Perioperative Buprenorphine Management

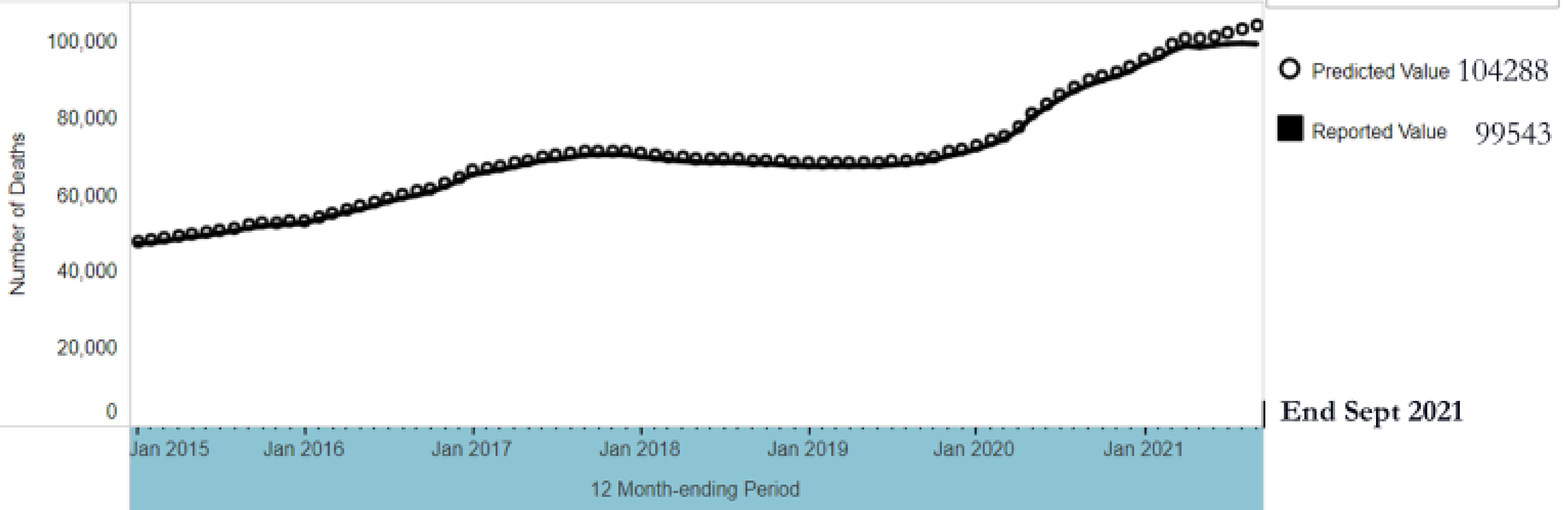
Thomas Hickey, MS MD
Staff Anesthesiologist, VACT HCS
Assistant Professor, Yale SOM

Caroline Falker, MD
Health Professions Trainee
VA Connecticut Healthcare System
Internal Medicine Specialist, Yale SOM

Outline / CME Objectives

- Opioid Crisis
- Surgery’s Role
- Illustrative BUP + Surgery Story
- Acute Postoperative Pain
- Multimodal Analgesia Primer
- BUP - Unique Pharmacology
- BUP - Perioperative Trends
- ER-Buprenorphine (Sublocade™)
- Case Discussion

Overdose deaths (combined)



Surgery & Opioids – by the Numbers

- US: **~ 50 million** surgeries/year
- 2012: **10%** of ALL opioid prescriptions by surgeons

Levy B, Paulozzi L, Mack KA, Jones CM. Trends in opioid analgesic-prescribing rates by specialty, U.S., 2007–2012. *Am J Prev Med.* (2015) 49:409–13. doi: 10.1016/j.amepre.2015.02.020

- Australia: **6.6%** of ALL opioid initiations by surgeons

Lalic S, Ilomaki J, Bell JS, Korhonen MJ, Gisev N. Prevalence and incidence of prescription opioid analgesic use in Australia. *Br J Clin Pharmacol.* (2019) 85:202–15. doi: 10.1111/bcp.13792

Persistent Postop Opioids

- Total Hip Arthroplasty (THA):
  - 20% at 3 months, 17% at 6 months, 16% at year

- THA and Total Knee:
  - 10% in opioid-naïve vs. 50% in opioid-tolerant

Am J Health-Syst Pharm. 2022;79:147-164

Surgeon: “Can we all get on the same page?”

Novel BUP Strategy - 2016

- Mild pain → Continue BUP
- **Moderate or greater → 72h abstinence**
- Committee decision
- Multimodal analgesia

Acute Postoperative Pain – Who Cares?

2003 Survey

- 80% had postop pain
  - For 86% of which was ≥ moderate
- 60% - pain top concern

Apfelbaum et al. Anesth Analg 2003; 97:534-40

2013 Survey

- 86% had postop pain
  - For 75% of which was ≥ moderate
  - …*even* at discharge
- Majority – pain top concern
- Half ≥ high anxiety (about pain)

Gan et al. Current Medical Research & Opinion. Vol 30, No. 1, 2014, 149-160.

Postop Pain – Who Cares?

- Poorly controlled ACUTE pain → CHRONIC pain
- 10% ↑ in severe acute pain → 30% ↑ in persistent pain a year later
- Inguinal hernia: 10% chronic pain, 2-4% disabling
- Thoracotomy: 30-40% chronic pain, 10% disabling

Kehlet et al. Lancet 2006; 367: 1618-25

Multimodal Analgesia

The Big 3

- **Acetaminophen**
- **NSAID**
- **Blocks** whenever possible

Creative Commons

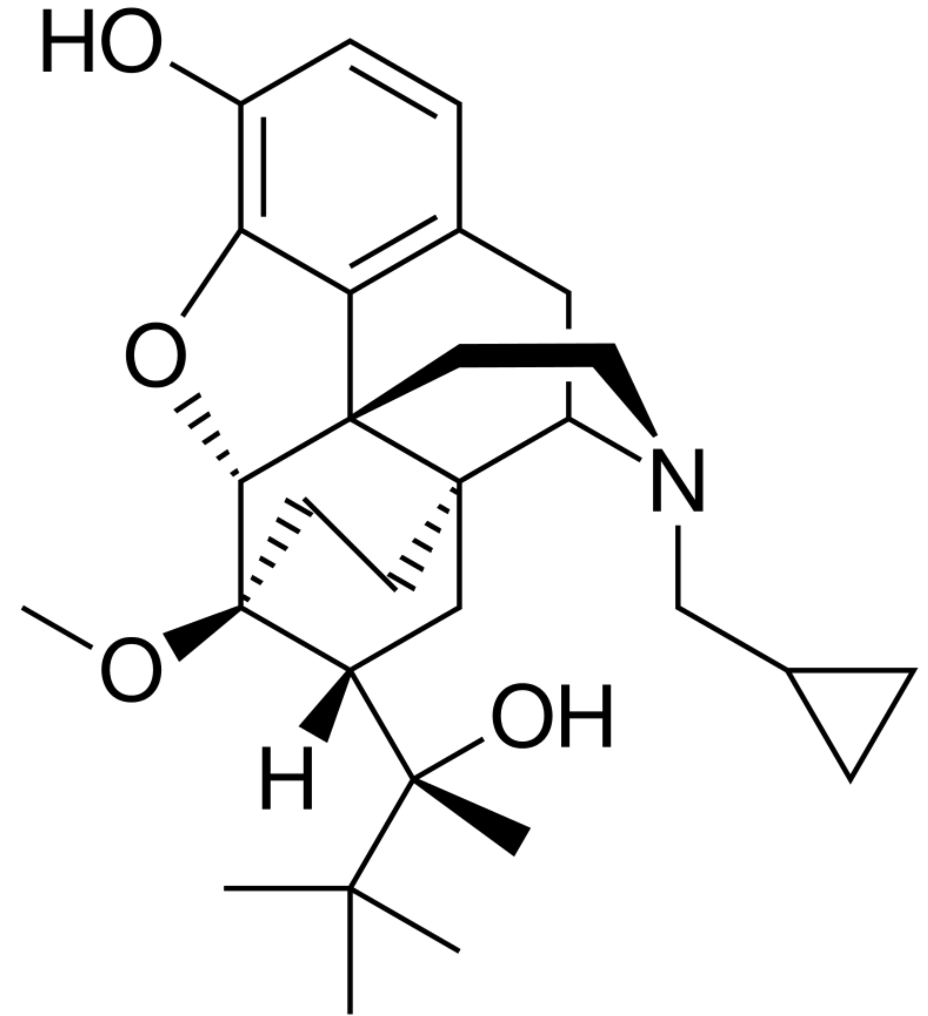
The Rest

- Continue home meds
- Alpha 2 agonist (i.e. clonidine)
- Magnesium
- Dexamethasone
- Lidocaine infusion
- Ketamine…mixed
- Gabapentinoids…mixed
- Non-Pharm: CBT/TENS

The Journal of Pain, Vol 17, No 2 (February), 2016: pp 131-157

BUP

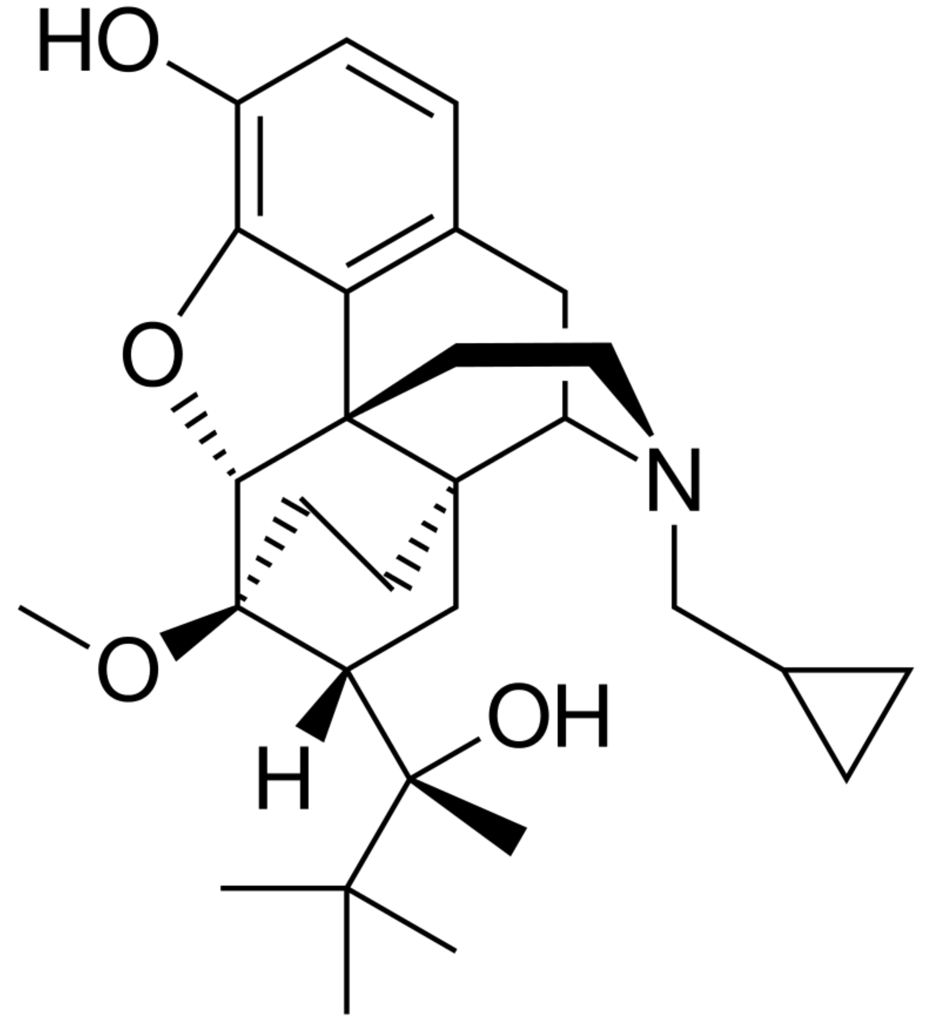
- Discovered 1966 as result of an effort to replace the OTC aspirin/codeine drug with a:
  - Safe, *OTC* opioid,
  - that provides analgesia,
  - without addicting qualities.



Lewis J. Nathan B. Eddy Award lecture: In pursuit of the Holy Grail. The College on Problems of Drug Dependence (CPDD) website. https://cpdd.org/Media/Index/AwardSpeeches/LewisJ._Eddy1998.pdf. 1998.

BUP

- FDA approved as analgesic!
- Lower intrinsic μOR activity → “partial agonist”
- High affinity for μOR → Long duration *and* interference with FAO binding (antagonist)



BUP and Acute Pain - Evidence

BUP Does Not Impair Opioid Analgesia

Study	Design	Population	Intervention	Outcome
Mercandante et al 2006	Prospective cohort	29 patients with cancer treated with transdermal BUP for cancer-related pain	IV morphine for breakthrough pain	"IV morphine safe and effective" - 92% of episodes treated successfully with IV morphine - with 88% of these achieving over 50% pain decrease in pain intensity within 15 minutes

Continued BUP Does Not Impair Post-Op Analgesia

Study	**Design**	**Population**	**Intervention**	**Outcome**
Jones et al 2009	Case Series	8 women treated with BUP for OUD undergoing vaginal delivery	Routine pain management	- Routine opioid analgesics effective - Pain scores consistent with those reported separately for non-opioid dependent patients.

Continued BUP Better than Discontinued

Study	Design	Population	Intervention	Outcome
Quaye et al, 2020	Retrospective cohort	55 patients treated with BUP for OUD who underwent surgery	38 patients continued BUP versus 17 held	Patients continued on BUP experienced: - ↓ PACU pain scores - ↓opioid prescriptions dispensed - ↓ MME dispensed.

Analgesia: BUP = Morphine In Opioid-Naïve Pts

Study	Design	Population	Intervention	Outcome
Jalili et al 2012	RCT	Adults presenting to emergency department with acute bone fractures	44 patients treated with BUP (0.4mg sublingual) and 45 patients with morphine (5mg IV)	"BUP is as effective and safe as morphine"

BUP Periop Pain Regimen Superior to Morphine

Study	**Desig n**	**Population**	**Intervention**	**Outcome**
Oifa et al 2009	RCT	120 opioid-naïve patients undergoing major abdominal surgery	Four arms - PCA bolus:infusion - BUP:BUP - BUP:MO - MO:BUP - MO:MO	- Pain lowest in BUP:BUP - PCA demand:deliver ratio lowest in BUP:BUP - Satisfaction highest in BUP:BUP - BUP did not inhibit MO analgesia

BUP vs. Morphine – Efficacy and Adverse Effects

- Primary Outcomes:
  - Pain: No significant difference
  - Resp Depression: No significant difference
  - Sedation: No significant difference

British Journal of Anaesthesia, 120 (4): 668–678 (2018)

BUP vs. Morphine – Efficacy and AE

- Secondary Outcomes:
  - Nausea: No difference
  - Vomiting: No difference
  - Dizziness: No difference
  - Hypotension: No difference
  - Pruritis: Less with BUP
  - Rescue analgesia requirement: No significant difference
  - Time to rescue analgesia: Trend to BUP

British Journal of Anaesthesia, 120 (4): 668–678 (2018)

Perioperative BUP: Rapid Change

2016

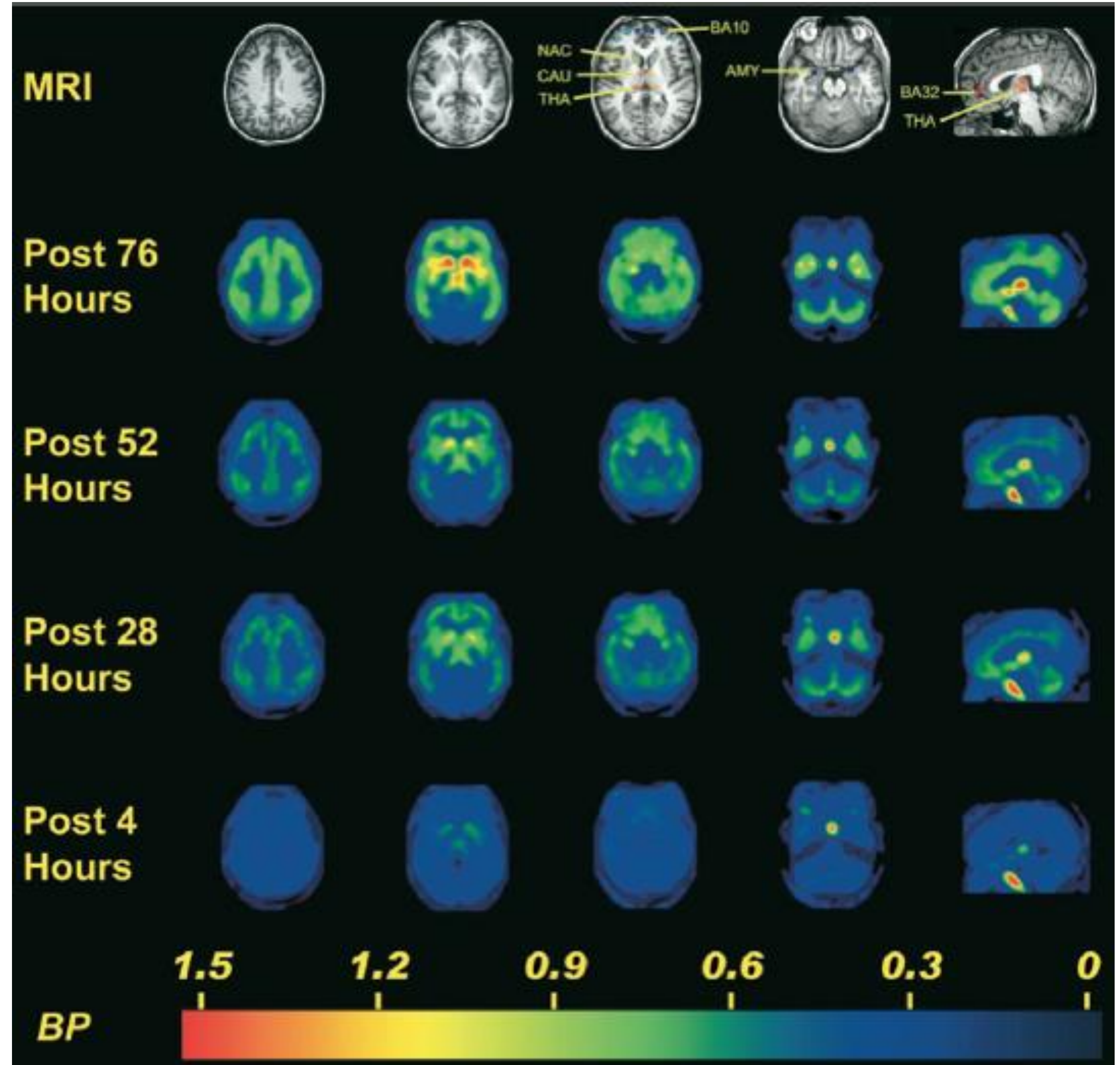
- ≥ Moderate pain expected
  - → **72h abstinence**

2019

- ≥ Moderate pain expected
- → **Continue BUP**

Periop BUP

What's the right dose?



M. Greenwald et al

BIOL PSYCHIATRY 2007;61:101–110

Periop BUP Dose – Greenwald Observations

- Therapeutic Effect in OUD
  - Withdrawal typically suppressed up to ~ 50 µOR availability
- DOSE & TIME:
  - ~ 60% µOR available 4h after 2mg BUP maintenance dose (0.5ng/mL)
  - ~ 20% µOR available 4h after 16mg BUP maintenance dose (2.5ng/mL)

BIOL PSYCHIATRY 2007;61:101–110

Periop BUP - Analgesia

- Oifa Trial:
  - Average combined IV BUP was 972 mcg/day
  - Assuming 30% oral bioavailability
  - That’d be about 3mg (300mcg) SL

Oifa et al 2009

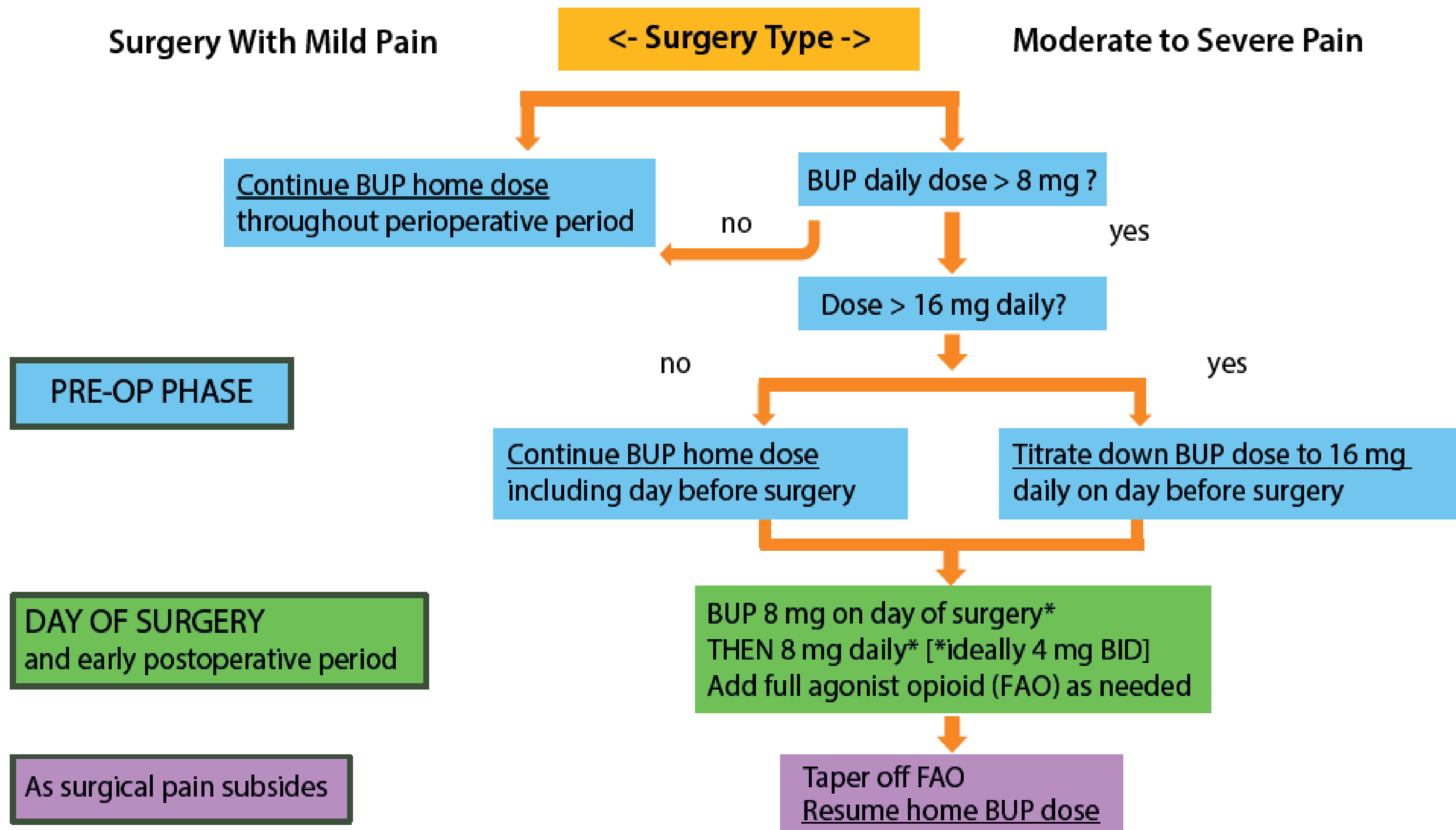


Figure 2. MGH Department of Anesthesia Critical Care and Pain Medicine Guideline for Perioperative Buprenorphine Management[a]
Surgery With Mild Pain
<- Surgery Type ->
Moderate to Severe Pain
Continue BUP home dose throughout perioperative period
BUP daily dose > 8 mg ?
no
yes
Dose > 16 mg daily?
PRE-OP PHASE
no
yes
Continue BUP home dose including day before surgery
Titrate down BUP dose to 16 mg daily on day before surgery
DAY OF SURGERY and early postoperative period
BUP 8 mg on day of surgery*
THEN 8 mg daily* [*ideally 4 mg BID]
Add full agonist opioid (FAO) as needed
As surgical pain subsides
Taper off FAO
Resume home BUP dose
[a]Protocol implemented at Massachusetts General Hospital (MGH) in March 2018 (revised by G.A.A. February 2019).
Abbreviations: BUP = buprenorphine, PRE-OP = preoperative.

ER-Buprenorphine (Sublocade™)

- 300mg and 100mg SC monthly regimens
- Steady state in 4-6 months
- Therapeutic half life: > 38 days

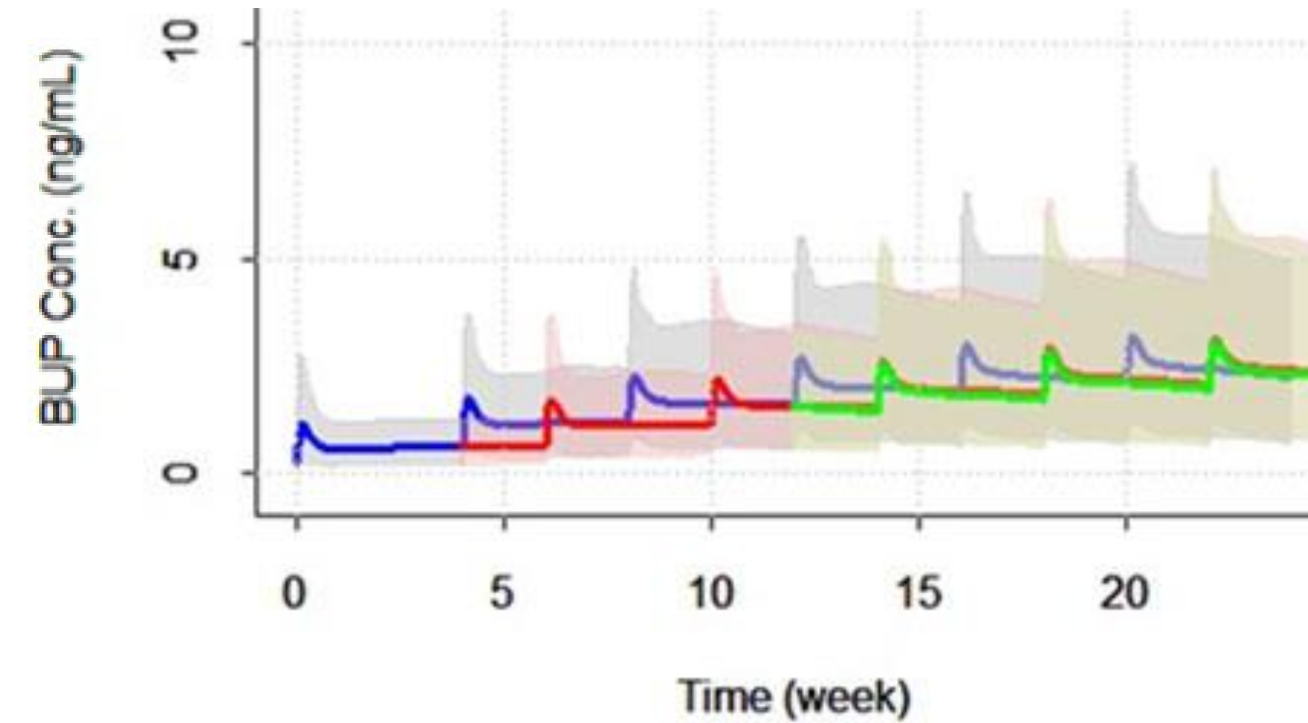
U.S. Food and Drug Administration/Center for Drug Evaluation and Research. FDA Briefing Document on NDA 209819 for RBP-6000 (buprenorphine injectable) for treatment of opioid dependence. 10 31, 2017a.

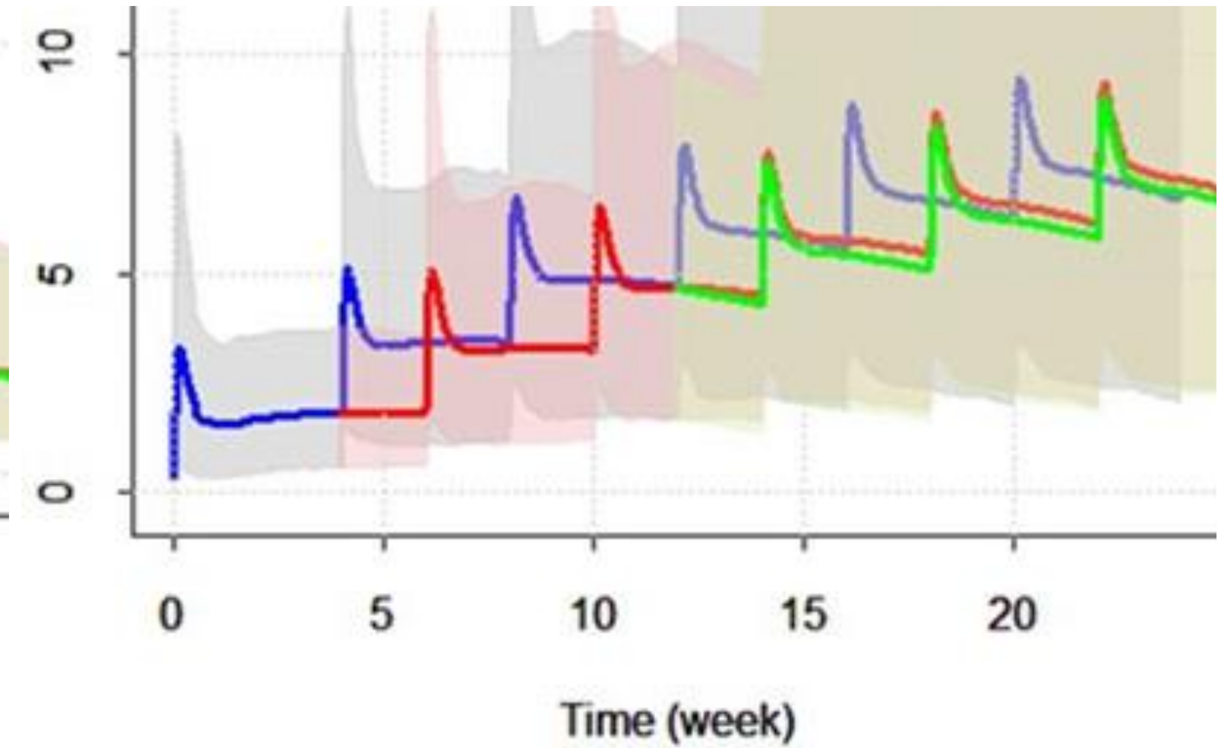
BUP Concentrations – SL vs. ER

	SL BUP		ER-BUP	
Dose	8 mg	24 mg	100 mg	300 mg
Cavg (ng/mL)	**1.4**	**2.8**	**2.9**	**6.3**
μOR Avail			**~40%**	**~ 20%**

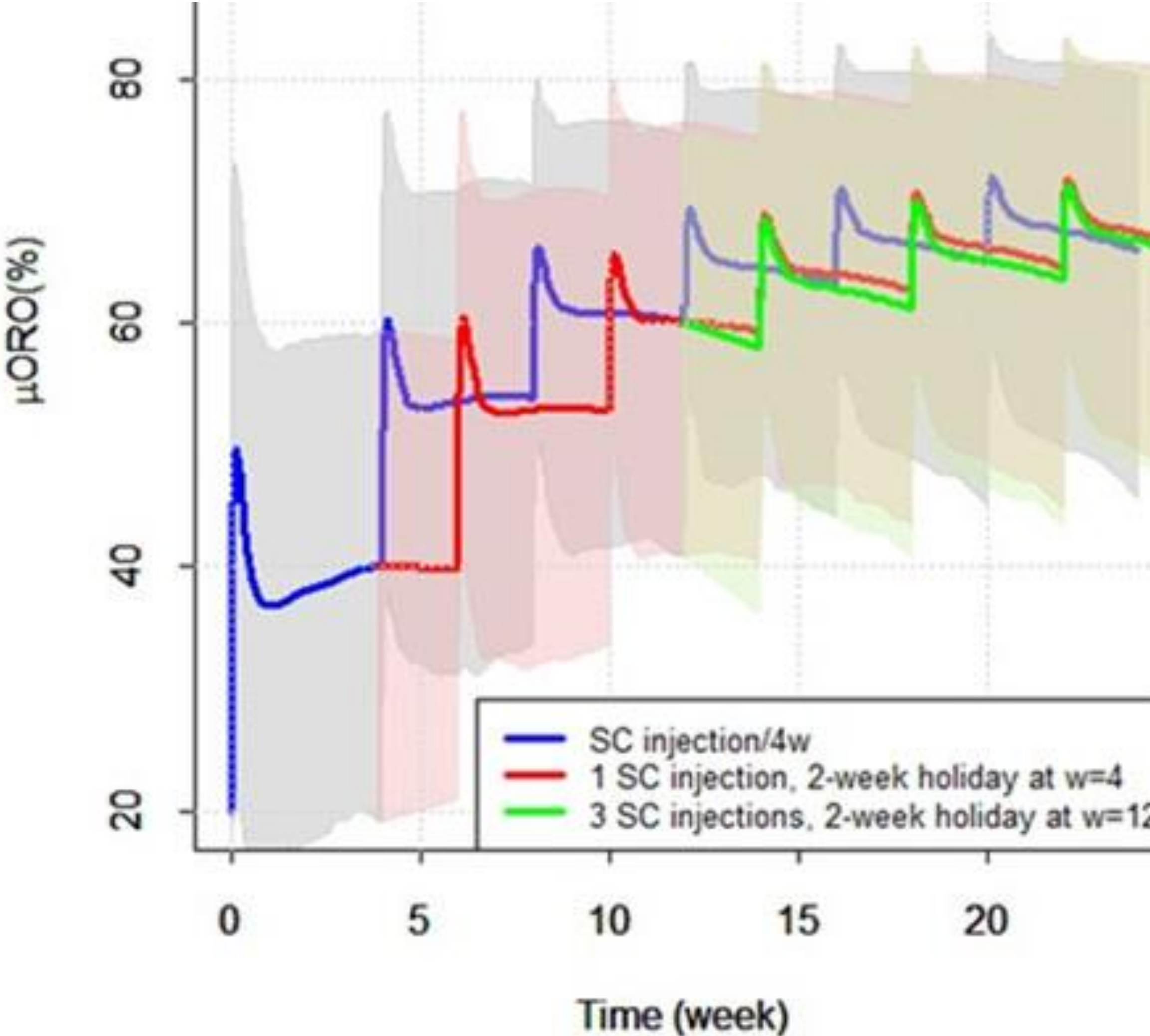
Laffont CM, Gomeni R, Heidbreder C, Jones JP 3rd, Nasser AF. Population Pharmacokinetic Modeling After Repeated Administrations of RBP-6000, a New, Subcutaneously Injectable, Long-Acting, Sustained-Release Formulation of Buprenorphine, for the Treatment of Opioid Use Disorder. J Clin Pharmacol. 2016 Jul;56(7):806-15. doi: 10.1002/jcph.665. Epub 2016 Mar 11.

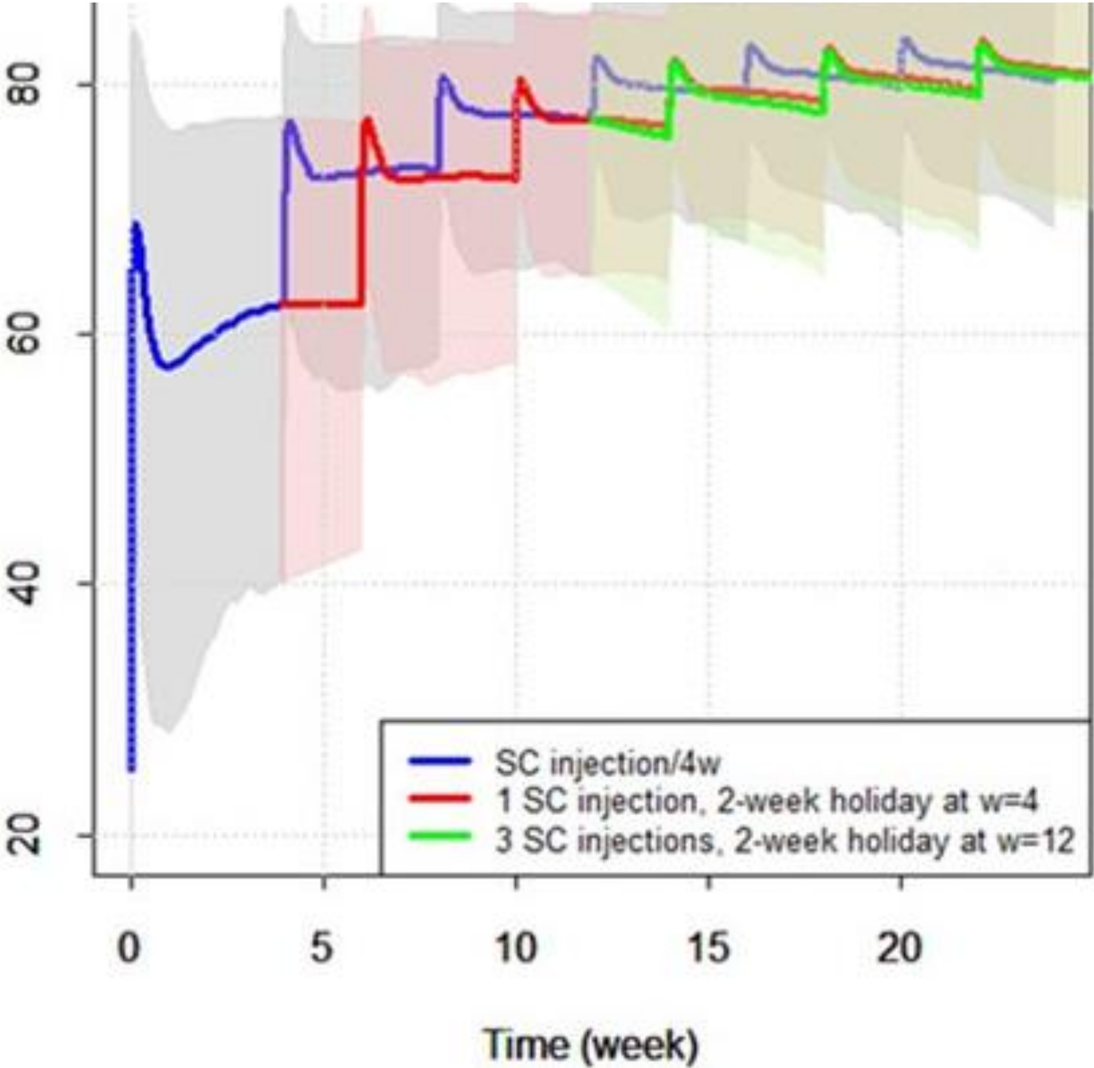
BUP Concentrations – 100mg & 300mg ER-BUP





MOR Occupancy – 100mg & 300 mg ER-BUP





ER-BUP – Best Practice?

- To our knowledge: Nobody knows
- Always vital: Multidisciplinary approach emphasizing multimodal analgesia
- Reasonable: Surgery at trough (i.e. at time of next scheduled dose)

Cases

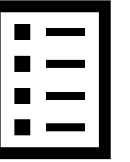
Consult Question

- “Recommendations for buprenorphine adjustment before dental surgery”

History of Present Illness

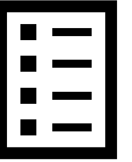
- A 64-year-old male with opioid use disorder (OUD) in remission and chronic low back pain maintained on sublingual buprenorphine/naloxone (bup/nalox) 24mg/6mg total daily dose was scheduled for an elective dental procedure.
- He was stable on bup/nalox without opioid cravings, aberrancies, or return to non-prescribed opioid use. Chronic pain was well-controlled.

Medical and Psychiatric Diagnoses



- Coronary artery disease
- Hypothyroidism
- Spinal stenosis complicated by chronic low back pain
- Opioid use disorder in sustained remission
- Alcohol use disorder in sustained remission

Psycho/social/spiritual History



- Lives with wife of 40+ years, has one adult daughter who lives independently. Siblings who live locally (2 brothers, 1 sister).
- Completed 10th grade; GED after military service. Prior work as chef in long term care facility, now on disability.
- Protestant, not practicing.
- Relevant family history:
  - Mother: deceased; hx alcohol use disorder
  - Father: deceased; hx alcohol use disorder

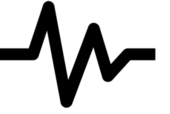
Current Medication Treatments

- Bup/nalox 8mg/2mg SL TID (24mg total daily dose)
- Aspirin 81mg
- Levothyroxine 125 mcg
- Fish oil

Current or Completed Psychotherapy Treatments

- Private counseling: current
- Inpatient alcohol treatment programs x 5 episodes (last 20+ years ago)

Relevant Data



- Labs all wnl
- Urine toxicology +buprenorphine only (as expected)
- Other
  - PHQ-9: score 3

Recommendations for continuing perioperative buprenorphine

	Baseline regimen	Day before procedure	Day of procedure	Day after procedure	Ongoing regimen
Buprenorphine/ naloxone	8mg/2mg SL TID (24mg TDD)	8mg/2mg SL TID (24mg TDD)	8mg/2mg SL BID (16mg TDD)	8mg/2mg SL TID (24mg TDD)	8mg/2mg SL TID (24mg TDD)
				Acetaminophen	
			Ice packs	Ice packs	

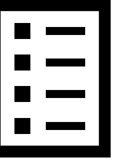
Consult Question

- “Perioperative buprenorphine recs for patient undergoing cardiac valve replacement”

History of Present Illness

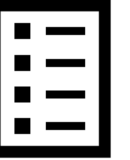
- A 35-year-old female with severe OUD and injection drug use-related infective endocarditis (IDU-IE) was admitted to the hospital and scheduled for aortic and mitral valve replacement.
- She initially presented for fever and malaise. She'd been injecting 15 bags of heroin daily for the last 8 months (with hx opioid use dating back 10 years).
- She was prescribed bup/nalox 24mg/6mg SL QD for years, but wasn't consistently taking it before admission.
- At the time of your evaluation, she has been in the hospital for 14 days and has been stable on bup/nalox 24/6mg SL QD. She is scheduled for surgery in 2 days.

Medical and Psychiatric Diagnoses



- Infective endocarditis
- Methicillin-susceptible staphylococcus aureus (MSSA) bacteremia
- Severe opioid use disorder
- Rule out anxiety disorder

Psycho/social/spiritual History



- Parents and 2 siblings living locally but strained relationship.
- Living with friend prior to admission, +housing insecurity.
- Completed high school and 2 years of college, stopped attending due to issues related to substance use. Prior work as administrator at Veterinary clinic, currently unemployed.
- No relevant family hx.

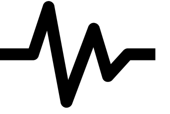
Current Medication Treatments

- Bup/nalox 24mg/6mg SL QD
- Gabapentin 300mg BID
- IV nafcillin
- Acetaminophen 650mg q6h PRN

Current or Completed Psychotherapy Treatments

- Patient describes past group and individual counseling at times when she was admitted to residential treatment programs, and did required groups years ago that were part of methadone maintenance treatment.
- Not currently receiving psychotherapy

Relevant Data



- Labs – stable renal and hepatic function, improving leukocytosis
- Urine toxicology on admission +opiates +fentanyl +benzos
- Other
  - PHQ-9: score 1

Recommendations for continuing perioperative buprenorphine

	Baseline regimen	Day before procedure	Day of procedure	Day after procedure	Ongoing regimen
Buprenorphine/ naloxone	24mg/6mg SL QD	8mg/2mg SL TID (24mg TDD)	8mg/2mg SL TID (16mg TDD*) *received 2 doses pre-op	8mg/2mg SL TID (24mg TDD)	24mg/6mg SL QD
			IV hydromorphone, IV fentanyl	PO hydromorphone	PO oxycodone x 5 days
Non-opioid medications					

Consult question

- “Patient on extended release buprenorphine. Recommendations for upcoming CT surgery”

History of Present Illness

- A 37-year-old male with remote IDU-IE s/p tricuspid valvectomy presented for planned tricuspid valve replacement while maintained on extended-release injection buprenorphine.

Current Medication Treatments

- Buprenorphine 100mg SQ once monthly

Recommendations for continuing perioperative buprenorphine

	Baseline regimen	Day before procedure	Day of procedure	Day after procedure	Ongoing regimen
Buprenorphine	100mg SQ once monthly	100mg SQ once monthly (day 27)	4mg/1mg SL TID (12mg TDD); day 28	4mg/1mg SL TID (12mg TDD)	100mg QS once monthly
				PO hydromorphone	PO oxycodone (tapered over a week)
Non-opioid medications					

Thank you!