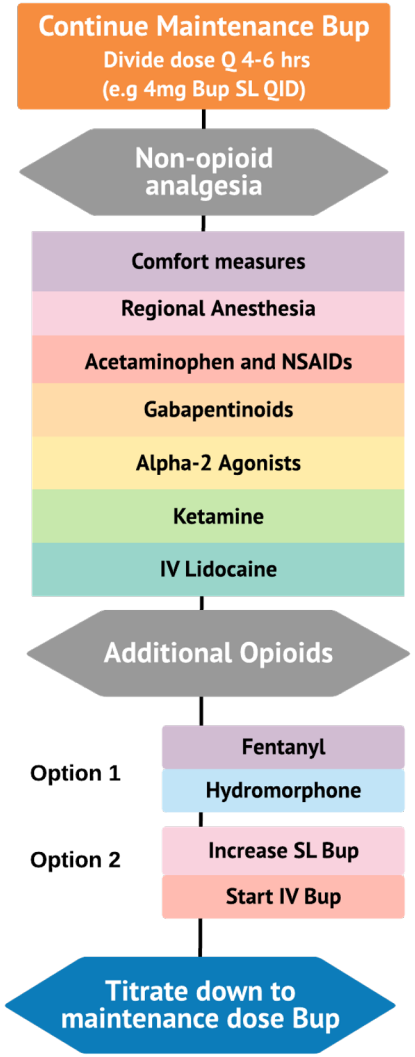
ED Acute Pain Management



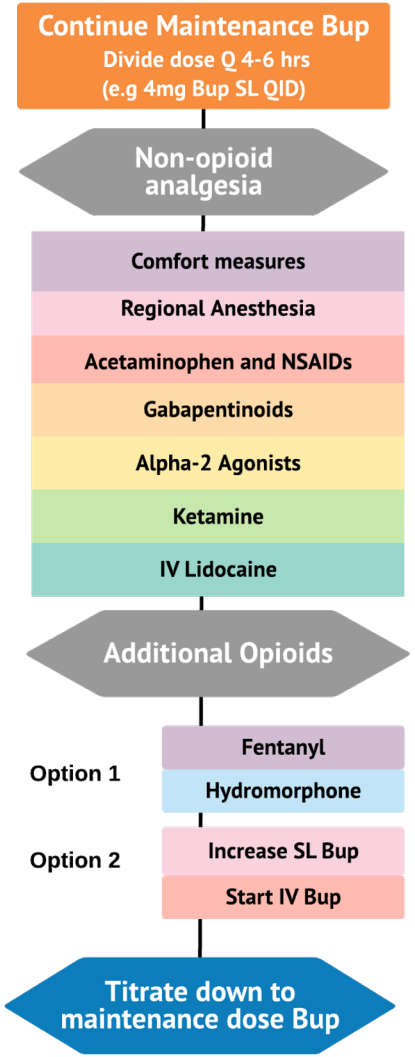
Use the column on the left as a guide.

Always consider, as applicable:

- Standard non-opioid treatment, including:
  - Ice, immobilization, and relaxation techniques as appropriate
  - Acetaminophen and NSAIDS
- Alternatives To Opioids (“ALTO”), such as:
  - Trigger point injections
  - Lidocaine IV and lidocaine patches
  - Gabapentinoids
  - Regional nerve blocks (e.g. for rib fractures)
  - Hematoma blocks

Liu B, 2017

ED Acute Pain Management



Continuing with the column on the left:

More advanced regional nerve blocks:

- Serratus Anterior plane block
- Femoral nerve block
- Fascia Iliaca block

Sub-dissociative ketamine

IV push doses

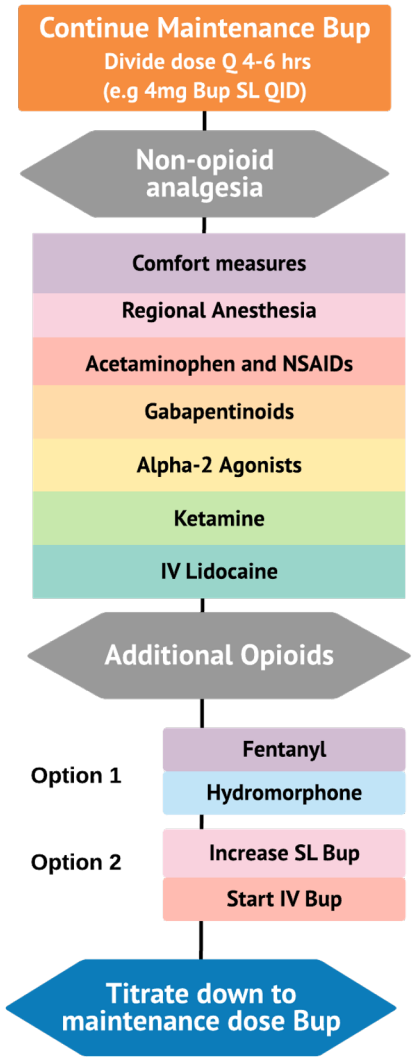
Continuous IV infusions (drips)

Alpha-2 Adrenoceptor agonists:

- Clonidine
- Dexmedetomidine

Khalil A, 2017
Khan Z, 1999

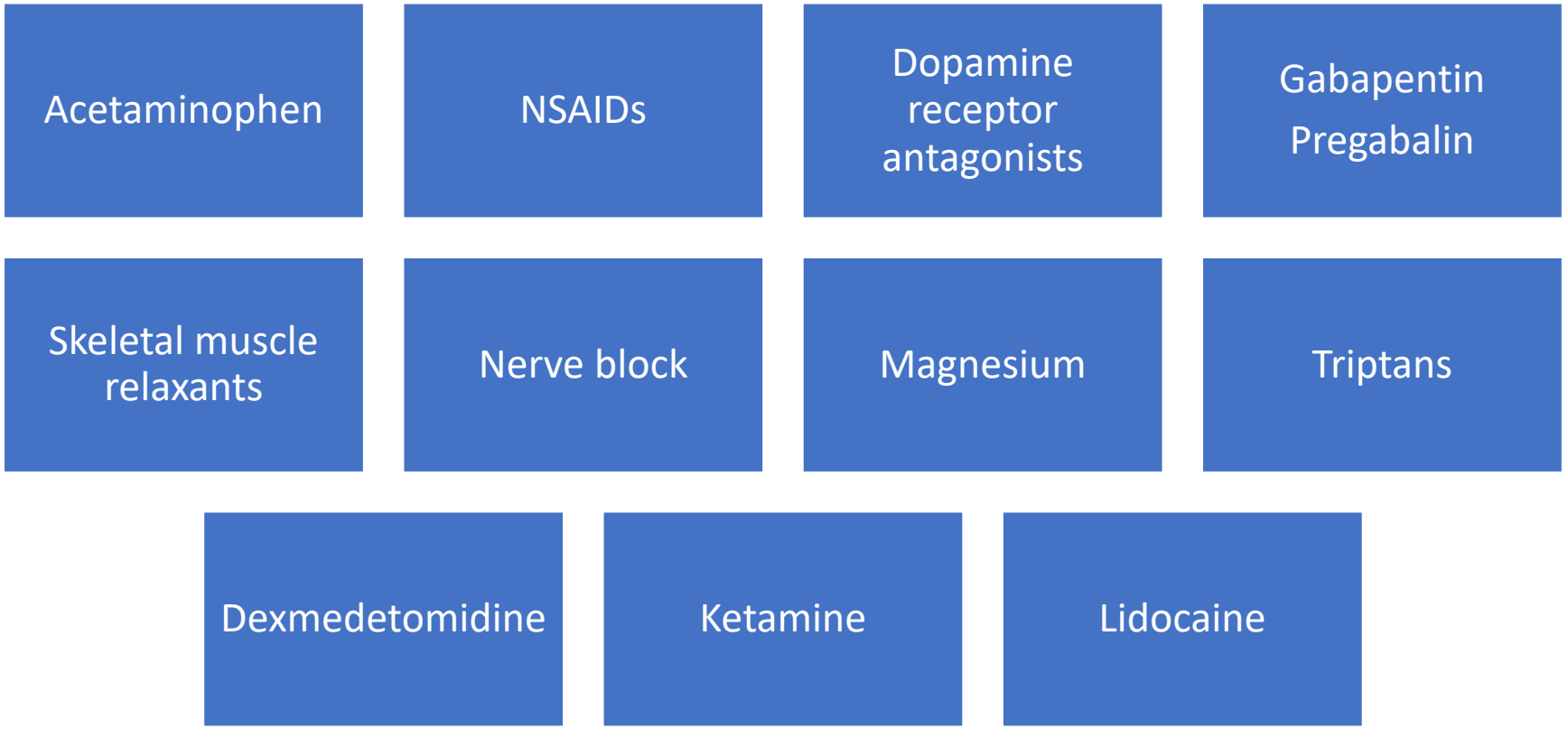
ED Acute Pain Management

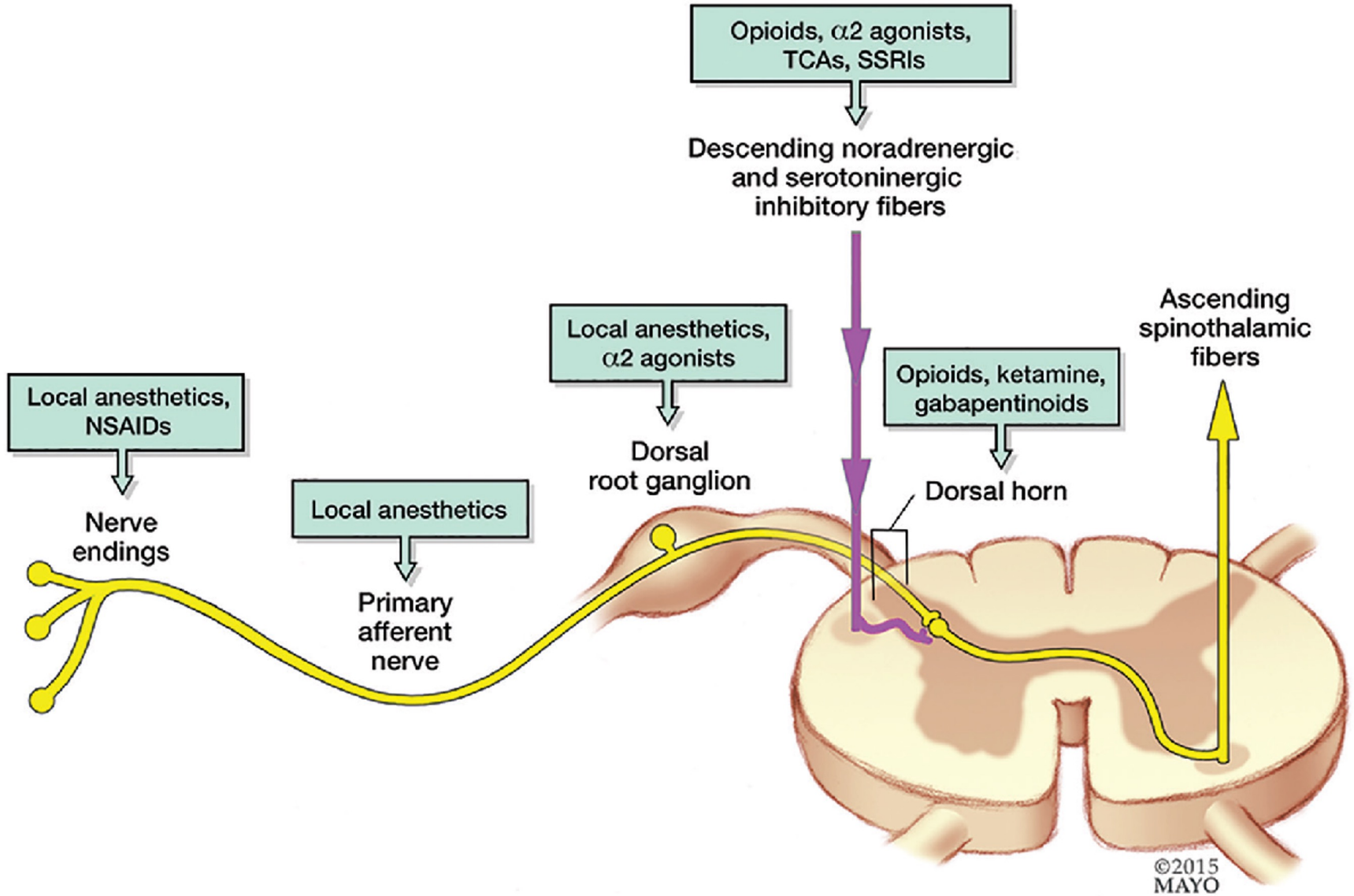


Mastering non-opioid techniques of pain management is particularly important in patients on MOUD

- Patients on MOUD have a high opioid tolerance
- Naltrexone has a very high mu receptor binding affinity - pain difficult to treat with most opioids
- Buprenorphine has a high binding affinity – requires strategy with applying additional opioids
- Methadone is long half-life full mu agonist

Non-Opioid Alternatives





Non-Opioid Alternatives

A. Gorlin et al. J Anaesthesiol Clin Pharmacol 32.2 (2016) 160

Effect of a Single Dose of Oral Opioid and Nonopioid Analgesics on Acute Extremity Pain in the Emergency Department
A Randomized Clinical Trial

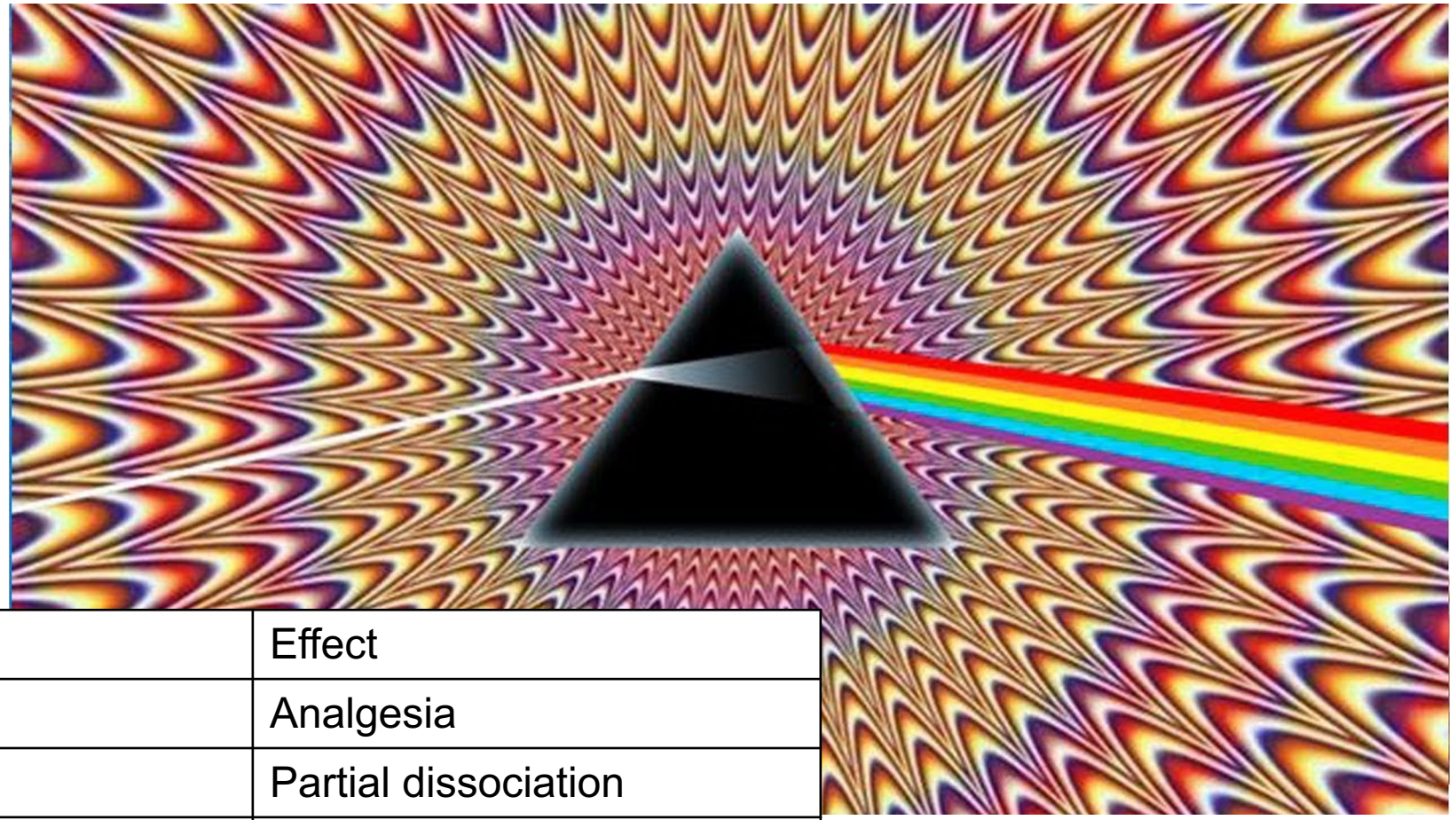
Andrew K. Chang, MD, MS; Polly E. Bijur, PhD; David Esses, MD; Douglas P. Barnaby, MD, MS; Jesse Baer, MD

Objective	To compare the efficacy of 4 oral analgesics
Study Design (n = 416)	Randomized controlled trial
Interventions	1. 400 mg of ibuprofen and 1000 mg of acetaminophen 2. 5 mg of oxycodone and 325 mg of acetaminophen 3. 5 mg of hydrocodone and 300 mg of acetaminophen 4. 30 mg of codeine and 300 mg of acetaminophen
Results	No significant differences in pain reduction at 2 hours between groups (4.3 vs. 4.4 vs. 3.5 vs. 3.9)

Non-Opioid Alternatives

A. Chang et al. JAMA 318.17 (2017) 1661-7

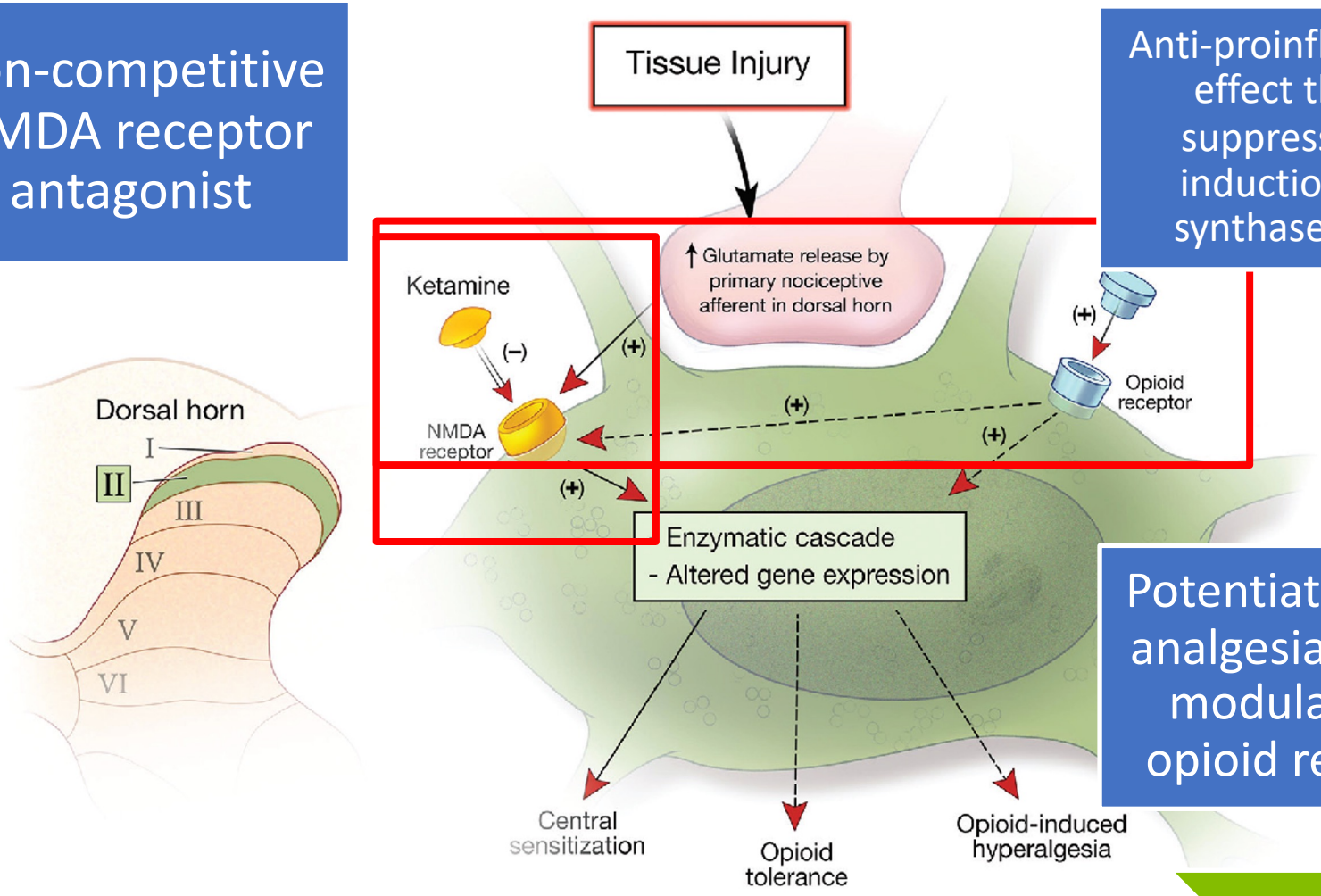
Ketamine



IV Bolus Dose	Effect
0.1-0.4 mg/kg	Analgesia
0.5-0.9 mg/kg	Partial dissociation
1-2 mg/kg	Full dissociation

Mechanism of Action

Non-competitive NMDA receptor antagonist



Anti-proinflammatory effect through suppressing the induction of NO synthase activity

Potentiates opioid analgesia through modulation of opioid receptors

Ketamine

A. Gorlin et al. J Anaesthesiol Clin Pharmacol. 32.2 (2016) 160

Intravenous Subdissociative-Dose Ketamine Versus Morphine for Analgesia in the Emergency Department: A Randomized Controlled Trial

Sergey Motov, MD*; Bradley Rockoff, MD; Victor Cohen, PharmD; Illya Pushkar, MPH; Antonios Likourezos, MA, MPH; Courtney McKay, PharmD; Emil Soleyman-Zomalan, MD; Peter Homel, PhD; Victoria Terentiev, BA; Christian Fromm, MD

Objective	To assess and compare the analgesic efficacy and safety of subdissociative IV ketamine with morphine
Study Design (n = 90)	Randomized controlled trial
Interventions	1. Ketamine 0.3 mg/kg IV push in 10 mL NS 2. Morphine 0.1 mg/kg IV push in 10 mL NS
Outcomes	**Primary:** Reduction in numeric rating scale pain scores at 30 minutes **Secondary:** Need for rescue analgesia at 30 and 60 minutes

Ketamine

S. Motov et al. Ann Emerg Med. 66.3 (2015) 222-29

Intravenous Subdissociative-Dose Ketamine Versus Morphine for Analgesia in the Emergency Department: A Randomized Controlled Trial

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Inclusion Criteria	• 18 to 55 years old • Presents with acute (onset within 7 days) abdominal, flank, back, or musculoskeletal pain score of 5 or more
Exclusion Criteria	• Pregnant • Altered mental status • Weight < 46 kg or > 115 kg • Unstable vitals • History of hepatic or renal insufficiency

Ketamine

S. Motov et al. Ann Emerg Med. 66.3 (2015) 222-29

Intravenous Subdissociative-Dose Ketamine Versus Morphine for Analgesia in the Emergency Department: A Randomized Controlled Trial

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Characteristics	Group		Difference (95% CI)
	Ketamine	Morphine	
No. of patients	45	45	
Age, mean (SD), y	35 (9.5)	36 (10.5)	−1 (−5.1 to 3.3)
Sex			
Female, No. (%)	30 (67)	28 (62)	5 (−16 to 25)
Weight, mean (SD), kg	74 (15.9)	78 (16.6)	−4 (−11.4 to 2.2)
Blood pressure, mean (SD), mm Hg			
Systolic	125 (18.2)	127 (16.1)	−2 (−8.8 to 5.6)
Diastolic	76 (13.2)	74 (12.7)	2 (−3.6 to 7.3)
Pulse rate, beats/min	79 (14.8)	79 (15.0)	0 (−6.8 to 5.6)
Source of pain, No. (%)			
Abdominal	33 (73)	31 (69)	4 (−15 to 24)
Flank	7 (16)	9 (20)	−4 (−21 to 12)
Other*	5 (11)	5 (11)	0 (−13 to 13)

*Other pain sources include back and musculoskeletal pain.

Ketamine

S. Motov et al. Ann Emerg Med. 66.3 (2015) 222-29

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Time Interval*	Group		Difference (95% CI)
	Ketamine	Morphine	
Pain NRS, mean (SD)			
Baseline	8.6 (1.5)	8.5 (1.5)	0.1 (−0.46 to 0.77)
15	3.2 (3.5)	4.2 (2.9)	−1.0 (−2.40 to 0.31)
30	4.1 (3.2)	3.9 (3.1)	0.2 (−1.19 to 1.46)†
60	4.8 (3.2)	3.4 (3.0)	1.4 (0.13 to 2.75)
90	4.8 (3.1)	3.9 (3.1)	0.9 (−0.37 to 2.28)
120	3.9 (2.9)	3.7 (2.9)	0.2 (−1.09 to 1.46)

Ketamine

S. Motov et al. Ann Emerg Med. 66.3 (2015) 222-29

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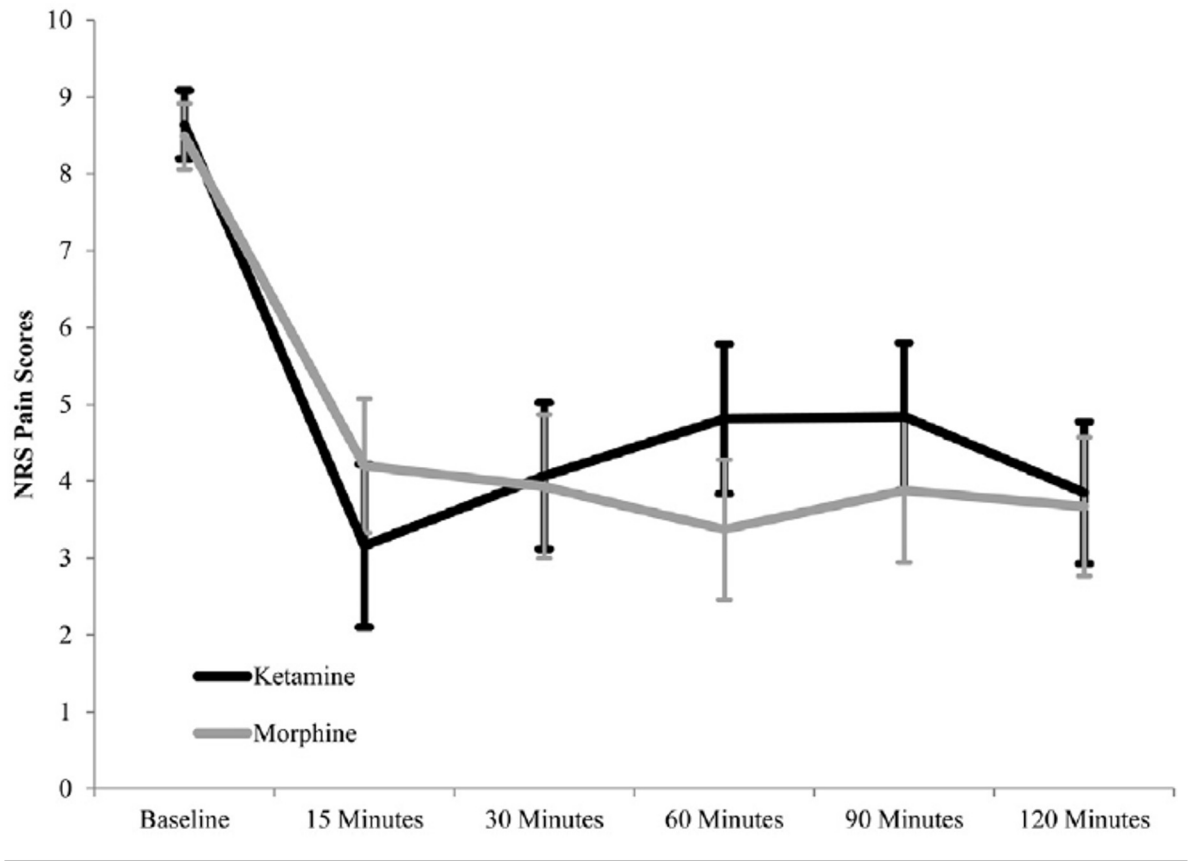


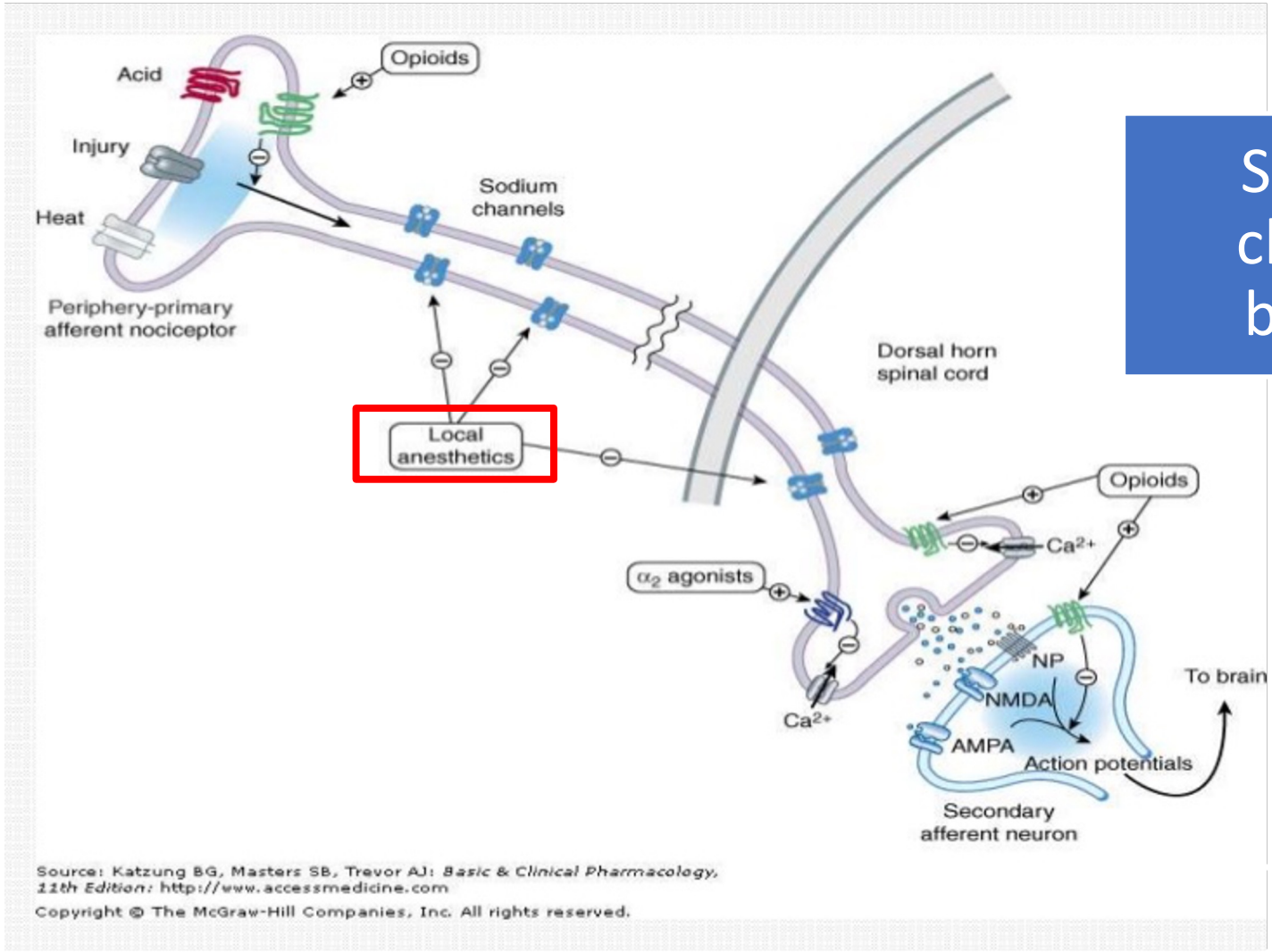
Ketamine

S. Motov et al. Ann Emerg Med. 66.3 (2015) 222-29

Lidocaine


50 mL
2% LIDOCAIN
Injection, USP
20 mg/mL
HOSPIRA, INC., LAKE FOREST, IL 60
30 mL Single-dose
Preservative-Free
1% LIDOCAINE HCl
Injection, USP
10 mg/mL
HOSPIRA, INC., LAKE FOREST, IL 60045 USA
LOT 62-236-DK
TIPLE-DOSE
OCAINE HCl
n, USP
g/mL
OREST, IL 60045 USA
-102-DK

Mechanism of Action



Sodium channel blocker

Lidocaine

Effectiveness of intravenous lidocaine versus intravenous morphine for patients with renal colic in the emergency department

Hassan Soleimanpour[1*], Kamaleddin Hassanzadeh[2], Hassan Vaezi[1], Samad EJ Golzari[3,4], Robab Mehdizadeh Esfanjani[5] and Maryam Soleimanpour[6]

Objective	To compare the efficacy of IV lidocaine with IV morphine for pain management in patients with renal colic
Study Design (n = 240)	Randomized controlled trial
Interventions	1. Lidocaine 1.5 mg/kg IV push in 10 mL NS (Group 1) 2. Morphine 0.1 mg/kg IV push in 10 mL NS (Group 2)
Primary Outcome	Reduction in numeric rating scale pain scores at 5, 10, 15 and 30 minutes

Lidocaine

H. Soleimanpour et al. BMC Urology. 12.1 (2012) 13

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	Group I	Group II	*P*-value
primary VAS	9.65 ± 0.88	9.74 ± 0.63	0.365
VAS_5	3.18 ± 2.27	4.45 ± 2.16	0.0001
VAS_{10}	1.83 ± 1.59	2.89 ± 2.07	0.0001
VAS_{15}	1.37 ± 1.32	2.55 ± 1.52	0.0001
VAS_{30}	1.13 ± 1.15	2.23 ± 1.57	0.0001

Lidocaine

H. Soleimanpour et al. BMC Urology. 12.1 (2012) 13

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Group I	perioral numbness	3 (2.5 %)
	transient dizziness	10 (8.3 %)
	dysrathria	2 (1.7 %)
	Without side effect	105 (87.5 %)
Group II	hypotension	3 (2.5 %)
	vertigo	2 (1.7 %)
	nausea	9 (7.5 %)
	vomiting	2 (1.6 %)
	Without side effect	104 (86.7 %)

Lidocaine

H. Soleimanpour et al. BMC Urology. 12.1 (2012) 13

Randomized Trial of Intravenous Lidocaine Versus Hydromorphone for Acute Abdominal Pain in the Emergency Department

Elliott Chinn, DO; Benjamin W. Friedman, MD, MS*; Farnia Naeem, BS; Eddie Irizarry, MD; Freda Afrifa, PharmD; Eleftheria Zias, RPh; Michael P. Jones, MD; Scott Pearlman, MD; Andrew Chertoff, MD; Andrew Wollowitz, MD; E. John Gallagher, MD

Objective	To compare the efficacy and safety of IV lidocaine with IV hydromorphone for the treatment of acute abdominal pain in the ED
Study Design (n = 154)	Randomized controlled trial
Interventions	1. 120 mg IV lidocaine infused over 10 minutes 2. 1 mg IV hydromorphone infused over 10 minutes • Patients could receive additional dose at 30 minutes if inadequate pain relief
Results	Reduction in numeric rating pain scale at 15, 30, 45, 60, 90, 120 and 180 minutes was larger with hydromorphone compared to lidocaine

Lidocaine

E. Chinn et al. Ann Emerg Med. 74.2 (2019) 233-40

Randomized Trial of Intravenous Lidocaine Versus Hydromorphone for Acute Abdominal Pain in the Emergency Department

Elliott Chinn, DO; Benjamin W. Friedman, MD, MS*; Farnia Naeem, BS; Eddie Irizarry, MD; Freda Afrifa, PharmD; Eleftheria Zias, RPh; Michael P. Jones, MD; Scott Pearlman, MD; Andrew Chertoff, MD; Andrew Wollowitz, MD; E. John Gallagher, MD

Time, Minutes	Lidocaine (n = 77)	Hydromorphone (n = 77)	Difference (95% CI)
Baseline	9.0 (1.3)	9.0 (1.2)	0.0 (−0.4 to 0.4)
15	6.6 (2.4)	5.6 (2.6)	1.0 (0.2 to 1.8)
30	6.1 (2.8)	4.6 (2.8)	1.5 (0.6 to 2.4)
45	5.6 (3.0)	4.1 (2.7)	1.5 (0.6 to 2.4)
60	5.4 (3.0)	3.9 (2.8)	1.5 (0.5 to 2.4)
90	5.2 (3.1)	4.0 (2.9)	1.2 (0.3 to 2.2)
120	5.1 (3.2)	3.7 (2.8)	1.4 (0.4 to 2.3)
180	4.8 (2.8)	3.8 (2.9)	1.0 (0.1 to 2.0)

Lidocaine

E. Chinn et al. Ann Emerg Med. 74.2 (2019) 233-40

Randomized Trial of Intravenous Lidocaine Versus Hydromorphone for Acute Abdominal Pain in the Emergency Department

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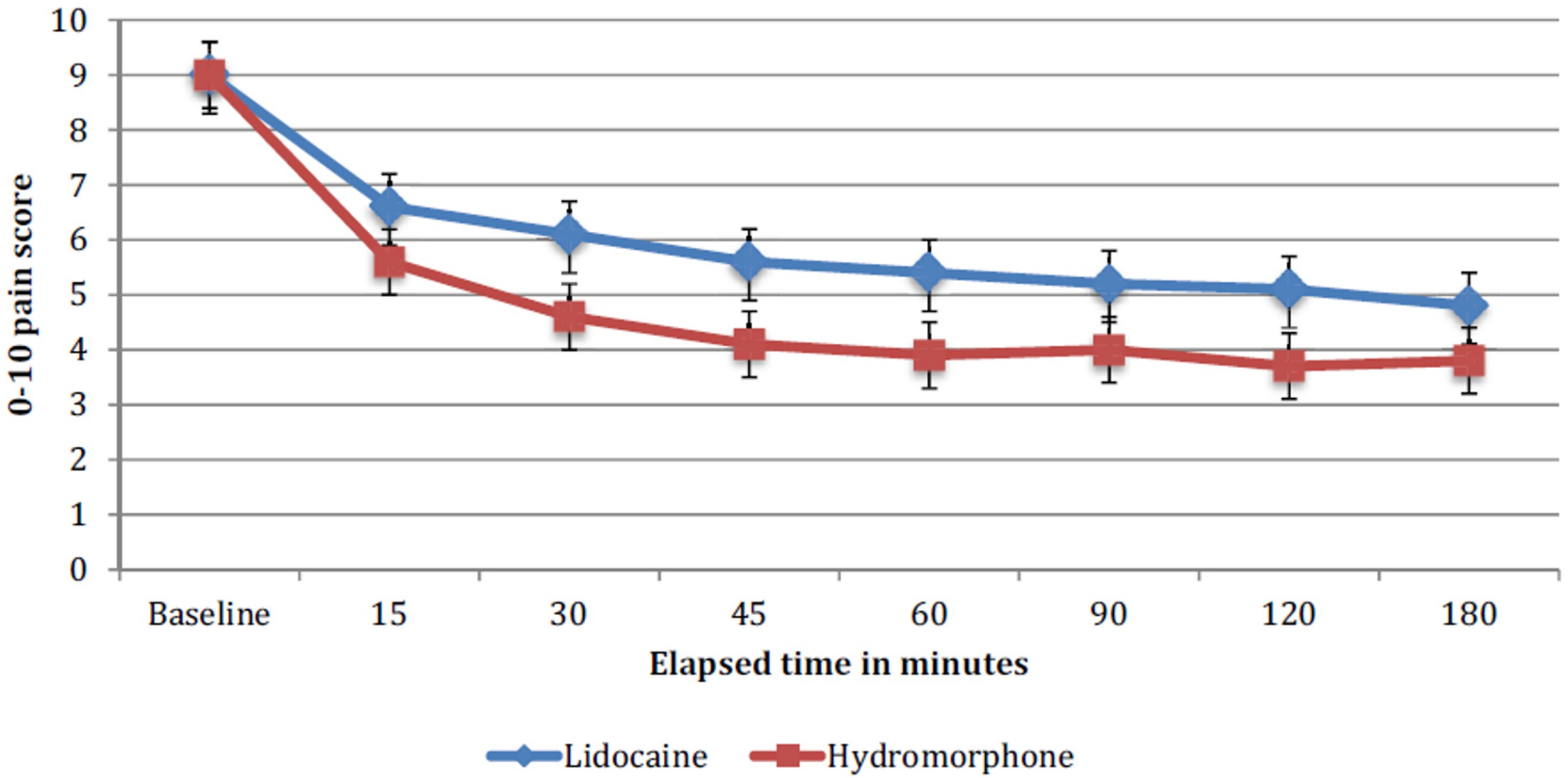


Lidocaine

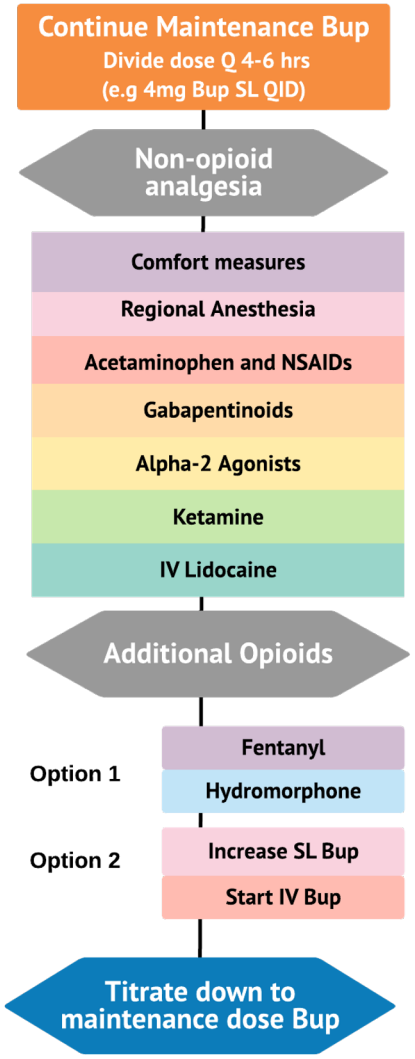
E. Chinn et al. Ann Emerg Med. 74.2 (2019) 233-40

ED Acute Pain Management for Patients with OUD

Just as you would for patients without OUD -- consider the etiology of the acute pain

- If the condition should not usually be treated with opioids (and the patient is not actively in opioid withdrawal) then don't consider an opioid
  - Example: Migraine headache in patient with OUD on methadone or buprenorphine
  - Just as for patients who do not have OUD, migraine headaches should not be treated with opioids

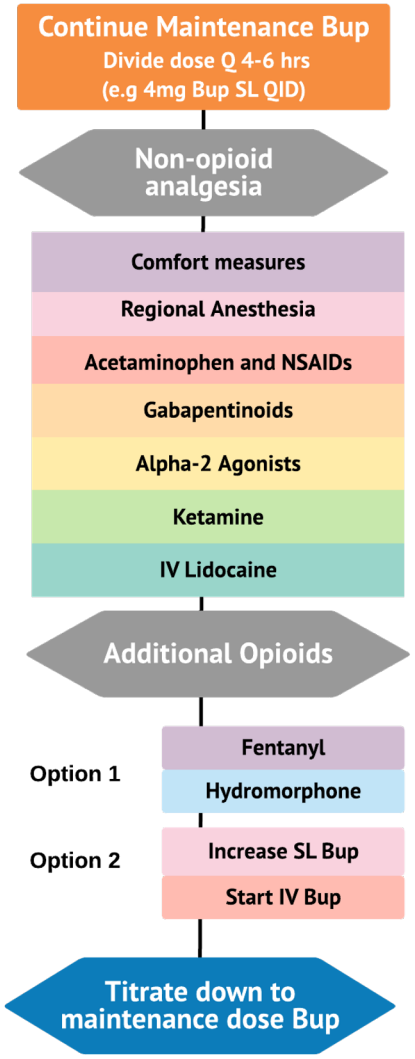
ED Acute Pain Management



Acute pain management for patients on **naltrexone** (particularly depot IM naltrexone):

- Employ all non-opioid techniques
- When it comes necessary to add an opioid, select an opioid with a high mu receptor binding affinity:
  - **Fentanyl:** high affinity, titratable, short-acting (but still may need very high doses to overcome naltrexone
  - **Hydromorphone:** higher binding affinity than fentanyl, longer acting (and less titratable)
  - **? Buprenorphine ?**

ED Acute Pain Management

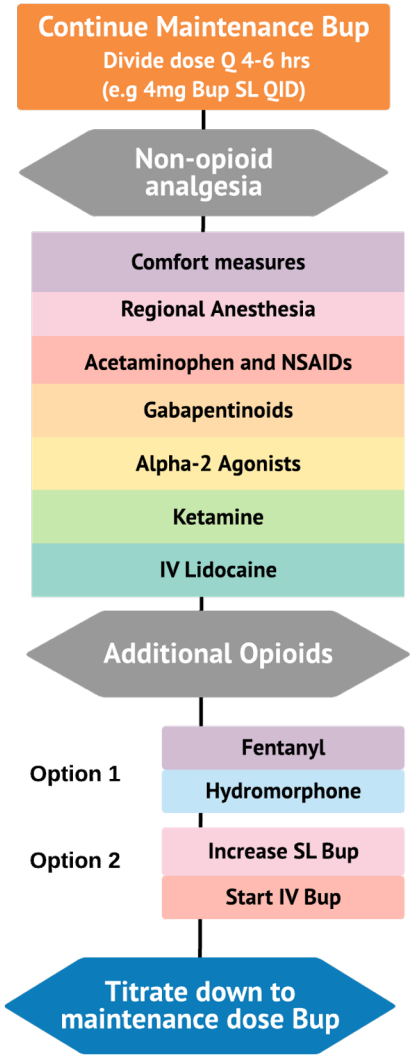


For patients on **Methadone:**

<u>Employ all non-opioid techniques</u>.

- Do NOT administer buprenorphine or butorphanol (“Stadol”) – both are high affinity partial agonists – may precipitate withdrawal
- For sustained pain relief, to reduce the need for additional opioids, adjust/divide methadone dosing to TID or BID
  - Methadone has a short half-life as an analgesic (~ 8 hours)
- May add other full mu agonists (temporarily)
- May increase total daily methadone dose (gradually)
- May want to consult an expert

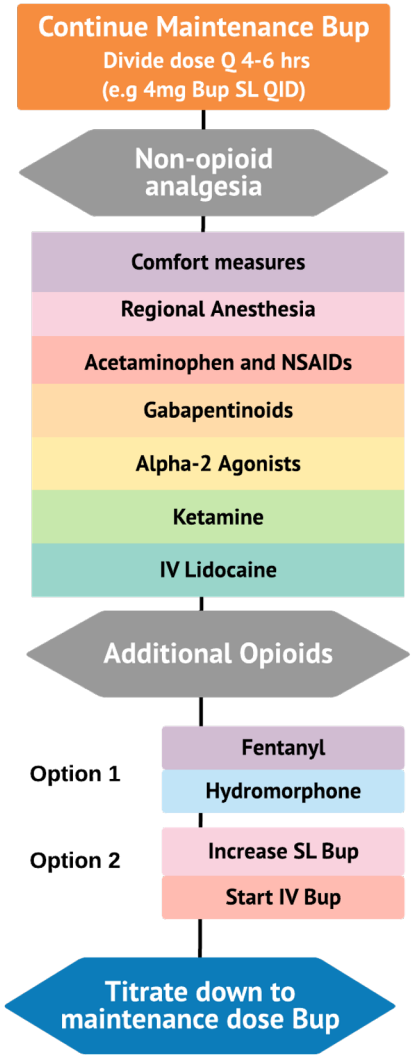
ED Acute Pain Management



Acute pain management for patients on **buprenorphine**:

- Employ non-opioid techniques (as applicable)
- First adjust buprenorphine dosing intervals:
- Divide dose to TID or QID if on daily dosing:
  - e.g. adjust 12mg daily to 4mg TID
  - e.g. adjust 16mg daily to 4mg QID
- May increase the dose of buprenorphine temporarily (examples):
  - e.g. increase from 8mg BID to 8mg TID
  - May increase to even shorter intervals (particularly if in the hospital)
  - Consider IV buprenorphine

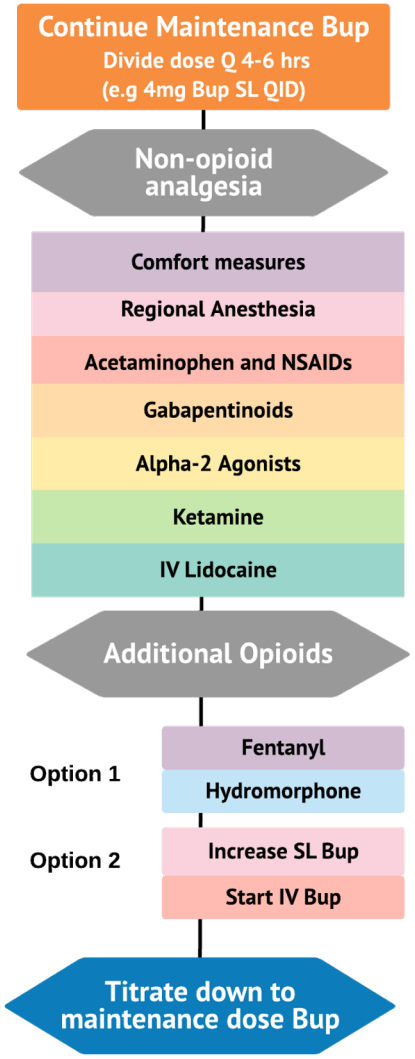
ED Acute Pain Management



Acute pain management for patients on **buprenorphine**:

- Employ all non-opioid techniques.
- When it becomes necessary to add an opioid, as with naltrexone, select an opioid with a high mu receptor binding affinity:
  - **Fentanyl:** high affinity, titratable, short-acting (may need relatively high doses)
  - **Dilaudid:** higher binding affinity than fentanyl, longer acting (and less titratable)

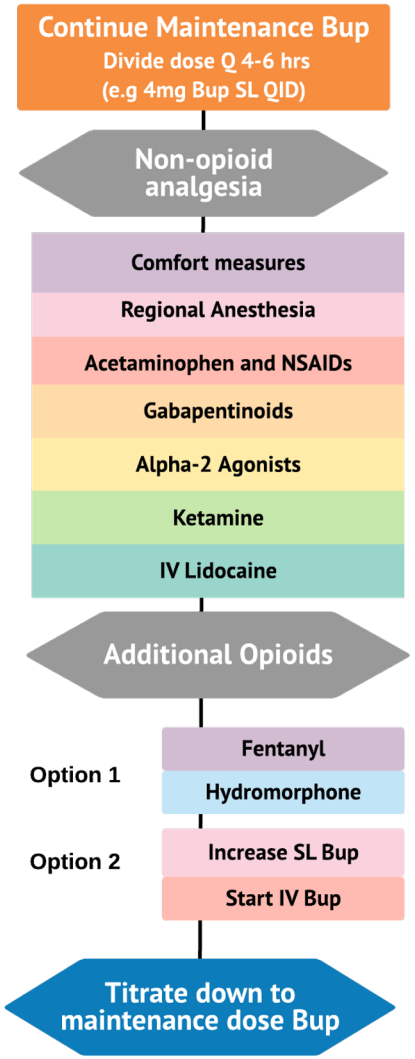
Pre-op Acute Pain Management



- Current evidence does not support the practice of routinely discontinuing Buprenorphine before surgery
- Buprenorphine is a powerful analgesic that can be combined synergistically with other opioids
  - **Buprenorphine onboard first, and maintained**

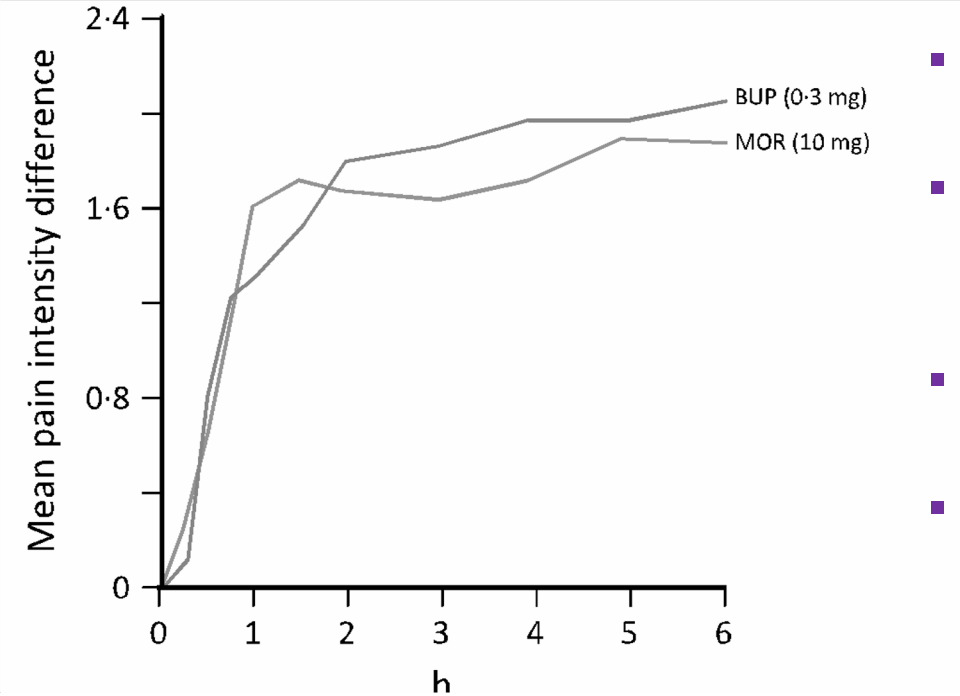
Harrison, T., 2018.
Quaye, A., 2018
Lembke, A., 2018

Buprenorphine for Acute & Chronic Pain Management



- Potent Mu agonist analgesic
- Synergistic additive analgesia when combined with full agonist opioids
- Potent anti-hyperalgesia via Kappa antagonism
- Increases Mu opioid receptor expression on the cell surface
- Blocks morphine induced receptor desensitization
- Reduced opioid tolerance
- Longer half-life (6-8 hours IV)
- Ceiling on respiratory depression
- Reduced constipation
- Reduced gonadal suppression
- Reduced immune suppression
- Reduced pancreatic and biliary duct tone

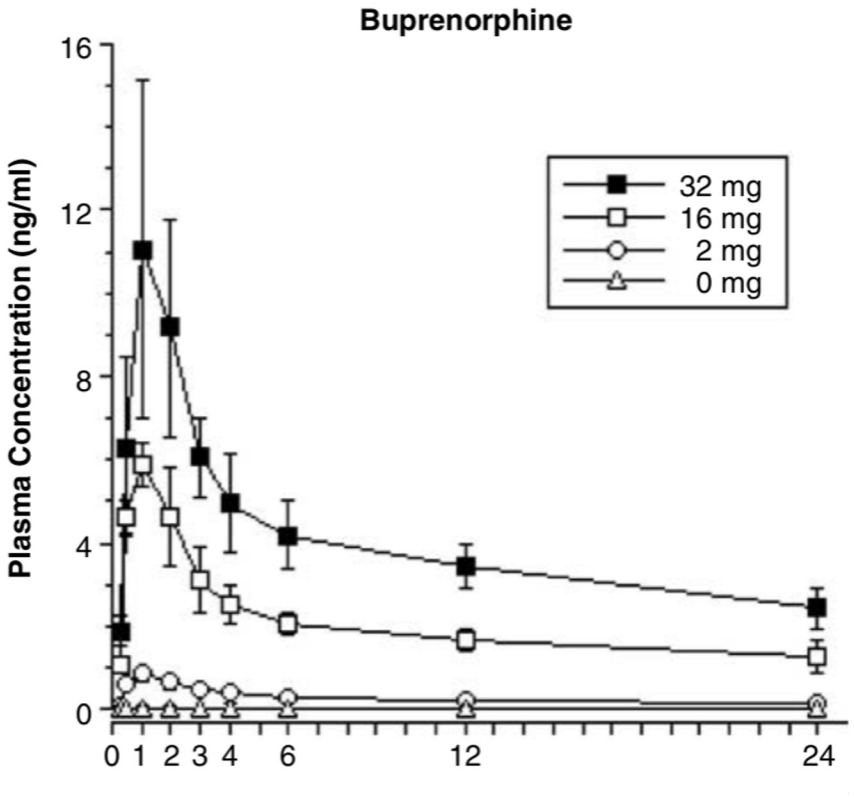
Pain Dosed Buprenorphine



White, L., 2018
Raffa, R., 2014.

- Buprenorphine is **30 to 40 times** more potent than morphine
- Clinically significant analgesia begins at 5-10% receptor occupancy
- Analgesic effect seen over the 0.1 to 10 mg range IV
- Reduced Side effects:
  - Hypotension
  - Respiratory depression
  - Sedation
  - Pruritis

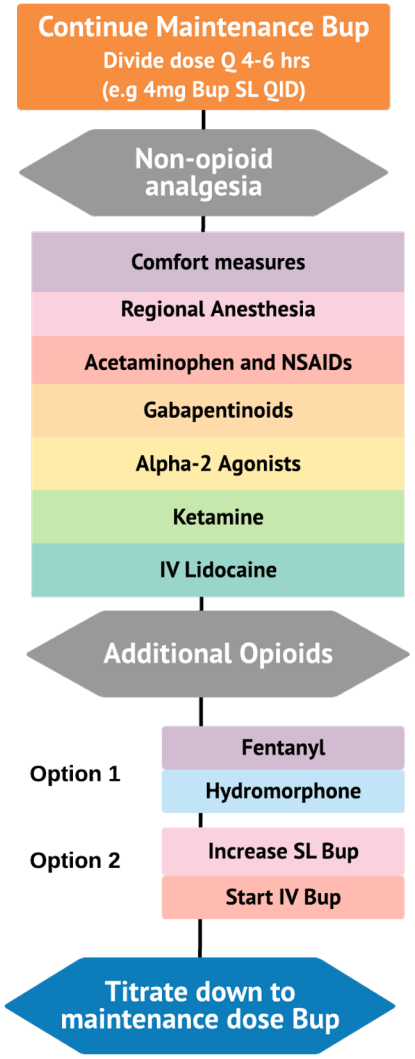
Pain Dosed Buprenorphine



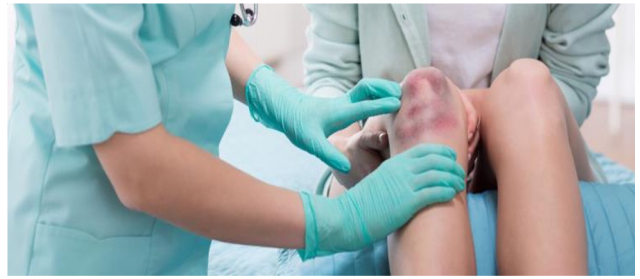
Greenwald, M. 2003

- **Increased frequency** of dosing
- Buprenorphine's analgesic duration is only a few hours
- **Increased total dose**
  - No clinical ceiling on analgesic effect

Acute Pain Management in Buprenorphine Maintained Patients



Recap:



- Use multimodal analgesia:
  - Regional anesthesia
  - Acetaminophen, NSAIDs
  - Ketamine, Magnesium
    Alpha-2 Agonists—clonidine
  - Gabapentinoids
  - IV lidocaine
- May continue same buprenorphine maintenance dose but add non-opioid analgesics
- May first divide current dose of buprenorphine into more frequent small supplemental doses of sublingual buprenorphine - Buprenorphine's analgesic duration is only a few hours
- May also increase the total daily dose of buprenorphine
- Combine high affinity (fentanyl or hydromorphone) full agonist therapy with maintenance Buprenorphine

Perioperative Management

- General:
  - Patients fear mistreatment, Providers fear deception
  - Lack of consensus in the field – often based on the preference of the surgical/ anesthesia teams

- Pre-Op:
  - Confirm Multi-Party Consent and Coordination of care with providers
  - In general buprenorphine should not be discontinued. Some clinicians may lower the dose to 8-16mg SL per day in divided doses during the perioperative period

Harrison, T. K. 2018,
Quaye, A., 2018.
Lembke, A, 2018.

Chronic Pain Patients

- Consider consulting a pain medicine specialist
- Consider Multidisciplinary Team Approach
- Try non-opioid and adjuvant analgesics
- Consider non-pharmacologic therapies
- For patients maintained on chronic opioids, consider transition to buprenorphine:
  - Safer
  - Fewer adverse effects than other opioids

Summary

- Patients with OUD treated with naltrexone, buprenorphine, and methadone, each present different challenges and opportunities for acute pain management
- Emergency physicians should develop a competency with multiple forms of non-opioid acute pain management techniques, nerve blocks, and non-opioid forms of analgesia
- Peri-operative pain management practices for patients with OUD are variable and require close coordination with surgical team
- Patients on buprenorphine can be maintained on buprenorphine through acute pain management, including peri-operative management