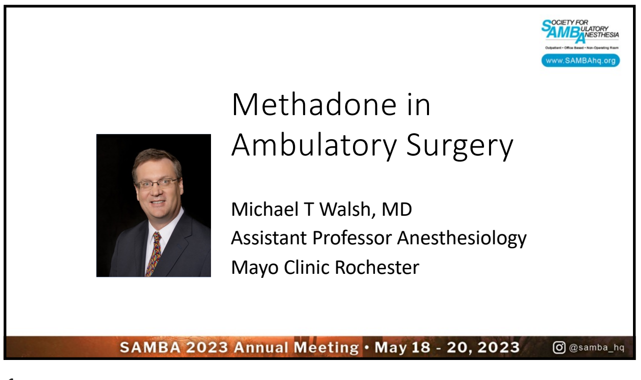

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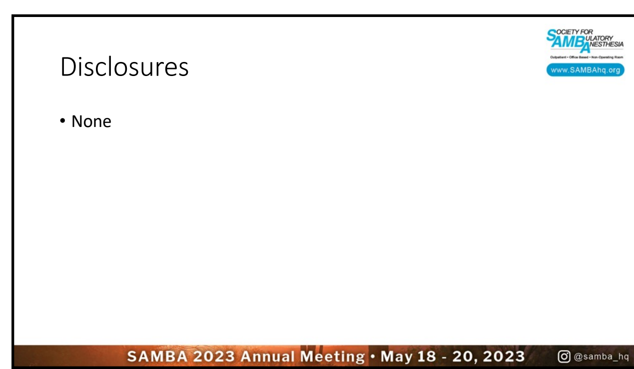

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Outline

- Focus on using methadone as a primary strategy to treat pain in ambulatory surgical patients
- Why?
- Advantages
- Inpatient Studies
- Outpatient **Study**
- Where do we go from here

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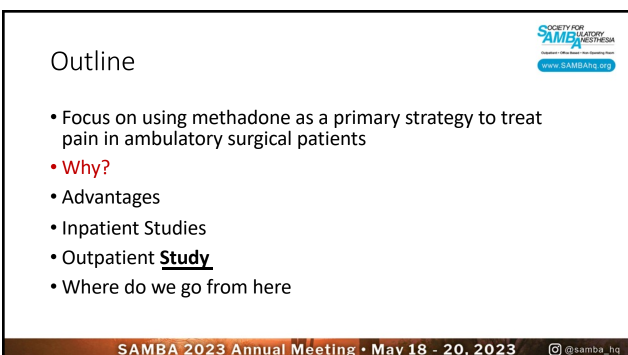

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Too many people with postop pain

- >50% - even in minor/medium level procedures

Journal of Clinical Anesthesia 16:200 –206, 2004
Ann Surg 2019;269:856–865
Jnl of Pain 2016;17(2):131-157
Ann Surg 2017;266:516–524

- Acute post op pain is biggest risk factor for chronic postsurgical pain

Pain Reports 2022;7(6):e1048
JPRAS Open 2022;31:32–49

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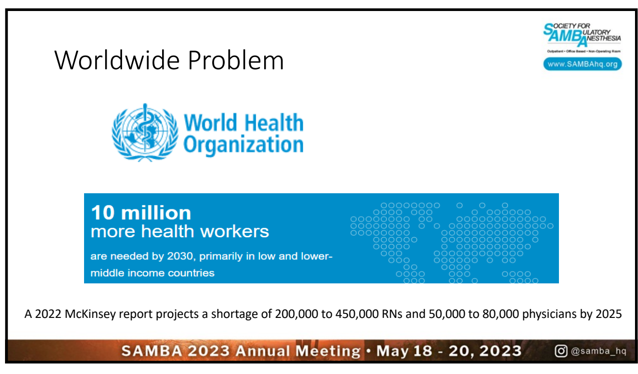

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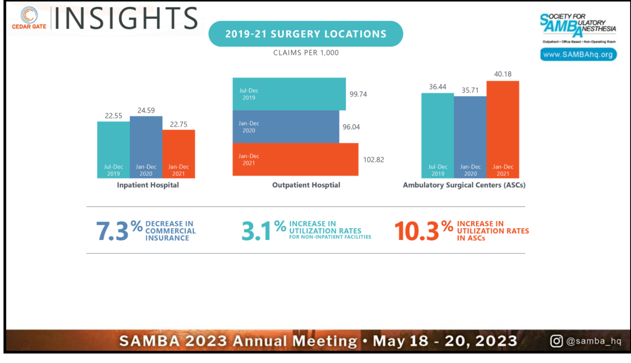

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Methadone Advantages

- Strong *u*-opioid receptor agonist
  - Incomplete cross tolerance with other opioids
- NMDA antagonist
- Inhibits reuptake serotonin and norepinephrine in CNS
- IV – "rapid" onset: t1/2 ke0 = 8 minutes
- Long half life (1-2 **days**) = long duration

Table 1. Onset of Effect and Elimination of Opioids

	$t_{1/2}k_{eo}$[a]	Elimination $t_{1/2}$
Remifentanil	1 minute	0.5 hour
Alfentanil	1 minute	1 hour
Sufentanil	6 minutes	8 hours
Fentanyl	5 minutes	8–10 hours
Morphine	2–4 hours	2–3 hours
Methadone	8 minutes	24–36 hours

Anesth and Analg 2011;112:13-16

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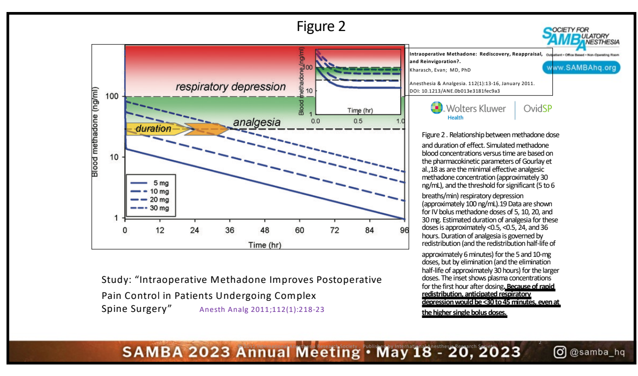

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Methadone Studies

"Intraoperative Methadone for the Prevention of Postoperative Pain: A Randomized, Double-blinded Clinical Trial in **Cardiac Surgical Patients**" — 156 patients

Anesthesiology 2015:122:1112-22

"Clinical Effectiveness and Safety of Intraoperative Methadone in Patients Undergoing Posterior **Spinal Fusion Surgery**: A Randomized, Double-blinded, Controlled Trial" — 115 patients

Anesthesiology 2017;126:822-33

"Perioperative Methadone and Ketamine for Postoperative Pain Control in **Spinal Surgical Patients**: A Randomized, Double-blind, Placebo-controlled Trial" — 130 patients

Anesthesiology 2021;134:697-708

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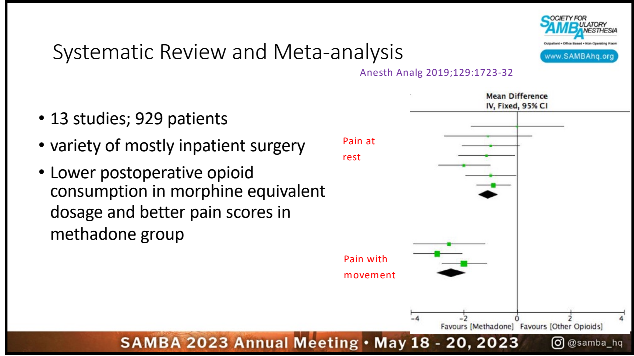

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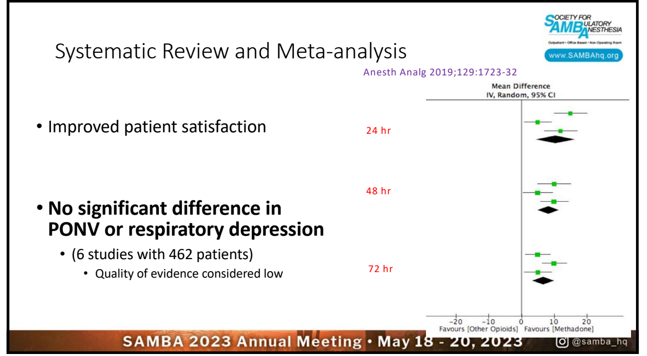

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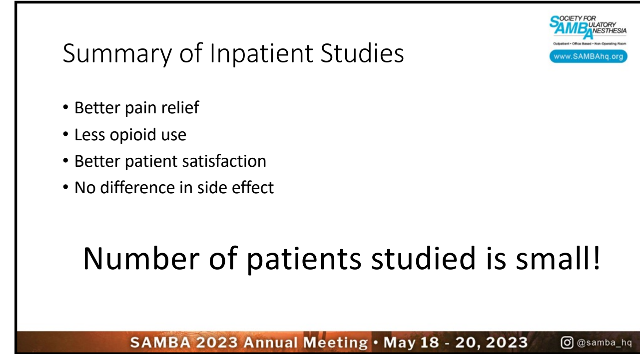

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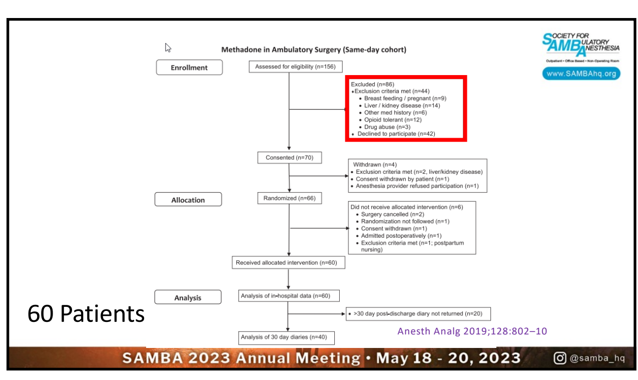
Intraoperative Methadone in Same-Day Ambulatory Surgery: A Randomized, Double-Blinded, Dose-Finding Pilot Study

Anesth Analg 2019;128:802–10

Helga Komen, MD,* L. Michael Brunt, MD,† Elena Deych, MS,‡ Jane Blood, RN,* and Evan D. Kharasch, MD, PhD*§||

- Dose-escalation study (ended up with 2 doses studied)
- Laparoscopic surgeries
  - Chole, tubal, salpingectomy/oophorectomy, inguinal hernia
- Looked at pain scores and narcotic usage both in hospital and post discharge
- Looked at complications



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- Cohort # 1 (18 pts) 0.1 mg/kg ideal body weight methadone
  - Median dose = 6 mg
- Cohort # 2 (21 pts) 0.15 mg/kg ideal body weight methadone
  - Median dose = 9 mg
- Controls (21 pts) fentanyl or fentanyl/hydromorphone
- Fentanyl/hydromorphone prn at end of case/PACU

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A — Pain at rest (0-10) vs. Time after PACU admission (hr); B — Sedation (MOAA/S score) vs. Time after PACU admission (hr). Control; Methadone 0.1 mg/kg IBW; Methadone 0.15 mg/kg IBW.

Table 2. In-Hospital Opioid Consumption

	Control (Short-Duration Opioid)	Methadone 0.1 mg/kg IBW	P Value Versus Control	Methadone 0.15 mg/kg IBW	P Value Versus Control
Primary outcomes					
Total intraoperative nonmethadone opioid (mg morphine equivalents)	25.0 (23.3–28.3)	0.1 (0.1–0.1)	<.0001	0.1 (0.1–0.1)	<.0001
Total PACU nonmethadone opioid (mg morphine equivalents)	9.3 (1.3–11.0)	5.0 (3.3–8.1)	.60	0.1 (0.1–3.3)	<.0001
Number of patients (%) needing no PACU opioid	5 (24%)	2 (11%)	.42	12 (57%)	.06
Total post-PACU nonmethadone opioid (mg morphine equivalents)	0.0 (0.0–2.9)	0.0 (0.0–0.6)	.19	0.0 (0.0–2.5)	.79
Total day of surgery non-OR (PACU + post-PACU) total nonmethadone opioid (mg morphine equivalents)	10.0 (2.5–14.3)	5.4 (3.3–9.6)	.42	3.3 (0.1–5.8)	.01
Total day of surgery nonmethadone opioid (mg morphine equivalents)	35.3 (25.0–44.0)	7.1 (3.7–10.0)	<.0001	3.3 (0.1–5.8)	<.0001
Total day of surgery opioid (mg morphine equivalents)	35.3 (25.0–44.0)	13.3 (8.9–16.4)	<.0001	12.3 (8.9–14.3)	<.0001

Results are the median (interquartile range).
Abbreviations: IBW, ideal body weight; OR, operating room; PACU, postanesthesia care unit.

Anesth Analg 2019;128:802–10

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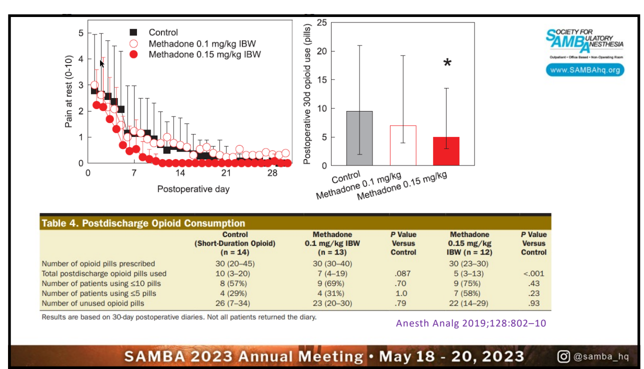

Table 4. Postdischarge Opioid Consumption

	Control (Short-Duration Opioid) (n = 14)	Methadone 0.1 mg/kg IBW (n = 13)	*P* Value Versus Control	Methadone 0.15 mg/kg IBW (n = 12)	*P* Value Versus Control
Number of opioid pills prescribed	30 (20–45)	30 (30–40)		30 (23–30)	
Total postdischarge opioid pills used	10 (3–20)	7 (4–19)	.087	5 (3–13)	<.001
Number of patients using ≤10 pills	8 (57%)	9 (69%)	.70	9 (75%)	.43
Number of patients using ≤5 pills	4 (29%)	4 (31%)	1.0	7 (58%)	.23
Number of unused opioid pills	26 (7–34)	23 (20–30)	.79	22 (14–29)	.93

Results are based on 30-day postoperative diaries. Not all patients returned the diary.

Anesth Analg 2019;128:802–10

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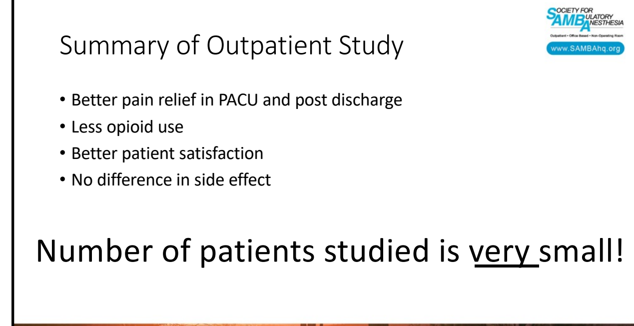

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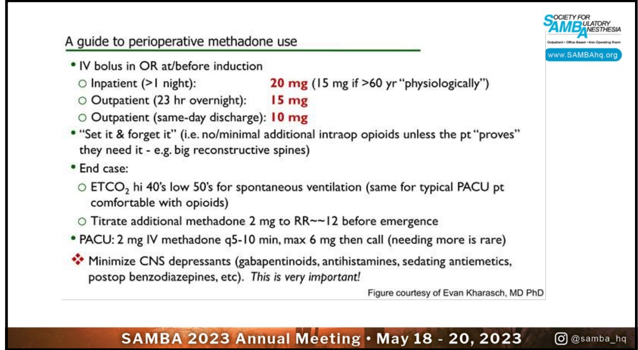

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Conclusions

- High confidence that pain control and patient satisfaction superior with methadone for acute postop pain
  - Lower opioid needs at home — May be helpful in opioid epidemic?
  - Better pain control at 30 days — May decrease chronic pain?
- No difference in adverse effects (low confidence)
  - Numbers too small to remark on safety
- Personal practice: still inpatient only - but looking into a protocol

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