

Mechanism of Transition from Acute to Chronic Pain

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Disclosures

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 - ...and by Donn M. Dennis M.D. Professorship in Anesthetic Innovation

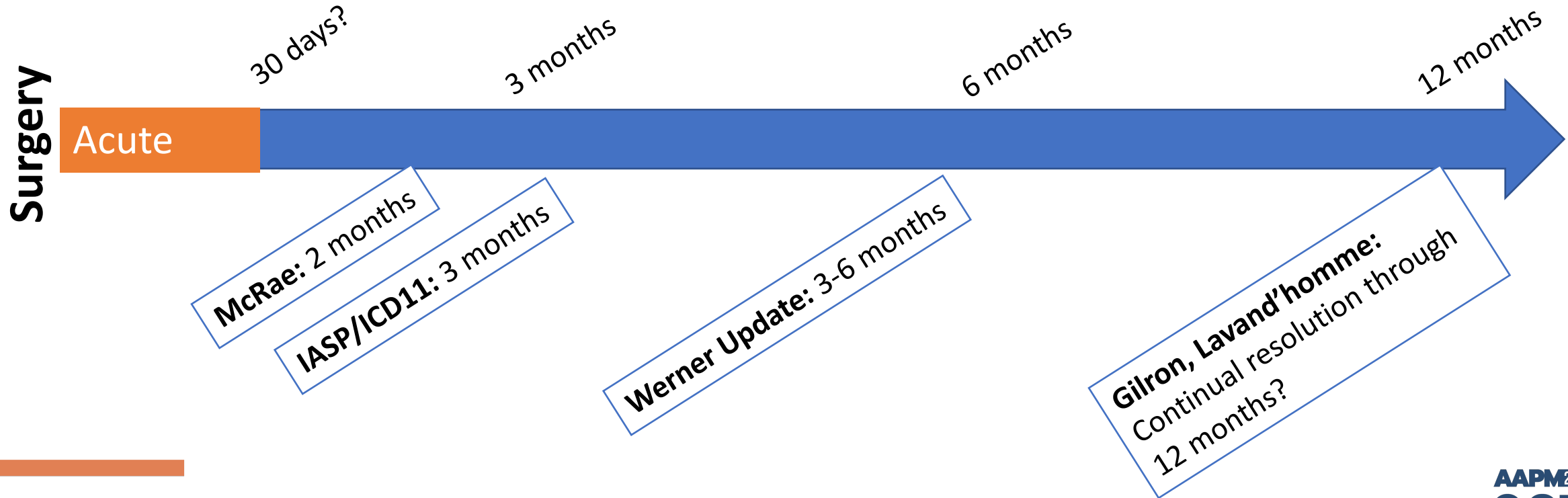
Objectives for Today

- Defining the Transition
- Theoretical Frameworks for Modeling Acute to Chronic Transition of Postoperative Pain
- Prediction Models



How Persistent is Persistent Postsurgical Pain?

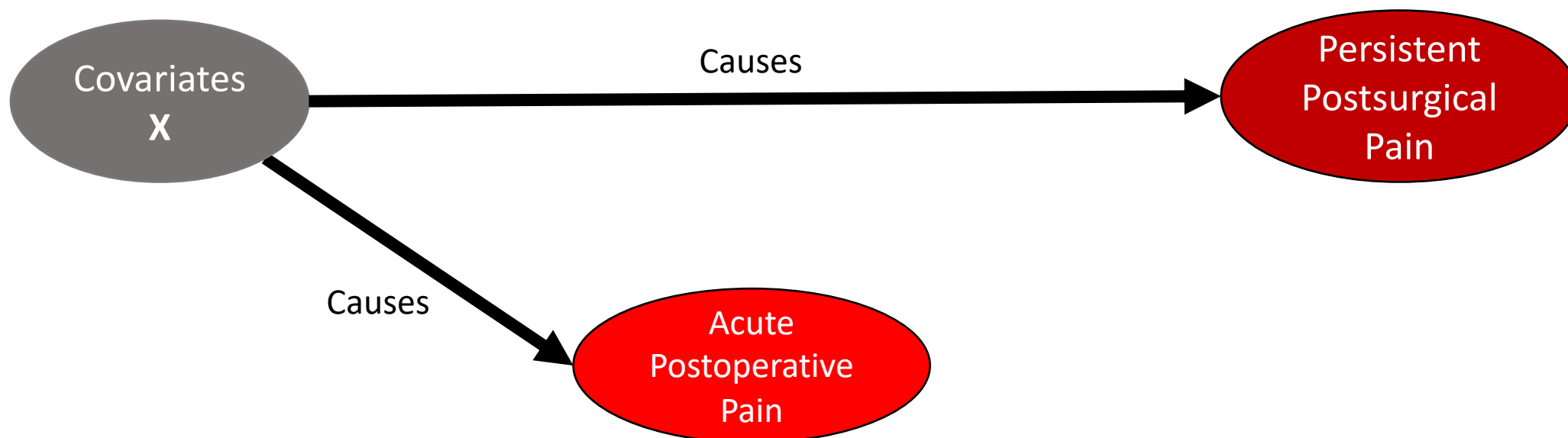
Does Time Matter?



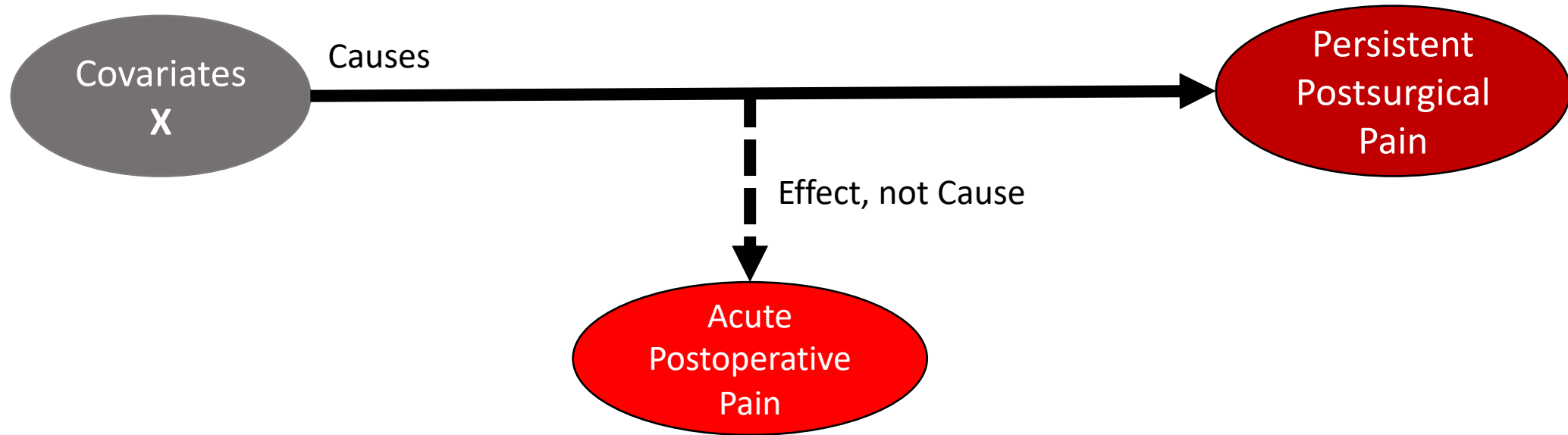
Theoretical Frameworks: A Causal Chain?



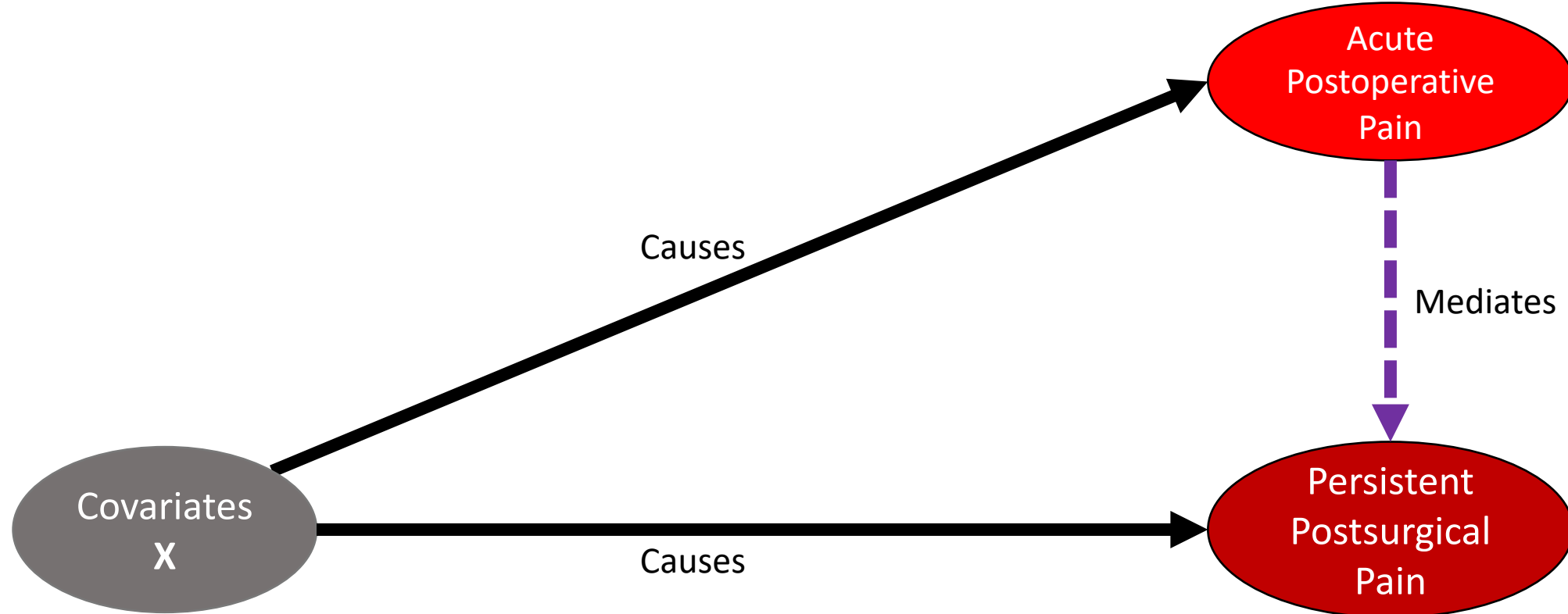
Theoretical Frameworks: Separate Chains?



Theoretical Frameworks: Effects & Causes?



Theoretical Frameworks: Mediation?



Risk Factors & Models

	Estimated incidence of chronic pain	Estimated chronic severe (disabling) pain (>5 out of score of 10)	US surgical volumes (1000s)†
Amputation ²	30–50%	5–10%	159 (lower limb only)
Breast surgery (lumpectomy and mastectomy) ³	20–30%	5–10%	479
Thoracotomy ^{4–7}	30–40%	10%	Unknown
Inguinal hernia repair ^{8–10}	10%	2–4%	609
Coronary artery bypass surgery ^{11–13}	30–50%	5–10%	598
Caesarean section ¹⁴	10%	4%	220

*Gall bladder surgery not included, since preoperative diagnosis of pain specifically from gall bladder is difficult and persistent postoperative pain could therefore be related to other intra-abdominal disorders. †National Center For Health Statistics, Ambulatory and Inpatients Procedures, USA, 1996.

Table 1: Estimated incidence of chronic postoperative pain and disability after selected surgical procedures*

	Neuropathic pain	Inflammatory pain
Positive symptoms and signs		
Spontaneous pain in damaged area	Yes	Yes
Heat hyperalgesia	Rarely	Often
Cold allodynia	Often	Rarely
Hyperpathia (increased threshold and explosive suprathreshold pains)	Often	Never
Aftersensations	Often	Rarely
Paroxysms	Often	Rarely
Burning pain	Often	Rarely
Throbbing pain	Rarely	Often
Negative symptoms and signs		
Sensory loss in damaged nerve territory	Yes	No
Motor deficit in damaged nerve territory	Often	No

Table 2: Characteristic features of neuropathic and inflammatory pain

Risk Factors & Models: Thoracotomy & VATS

Table 4. Preoperative Psychosocial Assessments

Variable	Pain at 6 Months (n = 27)	No Pain at 6 Months (n = 72)	P Value
Anxiety T	53.5±9.2	52.7±7.9	0.68
Depression T	49.5±7.3	49.0±7.5	0.78
Fatigue T	50.2±8.5	48.7±8.2	0.43
Physical function T	45.1±9.5	46.8±8.6	0.43
Sleep T	51.8±9.4	48.0±9.4	0.10
PCS total score	23 (14, 29)	17 (14, 22)	0.15
PCS total score > 30	5 (33.3%)	10 (66.7%)	0.51
≤ 30	22 (26%)	62 (74%)	
PCS rumination	9 (4, 12)	5 (4, 8)	0.20
PCS magnification	4 (3, 6)	4 (3, 5)	0.24
PCS helplessness	8 (6, 10)	7 (6, 10)	0.099
PTSD total score	23 (19, 35)	21 (19, 24)	0.27
AAQ total score	10 (7, 16)	10 (7, 13)	0.74

Table 6. Frequentist and Bayesian Multivariate Models for the Presence of Chronic Pain at 6 Months after Thoracic Surgery

Effect	Frequentist		Bayesian	
	Multivariate P Value	Multivariate, Relative Risk (99% CI)	Posterior, Mean (99% Credible Interval)	Relative Risk (99% Credible Interval)
Average severity of acute pain during the first 3 days (NRS, 0–10)	0.001	1.27 (1.12, 1.44)	0.19 (0.04, 0.41)	1.22 (1.04, 1.50)

The covariates considered for the frequentist and Bayesian multivariate models were age at surgery, preoperative pain at rest (or preoperative pain with coughing), preoperative opioid usage, average expected pain severity, any chest tube on day 3 after surgery, severity of acute postoperative pain during the first 3 days after surgery, standardized sleep disturbance score, and the pain catastrophizing scale total score. The final frequentist multivariate model using the modified Poisson regression approach: Logit (probability of chronic pain) = $-2.56 + 0.25$ acute pain. The final Bayesian multivariate model: Logit (probability of chronic pain) = $-2.33 + 0.19$ acute pain.

Risk Factors & Models: TKA

6 Months

Table 4 Final multivariate model of predictors of moderate to severe persistent postoperative pain 6 months after total knee arthroplasty. Odds ratios presented are for every 1 point change. OR, odds ratio; CI, confidence interval; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index; df, degrees of freedom; AIC, Akaike information criterion; AUC, area under the receiver operating characteristic curve

Variable	Z	P-value	OR	95% CI
Preoperative WOMAC pain (0–100)	3.39	0.001	1.06	1.03–1.10
Temporal summation (0–100)	0.91	0.360	1.01	0.98–1.05
Trait anxiety (20–80)	1.87	0.061	1.07	0.99–1.15
Expected pain (0–10)	1.46	0.146	1.37	0.90–2.09
Test	χ^2	df	P-value	
Overall model evaluation				
Likelihood ratio test	23.69	4	<0.001	
Goodness-of-fit test				
Hosmer and Lemeshow	286.13	295	0.634	
AIC	309.88			
AUC	0.70			
Sensitivity	0.72			
Specificity	0.64			
Correctly classified, %	65.67			

12 Months

Table 5 Final multivariate model of predictors of moderate to severe persistent postoperative pain 12 months after total knee arthroplasty. Odds ratios presented are for every 1 point change. OR, odds ratio; CI, confidence interval; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index; df, degrees of freedom; AIC, Akaike information criterion; AUC, area under the receiver operating characteristic curve

Variable	Z	P-value	OR	95% CI
Preoperative WOMAC pain (0–100)	1.84	0.066	1.03	0.99–1.07
Trait Anxiety (20–80)	0.55	0.580	1.02	0.95–1.10
Expected pain (0–10)	2.71	0.007	1.81	1.18–2.79
Test	χ^2	df	P-value	
Overall model evaluation				
Likelihood ratio test	12.90	3	0.005	
Goodness-of-fit test				
Hosmer and Lemeshow	279.97	290	0.589	
AIC	286.83			
AUC	0.66			
Sensitivity	0.61			
Specificity	0.67			
Correctly classified, %	66.00			

Petersen KK, Arendt-Nielsen L, Simonsen O, Wilder-Smith O, Laursen MB. Presurgical assessment of temporal summation of pain predicts the development of chronic postoperative pain 12 months after total knee replacement. Pain. 2015 Jan;156(1):55-61. doi: 10.1016/j.pain.000000000000022. PMID: 25599301.

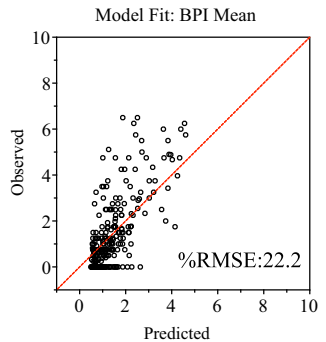
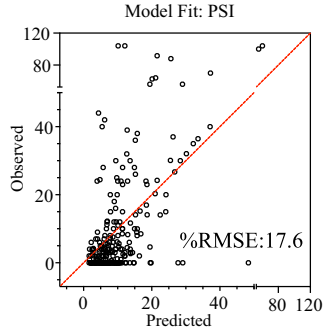
ROLE OF QST?!

Persistent postoperative pain after total knee arthroplasty: a prospective cohort study of potential risk factors

D. A. Rice^{1,3,*}, M. T. Kluger^{3,4,6}, P. J. McNair¹, G. N. Lewis¹, A. A. Somogyi^{7,8}, R. Borotkanics², D. T. Barratt⁷ and M. Walker², British Journal of Anaesthesia, 121 (4): 804–812 (2018)

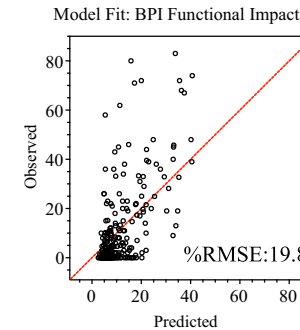
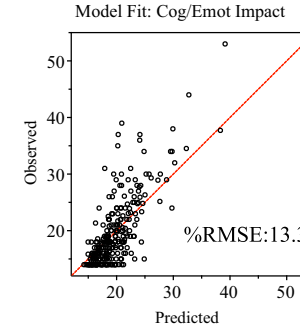
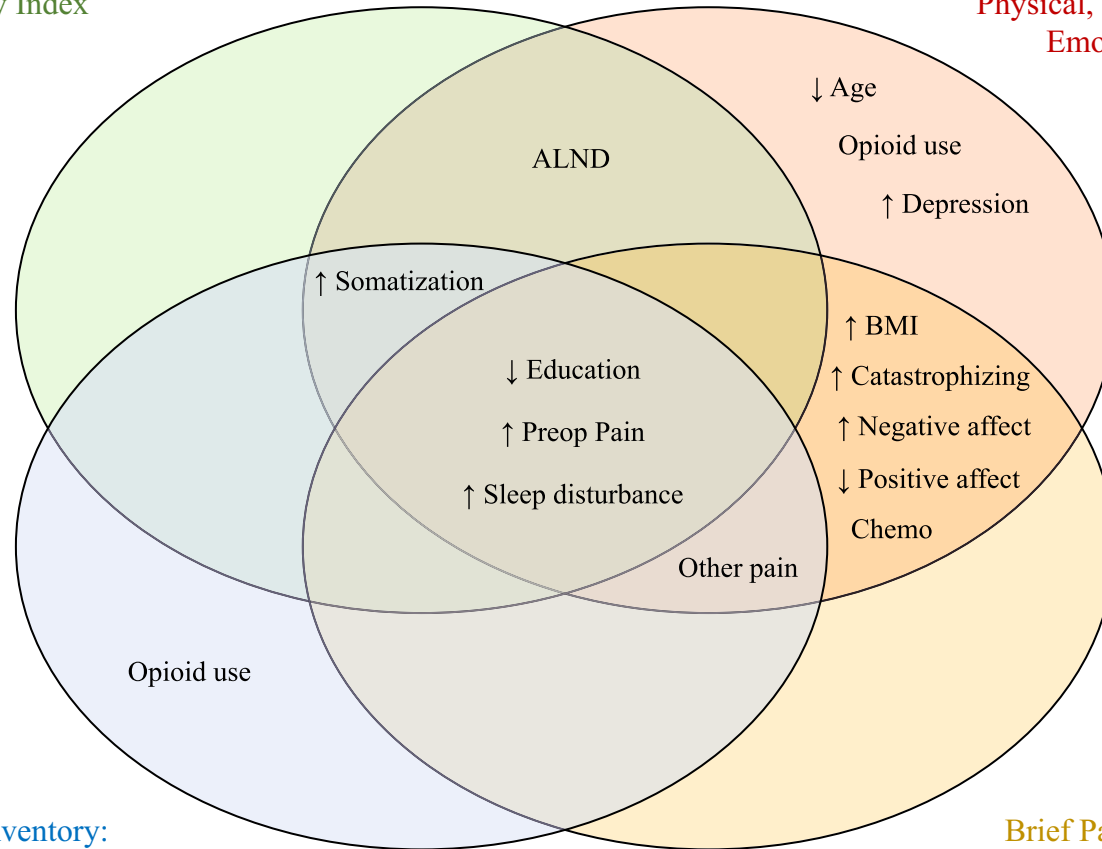
Risk Factors & Models: Breast Surgery

Breast Cancer Pain Questionnaire (BCPQ):
Pain Severity Index



Brief Pain Inventory:
BPI mean

Breast Cancer Pain Questionnaire (BCPQ):
Physical, Cognitive, &
Emotional Impact



Brief Pain Inventory:
BPI Interference

Persistent Post-Mastectomy Pain
@ 12 Months

Ann Surg Oncol
<https://doi.org/10.1245/s10434-020-09479-2>

Annals of
SURGICAL ONCOLOGY
OFFICIAL JOURNAL OF THE SOCIETY OF SURGICAL ONCOLOGY

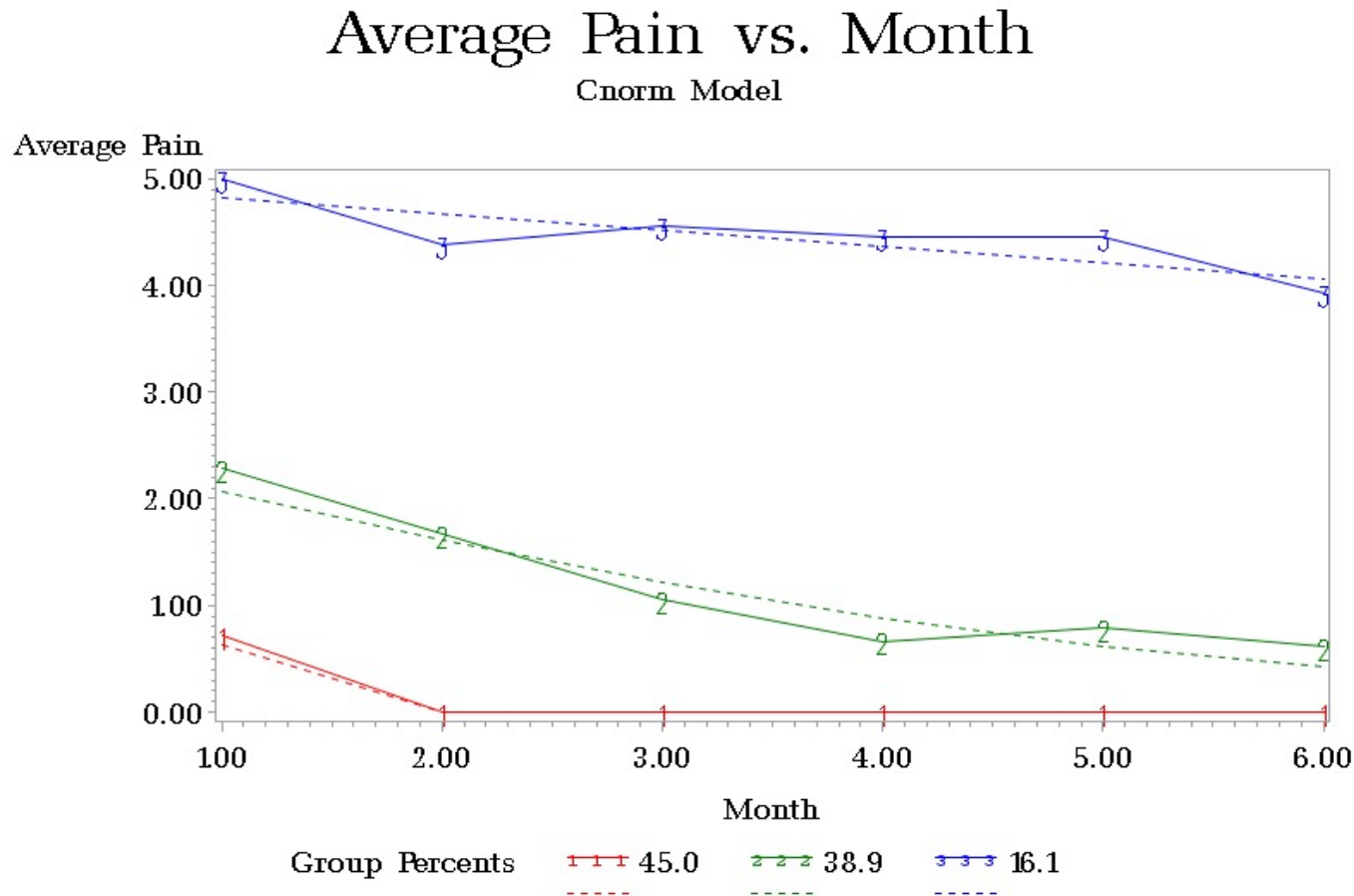
ORIGINAL ARTICLE - BREAST ONCOLOGY

Prediction of Persistent Pain Severity and Impact 12 Months After Breast Surgery Using Comprehensive Preoperative Assessment of Biopsychosocial Pain Modulators

Kristin L. Schreiber, MD, PhD¹, Nanthansorn Zinboonyahoon, MD², K. Mikayla Flowers, MS¹, Valerie Hruschak, PhD¹, Kara G. Fields, MS¹, Megan E. Patton, BS¹, Emily Schwartz, BS⁵, Desiree Azizoddin, PhD¹, Mieke Soens, MD¹, Tari King, MD⁴, Ann Partridge, MD⁵, Andrea Pusic, MD⁴, Mehra Golshan, MD⁶, and Rob R. Edwards, PhD¹

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Preliminary Analyses: Acute & Persistent Trajectories

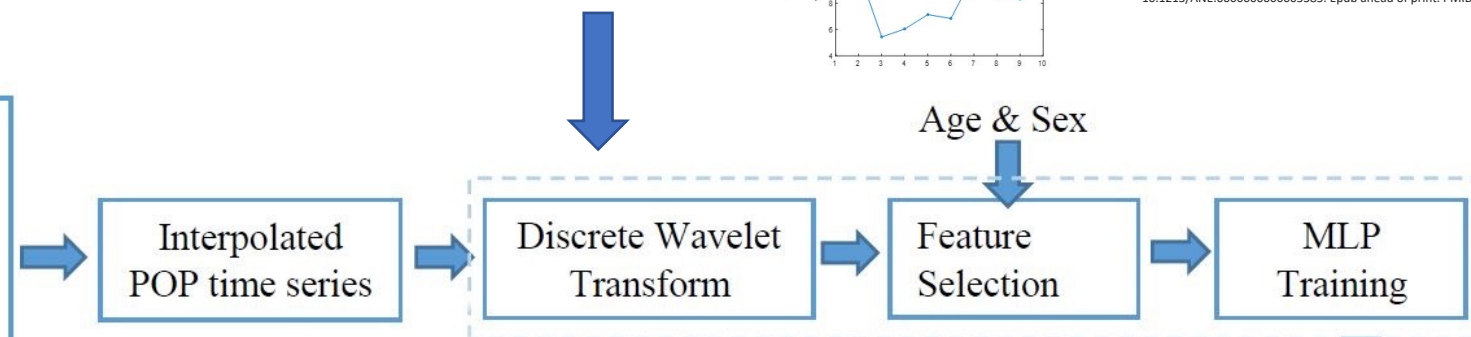
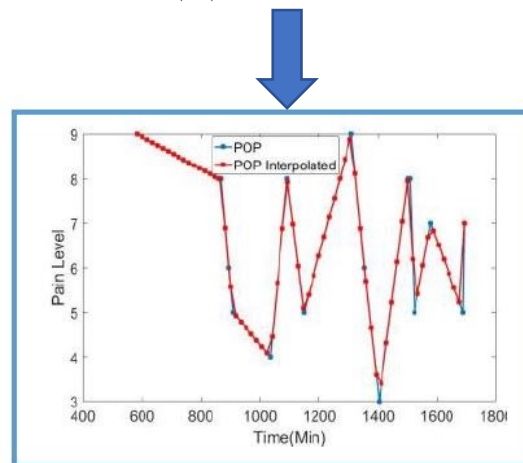
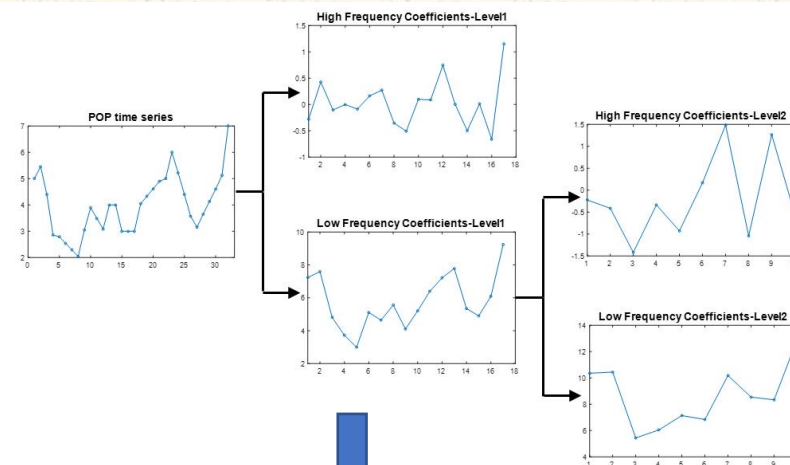
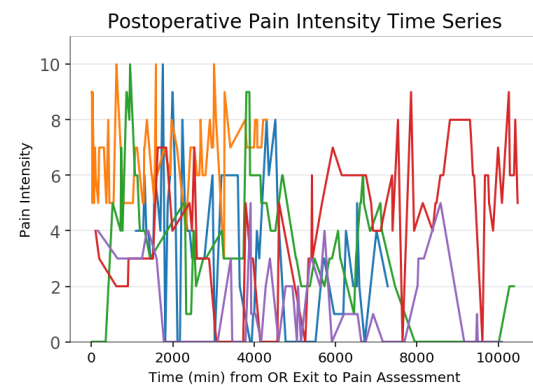


- **3 PPP Groups**
 1. Persistent moderate
 2. Persistent low-moderate
 3. Persistent low
- Acute postoperative pain trajectory group associated with PPP group assignment ($p < 0.001$)
- 90% in Persistent Moderate were in High or Moderate-High Acute Trajectory groups

Slow Dynamics of Acute Postoperative Pain Intensity Time Series Determined via Wavelet Analysis Are Associated With the Risk of Severe Postoperative Day 30 Pain

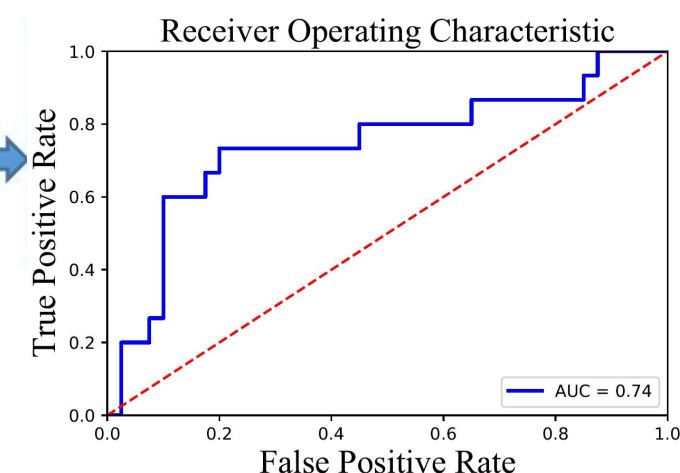
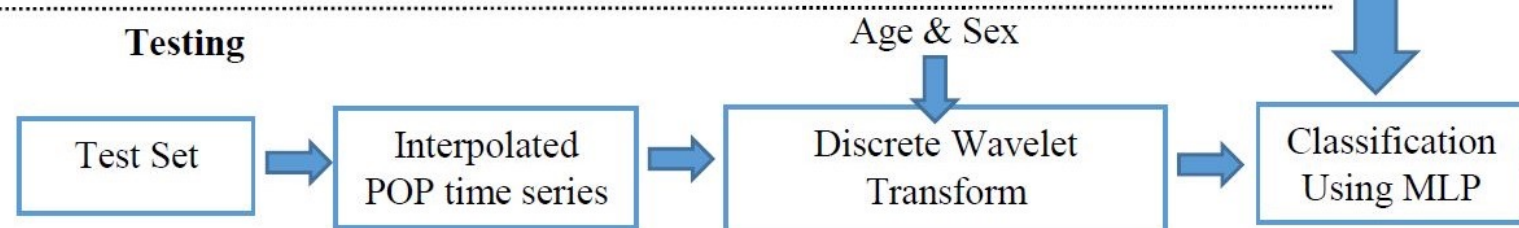
Raheleh Baharloo, MS,* Jose C. Principe, PhD,* Roger B. Fillingim, PhD,† Margaret R. Wallace, PhD,‡ Baiming Zou, PhD,§ Paul L. Crispen, MD,|| Hari K. Parvataneni, MD,¶¶ Hernan A. Prieto, MD,¶¶ Tiago N. Machuca, MD, PhD,# Xinlei Mi, PhD,** Steven J. Hughes, MD,# Gregory J. A. Murad, MD,†† Parisa Rashidi, PhD,* and Patrick J. Tighe, MD, MS‡‡

Baharloo R, Principe JC, Fillingim RB, Wallace MR, Zou B, Crispen PL, Parvataneni HK, Prieto HA, Machuca TN, Mi X, Hughes SJ, Murad GJA, Rashidi P, Tighe PJ. Slow Dynamics of Acute Postoperative Pain Intensity Time Series Determined via Wavelet Analysis Are Associated With the Risk of Severe Postoperative Day 30 Pain. *Anesth Analg*. 2021 Jan 15. doi: 10.1213/ANE.0000000000005385. Epub ahead of print. PMID: 33591118.



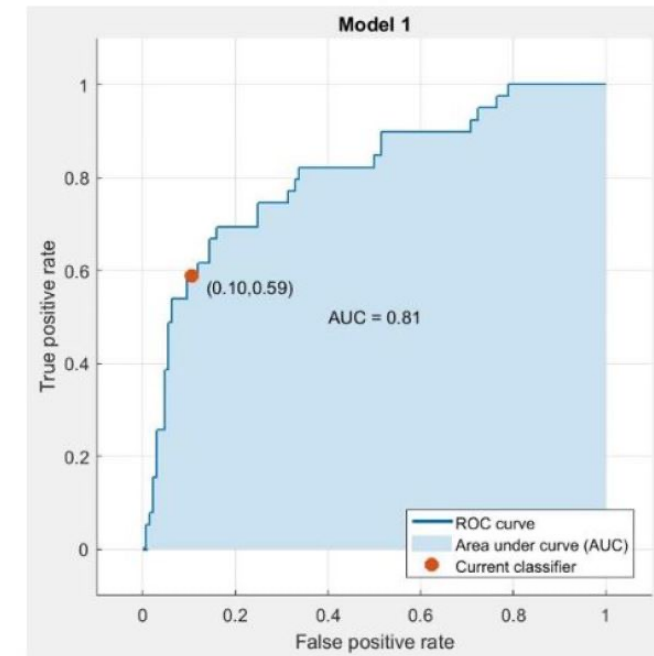
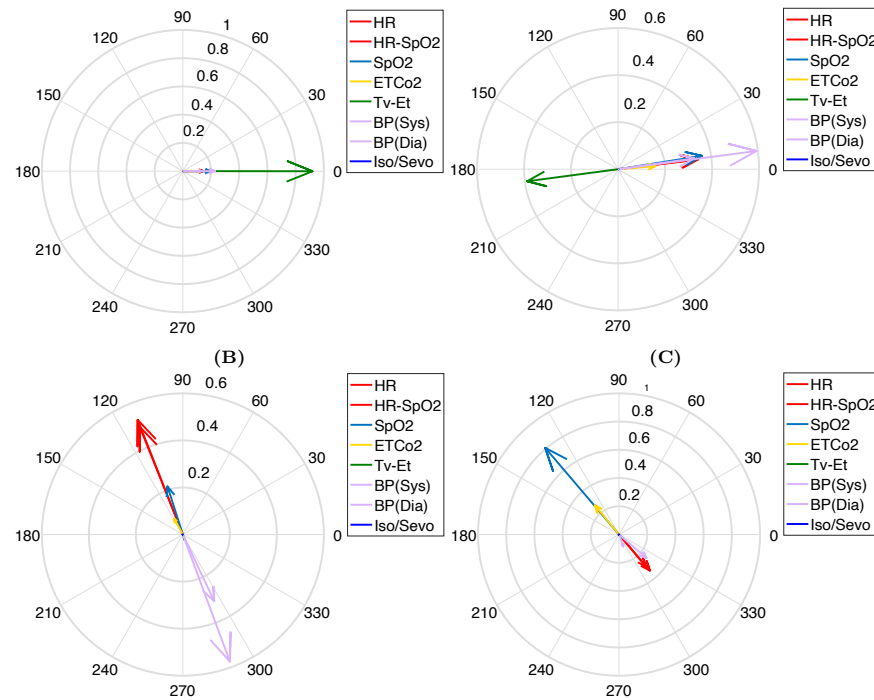
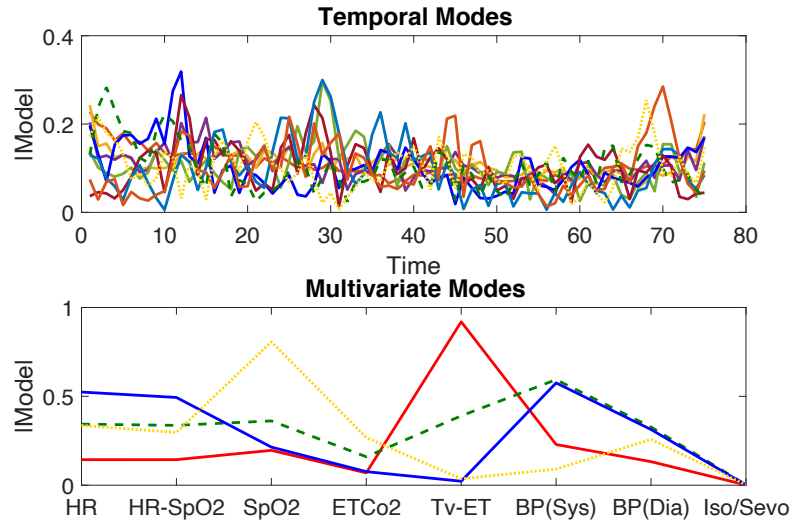
Training

Testing

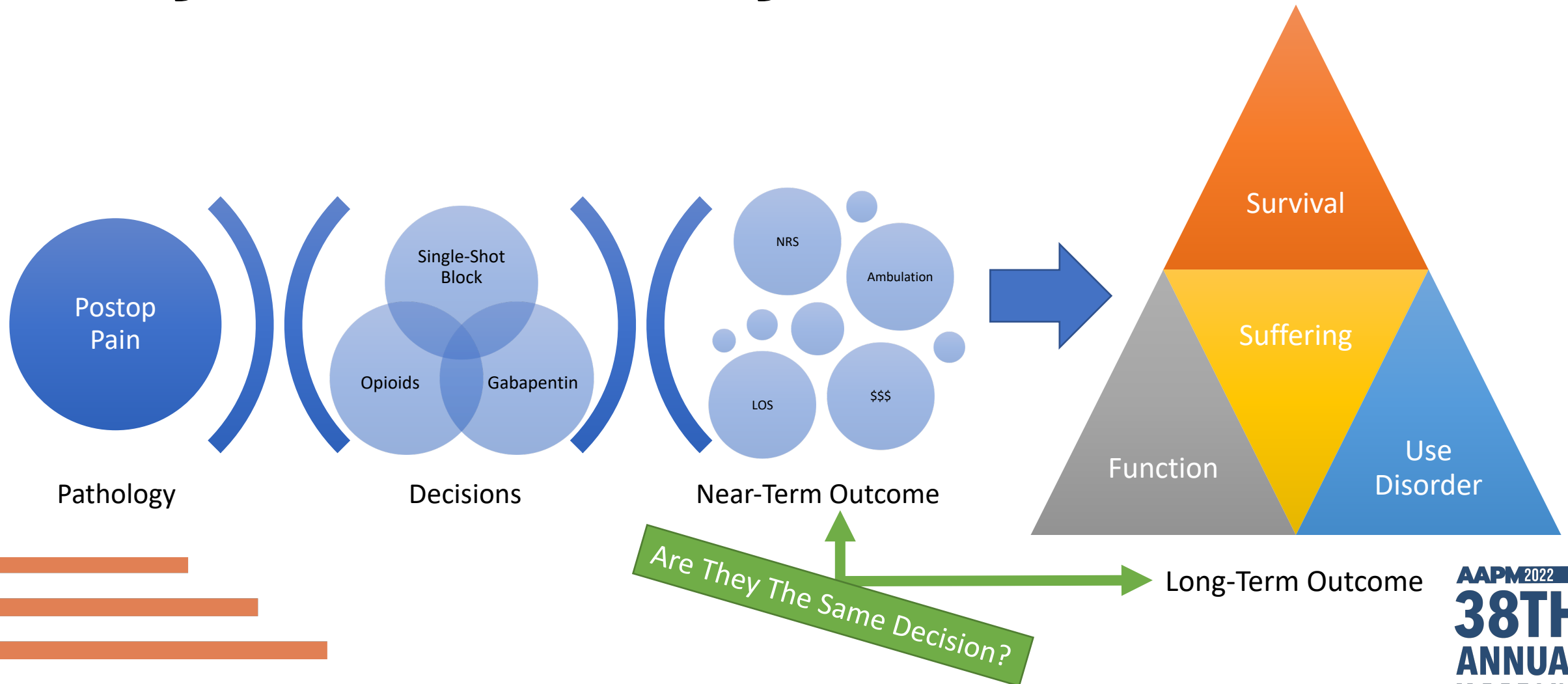


*Early TEMporal POstoperative pain Signatures (TEMPOS)
Forecast Pain Intensity 30 Days after Surgery*

AI Analysis of Intraoperative Vitals Predicts POD30 Pain Severity



Supporting Clinical Decisions to Optimize Long-term Function: Longitudinal Perspective



Summary

- *Defining the Transition: 3, 6, 12 months...or irrelevant?*
- *Theoretical Frameworks for Modeling Acute to Chronic Transition of Postoperative Pain: Causation Remains Elusive!*
- *Prediction Models Must Consider Patient, Surgical Factors*



Thank You!!!

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