Opioid Agonist Therapy 101: An Introduction to Clinical Practice

Acute, Chronic & Perioperative Pain Management in the Context of OAT

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- **Faculty:** Erin Knight
- **Relationships with commercial interests:**
  - None

Learning Objectives

- Review definitions, pathophysiology, and classification of pain
- Understand the epidemiology and management of chronic pain
- Outline rational pharmaceutical options for pain management
- Review current guidelines for Opiate Replacement Therapy (OAT) with respect to patients with concurrent pain
- Discuss management of pain for patients on OAT with acute and chronic pain through case-based learning

Case 1: Jim

- 52 year old male
- Long standing history of alcohol use disorder
- Introduced to opioids via his wife
- Stabilized on methadone for a few years with a few minor relapses only
- No other medical history or medications

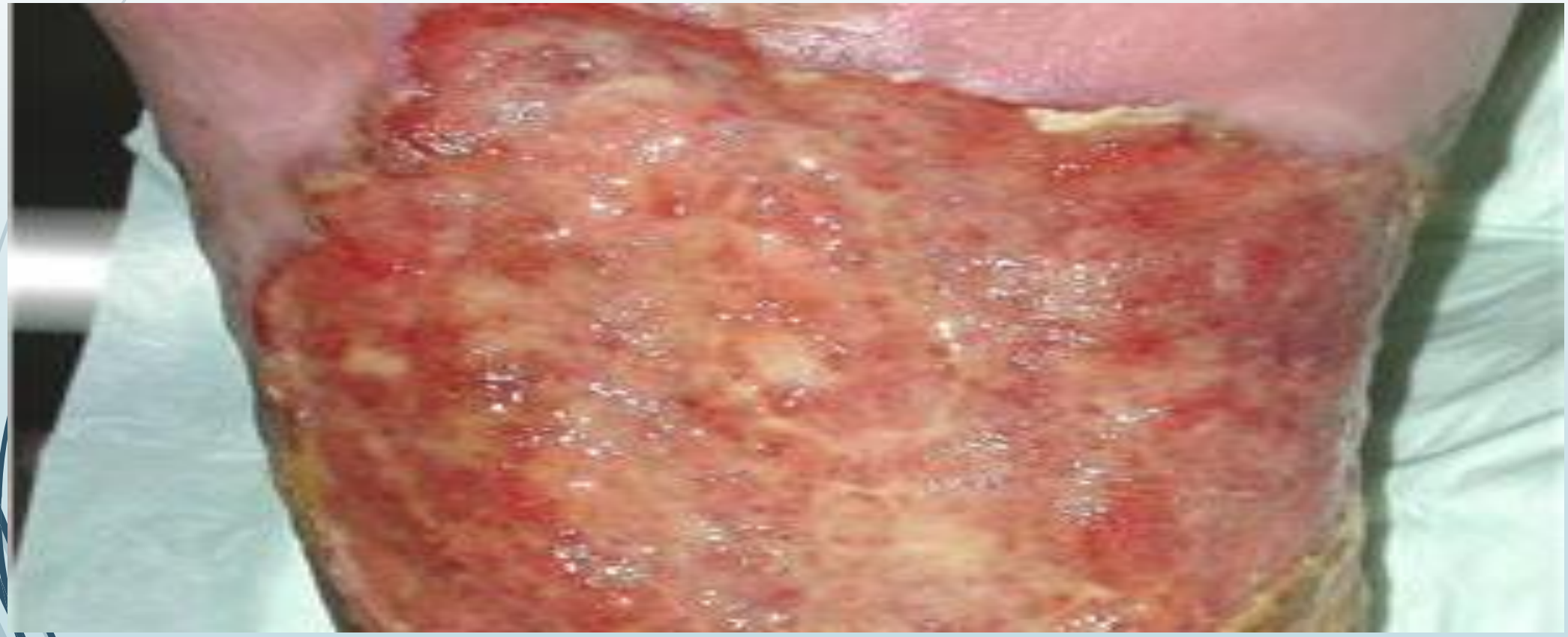
Case 1: Jim

- Jim's wife leaves for 2 weeks to visit with family
- Jim takes the opportunity to indulge in a few beer
- Unfortunately, while on a ladder, Jim falls and has an acute navicular fracture for non operative management
- He is having considerable pain, what do you do?

Case 2: Kathy

- Kathy is a 33 year old female
- She has a positive family history of substance use disorder
- She herself has a long standing history of an opioid use disorder for which she is on 28mg of buprenorphine/naloxone
- She also has known Crohn's Disease which is currently in remission
- She is transferred your clinic with the following….

Pyoderma Gangrenosum



Case 2: Kathy

- Kathy presents in crisis
- She is receiving Infliximab and prednisone and is being followed by a gastroenterologist as well as a dermatologist. She has had a poor response to therapy thus far
- She is in pain. How do you proceed?

Pain Overview

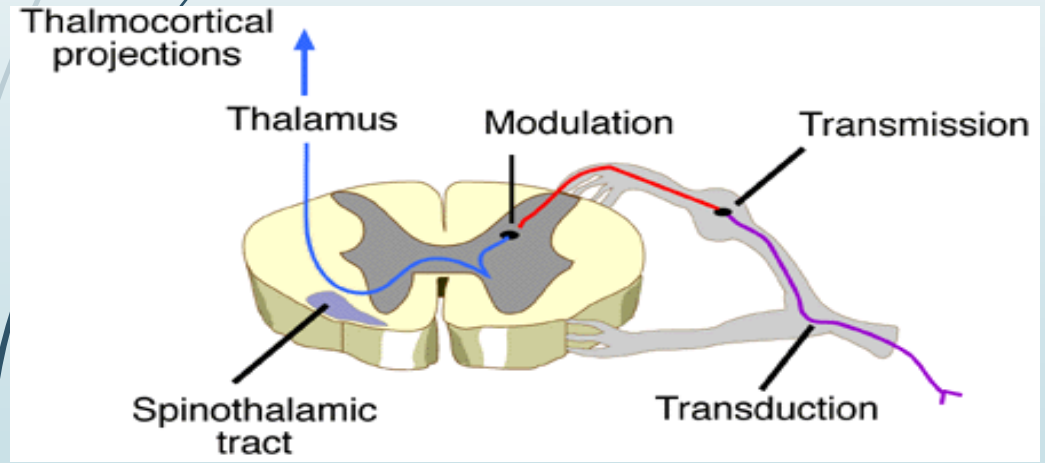
Definitions

- Nociception
  - The process by which information about a noxious stimuli is conveyed to the brain. It is the total sum of the neural activity that occurs ***prior to the cognitive processes*** that enable human to identify a sensation as pain

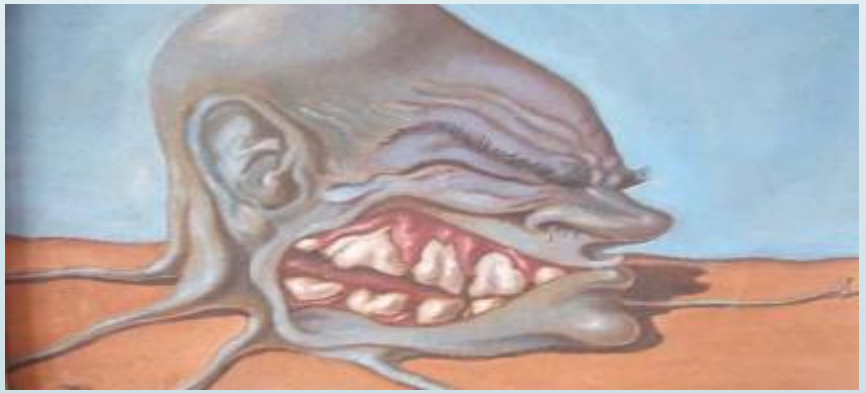
- Pain
  - An unpleasant sensory or emotional experience associated with actual or potential tissue damage, or described in terms of such damage….it is always subjective.

A picture is worth……

- Nociception



- Pain



Classification of Pain

- Type: nociceptive, neuropathic pain
- Temporal: acute pain, chronic pain
- Location: soft tissue, bones/joints, visceral pain

Goals of Chronic Pain Management

- Focus visits on function
- Identify complex interactions that may be driving or enhancing the pain experience
- Collaborative care models

Pain Overview

Pharmaceutical Options

Acute Nociceptive/Perioperative Pain

But what about the methadone/buprenorphine?

- Continue (and optimize) OAT
  - OAT dose is baseline for preventing withdrawal
  - Once daily dosing will not provide significant pain relief
- Split dosing may be an option for those eligible for carries
- If using opioids start with dosing similar to that used for a person not on OAT
  - Caveat: may need to be larger and/or more frequent doses, due to:
    1) Opioid tolerance
    2) More severe pain experience
- Avoid using person's previous or current drug of choice if possible
- Shared decision making is important, discussing risks, framing expectations
- Consideration of regional anaesthesia for perioperative pain

Buprenorphine hmmm…

- Buprenorphine binds tightly to the mu-opioid receptor as a partial agonist

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Uniform assessment and ranking of opioid Mu receptor binding constants for selected opioid drugs ☆

Donna A. Volpe [a,*], Grainne A. McMahon Tobin [a], R. Daniel Mellon [b], Aspandiar G. Katki [a], Robert J. Parker [a], Thomas Colatsky [a], Timothy J. Kropp [c], S. Leigh Verbois [c]

Drug	K_i (nM)	Drug	K_i (nM)	Drug	K_i (nM)
Tramadol	12,486	Hydrocodone	41.58	Butorphanol	0.7622
Codeine	734.2	Oxycodone	25.87	Levorphanol	0.4194
Meperidine	450.1	Diphenoxylate	12.37	Oxymorphone	0.4055
Propoxyphene	120.2	Alfentanil	7.391	Hydromorphone	0.3654
Pentazocine	117.8	Methadone	3.378	Buprenorphine	0.2157
		Nalbuphine	2.118	Sufentanil	0.1380
		Fentanyl	1.346		
		Morphine	1.168		

Drug Alcohol Depend. 2014 November 1; 0: 1–11. doi:10.1016/j.drugalcdep.2014.07.035.

Buprenorphine maintenance and *mu*-opioid receptor availability in the treatment of opioid use disorder: implications for clinical use and policy

Mark K. Greenwald[a,*], **Sandra D. Comer**[b], and **David A. Fiellin**[c]

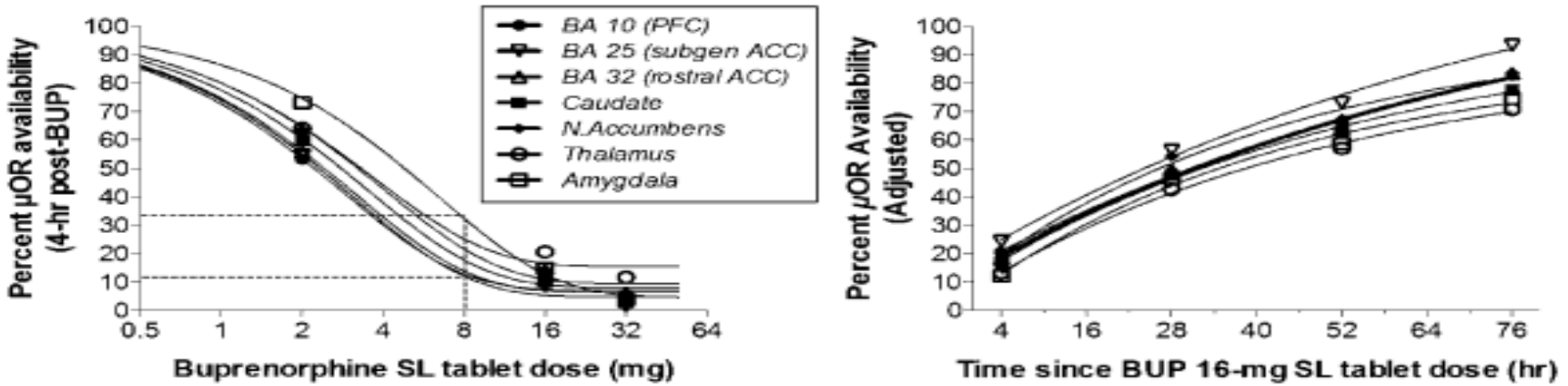
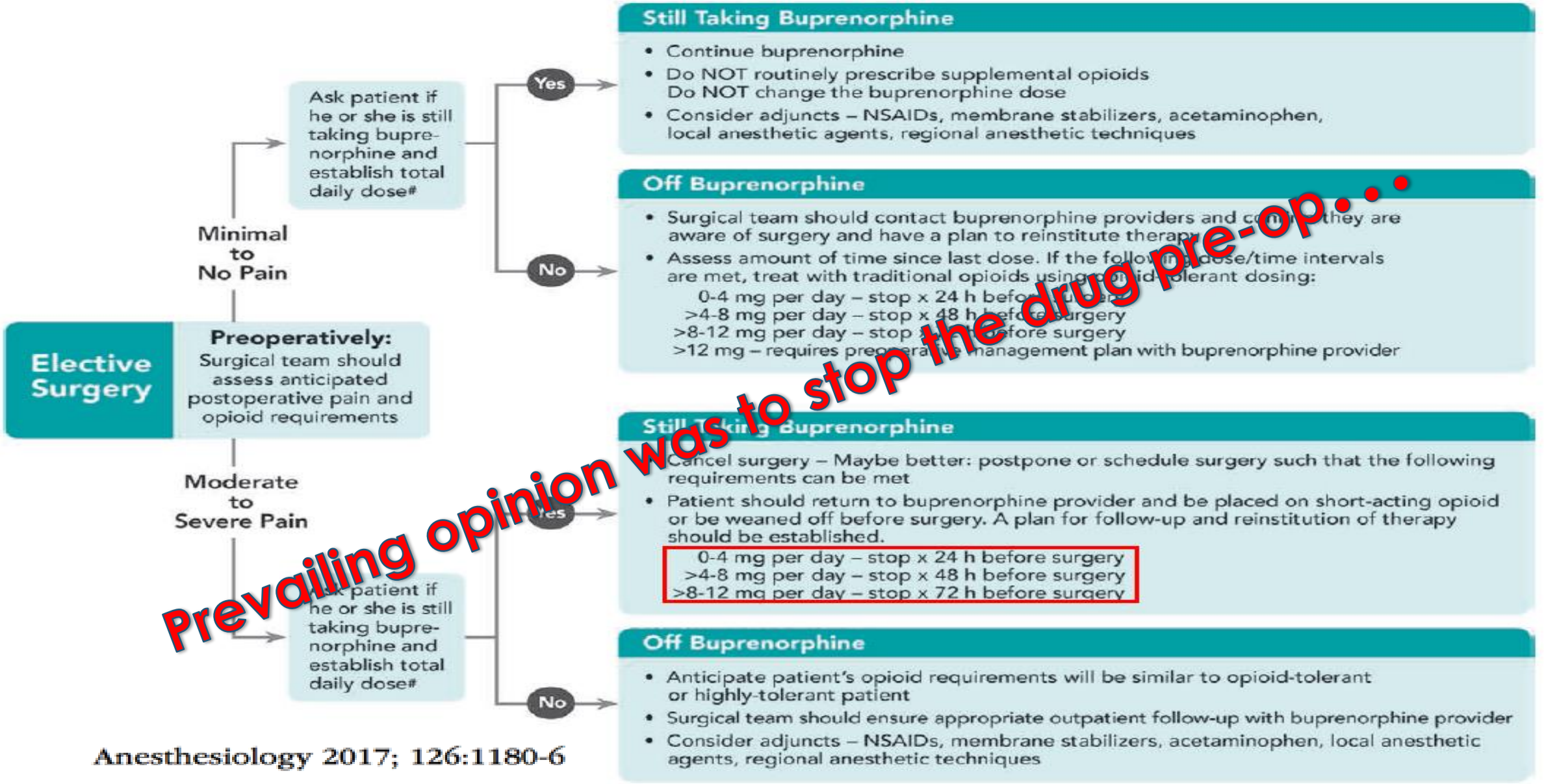


Fig. 1. Left panel: Non-linear regression curves on μOR availability (non-displaceable binding potential, BP_{ND}) fitted to brain region-of-interest (ROI) [^{11}C]-carfentanil PET data from Greenwald et al. (2003) for different buprenorphine (BUP) maintenance doses (log_2–linear plot) at 4-h post-dose. The seven ROIs illustrated are: Brodmann area (BA) 10 in prefrontal cortex (PFC); BA 25 in subgenual anterior cingulate cortex (ACC); BA 32 in rostral ACC; caudate nucleus; nucleus accumbens; thalamus; and amygdala. Dashed lines indicate estimated range of μOR availability across ROIs for an 8-mg/day BUP dose (12–33%). See Table 1 for estimates of μOR availability (based on these curve fits) for BUP doses that were not experimentally studied. Right panel: Non-linear regression curves on regional μOR availability (BP_{ND}) fitted to [^{11}C]-carfentanil PET data from Greenwald et al. (2007) following discontinuation of BUP 16-mg/day maintenance. The Y-intercept values at the 4-h time point for each ROI were adjusted to data for the identical condition (4 h after BUP 16-mg) in the Greenwald et al. dose-response study (2003).

- BUP 8 mg/d- approx. 65% receptor saturation, 35% of receptors are available.
- Doses above 16 mg/d- approx 95% receptor saturation



Prevailing opinion was to stop the drug pre-op. . .

Fig. 1. Suggestions are outlined for patients presenting for elective surgeries taking buprenorphine. NSAIDs = nonsteroidal anti-inflammatory drugs. #Transdermal buprenorphine need not be discontinued prior to elective surgery regardless of dose.

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Special Article

Perioperative Pain and Addiction Interdisciplinary Network (PAIN) clinical practice advisory for perioperative management of buprenorphine: results of a modified Delphi process

Akash Goel[1,2], Saam Azargive[1,3], Joel S. Weissman[2,4], Harsha Shanthanna[5], John G. Hanlon[1], Bana Samman[1], Mary Dominicis[1], Karim S. Ladha[1], Wiplove Lamba[6], Scott Duggan[3], Tania Di Renna[1], Philip Peng[1], Clinton Wong[7], Avinash Sinha[8], Naveen Eipe[9], David Martell[10], Howard Intrater[11], Peter MacDougall[9], Kwesi Kwofie[12], Mireille St-Jean[13], Saifee Rashiq[14], Kari Van Camp[15], David Flamer[1], Michael Satok-Wolman[15] and Hance Clarke[1,15,*]

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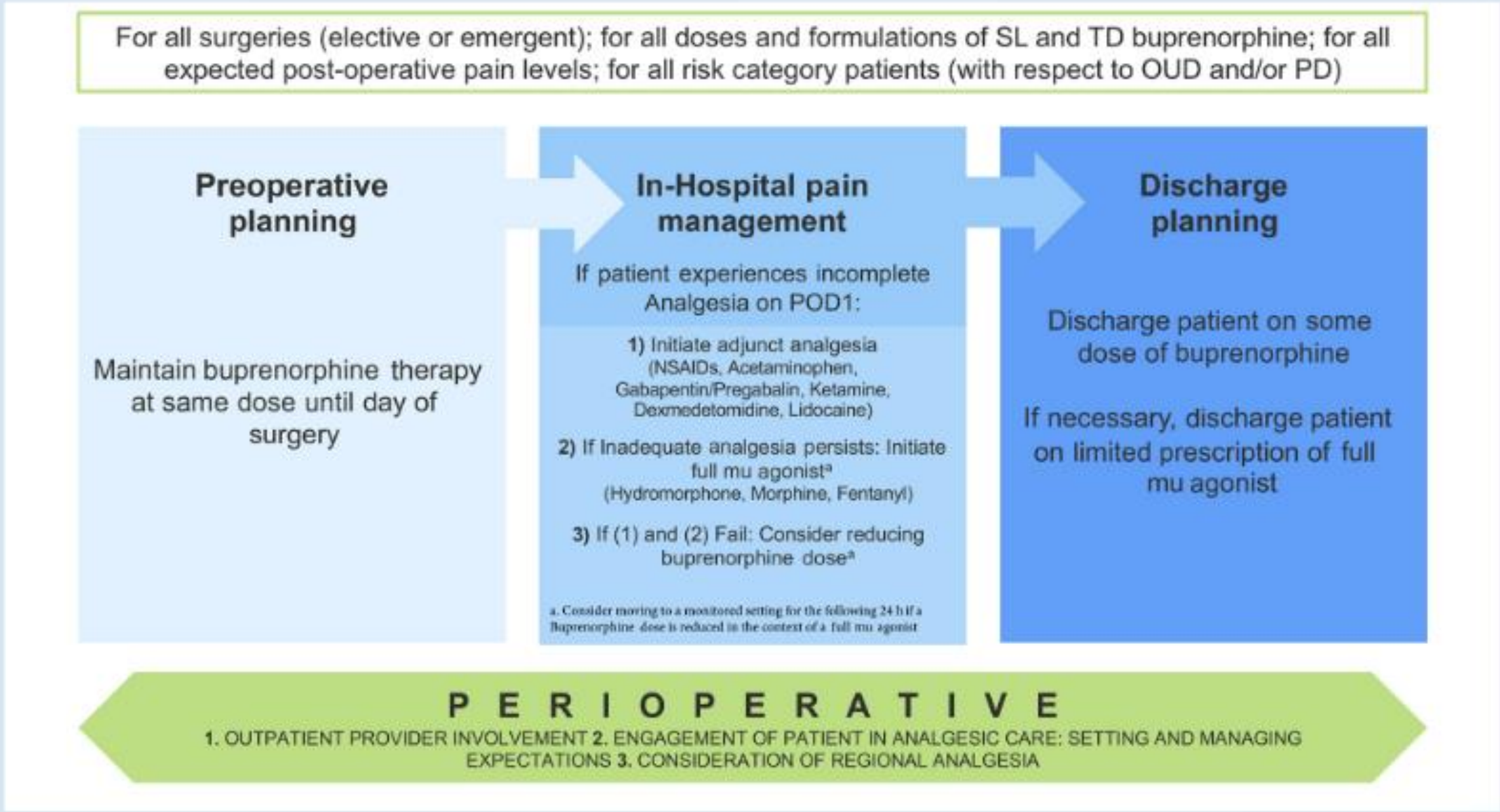

Fig. 3. A summary of recommendations for perioperative management of patients taking buprenorphine. OUD, opioid use disorder; PD, pain disorder; POD, postoperative day; SL, sublingual; TD, transdermal.

Other considerations

- Maximize rational non-opioid pharmacologic options
  - Consider potential for drug interactions, sedation and overdose risk
- Employ available non-pharmacologic options including "living with pain" groups, physiotherapy, occupational therapy, psychology
- Clear discussion regarding short term nature of opioid prescribing for acute pain issues, when necessary
  - Split dosing?
- Single prescriber, limited dispensing, close follow-up

Clinical Application

Case 1: Jim

- Jim's wife leaves for 2 weeks to visit with family
- Jim takes the opportunity to indulge in a few beer
- Unfortunately, while on a ladder, Jim falls and has an acute navicular fracture for non operative management
- He is having considerable pain, what do you do?

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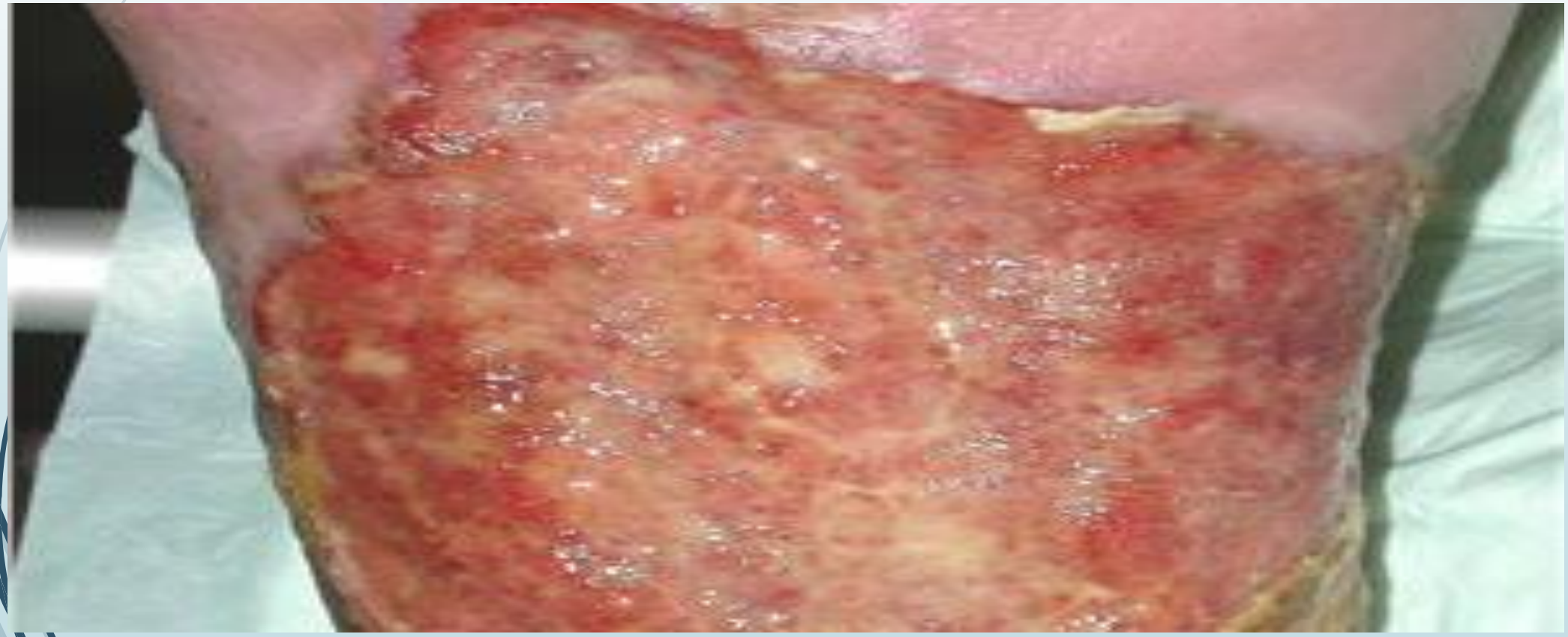

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Take Home Messages

- Appreciate the individual patient's pain experience
- Manage expectations early and set realistic goals, *focus on function*
- Be aware of awakening the addiction circuitry and be ready to tighten treatment parameters for safety
- More research is needed:
  - Treatment of concurrent chronic pain and OUD
  - Treatment of acute/peri-operative pain in patients with OUD
- Return to first principles
  - understand the type(s) of pain that you are attempting to treat
  - prescribe medications rationally
    - Pharmacologic category
    - Dose and timing
  - utilize safer prescribing principles

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Questions ???