

Combinatorial pharmacogenetic opioid-risk algorithms more accurately and reliably predict serious opioid and pain outcomes after lumbar spine surgery in adults



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INTRODUCTION

- Lumbar spinal fusion and decompression surgeries (LSS) are among the most common and most painful inpatient procedures for degenerative lumbar conditions
- LSS is associated with immediate and long-term pain and opioid-related adverse outcomes
- There are no proactive and reliable ways to predict and prevent these immediate & long-term adverse outcomes

OBJECTIVES

- To reliably predict short-term (hospital) and long-term (post-discharge) adverse outcomes including uncontrolled acute post-LSS pain, excessive opioid use, CPSP, persistent opioid use and OUD risks with integrated genomic and non-genomic features.

METHODS

Design: Prospective, genotype-blinded observational study.

Participants: 205 adults undergoing LSS for degenerative lumbar spine disease or lumbar spinal stenosis

Study Observation: Preoperative genotyping, standardized perioperative care and prospective clinical outcome data collection in the hospital and post-discharge.

Short-term Outcomes: (1) respiratory depression, (2) excessive sedation, (3) PONV, (4) severe postoperative pain (NRS ≥8), (5) total opioid consumption ≥250 MME within 48 hours, and (6) prolonged hospital stay (≥4 days).

Long-term Outcomes: 1) CPSP, defined as pain ≥3/10 persisting beyond 3 months, (2) persistent opioid use, defined as opioid prescriptions beyond 90 days, and (3) opioid dependence/misuse risk, assessed with the Clinical Opiate Withdrawal Scale (COWS) and COMM.

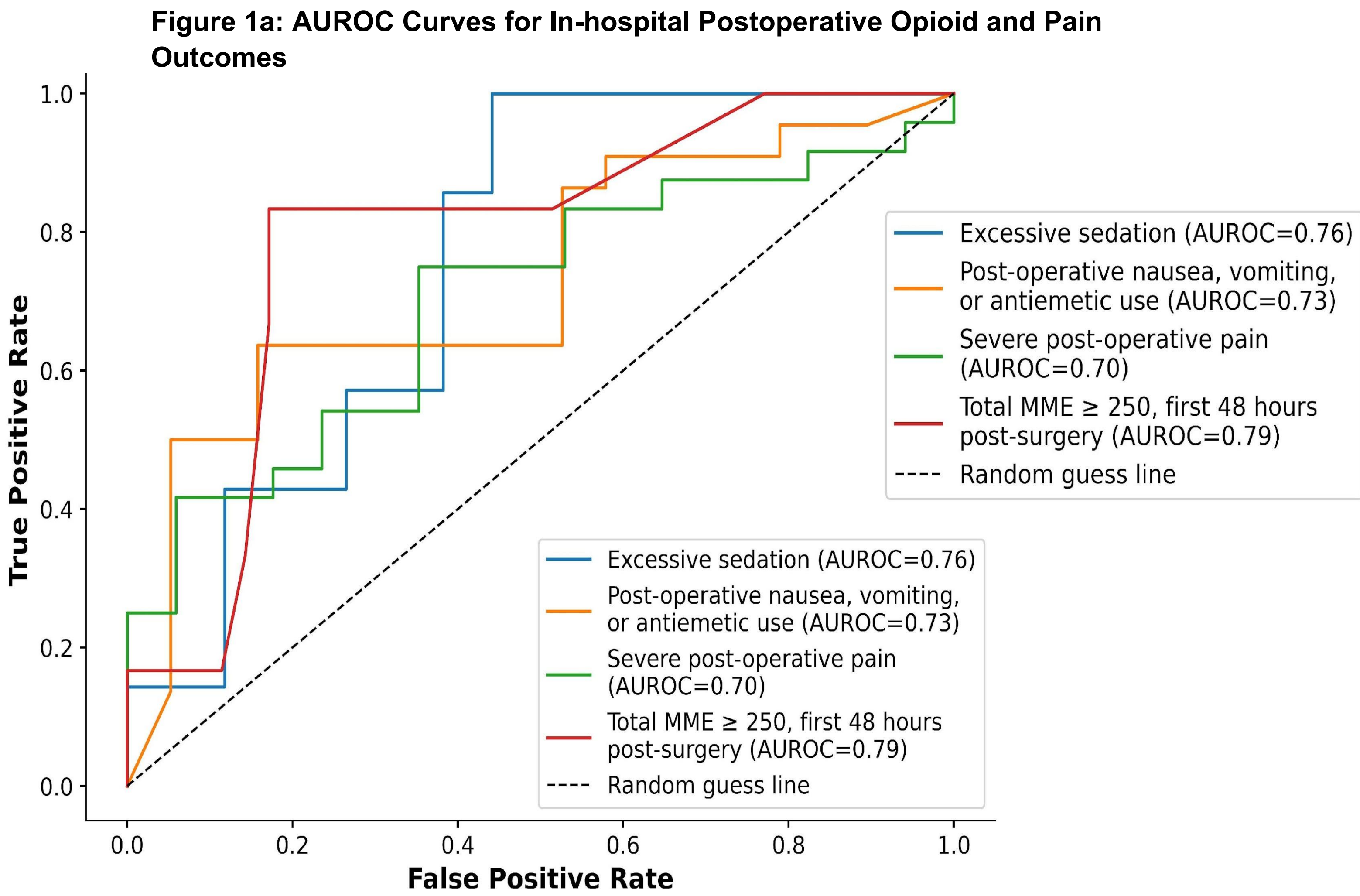
RESULTS

Table 1a: Robust Combinatorial Prediction and Validation of In-hospital Postoperative Opioid and Pain Outcomes

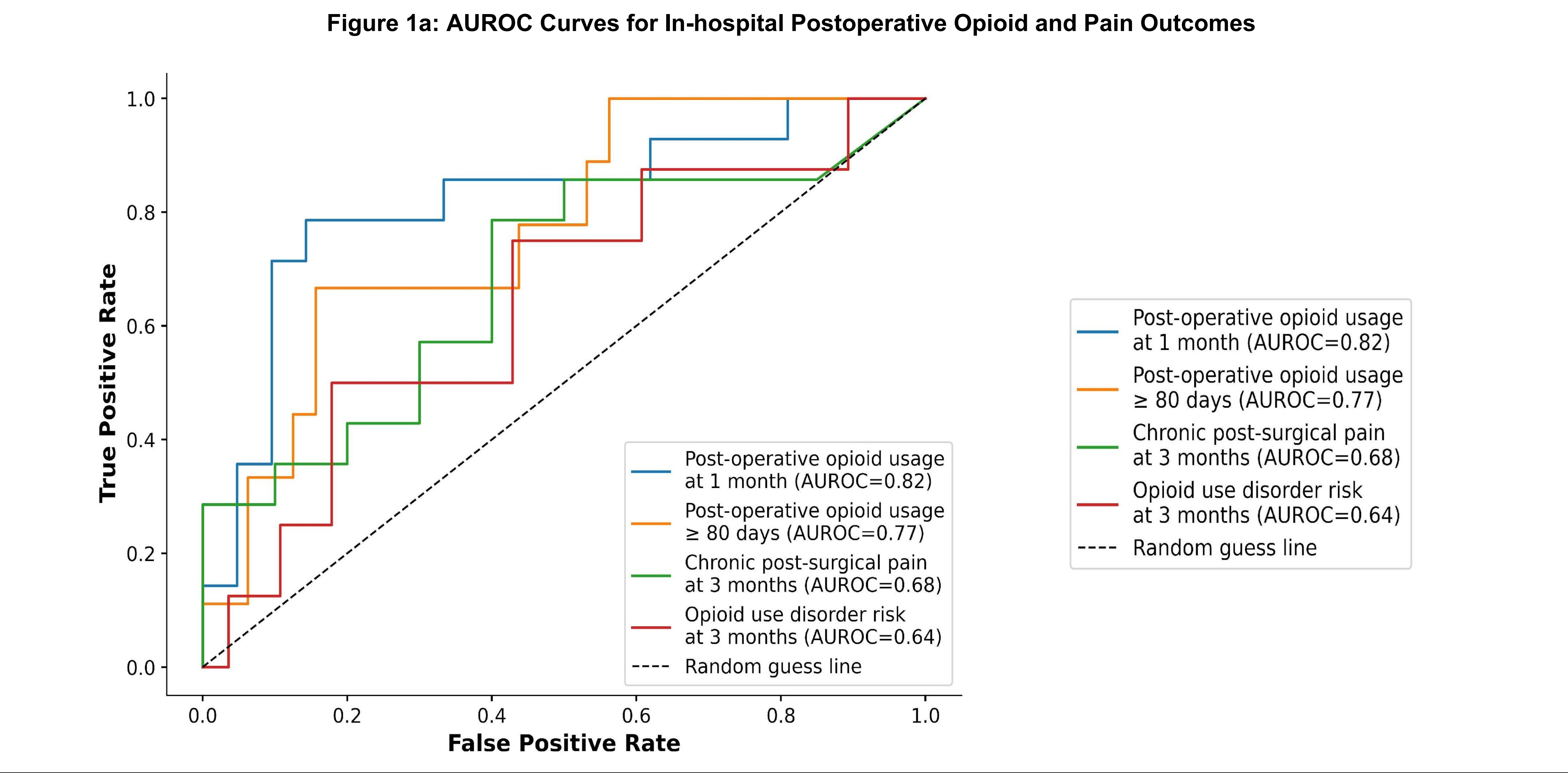
Postoperative Outcomes	Incidence Rate	AUROC (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
ES	13.7%	0.76 (0.43, 0.86)	0.57 (0.17, 1.00)	0.74 (0.58, 0.88)
PONV	56.1%	0.73 (0.46, 0.76)	0.64 (0.43, 0.83)	0.58 (0.35, 0.80)
RD	5.9%	0.69 (0.32, 0.92)	0.50** (0.00, 1.00)	0.74 (0.60, 0.87)
Severe pain 0-48 hr. post-op	67.3%	0.70 (0.52, 0.81)	0.75 (0.57, 0.91)	0.59 (0.35, 0.82)
≥ 250 MME 0-48 hr. post-op	13.7%	0.79 (0.51, 0.94)	0.67 (0.22, 1.0)	0.83 (0.69, 0.94)
Hospital stay ≥4 days	50.2%	0.67 (0.56, 0.84)	0.76 (0.56, 0.94)	0.65 (0.43, 0.86)

Table 1b: Robust Combinatorial Prediction and Validation of Post-discharge Opioid and Pain Outcomes

Postoperative Outcomes	Incidence Rate	AUROC (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
POU at 1 month	37.6%	0.82 (0.63, 0.92)	0.71 (0.46, 0.93)	0.86 (0.70, 1.00)
POU for ≥ 80 days	22.4%	0.77 (0.55, 0.90)	0.67 (0.33, 1.00)	0.81 (0.67, 0.94)
CPSP at 3 months	39.2%	0.68 (0.46, 0.80)	0.57 (0.30, 0.83)	0.70 (0.48, 0.90)
OUD risk at 3 months	19.3%	0.64 (0.40, 0.80)	0.50 (0.14, 0.86)	0.71 (0.54, 0.88)



RESULTS



DISCUSSION

Inadequacy of current standardized and even ERAS multimodal analgesia with high incidences of adverse outcomes

- Short-term outcomes: 67% with severe pain in the first 48 h, >50% with PONV, 14% with ES and 6% with RD and nearly 50% with prolonged hospitalization of >4 days.
- Long-term outcomes: 19% OUD, 39% CPSP and 22% persistent opioid use at 3 months

Need for personalized and precise risk prediction and prevention

Predictive algorithms using combined clinical, psychosocial, and genetic features have strong discriminatory performance across outcomes, with AUROC values ranging from 0.70 to 0.92.

Genetic factors significantly contribute to these predictions

CONCLUSION

- **Algorithms including clinical and genetic factors reliably predict short-term and long-term post-LSS pain and opioid-related outcomes**
- **Larger clinical trial comparing standard of care versus predictive algorithm-based care are needed to overcome current barriers to personalized care with optimal outcomes**