gaps in follow-up
  - Inadequate disposal of unused excess supply.

Brummett CM., et al. *JAMA Surg.* 2017;152(6):e170504.
Lee JS, et al. *J Clin Oncol.* 2017;35(36):4042-4049.
Harbaugh CM, et al. *Pediatrics.* 2018;141(1).
J Calif Dent Assoc. 2016;44(12):727.
Bicket MC, et al. *JAMA Surg.* 2017;152(11):1066-1071.

Prescription opioid misuse is a major risk factor for heroin use



3 out of 4 people who used heroin in the past year misused opioids first

7 out of 10 people who used heroin in the past year also misused opioids in the past year

Jones CM. Heroin use and heroin use risk behaviors among nonmedical users of prescription opioid pain relievers – United States, 2002-2004 and 2008-2010. Drug Alcohol Depend 2013

Pain Management Dilemma

- **Patient Education Needs and Conflict of Patient Expectations**
- **Opioid prescribed based on:**
  - Practice history
  - Manage patient's potentially severe post-operative pain
  - Ensure patient satisfaction
- **When prescribing for acute pain…**
  - Making judgement of patient's needs on basis of length of procedure and degree of surgical trauma

Moore PA, et al. JADA 2016:147:530-533.

Perceptions and Gaps – Patient Education

- Reasons for inconsistent patient education regarding risks associated with opioid use:
  - Believed patient already knew
  - Felt not necessary for short-term Rx
  - Patients would ignore education
  - Assume pharmacist would educate
  - Not enough time
  - Felt uncomfortable having the conversation
  - Patients would not understand

Majority of dentists perceived diversion to be either not much or not at all a problem in their practice

McCauley, et al. Subst Abus. 2016 ; 37(1): 9–14

North Carolina Controlled Substance Reporting System And Resources

Controlled Substance Drug Schedules

In 2012, over 17.4 million prescriptions for Schedule II-V controlled substances were dispensed in North Carolina

Schedule	DEA Definition	Rx Process for NC*	Refills/ Expiration	Examples
I	high potential for abuse with no accepted medical use in US	N/A	N/A	heroin, LSD, marijuana, peyote, ecstasy mescaline
II	high potential for abuse for which there is currently accepted medical use in US	- E-prescribe - Hard copy (HC)	None/ 6 months	oxycodone, cocaine, hydrocodone, methamphetamine, methadone, hydromorphone
III	lower potential for abuse than I and II	- Call - E-prescribe/HC	Max 5/ 6 months	Tylenol with codeine, ketamine, anabolic steroids
IV	lower potential for abuse than III	- Call - E-prescribe/HC	Max 5/ 6 months	Valium, Ambien, Xanax, Tramadol, Soma
V	even lower potential for abuse	- Call - E-prescribe/HC	No limit/ 6 months	Lomotil, Robitussin AC

*States other than NC may have differences and it will be important to review those when relocating

DEA website: https://www.dea.gov/druginfo/ds.shtml

NC General Assembly Report No. 2014-05: www.ncleg.net/PED

CDC Stance: Opioid Priority Areas

- Advancing the practice of ***pain management***
- Expanded availability and distribution of treatments for opioid overdoses (i.e. ***naloxone***)
- Expanded access to ***treatment and recovery services***
- Strengthening ***public health surveillance***
- Supporting ***cutting edge research***

https://www.cdc.gov/drugoverdose/pdmp/index.html

What is a Prescription Drug Monitoring Program (PDMP)?

https://www.cdc.gov/drugoverdose/pdmp/index.html

Risk Mitigatic

- Varies from state to state
- Mandatory Use Examples:
  - **New York**
    - 2012 Action: Required prescribers to check the PDMP before prescribing
    - 2013 Result: 75% drop in patients' seeing multiple prescribers for the same drugs.
  - **Tennessee**
    - 2012 Action: Required prescribers to check the PDMP before prescribing
    - 2013 Result: 36% decline in patients' seeing multiple prescribers for the same drugs.

Rasubala L, et al. PLoS ONE 2015. 10(8): e0135957

North Carolina Controlled Substance Reporting System (CSRS)

- Established to improve the state's ability to track prescribing and dispensing patterns of controlled substances in North Carolina

Responsible Prescribing Can Save Lives

NC General Assembly Report No. 2014-05: www.ncleg.net/PED
NC CSRS: www.ncdhhs.gov/divisions/mhddsas/csrs

*NC HB 243: Strengthen Opioid Misuse Prevention (STOP) ACT

- **Signed JUNE 2017**
- **Mandatory** use of PDMP (Initial and Q3 months)
- Limit doctors to prescribing no more than **5-day supply** of opioids during initial visit to treat patient's acute non post-op pain (**7-day supply** for post-op pain)
  - Can prescribe larger supply at follow-up
  - Limit not apply to cancer patients or others with chronic pain
- Medical providers would be **REQUIRED** to submit prescriptions electronically (E-prescribing)

NCGA NORTH CAROLINA GENERAL ASSEMBLY

https://www.ncdhhs.gov/opioids
http://www.ncleg.net/gascripts/BillLookUp/BillLookUp.pl?Session=2017&BillID=H243

When to use North Carolina CSRS*

- Confirm past treatments with controlled substances
  - Including opioids and benzodiazepines, based on referral information and patient-reported information provided during the initial visit.
- Uncover evidence of obtaining controlled substances from multiple providers and/or visiting multiple pharmacies.
- Queried periodically
  - At three-, six-, and twelve-month intervals for returning patients who are being managed with opioid therapy

NC General Assembly Report No. 2014-05: www.ncleg.net/PED

How to Encourage Your Practice to Use NC CSRS

- Suggestions/Recommendations:
  - Delegate accounts
    - Designated person(s) in office to access/generate reports
  - Query search types
    - Character matches
  - What to do if you find something incorrect
    - Corrections by pharmacy

Contact for Questions and Tips

- NC Health and Human Services: Opioid Action Plan 2017-2021
  - https://www.ncdhhs.gov/opioids
- Utilizing the system:
  - https://nccsrsph.hidinc.com/help_nc_query/index.html
  - https://nccsrsph.hidinc.com/NC_RxSentry_TrainingGuide_Practitioners.pdf
- North Carolina Controlled Substance Reporting System
  Division of Mental Health, Developmental Disabilities,
  and Substance Abuse Services
  3008 Mail Service Center, Raleigh, NC 27699-3008
  Phone: (919) 733-1765
  Email: nccontrolsubstance.reporting@dhhs.nc.gov

Importance of Assessing Patient History

- Crucial to assess history of use prior to prescribing opioids as patients may have other conditions or tolerance
  - Does the patient have a history of taking sustained/controlled release products?
  - How many tablets should be written for after a procedure?
  - Does the patient or family history indicate drug abuse?
- Additional Resources to Verify
  - Retail/Community pharmacies patient uses
  - Contacting primary care or specialty providers
  - NC Controlled Substance Reporting System

Dionne RA, et al. Compendium 2016; 37:372-379.

Importance of Provider-to-Provider Communication

- Physicians (Primary Care/Specialties) aware of patient factors
  - Resistance to changes in therapy
  - Deterioration in home/work
  - Abuse of other substances
  - Frequent ED visits
  - Unauthorized dose increases
  - Non-medical use
  - Refuses urine drug screen/referral to specialist
  - Pain contracts*

What can your local pharmacy/pharmacist do?

- Awareness of patient substance abuse factors and behaviors
  - Early refills/fill history
  - Lost/stolen prescriptions
  - Doctor shopping
  - Prescription forgery
  - Payment methods (cash)
- Drug Take Back Programs
  - Disposal (select locations, time of year)
- Naloxone dispensing*

Reynolds V. N C Med J. 2017;78(3):202-205.

Patient Education and Counseling 4

Communicate Education

- Discuss plan if patient already takes opioids chronically
- Severity of pain may not require opioid prescription to be filled
- Adverse effects of opioids
- Significant potential for misuse, abuse, and overdose
- Caution with *other* Combination Products
  - OTC acetaminophen, cough/cold products

SBIRT

- **Screening** quickly assesses the severity of substance use and identifies the appropriate level of treatment.
- **Brief intervention** focuses on increasing insight and awareness regarding substance use and motivation toward behavioral change.
- **Referral to Treatment** provides those identified as needing more extensive treatment with access to specialty care.

Patient Education and Counseling

Patient Medication Counseling

- Follow the labeled instructions
- Avoid alcohol and sedative drugs while taking an opioid pain reliever
- Never share with a friend or family member
- Keep in a secure location
  - Avoid leaving them in predictable, accessible places

Disposal of Unused Medications

- DEA Controlled Substance Public Disposal Locations
  - https://apps.deadiversion.usdoj.gov/pubdispsearch/spring/main?execution=e1s1
- National Prescription Drug Take Back Day (April and October)
  - https://www.deadiversion.usdoj.gov/
  - **Next Drug Take Back Day - October 27, 2018**
- FDA Safe Disposal
  - https://www.fda.gov/Drugs/ResourcesForYou/Consumers/BuyingUsingMedicineSafely/EnsuringSafeUseofMedicine/SafeDisposalofMedicines/ucm186167.htm#Flush_List
- Dispose of unused tablets properly:
  - Combine with coffee grinds or kitty litter. Place mixture in a sealed bag.

U.S. Department of Justice ★ Drug Enforcement Administration

DIVERSION CONTROL DIVISION

Controlled Substance Public Disposal Locations - Search Utility

Public Controlled Substance Disposal Locations:

Business Name	Address 1	Address 2	City, State Zip	Distance	Map
UNC CENTRAL OUTPATIENT PHARMACY	101 MANNING DRIVE	CB #7600	CHAPEL HILL, NC 27514	4 miles	Map
UNC EMPLOYEE PHARMACY	101 MANNING DRIVE	CB #7600	CHAPEL HILL, NC 27514	4 miles	Map
WALGREEN CO.	6405 FAYETTEVILLE ROAD		DURHAM, NC 27713	8 miles	Map
UNC HILLSBOROUGH OUTPATIENT PHARMACY	430 WATERSTONE DRIVE		HILLSBOROUGH, NC 27278	10 miles	Map
DUKE UNIVERSITY HOSPITAL MAIN	2301 ERWIN ROAD	DUMC #3089	DURHAM, NC 27710	11 miles	Map
WALGREENS OF NORTH CAROLINA INC.	3905 NORTH ROXBORO STREET		DURHAM, NC 27704	14 miles	Map
CAROLINA BEHAVIORAL CARE PHARMACY	4102 BEN FRANKLIN BLVD		DURHAM, NC 27704	14 miles	Map

Opioid Use Disorder (OUD)

For a patient using opiates with ≥ 2 of the following behaviors within a 12-month period:

- Taking more opioid drugs than intended or prescribed
- Wanting or trying to control opioid drug use without success
- Spending a lot of time obtaining, taking, or recovering from opioid use
- Ongoing cravings for opioids
- Fails to carry out important roles at home, work, or school due to use
- Continuing to use despite causing relationship or social problems

Criteria
Mild = 2 to 3
Moderate = 4 to 5
Severe > 6

Current Context of Opioid Use, American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders, fifth edition, American Psychiatric Association, 2013.

Opioid Use Disorder (OUD)

For a patient using opiates with ≥ 2 of the following behaviors within a 12-month period:

- Giving up or reducing other activities because of opioid use
- Using opioids even when it is physically unsafe
- Knows that opioid use is causing a physical and/or psychological problems, but continues to take the drug anyway
- Tolerance
- Withdrawal

Criteria
Mild = 2 to 3
Moderate = 4 to 5
Severe > 6

Current Context of Opioid Use, American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders, fifth edition. American Psychiatric Association, 2013.

Provider and patient resources

Substance Abuse and Mental Health Services Administration (SAMHSA) - http://www.samhsa.gov/

- Program directories (behavioral health, opioid treatment, etc.)
- Information topics on substance abuse and mental illness

National Institute of Drug Abuse (NIDA) - https://www.drugabuse.gov/

- Provider information related to science of drug abuse

Centers for Disease Control and Prevention (CDC) -

- **Recent Landscape for Guidelines:**

Small Number
Outdated
Not Conflict Free

- **Solution....** CDC

Opioid Prescribing Guidelines

- **Intended for primary care providers**
- **Applies to patients >18 years old in chronic pain outside of end-of-life care**
- **Builds on joint CDC, NIDA, ONC, SAMHSA summary on "Common Elements in Guidelines for Prescribing Opioids for Chronic Pain" and the NIH Pathways to Prevention for Opioids in Treating Chronic Pain**
- **PUBLISHED MARCH 15, 2016**

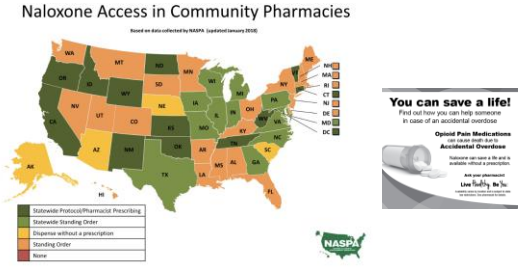
Wilson M. Compton, M.D., M.P.E., Deputy Director, National Institute on Drug Abuse

Recommendation 8

8. Before starting and periodically, evaluate risk factors for opioid-related harms. Incorporate strategies to mitigate risk such as offering naloxone when factors that increase risk for opioid overdose:
   - history of overdose (may consider non-opioid therapy)
   - history of substance use disorder
   - higher opioid dosages (≥ 50 MME/day), or
   - concurrent benzodiazepine use (A-4).

Dowell D, et al. *JAMA*. 2016;315(15):1624-1645

Naloxone Access in Community Pharmacies



https://naspa.us/resource/naloxone-access-community-pharmacies/

Naloxone Standing Orders

- Past in North Carolina: More than 1,000 people died each year from prescription opioid and heroin overdoses.
- As of 6.20.16, North Carolina pharmacies can make naloxone available without a prescription, the third state to issue a statewide standing prescription order.
- Good News: In 2015, the number of opioid overdose reversals exceeded the number of overdose deaths.
- Since 8.1.13, # overdose reversals via naloxone in NC = **6,280*** (as of 2.22.17) = www.nchrc.org/programs-and-services/nc-od-reversals/

Which North Carolina Pharmacies Have Naloxone?

Via standing order, pharmacies can dispense naloxone to:
- Persons who are at risk of experiencing an opiate-related overdose.
- Persons who are the family member or friend of a person at risk of experiencing an opiate-related overdose.
- Persons who are in the position to assist a person at risk of experiencing an opiate-related overdose.

http://www.naloxonesaves.org/n-c-pharmacies-that-offer-naloxone/

CDC Guideline for Prescribing Opioids for Chronic Pain

- Published on March 18, 2016, CDC reviewed evidence, expert opinion, stakeholders (professional organizations), and public comments
- Intended for primary care providers treating patients with chronic pain (pain **≥ 3 months**)
- *Not* intended for dental practice, emergency physicians, or medication-assisted treatment for an opioid use disorder, But…

Dowell D, et al. *JAMA*. 2016;315(15):1624-1645
https://www.cdc.gov/drugoverdose/prescribing/providers.html

What else is CDC doing?

- The new prescribing guideline is just one of the strategies to reduce the number of people who suffer from opioid use disorder or overdose related to these drugs. Other efforts include:
  - Enhancing and maximizing the use of PDMPs
  - Helping states scale up effective programs through the Prevention for States program
  - Conducting policy evaluations
  - Developing and implementing Rapid Response Projects
  - Improving data quality and tracking trends to monitor the epidemic

Dowell D, et al. *JAMA*. 2016;315(15):1624-1645
https://www.cdc.gov/drugoverdose/prescribing/providers.html

Interprofessional Outreach Barriers

- Assumptions of education
- Time limitations
- Practice and communication limitations
- Preventative vs. Reactive

Example: Narcotic Prescribing Practice Policy Guidelines/Steps

1. Run CSRS report on patient **prior** to patient's scheduled appointment (completed by: _____)
2. Verify full medication history **during** appointment (including history of pain management)
   a. Determine amounts of "as needed" pain medications (over-the-counter or prescription)
   b. Determine previous use of controlled substances
3. Verify primary pharmacy patient fills prescriptions (completed by: _____)
4. Screen for use/abuse – not just yes/no questions
   a. Tobacco
   b. Alcohol
   c. Illicit drug
   d. Prescription drug
5. Consider development and having patient sign a policy related to opioid prescribing
6. At receipt of prescription, verbally review and provide patient:
   a. Education sheet related to pain medication side effects (opioid/NSAIDs)
   b. Risks associated to abuse/misuse of opioids
   c. Secure storage and disposal of opioids unused
      i. Closest pharmacy to practice site for disposal: _____
      ii. Drug Take Back Day and Location: _____

Pharmacological Approaches To Acute Pain And Patient Considerations

Types of Pain

Nociceptive

- Tissue Injury
- Inflammation

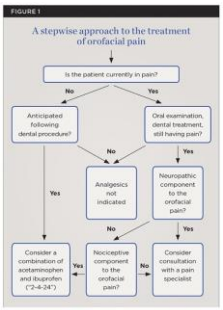
Neuropathic

- Primary lesion
- Dysfunction of nervous system

Donaldson M. *Compend Contin Educ Dent*. 2017;38:334-335.
Goodchild JH, et al. *Three Drug Classes Every Dentist Should Know*, Western Books, 2015, Available from: Ebook library (Accessed May 2017)

Pain Type Should Drive Treatment

- Stepwise approach examples have been published



Donaldson M. *Compend Contin Educ Dent*. 2017;38:334-335.
Goodchild JH, et al. *Three Drug Classes Every Dentist Should Know*, Western Books, 2015, Available from: Ebook library (Accessed May 2017)

Pathophysiology of Pain

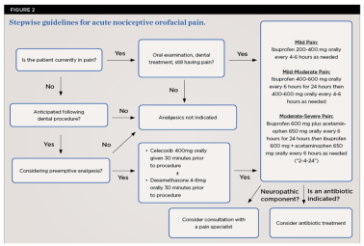
- Tissue damage stimulates release of inflammatory mediators
  - ***Prostaglandins***
  - Kinins
  - Leukotrienes
  - Substance P
  - Histamine

Donaldson M. *Compend Contin Educ Dent*. 2017;38:334-335.
Goodchild JH, et al. *Three Drug Classes Every Dentist Should Know*, Western Books, 2015, Available from: Ebook library (Accessed May 2017)

Terminology and Abbreviations

- OTC - Over-the-counter
- PRN - as needed
- Rx – Prescription
- APAP - Acetaminophen (Tylenol)
- NSAID - Non-steroidal anti-inflammatory
- COX - Cyclooxygenase
- ASA - Aspirin

Stepwise Guidelines Overview: Drugs & Doses



Donaldson M. *Compend Contin Educ Dent*. 2017;38:334-33

ADULT Acute Orofacial Pain Guidance Management

Pain Level	Treatment Examples	
Mild	OTC/Rx ibuprofen, naproxen, ketoprofen PRN	Ibuprofen 200-400 mg PO every 4-6 hours PRN
Mild-to-Moderate	Ibuprofen 400 mg to 600 mg every 4-6 hours for first 48-72 hours prn	Ibuprofen 400-600 mg PO every 6 hours x 24 hours, then every 4-6 hours PRN
Moderate-to-Severe	- Rx dose NSAID administered prior to procedure or immediately afterward - Administer a longer acting local anesthetic 0.5% bupivacaine - Post-op administration of Rx NSAID + APAP 650 mg for 48-72 hrs	Ibuprofen 600 mg + APAP 650 mg every 6 hours x 24 hours, then every 4-6 hours PRN **"2-4-24 Regimen"**
Severe	Rx Opioid (3-day supply) + APAP combo only if pain relief not achieved	

(AVOID exceeding maximum doses!)

Dionne RA, et al. Compend Contin Edu Dent. 2016; 37:372-379.
Donaldson M. *Compend Contin Educ Dent*. 2017;38:334-335.

Treatment (Nociceptive pain) – General ADULT Med Practice

- **Risk factors**: advanced age, renal / hepatic dysfunction, cardiovascular disease
- **Mild / Moderate Pain**:
  - (1) topical agents → (2) APAP → (3) NSAIDs or COX-2 → (4) Tricylic antidepressants (TCA) or Serotonin-Norepinephrine Reuptake Inhibitors (SNRI)
- **Moderate / Severe Pain:**
  - (1) NSAIDs → (2) APAP → (3) TCA / SNRI

RESERVE OPIOIDS

J Pain 2009; 10(2): 113
Herdon, 2016: *Principles of Analgesic Use*

NSAID Use in Pediatrics

- Main risk in taking NSAIDs = dosage errors resulting in overdose, which can cause substantial morbidity, or even death.
- Among NSAIDs, the most popular in pediatrics are **ibuprofen** followed by **naproxen**.
- Overall, between all analgesics, **acetaminophen** is the most broadly used drug in children and the preferred first-line agent because of its superior tolerability profile.

Laskarides C. Dent Clin N Am 2016;60: 347–366.

NSAID Use in Pediatrics

- In general NSAIDs should be avoided in children with:
  - Currently treatment for asthma
  - History of asthma, urticaria, rhinitis, or sinusitis precipitated by NSAIDs
  - Impaired renal function
  - Impaired coagulation mechanism
  - Anticoagulant medications
  - Nephrotoxic medications, like aminoglycoside antibiotics (eg, gentamycin, neomycin, and amikacin).

Laskarides C. Dent Clin N Am 2016;60: 347–366.

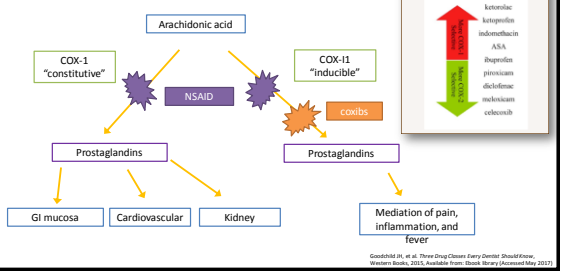
NSAID Use in Pediatrics

Medication	Dose (mg/kg)	Frequency (h)	Max per day (mg/kg/d)
Aspirin*	10-15	4-6	90 (4 g/day)
Ibuprofen	4-10	6-8	40
Naproxen	5-10	12	15

*Aspirin carries risk of Reye's syndrome (a rare disorder presented by symptoms of encephalitis and evidence of liver failure) in children < 12 years old recovering from chickenpox or flu symptomes and should be avoided

Aspirin. Lexi-comp, Inc (Lexi-Drugs®); 2017.
Ibuprofen. Lexi-comp, Inc (Lexi-Drugs®); 2017.
Naproxen. Lexi-comp, Inc (Lexi-Drugs®); 2017.

Why NSAIDS?



Goodchild JH, et al. *Three Drug Classes Every Dentist Should Know*. Western Books, 2015, Available from: Ibook library (Accessed May 2017)

NSAIDs (ibuprofen, naproxen, indomethacin, ketoprofen)

- NSAIDs - Effective in acute inflammation from dental procedures

NSAID	Adult General Dosing	Max Daily Dose
Ibuprofen	**Rx/OTC:** 200-400 mg Q4-6H	**Rx**: 3200 mg **OTC**: 1200 mg
Naproxen (Naproxen Sodium)	**Rx**: 500 mg, then 250 mg Q6-8H OR 500 mg Q12H **OTC**: 200-400 mg Q8-12H	**Rx:** 1250mg **OTC:** 600mg

– Pediatric Dosing: refer to OTC weight-based recommendations

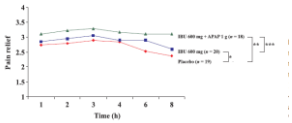
Lexi-comp. Lexi-Drugs
Dionne RA, et al. Compendium 2016; 37:372-379.

Why APAP?

- Mechanism for analgesia not well understood
  - Believed to be weak inhibitor of prostaglandin synthesis in the Central Nervous System (weak anti-inflammatory)
  - Work peripherally to block pain impulse

"When Two are Better than One"
Post-operative endodontic pain

- Avoid Ceiling-dose effect



Menhinick KA, et al. Int Endod J 37 (8), 531-541. 8 2004
Moore PA, et al. JADA 2013;144(8):898-908.

Acetaminophen (APAP)

– Generally safer option

- General Dosing
  - 325 mg – 650 mg every 4-6 hours as needed
  - 500 mg – 1000 mg every 6-8 hours as needed
- Maximum Daily Dose: 3000 mg or 3 g (some references state 4g)
- Provide synergistic effect when combined in alternating schedule with ibuprofen
- In 2013, FDA limited APAP components in combination products
  - Most opioid combos have suboptimal APAP dose in 1 tablet

Moore PA, et al. JADA 2013;144(8):898-908.
Moore PA, et al. JADA 2016;147:530-533

Acetaminophen Weight-Based Pediatric Dosing

Medication	Dose (mg/kg)	Frequency (h)	Max per day (mg/kg/d)
Acetaminophen	10-15	4-6	75 (3 g/day)

OTC Labeling Acetaminophen

- Children 6 to 11 years: 325 mg every 4 to 6 hours; maximum daily dose: 1,625 mg/**day**
- Children ≥12 years and Adolescents:
  - *Regular strength:* 650 mg every 4 to 6 hours
  - *Extra strength:* 1,000 mg every 6 hours
  - Extended release: Children ≥12 years and Adolescents: 1,300 mg every 8 hours
- Maximum daily dose: **3,000 mg/day (≤4,000 mg under physician supervision)**

Acetaminophen. Lexi-comp, Inc (Lexi-Drugs®); 2017.

Acetaminophen Fixed Dosing in Pediatrics

Weight (preferred)*		Age	Dosage (mg)
kg	lbs		
2.7 to 5.3	6 to 11	0 to 3 mo	40
5.4 to 8.1	12 to 17	4 to 11 mo	80
8.2 to 10.8	18 to 23	1 to 2 y	120
10.9 to 16.3	24 to 35	2 to 3 y	160
16.4 to 21.7	36 to 47	4 to 5 y	240
21.8 to 27.2	48 to 59	6 to 8 y	320
27.3 to 32.6	60 to 71	9 to 10 y	400
32.7 to 43.2	72 to 95	11 y	480

*Manufacturer's recommendations are based on weight in pounds (OTC labeling); OTC labeling instructs consumer to consult with physician for dosing instructions in infants and children under 2 years of age.

Why Both? Why Scheduled?

- Around the Clock Synergy – Scheduled reduced overall need for pain medication
  – "2-4-24"
- Scheduled Together or Staggered = Similar benefit
  – Patient Preference
  – Greater than PRN or "chasing pain"

Moore PA, et al. JADA 2013;144(8):898-908.

General Dosing Recommendations

- Oral administrations should be preferred when possible
- Dosing instructions should be clear, especially for pediatric patients where the risk of accidental overdose is high
- **Measurement tools** of milliliters for suspensions or liquids (teaspoon vs tablespoon) should be standardized and administration instructions clear
- If needed, analgesics should be given at regular intervals. The dosage is calculated according to patients' weight, pain level, and adjusted until pain dissipates.

Patient Factors to Consider

- What is important to assess
  - Age
  - Pre-existing medical conditions
- When to avoid/reduce NSAIDS
  - Prime example: Geriatric patients with history of gastric bleeding, renal dysfunction, or cardiovascular disease
  - Caution for less common NSAIDs (insurance coverage/access issues) - Ketoprofen
- When to avoid/reduce APAP
  - Hepatotoxicity
  - Patients with high alcohol use

Mehlisch DR, JADA 2002;133:861-871.

NSAIDs: When to Reduce/Avoid use

Pre-existing Medical Conditions	Possible Adverse Effects
Gastric ulcer	Internal bleeding
Asthma	Asthmatic attack
Diabetes	Reduce effect of diabetic treatment
Gout	Alternation in plasma urate levels
Concurrent ASA use (CV)	
Hypertension	Reduce hypotensive effect of beta-blockers if use prolonged > 3 weeks Decreased renal function in combination with diuretic or angiotensin-converting enzyme inhibitors (e.g. lisinopril, enalapril)
Heart Failure	Fluid retention/edema
Anticoagulation	Increased risk of bleeding following surgery, potential for CV events
Influenza, varicella	Reye syndrome in children

Dionne RA, et al. Compendium 2016; 37:372-379.

APAP: When to avoid/reduce use

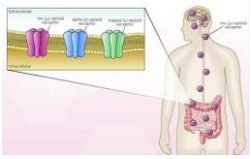
- Assess for history of liver dysfunction
- APAP is not viable if hepatic disease – for hepatic disease avoid use and no NSAIDs either

Check for drug interactions (oral anticoagulants)

Dionne RA, et al. Compendium 2016; 37:372-379.

Why Opioids?

- Opioid drugs act in the **brain stem and peripheral receptors** → targeted actions plus adverse effects:
  - **mu: *analgesia***, respiratory depression, ***euphoria***, GI motility, miosis
  - **delta:** physical dependence
  - **kappa: *analgesia***, dysphoria, miosis



Evidence to Support Opioids?

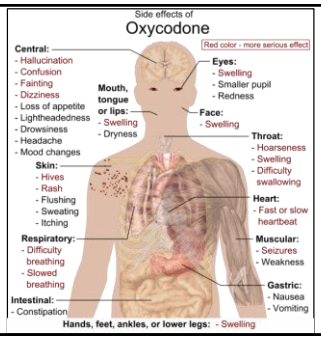
- Opioid-based analgesics are NOT anti-inflammatory, so not drugs of choice for the major categories of nociceptive orofacial pain
- Reserved for small percentage of dental patients with severe, uncontrolled orofacial and postoperative pain
- Best prescribed as combination product with clear instructions

Goodchild JH, et al. *Three Drug Classes Every Dentist Should Know*, Western Books, 2015, Available from: Ibook library (Accessed May 2017)

Opioid use in Pediatrics

Opioid*	Starting Dose for Children (oral)
Hydrocodone	100-200 mcg/kg Q4H
Oxycodone	Immediate Release (IR): 125-200 mcg/kg Q4H (max 5 mg/dose) Sustained Release (SR): 5 mg Q12H
Morphine	Immediate Release: 1-2yr: 200-400 mcg/kg Q4H 2-12 yr: 200-500 mcg/kg Q4H (max 5 mg)
Hydromorphone	30-80 mcg/kg Q3-4H (max 2 mg/dose)

*Of these opioids, only hydrocodone and oxycodone in combination with acetaminophen would be deemed acceptable for use in pediatric dental pain



Opioid Pain Medications

Avoid Range Instructions
(i.e. 1-2 tablets Q4-6 hours)

- Opioids: Hydrocodone, oxycodone, codeine
- Immediate release vs. Sustained/Controlled release
- Recommend dosing in limited quantities and in combination
- Examples:
  - Hydrocodone-APAP (Norco® or Vicodin®) 5 mg-325 mg, 5 mg-300 mg
  - Oxycodone-APAP (or Percocet®) 5 mg-325 mg, 10 mg-325 mg
  - Codeine-APAP 30 mg-300 mg
  - Off-market/Not recommended: Oxycodone-Aspirin, Propoxyphene-APAP (2010)

Dionne RA, et al. Compendium 2016; 37:372-379.

What about Tramadol in Adults?

- Centrally acting analgesic
  - Weak opioid receptor action
  - Norepinephrine and serotonin reuptake inhibition
- Limited therapeutic advantage for managing acute postoperative pain as monotherapy
- Efficacy (studied at doses of 50-100 mg)
  - Similar to Codeine (at doses of 60 mg) monotherapy
  - Less than opioid combination (Codeine + APAP)

Moore PA. JADA 1999;130:1075-1079
Mehlisch DR, JADA 2002;133:861-871

What about Tramadol in Adults?

- Recommended Use:
  - When patient has intolerances/contraindications to Tylenol #3 (codeine/APAP) and NSAIDs (Side effects: nausea, vomiting, dizziness)
  - Potentially in combination with NSAID (not well studied)
- Still carries abuse potential

Moore PA. JADA 1999;130:1075-1079
Mehlisch DR, JADA 2002;133:861-871

Codeine and Tramadol NOT for use in Pediatrics

Due to case reports involving morbidity and mortality, in April 2017, the FDA issued a new warning that recommends against use of codeine and tramadol in children younger than 12 years.

Jin J. *JAMA*. 2017;318(15):1514

Special Populations – Pregnant/Breast-feeding Patients

- Consider pregnancy risk category by trimester (1st/2nd/3rd)
- Ibuprofen and naproxen risks
  - Embryonic implantation disturbances
  - Parturition inhibition
  - Gastroschisis
  - Maternal pulmonary hypertension
- Glucocorticoids
  - Oral clefts (1st trimester use)
- Safest option → Acetaminophen

Donaldson M, et al. JADA 2012;143(8):858-71
Drugs in Pregnancy and Lactation: A Reference Guide to Fetal and Neonatal Risk

Pregnant/Breast-feeding Patients

Medication	FDA Risk Category	Safe During Pregnancy?	Safe During Breastfeeding?
Acetaminophen	B	Yes	Yes
Aspirin	C/D	Avoid	Avoid
Codeine	C	Use with caution	Yes
Glucocorticoids (dexamethasone, prednisone)	C	Avoid	Yes
Hydrocodone	C	Use with caution	Use with caution
Ibuprofen	C/D	Avoid in 3rd trimester	Yes
Oxycodone	B	Use with caution	Use with caution

Donaldson M, et al. JADA 2012;143(8):858-71
Drugs in Pregnancy and Lactation: A Reference Guide to Fetal and Neonatal Risk

For more information…

- Journal of American Dental Association – April 2018 Issue
  - Moore PA, et al. – Benefits and harms associated with analgesic medications used in the management of acute dental pain
  - Gupta N, et al. - Opioid prescribing practices from 2010 through 2015 among dentists in the United States
  - Keith DA, et al. – The prescription monitoring program data
  - Janakiram C, et al. – Sex and race or ethnicity disparities in opioid prescriptions for dental diagnoses among patients receiving Medicaid

Acknowledgments

- Timothy Ives, PharmD, MPH, FCCP, CPP
- Ray Dionne, DDS, MS, PhD
- Anne Perry, Program Coordinator - NC CSRS Contact
- Wilson M. Compton, M.D., M.P.E, Deputy Director, National Institute on Drug Abuse

Contact: kim.sanders@unc.edu

QUESTIONS?

Chronic Pain Conditions And CDC Guidelines

What about Chronic Pain?

- New CDC guidelines Purpose
  - Make informed decisions about pain treatment
  - Use non-opioid therapies (exercise, cognitive behavioral therapy, anti-inflammatories)
  - Start low and go slow (lowest effective dose, limited quantity
  - Follow-up (regular monitoring, improvement, realistic goals, optimize/taper)
  - *Who the guideline is not intended for*: active cancer treatment, palliative care, or end-of-life care patients
- Primary reason for new CE requirement – due diligence

CDC Guideline for Prescribing Opioids for Chronic Pain

- Published on March 18, 2016, CDC reviewed evidence, expert opinion, stakeholders (professional organizations), and public comments
- Intended for primary care providers treating patients with chronic pain (pain ≥ 3 months)
- *Not* intended for dental practice, emergency physicians, or medication-assisted treatment for an opioid use disorder, But…

CDC Guidelines: Three Main Focus Areas

1. Determining when to initiate or continue opioids for chronic pain

- Selection of non-pharmacologic therapy, non-opioid pharmacologic therapy, opioid therapy
- Establishment of treatment goals
- Discussion of risks and benefits of therapy with patients

2. Opioid selection, dosage, duration, follow-up and discontinuation

- Selection of immediate-release or extended-release and long-acting opioids
- Dosage considerations
- Duration of treatment
- Follow-up considerations and discontinuation of opioid

Dowell D, et al. *JAMA*. 2016;315(15):1624-1645
https://www.cdc.gov/drugoverdose/prescribing/providers.html

CDC Guidelines: Three Main Focus Areas

3. Assessing risk and addressing harms of opioid use

- Evaluation of risk factors for opioid-related harms and ways to mitigate/reduce patient risk
- Review of PDMP data
- Use of urine drug testing
- Considerations for co-prescribing benzodiazepines
- Arrangement of treatment for opioid use disorder

Dowell D, et al. *JAMA*. 2016;315(15):1624-1645
https://www.cdc.gov/drugoverdose/prescribing/providers.html