Buprenorphine

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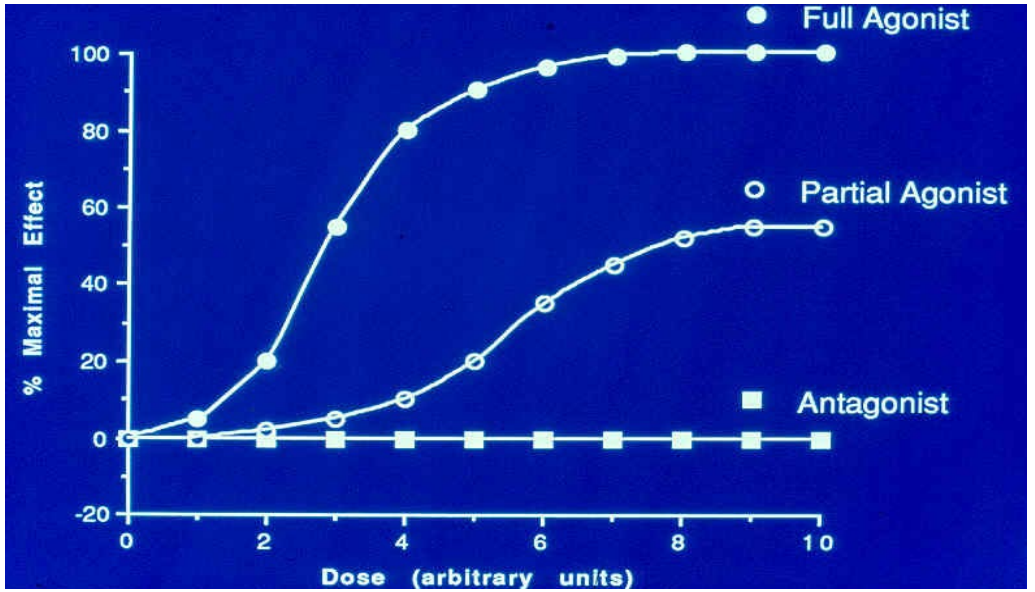
Buprenorphine primer

- Synthetic opioid, partial agonist at the mu opioid receptor
  - Potent analgesic
  - Ceiling effects on resp. depression
- High affinity (tight binding)
- Originally developed as a pain medication
- Multiple formulations:
  - High-dose: FDA approved for opioid use disorder
  - Low-dose: FDA approved for pain



Compelling rationale for buprenorphine in co-occurring pain and opioid use spectrum

- Treats physiologic dependence
- May improve pain control
- Reduces (full agonist) opioid burden, overdose risk

Veterans' Pain Care Organizational Improvement Comparative Effectiveness (VOICE) Trial (PCORI OPD-1511-33052)

- 10 VA sites, N=207 patients on ≥ 70 mg morphine equivalent daily dose for moderate-severe chronic pain, followed for 1 year in a collaborative care pain treatment clinic

Standard taper

- Patient-centered motivational interviewing
- Gain-framing; reassurance
- Slow, stepwise decrease
- Bolster other treatments

Optional buprenorphine

- Switch discussed with patient before month 9 *unless team determined patient not a good candidate*
- Gain-framing; reassurance
- Overlap initiation protocol
- Bolster other treatments

Study participants, baseline

	Std (n=103)	BUP/NX (n=104)
Age, years	62	60
Female	7%	14%
White	79%	81%
Black	13%	15%
Opioid daily dose, mean	165.4 ME mg	156.5 ME mg
Opioid daily dose, median	135.0 ME mg	124.7 ME mg
Brief Pain Inventory (BPI) total score	6.8	6.8

	Buprenorphine option (n=104)			No buprenorphine option (n=103)			
Outcome							p-value*
Primary outcome							
BPI total score							
Baseline		--	104	6.76 (1.57)	--	103	
3 months							0.91
6 months							
9 months							0.38
12 months							
Main secondary outcome							
Opioid daily dose, ME mg							
Baseline							
3 months							
6 months	116.5 (89.8)						0.54
9 months							
12 months	**91.8 (98.2)**						**0.55**
15 months							

Key take-homes

- Optional buprenorphine did not improve pain, did not lead to greater opioid reductions
- However, low rates of switching limited ability to detect a difference
- Future studies should be more “buprenorphine forward”

VA Study - Lagisetty & Bohnert (I01 HX003411)

Use VA medical records data to:

1. Identify a cohort of patients on long-term opioids with opioid misuse behaviors
2. Target trial emulation comparing treatment options:
    1. Continue treatment relatively unchanged
    2. Tapering
    3. Rotate to buprenorphine

Identifying Opioid Misuse

- Stage 1 – detailed chart review with physician adjudication

Variation in Clinical Characteristics and Longitudinal Outcomes in Individuals with Opioid Use Disorder Diagnosis Codes

Victoria D. Powell, MD[1,2], Colin Macleod, MA[3], Jeremy Sussman, MD[3,4], Lewei A. Lin, MD, MSc[4,5], Amy S. B. Bohnert, PhD, MHS[4,6], and Pooja Lagisetty, MD, MSc[3,4]

KEY RESULTS: Veterans (n = 483) were categorized as likely OUD (62.1%), limited aberrant use (17.8%), and prescribed, non-aberrant use (20.1%). Age, proportion

Identifying Opioid Misuse

- Stage 2 - Elastic Net Regression (ENR) to make process scalable

- Some key results:
  - Prediction worse in those with other serious illness (e.g., palliative care codes)
  - Good prediction after exclusions, i.e.:
    - Positive predictive value ~.90

Target Trial Emulation Study

- Improvements on conventional observational studies to reduce bias
  - Time anchor alignment
  - Advanced confounding adjustment
  - Avoid selection effects of who enrolls in trials

- Primary outcome: pain intensity
  - Change in pain score from baseline (avg of 6 months) to 6 months follow up (avg)

Target Trial Emulation Study - Results

	OVERALL N = 2916		LOW BASELINE PAIN [0, 4) N = 805		MODERATE BASELINE PAIN [4, 6] N = 1063		HIGH BASELINE PAIN (6, 10] N = 1048	
	Unweighted	Weighted	Unweighted	Weighted	Unweighted	Weighted	Unweighted	Weighted
BUP vs TAU	-0.37* (-0.63, -0.11)	**-0.37* (-0.63, -0.11)**	-0.29 (-0.91, 0.32)	-0.19 (-0.81, 0.43)	-0.21 (-0.61, 0.18)	-0.12 (-0.52, 0.27)	-0.61* (-1.01, -0.20)	**-0.78* (-1.20, -0.37)**
Taper vs TAU	0.01 (-0.17, 0.19)	-0.03 (-0.22, 0.15)	0.23 (-0.13, 0.60)	0.29 (-0.08, 0.67)	0.09 (-0.21, 0.38)	0.02 (-0.27, 0.31)	-0.24 (-0.55, 0.06)	-0.27 (-0.58, 0.04)

Key Takeaways

- Opioid misuse can be identified from medical charts, but not perfectly
- Need to better understand when buprenorphine is the best option
- Target trial emulation can fill in gaps of what is not is possible to study by RCT better than conventional observational studies

What about Serious Illness?

- Less research on comparative effectiveness in those with serious illness, e.g., cancer
- Debate on role of opioid sparing strategies
- Growing interest in buprenorphine
- Unclear how to integrate into the delivery of other intensive therapies (e.g., chemotherapy, dialysis)