



Toward the Prediction and Prevention of Chronic Post-Surgical Pain: Evidence from the China Surgery and Anaesthesia Cohort (CSAC)

Huan Song
West China Hospital
Sichuan University
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PART 1- Cohort Introduction

PART 2- Use our data to understand Chronic Post-Surgical Pain (CPSP)

Project 1: Associations between pre-operative psychological distress and CPSP (BJA, 2023)

Project 2: Genetic variants associated with CPSP (BJA, 2025)

PART 3- Towards CPSP intervention

Project 3: Development and Validation of an Interpretable Machine Learning Prediction Model for CPSP (manuscript)

Project 4: The impact of intraoperative xxxx use on CPSP: a target trial emulation and a clinical randomization trial (ongoing)



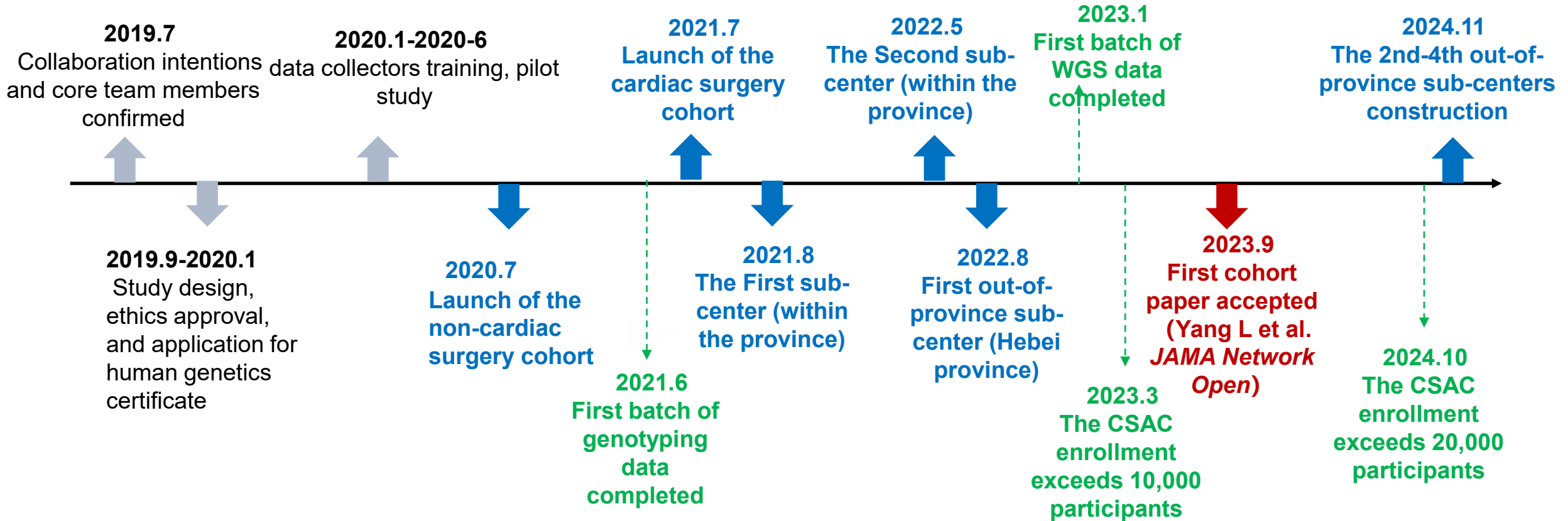


— 四川大學 —
華西醫院
WEST CHINA HOSPITAL, SICHUAN UNIVERSITY

The China Surgery and Anesthesia Cohort (CSAC,)

Aim: To establish a **multiple-center cohort** with detailed perioperative information, for **understanding the complex interplays of environmental and genetic components on a wide range of surgery/anesthesia-related outcomes**, with a primary focus on modifiable factors such as perioperative psychological conditions.

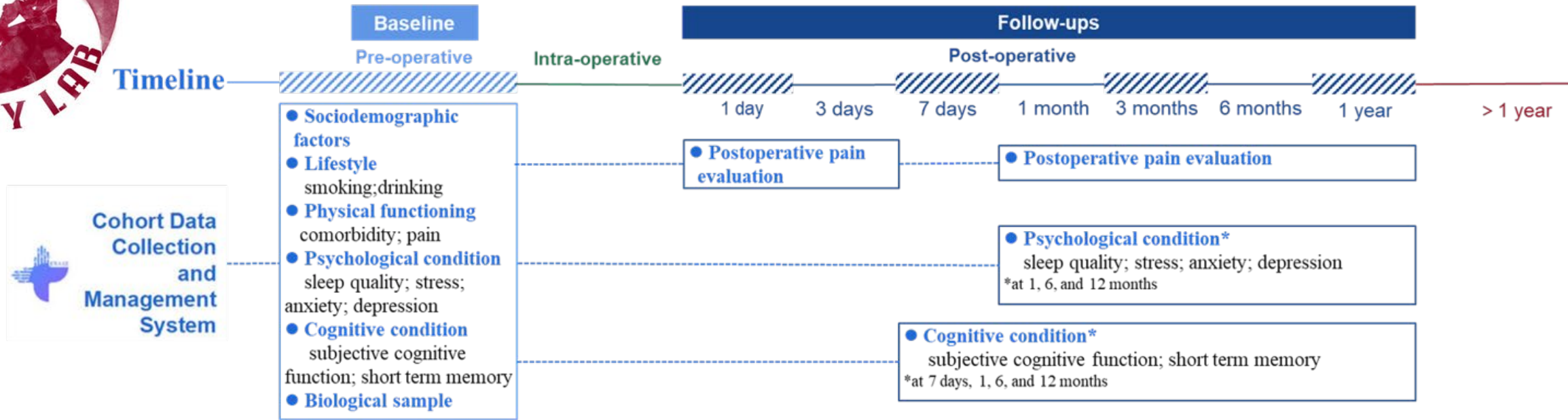
CSAC milestones



➤ The CSAC is an ongoing multicenter prospective cohort study recruiting all patients aged **40-65 years** who underwent **surgeries with general anesthesia** in **West China Hospital** (since Jul 2020) and **6 other medical centers** in China.



Key features of the CSAC



- **Full period:** Preoperative, intraoperative, and postoperative (short- and long-term)
- **Multiple data recourses:** EDC/HIS/LIS/AIMS/linked data from other system
- **Multidimensional data:** questionnaires, clinical management data, intraoperative vital sign, wristwatch data, image data, sequencing data
- **Biological samples:** blood, hair
- **High Quality!:** Full-time data collection team + multiple approaches for stringent quality control





厚德 | 精业 | 求实 | 创新

◆ Updates: until 2025.2

- ✓ 6 medical centers in China
- ✓ Number of participants: **26,909** (baseline response rate =96.82%)
- ✓ Proportions of participants who agreed to donate blood and hair samples: **69.23%** and **70.85%**, respectively
- ✓ Follow-up rates: 1 day, 3 days, 7 days, 1 month, 3 months, 6 months and 1 year after surgery were **99.45%, 99.30%, 98.13%, 96.13%, 92.78%, 93.64%, 92.63%**, respectively
- ✓ Genotyping data: $1978+3215+2517+1532+3200=12,442$
- ✓ WGS: 528
- ✓ Linked data from administrative system: 23,237



Cohort profile: The China Surgery and Anesthesia Cohort (CSAC),
European Journal of Epidemiology, 2024
(IF=13.6, HXB)



The China Surgery And Anesthesia Cohort (CSAC)

The China Surgery and Anesthesia Cohort (CSAC), launched in 2020, is a multicenter cohort study jointly founded by Prof. Qian Li from the Department of Anesthesiology, and Prof. Huan Song from the Biomedical Big Data Center, West China Hospital, Sichuan University. Until June 2023, CSAC has recruited more than 12,000 middle-aged (40-65 years) Chinese surgical population with both active (phone contacts within one year) and passive (linkage with administrative systems) follow-ups. The overarching aim of CSAC is to provide a reliable data source, with detailed perioperative multidimensional information (e.g., lifestyle, somatic conditions, neuropsychological conditions, genetic information, anesthesia-related information, including intraoperative vital signs and events), for understanding the complex interplay of environmental and genetic components on a wide range of interested surgery/anesthesia-related outcomes, with a primary focus on modifiable factors such as perioperative neuropsychological conditions. Currently, the data of CSAC are not available to public for data protection and privacy policy. But we welcome clinicians and researchers contact us, for initiating collaborative projects or joining CSAC as a new recruitment center.

A reliable research database & national benchmark cohort for anesthesia-related outcome studies.

<https://biomedbdc.wchscu.cn/JoylabErasePM/joylab-portals-web/#/queue/01/index>





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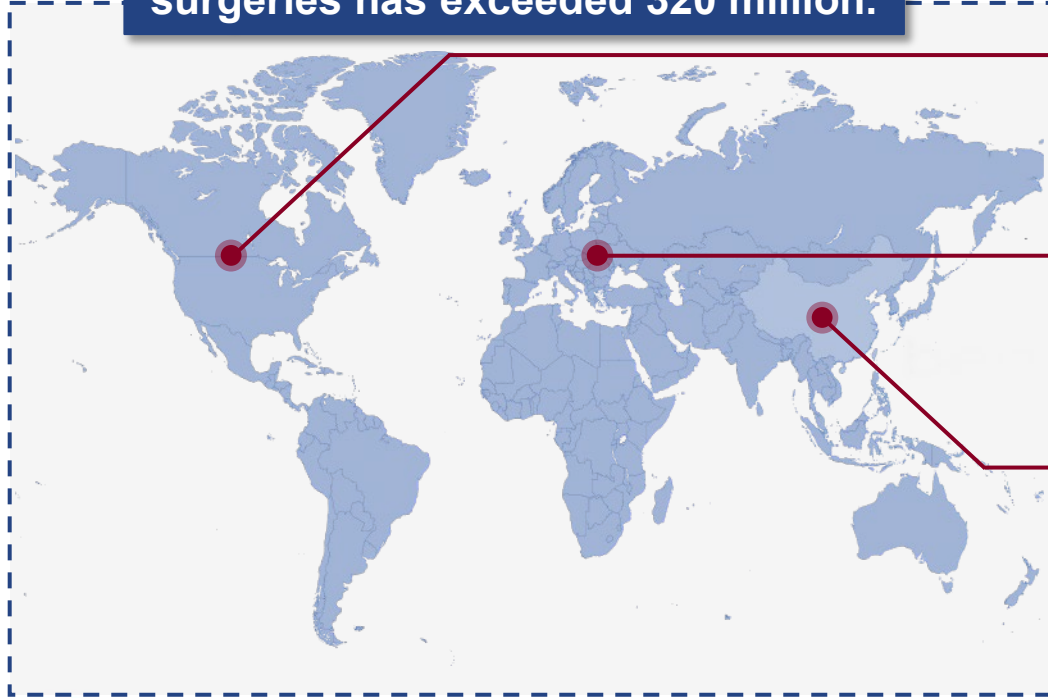
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Background - Chronic postsurgical pain, CPSP

ICD-11 Definition: pain that increases in intensity after a surgery and persists for **≥3 months** (i.e., beyond the healing process)

The global annual number of surgeries has exceeded 320 million.



1

- International (North America), multicenter prospective cohort study (n=2,054). (**12%** of CPSP incidence following day surgery)

2

- International (European), multicenter prospective cohort study (n=2,494). (**10.5%** of CPSP incidence following elective surgery)

3

- Our team (China), multicenter prospective cohort study (n=8,350). (**15.6%** of CPSP incidence following elective surgery) (CSAC)

The incidence of CPSP is relatively **high**, affecting at least **10%** of adult surgical patients.

[1] Lancet. 2015 Apr 27;385 Suppl 2:S11.

[2] Anesthesiology. 2024 Aug 1;141(2):286-299.

[3] Eur J Anaesthesiol. 2024 May 1;41(5):351-362.

[4] Br J Anaesth. 2024 Feb;132(2):359-371.





- Delayed rehabilitation
- Disability
- Opioid dependence



- Anxiety
- Depression
- Sleep disturbance



- Quality of life
- Economic burden
- Social impact

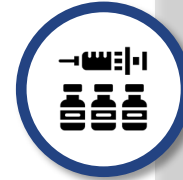
CPSP has severe and lasting impacts.



- General condition
- Physical illness
- Mental stress



- Surgical methods
- Surgical site
- Extent of injury



- Anesthesia medication
- Pain management.

Difficult to identify CPSP risk population.

[5] Br J Anaesth 2022, 129(3):407-415.

[6] Curr Opin Anaesthesiol 2023, 36(5):580-588.





Project 1: Associations between pre-operative psychological distress and CPSP

Rationale

- The perioperative period is highly stressful.
- Many psychological symptoms **co-occur**, yet previous studies examined them one by one.

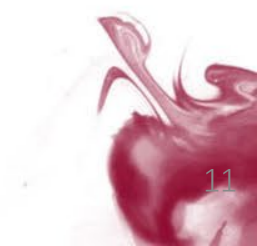


BJA, 2023

- the overall aim of this study was to assess the association of individual and patterns of preoperative psychological symptoms with subsequent risk of CPSP

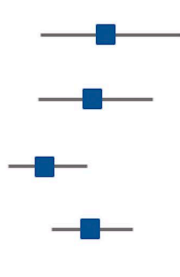


Dr. Dongxu Chen
Department of Anesthesia,
Sichuan University



Results

Preoperative psychological symptoms	No. of cases/ total number (incidence rate, %)		Adjusted OR* (95% CI)	
	exposed group	unexposed group		
<i>Individual preoperative psychiatric symptoms</i>				
Anxiety	143/604 (23.7)	1,159/7,746 (15.0)	1.52 (1.23, 1.86)	
Depression	204/910 (22.4)	1,098/7,440 (14.8)	1.46 (1.22, 1.73)	
Stress reaction	379/1,884 (20.1)	923/6,466 (14.3)	1.25 (1.09, 1.44)	
Sleep quality	764/4,045 (18.9)	538/4,305 (12.5)	1.45 (1.28, 1.64)	

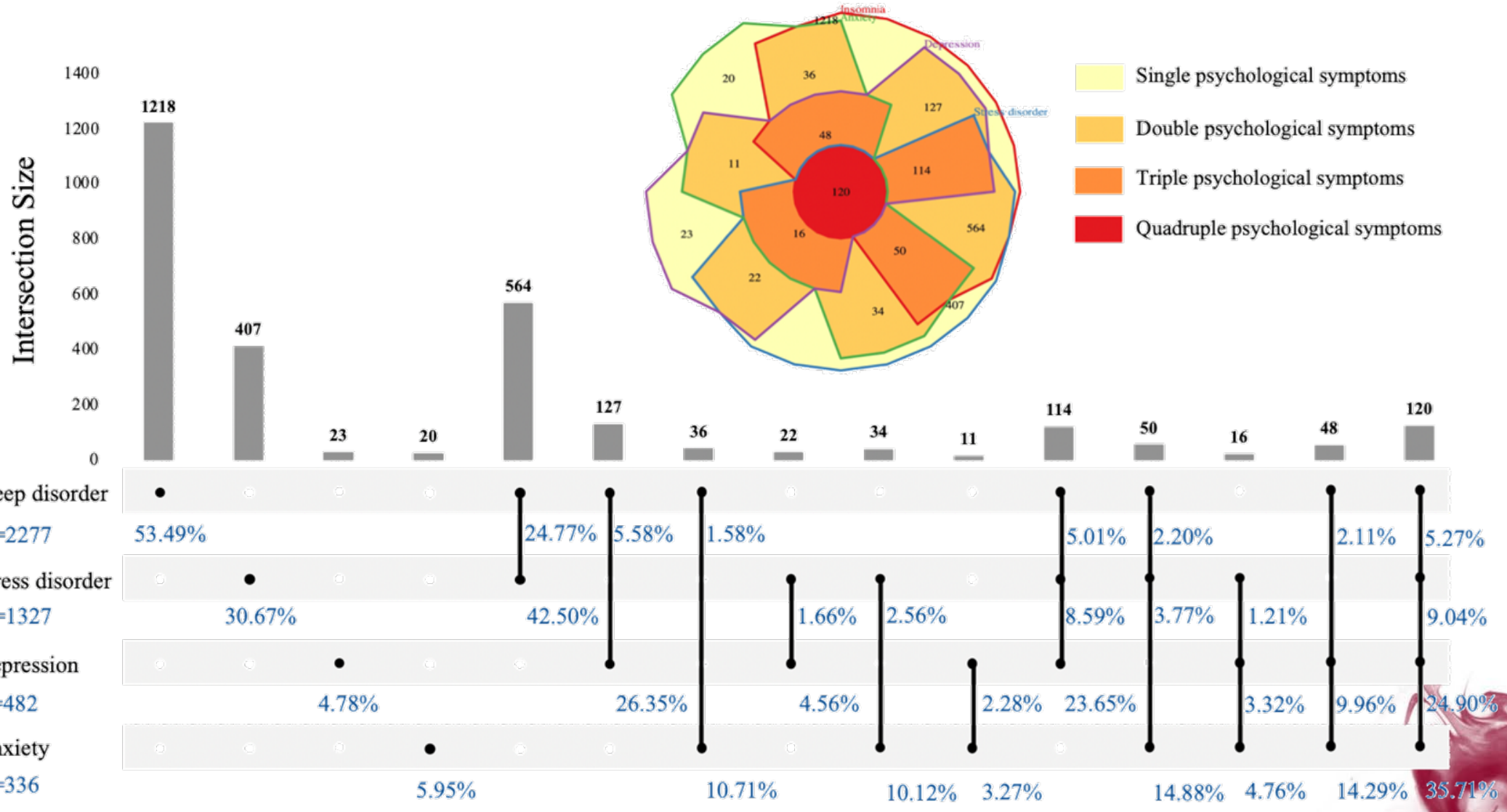


- At 3 months after surgery, we in total identified **1,302 (15.6%) CPSP cases**.
- We observed an elevated risk of CPSP among patients with individual psychological symptoms





- **Concern:** due to physical and psychological vulnerability during the preoperative period, the co-occurrence of different psychological symptoms is common



- **Solution:** we attempted to identify major clusters of patients with distinct preoperative psychological patterns using the k-means clustering algorithm

A Cluster 1 Minor symptom

Anxiety	-0.437 (0.331)
Depression	-0.533 (0.386)
Stress reaction	-0.561 (0.402)
Sleep quality	-0.571 (0.539)

Cluster 2 Mild sleep and stress disorders

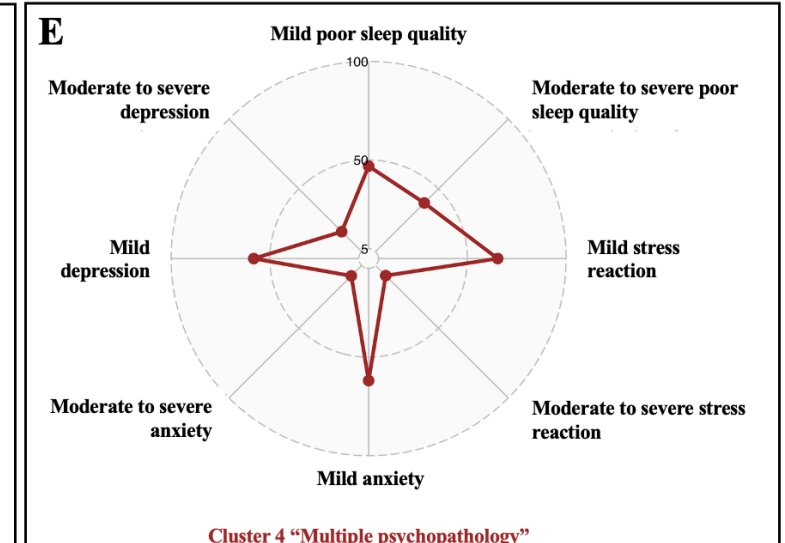
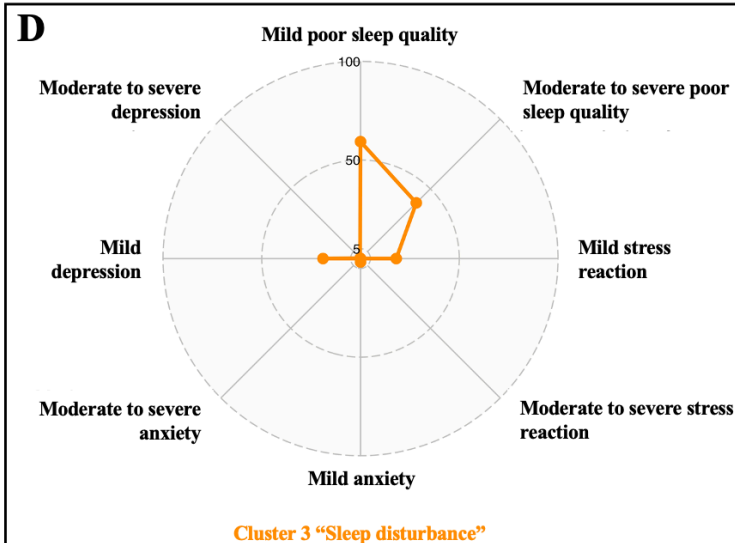
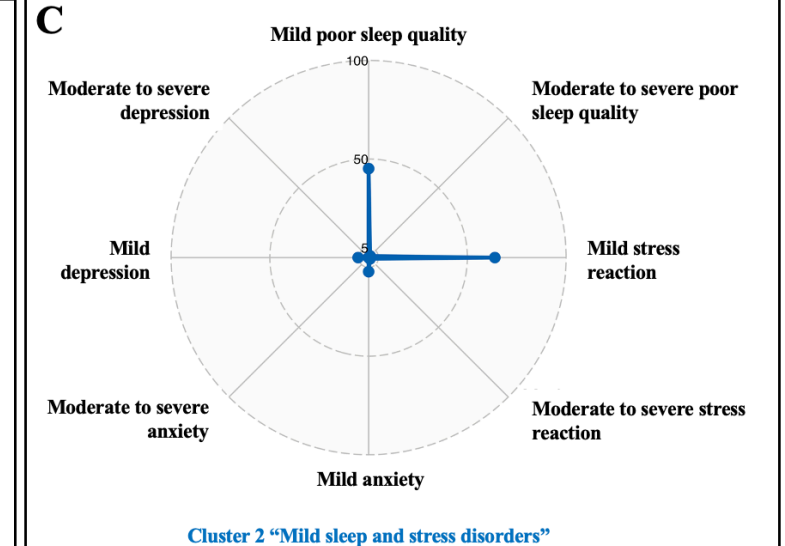
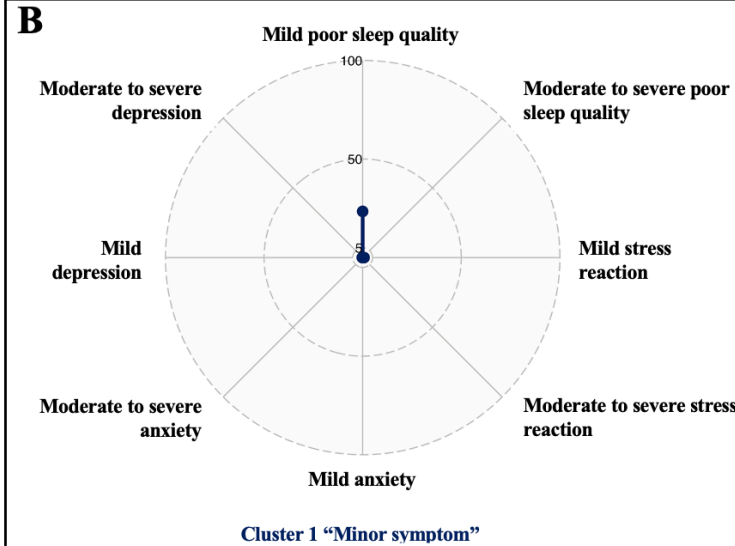
Anxiety	0.294 (0.786)
Depression	0.025 (0.619)
Stress reaction	0.884 (0.818)
Sleep quality	-0.208 (0.600)

Cluster 3 Sleep disturbance

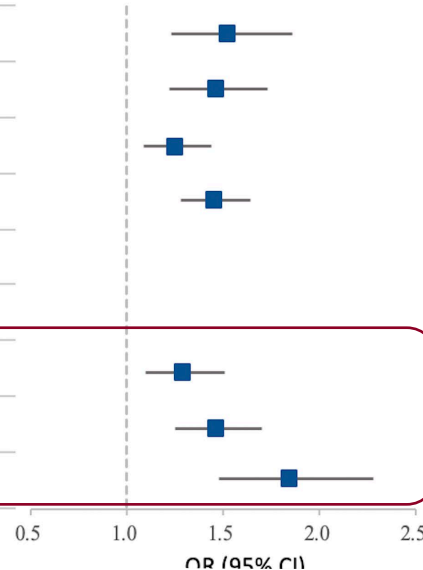
Anxiety	-0.062 (0.639)
Depression	0.522 (0.744)
Stress reaction	-0.032 (0.669)
Sleep quality	1.236 (0.722)

Cluster 4 Multiple psychopathology

Anxiety	2.505 (1.474)
Depression	2.226 (1.491)
Stress reaction	1.726 (1.459)
Sleep quality	1.081 (1.071)



Preoperative psychological symptoms	No. of cases/ total number (incidence rate, %)		Adjusted OR* (95% CI)		Attributable risk (95% CI)
	exposed group	unexposed group			
<i>Individual preoperative psychiatric symptoms</i>					
Anxiety	143/604 (23.7)	1,159/7,746 (15.0)	1.52 (1.23, 1.86)		34.2 (3.8, 87.7)
Depression	204/910 (22.4)	1,098/7,440 (14.8)	1.46 (1.22, 1.73)		31.5 (3.2, 86.1)
Stress reaction	379/1,884 (20.1)	923/6,466 (14.3)	1.25 (1.09, 1.44)		20.0 (1.2, 84.1)
Sleep quality	764/4,045 (18.9)	538/4,305 (12.5)	1.45 (1.28, 1.64)		31.0 (3.1, 86.1)
<i>Different psychological pattern</i>					
Minor symptom	534/4,353 (12.3)		Reference		
Mild sleep and stress disorders	285/1,633 (17.5)		1.29 (1.10, 1.51)		22.5 (1.5, 84.1)
Sleep disturbance	332/1,752 (19.0)		1.46 (1.25, 1.70)		31.5 (3.2, 86.1)
Multiple psychological symptoms	151/612 (24.7)		1.84 (1.48, 2.28)		45.7 (7.5, 89.1)



Adjusted OR (95% CI)

- Compared with patients clustered in the minor symptom group, a risk elevation of CPSP was observed among individuals with **psychological symptom patterns featured by mild sleep and stress disorders, sleep disturbance, and multiple psychological symptoms.**



Table. Mediating pathways within patterns identified by *k*-means and chronic postsurgical pain.

	Between mild sleep and stress disorders pattern, and chronic postsurgical pain [↙]				Between <u>sleep disturbance pattern</u> and chronic postsurgical pain [↙]				Between <u>multiple psychological symptoms</u> and chronic postsurgical pain [↙]			
	ACME, (95%CI) [↙]	ADE, (95%CI) [↙]	Total effect, (95%CI) [↙]	Percentage mediation (95%CI) [↙]	ACME, (95%CI) [↙]	ADE, (95%CI) [↙]	Total effect, (95%CI) [↙]	Percentage mediation (95%CI) [↙]	ACME, (95%CI) [↙]	ADE, (95%CI) [↙]	Total effect, (95%CI) [↙]	Percentage mediation (95%CI) [↙]
Duration of surgery [↙]	0.000(0.001, 0.000) * [↙]	0.029(0.009, 0.050) * [↙]	0.031(0.011, 0.050) * [↙]	5.1 (-1.4, 15.0)[↙]	0.000(-0.001, 0.000) [↙]	0.045(0.025, 0.070) * [↙]	0.045(0.026, 0.070) * [↙]	0.9 (-1.4, 4.0)[↙]	0.000(-0.001, 0.000) [↙]	0.087(0.054, 0.130) * [↙]	0.088(0.055, 0.130) * [↙]	0.5 (-1.8, 3.0)[↙]
Acute/subacute pain scores[↙]												
Pain score at postoperative 1 day [#] [↙]	0.005(0.003, 0.010) * [↙]	0.026(0.007, 0.040) * [↙]	0.031(0.011, 0.050) * [↙]	16.4 (7.8, 44.0) *[↙]	0.005(0.002, 0.010) * [↙]	0.040(0.020, 0.060) * [↙]	0.046(0.025, 0.070) * [↙]	11.4 (5.3, 22.0) *[↙]	0.010(0.006, 0.010) * [↙]	0.077(0.044, 0.110) * [↙]	0.087(0.052, 0.120) * [↙]	11.5 (6.4, 20.0) *[↙]
Pain score at postoperative 3 days [†] [↙]	0.004(0.002, 0.010) * [↙]	0.027(0.008, 0.050) * [↙]	0.031(0.012, 0.050) * [↙]	13.5 (5.9, 35.0) *[↙]	0.007(0.004, 0.010) * [↙]	0.039(0.019, 0.060) * [↙]	0.045(0.025, 0.070) * [↙]	14.4 (8.3, 27.0) *[↙]	0.011(0.006, 0.020) * [↙]	0.077(0.044, 0.110) * [↙]	0.088(0.054, 0.120) * [↙]	12.2 (6.8, 21.0) *[↙]
Pain score at postoperative 1 month ^{††} [↙]	0.006(0.003, 0.010) * [↙]	0.023(0.003, 0.040) * [↙]	0.029(0.009, 0.050) * [↙]	19.9 (7.6, 56.0) *[↙]	0.009(0.006, 0.010) * [↙]	0.033(0.013, 0.050) * [↙]	0.043(0.023, 0.060) * [↙]	21.9 (12.4, 41.0) *[↙]	0.020(0.013, 0.030) * [↙]	0.066(0.035, 0.100) * [↙]	0.086(0.052, 0.120) * [↙]	23.2 (14.5, 37.0) *[↙]
Psychopathology assessment at postoperative 1 month[↙]												
Anxiety [↙]	0.007(0.003, 0.050) * [↙]	0.024(0.004, 0.050) * [↙]	0.031(0.010, 0.050) * [↙]	21.5 (9.5, 61.0) *[↙]	0.005(0.002, 0.010) * [↙]	0.041(0.021, 0.060) * [↙]	0.045(0.025, 0.070) * [↙]	10.1 (4.5, 20.0) *[↙]	0.024(0.013, 0.040) * [↙]	0.062(0.025, 0.100) * [↙]	0.086(0.050, 0.120) * [↙]	27.9 (13.9, 53.0) *[↙]
Depression [↙]	0.009(0.006, 0.010) * [↙]	0.022(0.001, 0.040) * [↙]	0.031(0.009, 0.050) * [↙]	29.6 (16.2, 91.0) *[↙]	0.013(0.008, 0.020) * [↙]	0.033(0.013, 0.050) * [↙]	0.046(0.026, 0.070) * [↙]	27.7 (15.5, 52.0) *[↙]	0.032(0.021, 0.050) * [↙]	0.053(0.017, 0.090) * [↙]	0.085(0.052, 0.120) * [↙]	37.7 (21.8, 67.0) *[↙]
Stress reaction [↙]	0.008(0.005, 0.010) * [↙]	0.023(0.002, 0.040) * [↙]	0.031(0.011, 0.050) * [↙]	25.1 (12.2, 75.0) *[↙]	0.009(0.006, 0.010) * [↙]	0.037(0.017, 0.060) * [↙]	0.046(0.027, 0.070) * [↙]	19.2 (10.8, 35.0) *[↙]	0.027(0.017, 0.040) * [↙]	0.058(0.021, 0.100) * [↙]	0.085(0.049, 0.120) * [↙]	31.6 (18.0, 58.0) *[↙]
Sleep quality [↙]	0.008(0.005, 0.010) * [↙]	0.023(0.003, 0.040) * [↙]	0.031(0.011, 0.050) * [↙]	25.7 (13.1, 71.0) *[↙]	0.025(0.016, 0.030) * [↙]	0.020(0.009, 0.040) * [↙]	0.045(0.025, 0.070) * [↙]	56.3 (31.3, 106.0) *[↙]	0.034(0.022, 0.050) * [↙]	0.052(0.018, 0.090) * [↙]	0.086(0.052, 0.120) * [↙]	39.9 (23.0, 67.0) *[↙]

- The presence of postoperative **acute or subacute pain and psychopathology** occurring at 1 month after surgery were significant mediators.
- This suggests that **a psychological cascade** contributes to CPSP development.





Implications:

- ❖ Screening psychological distress before surgery is necessary
- ❖ Different psychological symptoms jointly effect the development of CPSP
- ❖ Early pain and mental health interventions after surgery may help prevent CPSP



Project 2: Genetic variants associated with CPSP (BJA, 2025)



Dr. Jie Song
Associate prof.
Sichuan
University

- **Epidemiological studies:** established risk factors (demographic and environmental factors) cannot fully explain the observed interpatient variability
- **Twin studies:** **moderate** heritability (20-70%) for chronic pain
- **Genome-wide association studies (GWAS)** ¹⁻⁴:
 - ✓ First GWAS (N=303+203 for discovery & replication) found **no genomic loci**
 - ✓ One GWAS (N= 1,350) suggests adaptive immune system involved in the development of CPSP **across 5 surgical types and 6 cohorts**



CPSP is moderately heritable, yet CPSP GWASs have been limited or inconclusive — especially in East Asian populations.

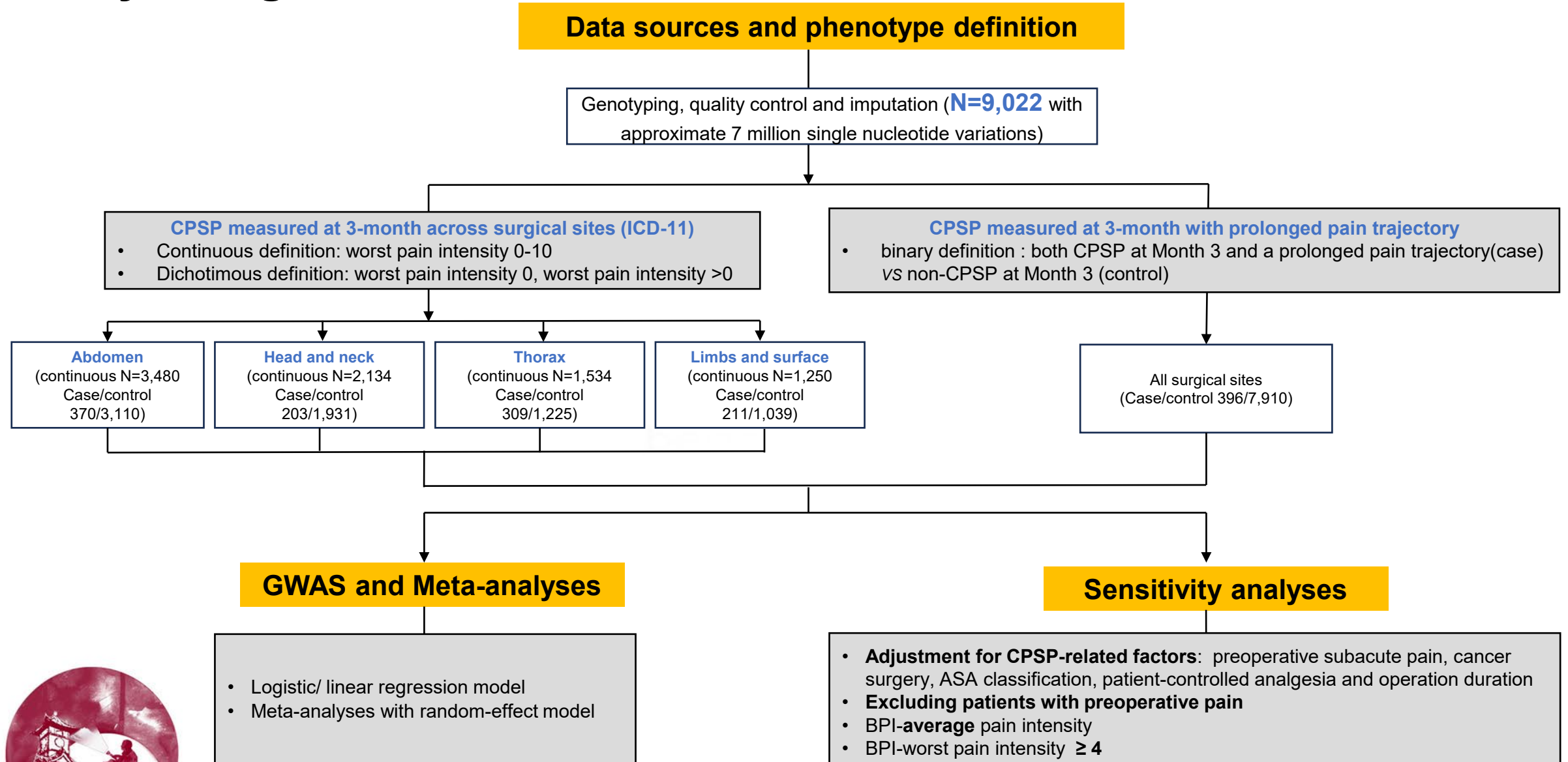


Yanan Zhang
PhD student
Sichuan
University

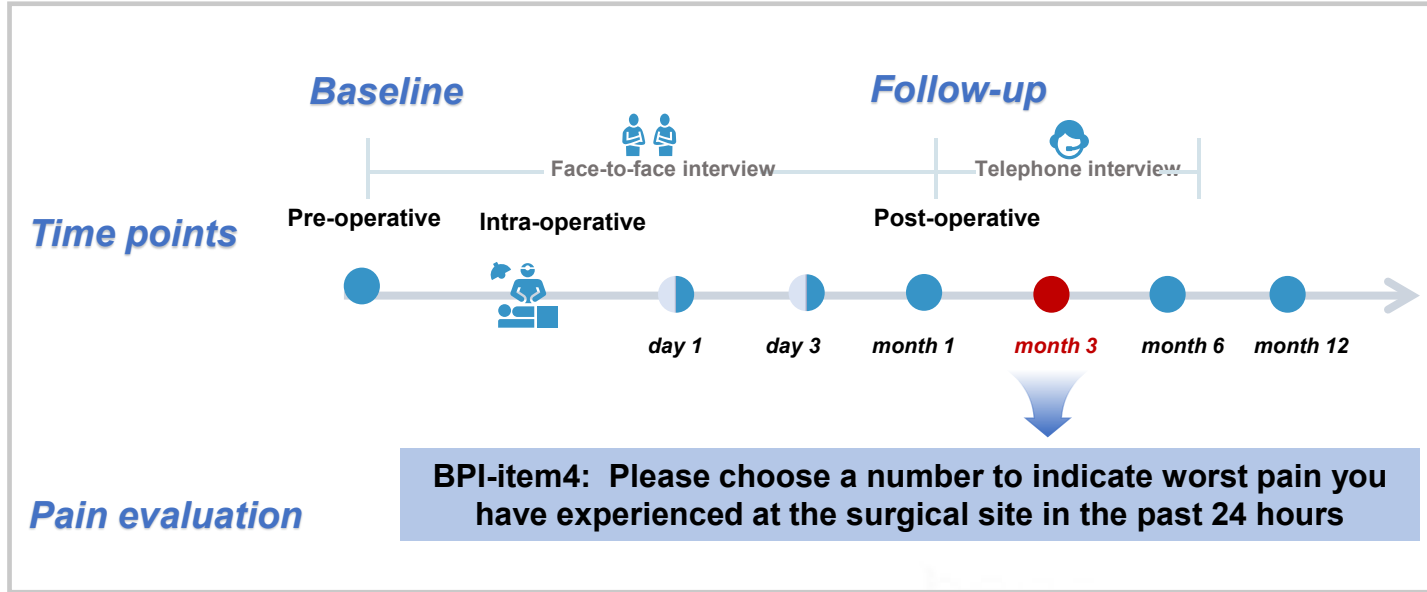


- [1] van Reij RRI, *et al. Anaesthesia*. 2020;75 Suppl 1:e111-e120. doi:10.1111/anae.14832
[2] Parisien M, *et al. Br J Anaesth*. 2024;133(2):360-370. doi: 10.1016/j.bja.2024.04.053.
[3] Li S, *et al. Anaesthesia*. 2025;80(5):499-510. doi:10.1111/anae.16528
[4] Li S, *et al. Br J Anaesth*. 2025;134(3):783-792. doi:https://doi.org/10.1016/j.bja.2024.12.008

Study design



CPSP ascertainment



Chinese version of Brief Pain Inventory (BPI-C)

Item 1: Do you feel pain at the surgical site?

(1) No (2) Yes

Item 2: The location of the pain is as follows (If there is no pain at the surgical site, please write "none")

Item 3: Please choose a number to indicate the level of pain at the surgical site right now.

(No pain) 0 1 2 3 4 5 6 7 8 9 10 (Worst pain)

Item 4: Please choose a number to indicate the worst pain you have experienced at the surgical site in the past 24 hours.

(No pain) 0 1 2 3 4 5 6 7 8 9 10 (Worst pain)

Item 5: Please choose a number to indicate the least pain you experienced at the surgical site in the past 24 hours.

(No pain) 0 1 2 3 4 5 6 7 8 9 10 (Worst pain)

Item 6: Please choose a number to indicate the average level of pain you have experienced at the surgical site in the past 24 hours.

(No pain) 0 1 2 3 4 5 6 7 8 9 10 (Worst pain)

Item 7: What medication or treatment have you received to control the pain at the surgical site?

Item 8: In the past 24 hours, how much relief have you experienced from the medication or treatment? Please choose a percentage to indicate the level of pain relief (Note: 0% means no relief, 100% means complete relief).

(No relief) 0 10% 20% 30% 40% 50% 60% 70% 80% 90% 100% (Complete relief)

Item 9: Please choose a number to indicate the impact of the pain at the surgical site on the following aspects in the past 24 hours

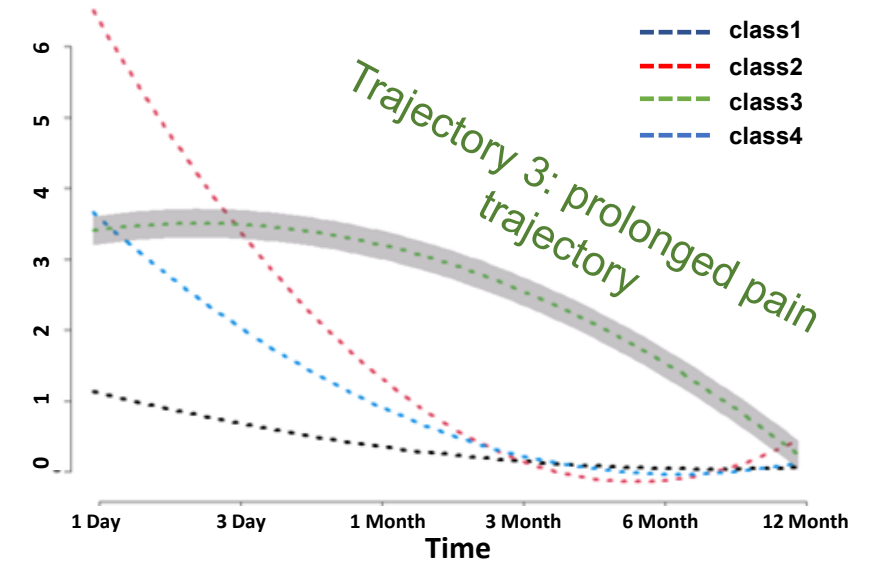
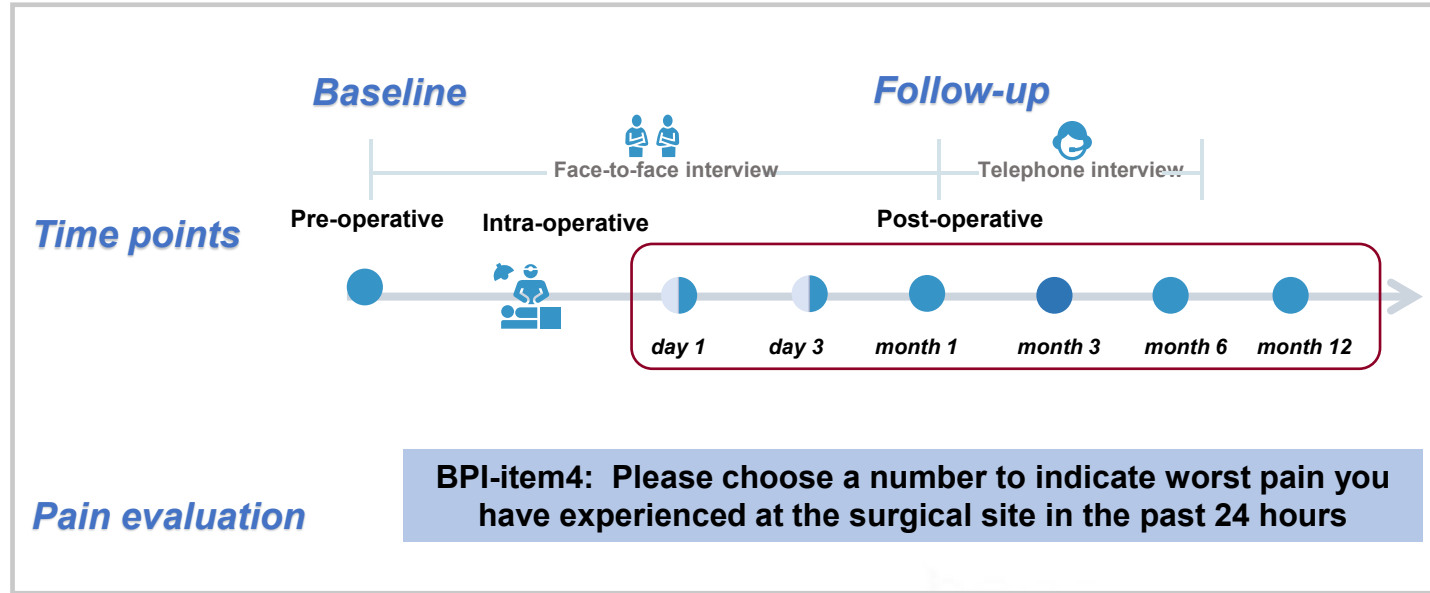
(1) daily life (2) emotions (3) walking ability (4) daily work (5) relationships with others (6) sleep (7) interest in life

Phenotype definition 1: CPSP according to the ICD-11 criteria

- ✓ Based on **Chinese version of Brief Pain Inventory (BPI-C)** questionnaire by **Numeric Rating Scale (NRS)**
- ✓ Defined by **BPI-worst pain intensity at Month 3**
 - Continuous phenotype (pain intensity 0-10)
 - Binary phenotype (pain intensity 0, pain intensity >0)
- ✓ Stratified by **four surgical sites** according to surgical department: **head and neck, thorax, abdomen, limbs and surface**
- ✓ Ensured that the Pain was **chronic, surgery-related, and not caused** by other conditions



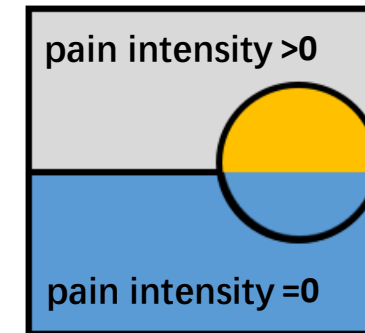
CPSP trajectory (-12 month)



Trajectories of postoperative pain within 12 months

Phenotype definition 2: CPSP with prolonged pain trajectory

- ✓ **Latent class trajectory model** using all available information on pain intensity at **different time points**
- ✓ **Case (yellow)**: the patients with CPSP (worst pain intensity >0) and with prolonged pain trajectory
- ✓ **Control (blue)**: the patients without CPSP (worst pain intensity =0)

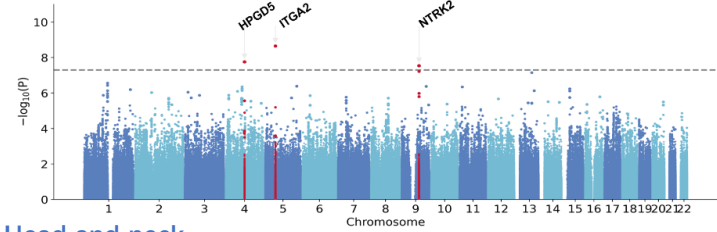


- Prolong pain trajectory
- CPSP measured by the worst pain intensity at Month 3

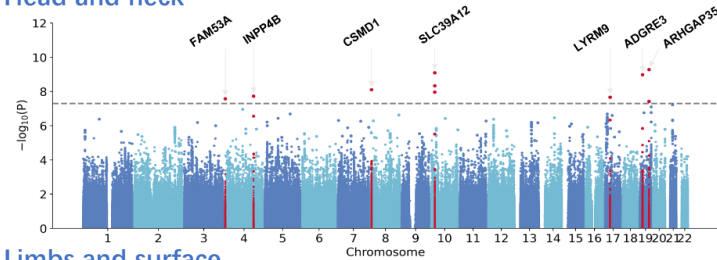
GWAS and meta-analyses

A. CPSP by continuous pain intensity at Month 3 B. CPSP by binary pain intensity at Month 3

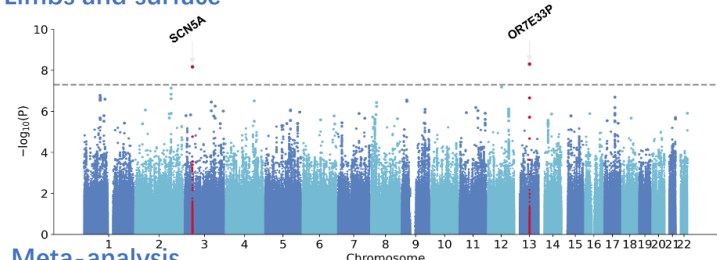
Abdomen



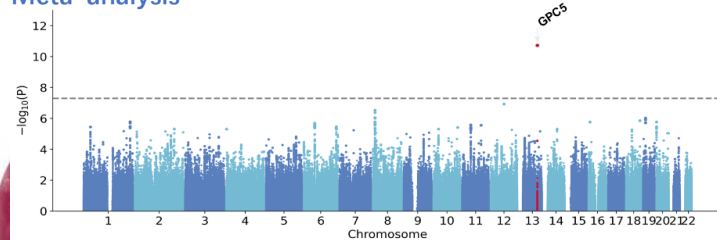
Head and neck



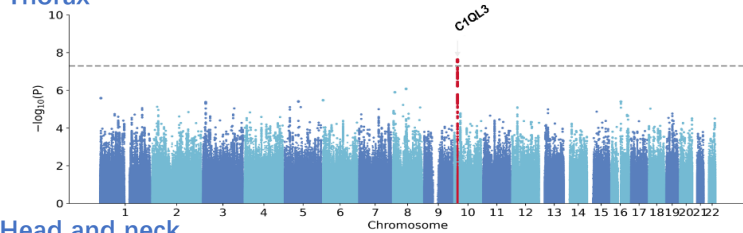
Limbs and surface



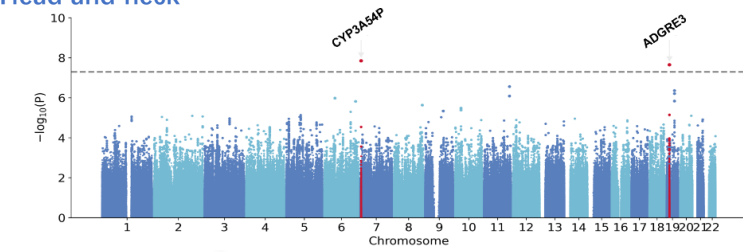
Meta-analysis



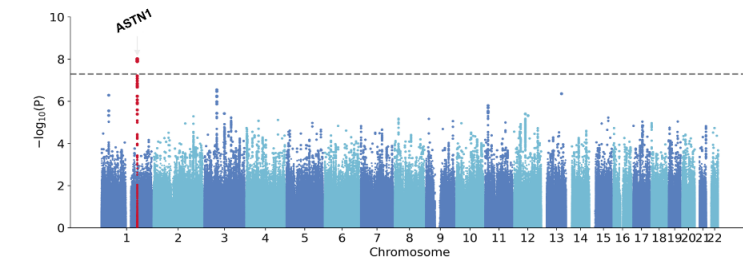
Thorax



Head and neck



C. CPSP with prolonged pain trajectory



The 16 genomic loci associated with CPSP across various assessments

CPSP by continuous definition	Lead SNP	BETA	P	Nearest gene
Abdominal surgery	rs75010196	0.60	1.77×10^{-8}	<i>HPGD5</i>
	rs139704993	0.57	2.26×10^{-9}	<i>ITGA2</i>
	rs12347629	0.50	2.92×10^{-8}	<i>UBE2V1P10</i>
Head and neck surgery	rs200348292	0.69	1.89×10^{-8}	<i>INPP4B</i>
	rs798715	0.70	2.69×10^{-8}	<i>FAM53A</i>
	rs148769945	0.79	7.94×10^{-9}	<i>CSMD1</i>
	rs553680819	0.59	8.15×10^{-10}	<i>SLC39A12</i>
	rs150447567	0.70	2.18×10^{-8}	<i>LYRM9</i>
	rs140124007	0.63	1.06×10^{-9}	<i>ADGRE3</i>
	rs73059314	0.56	5.29×10^{-10}	<i>ARHGAP35</i>
Limbs and surface surgery	rs143626305	1.39	6.79×10^{-9}	<i>SCN5A</i>
	rs186073562	1.66	4.96×10^{-9}	<i>OR7E33P</i>
Meta-analysis by four surgical sites	rs17668169	0.49	1.89×10^{-11}	<i>GPC5</i>
CPSP by binary definition	lead SNP	OR	P	Nearest gene
Thoracic surgery	rs10904771	2.28	2.4×10^{-8}	<i>C1QL3</i>
Head and neck surgery	rs76366961	4.96	1.42×10^{-8}	<i>CYP3A54P</i>
	rs140124007	4.89	2.24×10^{-8}	<i>ADGRE3</i>
All surgical sites with prolong pain trajectory	rs61075998	3.01	9.76×10^{-9}	<i>ASTN1</i>

Manhattan plots for main GWASs



Genes with strongest evidence

Ras Suppressor-1 (RSU1) associated with CPSP in **thoracic/ head and neck** surgery

- Participates in the **extracellular signal-regulated kinase (ERK) signaling** pathway

Nitric oxide synthase 2 (NOS2) associated with CPSP in **head and neck** surgery

- An exonic variant (rs150447567, **missense mutation**, T>C: p.Thr747Ala)
- **Neurotransmitter:** central sensitization and nociceptive process in the peripheral nervous system

Astrotactin-1 (ASTN1) associated with CPSP with a **prolonged pain trajectory**

- Identified with the highest number of evidence
- Encodes the neuronal adhesion molecule astrotactin 1 that involved in brain development



Conclusion

- ✓ Identified different genetic variants in the *RSU1* (for thoracic surgery), *ASTN1* (for CPSP with prolonged pain) and *NOS2* (for head and neck surgery) genes
 - ✓ Advances our understanding of the genetic architecture of CPSP, which is likely to be **heterogenous across different surgical sites**
-
- Provides **first large-scale genetic evidence in a Chinese cohort**
 - Supports **surgical-site-specific mechanisms**
 - Suggests novel **therapeutic targets**





PART 1- Cohort Introduction

PART 2- Use our data to understand Chronic Post-Surgical Pain (CPSP)

Project 1: Associations between pre-operative psychological distress and CPSP (BJA, 2024)

Project 2: Genetic variants associated with CPSP (BJA, 2024)

PART 3- Towards CPSP intervention

Project 3: Development and Validation of an Interpretable Machine Learning Prediction Model for CPSP (manuscript) →early identification of high-risk population

Project 4: The impact of intraoperative xxxx use on CPSP: a target trial emulation and a clinical randomization trial (ongoing) →early prevention



Project 3: Development and Validation of an Interpretable Machine Learning Prediction Model for CPSP (manuscript)

- Objective: to develop an **explainable and applicable** prediction model for CPSP using **Machine Learning** approaches based on the extensive perioperative data from the CSAC

To enable early identification of high-risk patients — before pain becomes chronic.

Study population

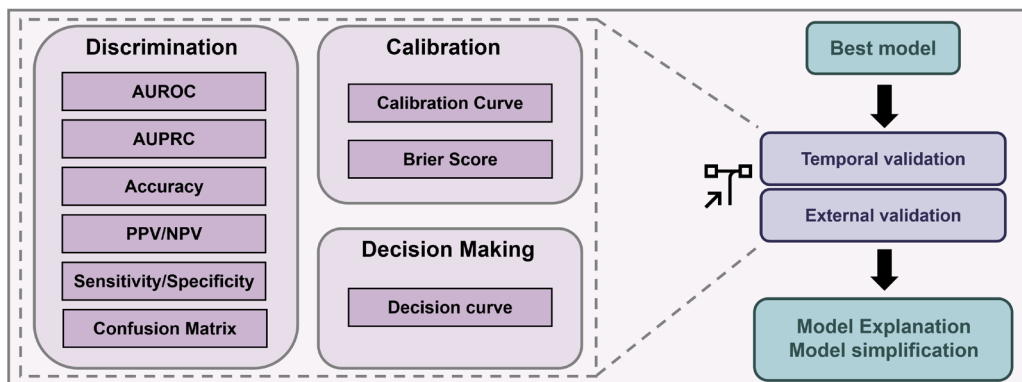
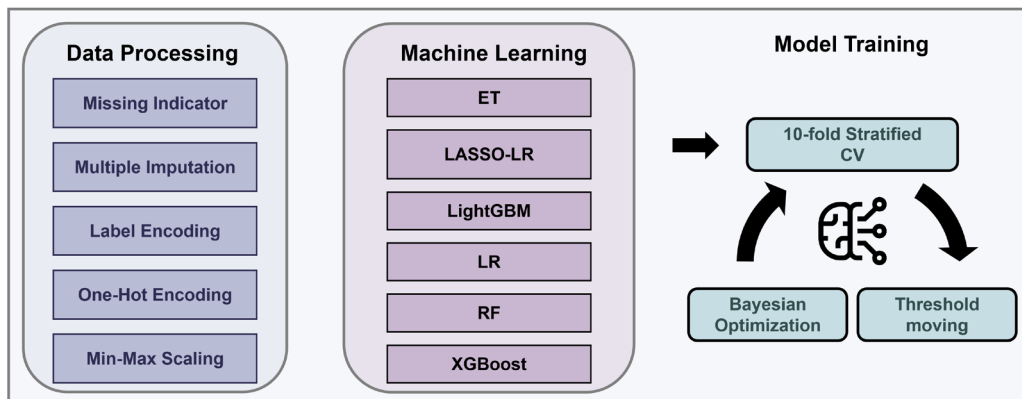
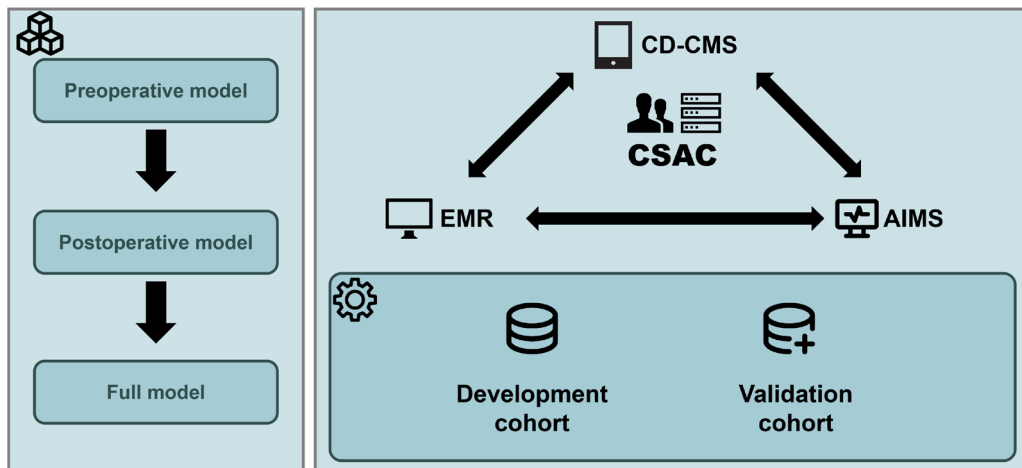
The data collected from July 2020 to March 2025 from **West China Hospital** constituted the development cohort for model development and internal validation (n= **13,256**). Whereas the data between January 2022 and December 2024 from **Tianfu Hospital** served as the validation cohort for external validation (n= **4,399**).



Yanjie Dong,
PhD student
Sichuan University



Method - Study design



1.Candidate features and prediction time points

Preoperative model: Preoperative features

Postoperative model (Day 1): Features obtained till POD1

Postoperative model (Day 30): All perioperative accessible features

2.Model selection

Six ML algorithms: Tree-based models and most used models

Fine-tuning: Bayesian optimization

Class imbalance: Threshold moving (Youden index)

Model performance:

- ❑ Discrimination
- ❑ Calibration
- ❑ Decision making

3.Model explanation and deployment

Model explanation and simplification: SHAP

Model Deployment: Web calculator (Streamlit)

Method – selection of candidate features and prediction time points

Social-demographics: i.e., Gender, Age, Education, Occupation

Physical status: i.e., Comorbidity, Pain history, Analgesic use

Mental status: i.e., Anxiety, Depression, Sleep disorder, Stress reaction

Anesthesia-surgical factors: i.e., ASA, Surgical site, Surgical month

Pre

Lab test: i.e., Complete blood count
Liver and kidney function test,
Coagulation tests, Electrolytes

Nurse test: i.e., Vital signs, Fall risk,
Self-care ability, Thrombosis risk, Ulcer risk.

**Prediction Time 1:
before the surgery**

Surgical: i.e., Surgical duration, Surgery type, Surgical grade, Blood loss.

Vital signs: i.e., Systolic pressure, Diastolic pressure, Mean arterial pressure, Heart rate

Intra

Anesthesia: i.e., Anesthesia method, Nerve block, Sedative medication, NSAIDs, Esketamine, Dexmedetomidine, Opioids, Muscle relaxant, Vasoactive medication, Anesthetic adjuvant medication, Crystalloid input, Colloid input, Intraoperative blood transfusion.

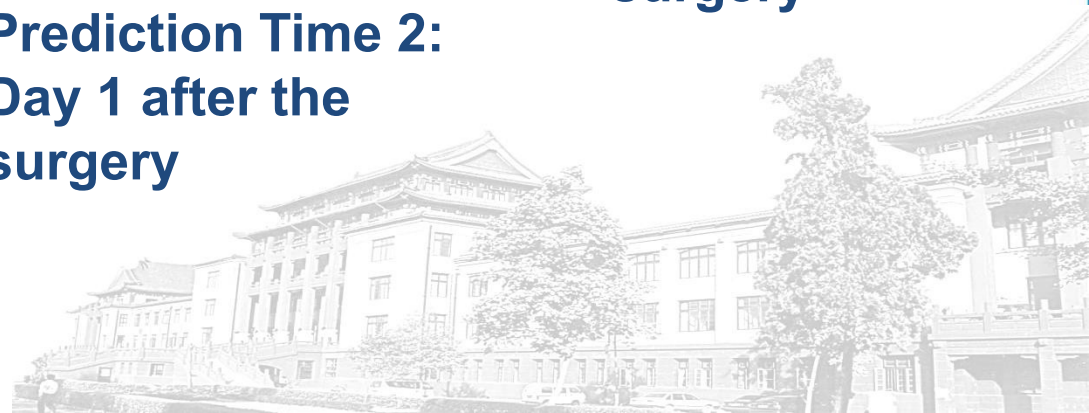
**Prediction Time 2:
Day 1 after the surgery**

Post

Pain management: i.e., acute pain at POD 1/3, PCA, NSAIDs at POD 1/2/3, Opioids at POD1/2/3

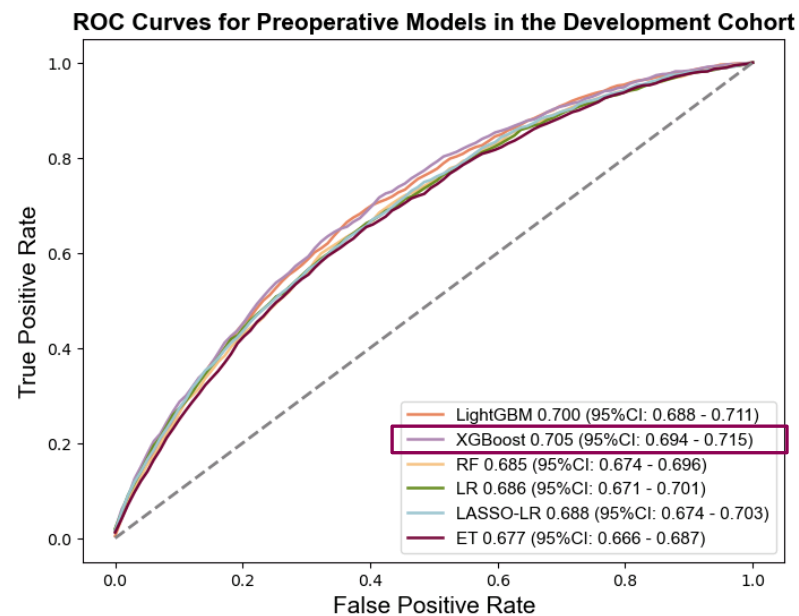
Rehabilitation: i.e., Length of hospitalization, Hospitalizing expenses, Rehabilitation at POD 30, Subacute pain at POD30

**Prediction Time 3:
Day 30 after the surgery**

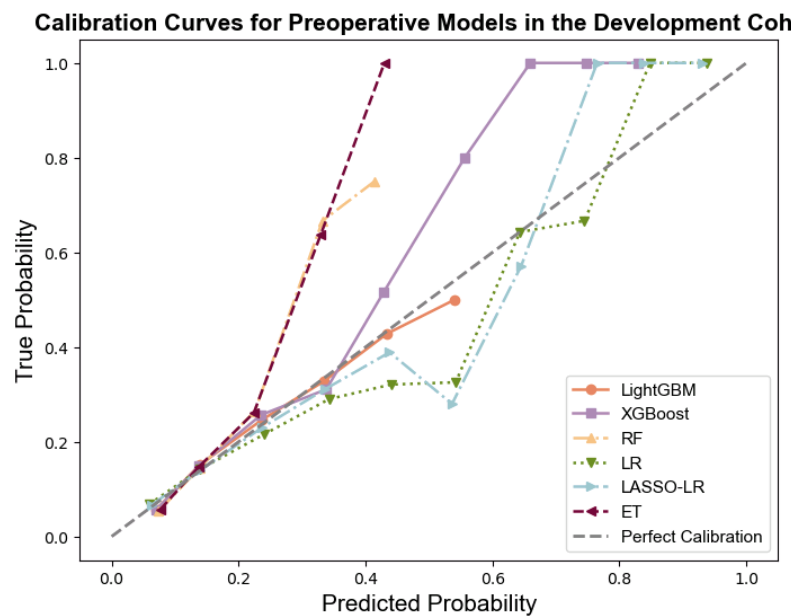


Result – Model selection (example. preoperative model)

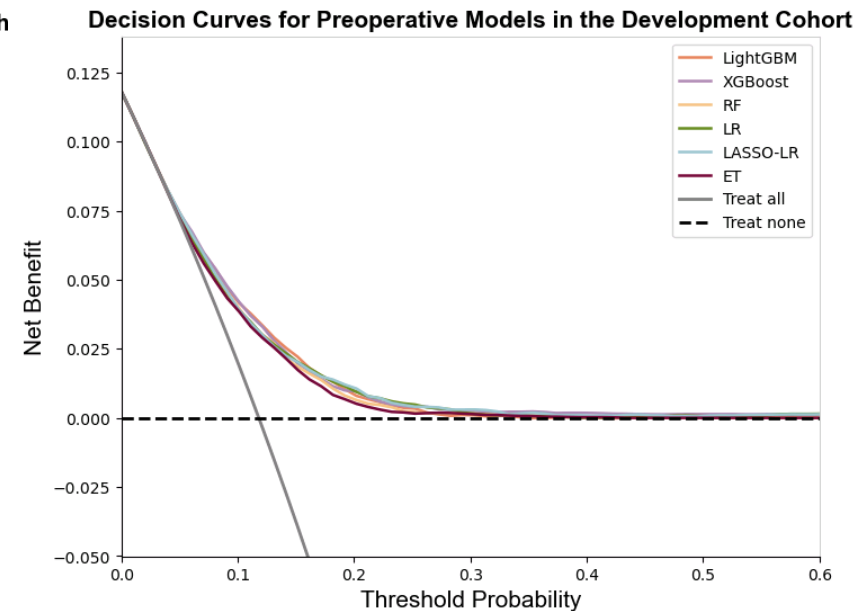
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B.



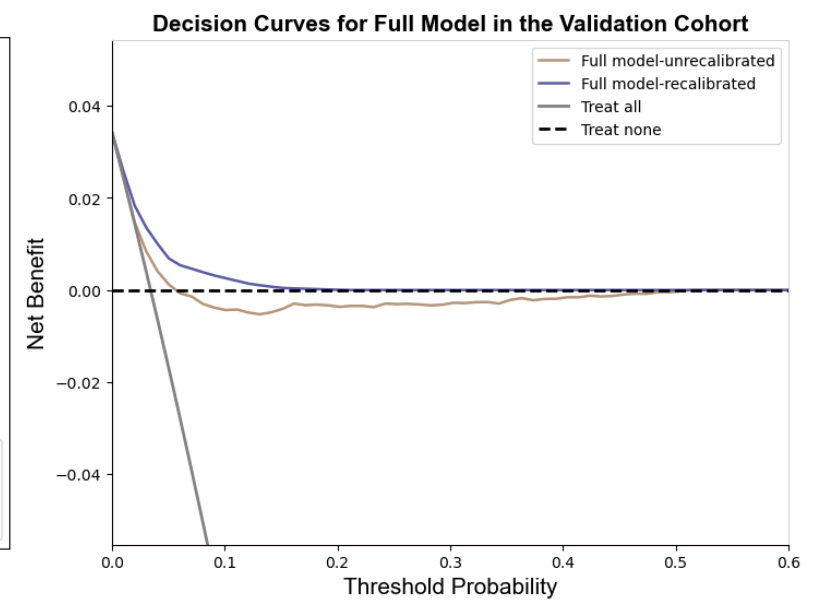
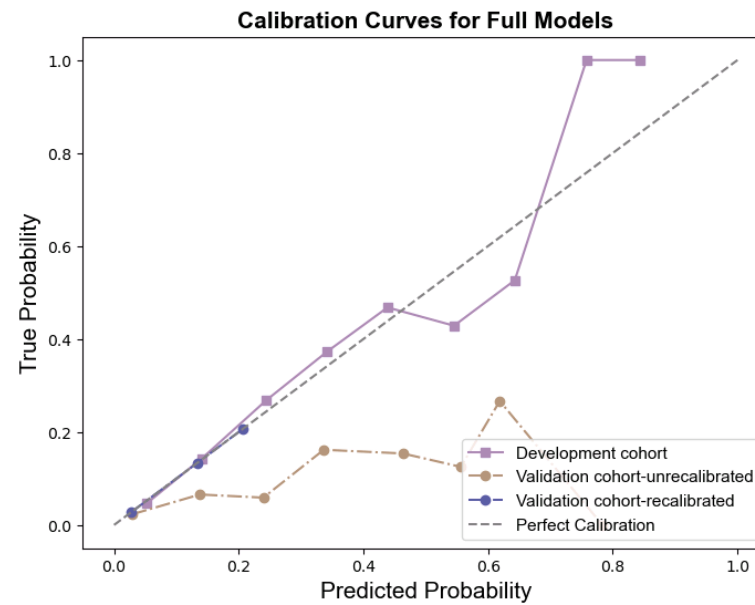
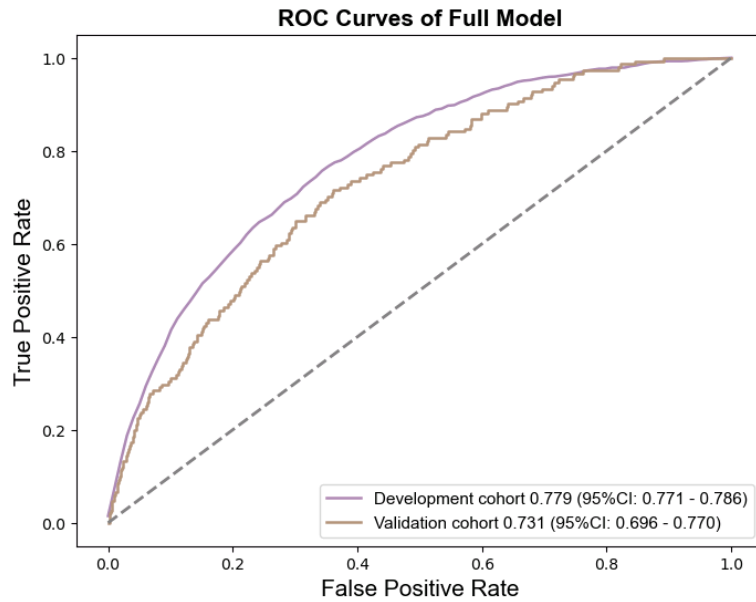
C.



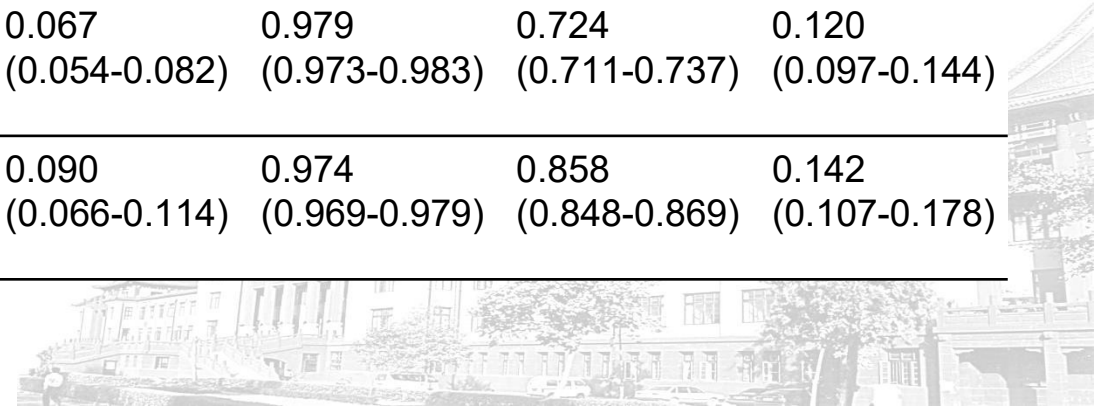
ML

algorithms	AUROC	AUPRC	Sensitivity	Specificity	PPV	NPV	Accuracy	F1 score
ET	0.677 (0.667-0.688)	0.228 (0.215-0.240)	0.684 (0.631-0.742)	0.598 (0.543-0.648)	0.188 (0.180-0.196)	0.935 (0.929-0.943)	0.608 (0.566-0.646)	0.293 (0.286-0.301)
Lasso-LR	0.688 (0.674-0.702)	0.248 (0.230-0.265)	0.642 (0.605-0.682)	0.644 (0.606-0.682)	0.197 (0.186-0.207)	0.931 (0.927-0.936)	0.643 (0.614-0.673)	0.300 (0.289-0.309)
LightGBM	0.700 (0.687-0.710)	0.236 (0.225-0.247)	0.680 (0.635-0.727)	0.639 (0.595-0.680)	0.204 (0.193-0.216)	0.938 (0.932-0.944)	0.644 (0.609-0.675)	0.312 (0.301-0.324)
LR	0.686 (0.670-0.701)	0.249 (0.230-0.269)	0.662 (0.615-0.708)	0.625 (0.580-0.671)	0.194 (0.183-0.207)	0.933 (0.928-0.938)	0.630 (0.593-0.664)	0.298 (0.286-0.311)
RF	0.685 (0.674-0.695)	0.236 (0.221-0.251)	0.668 (0.620-0.718)	0.630 (0.592-0.666)	0.196 (0.189-0.202)	0.935 (0.929-0.941)	0.634 (0.606-0.661)	0.301 (0.295-0.308)
XGBoost	0.705 (0.695-0.714)	0.253 (0.242-0.265)	0.709 (0.670-0.747)	0.619 (0.575-0.668)	0.203 (0.191-0.218)	0.941 (0.938-0.945)	0.630 (0.596-0.667)	0.314 (0.191-0.218)

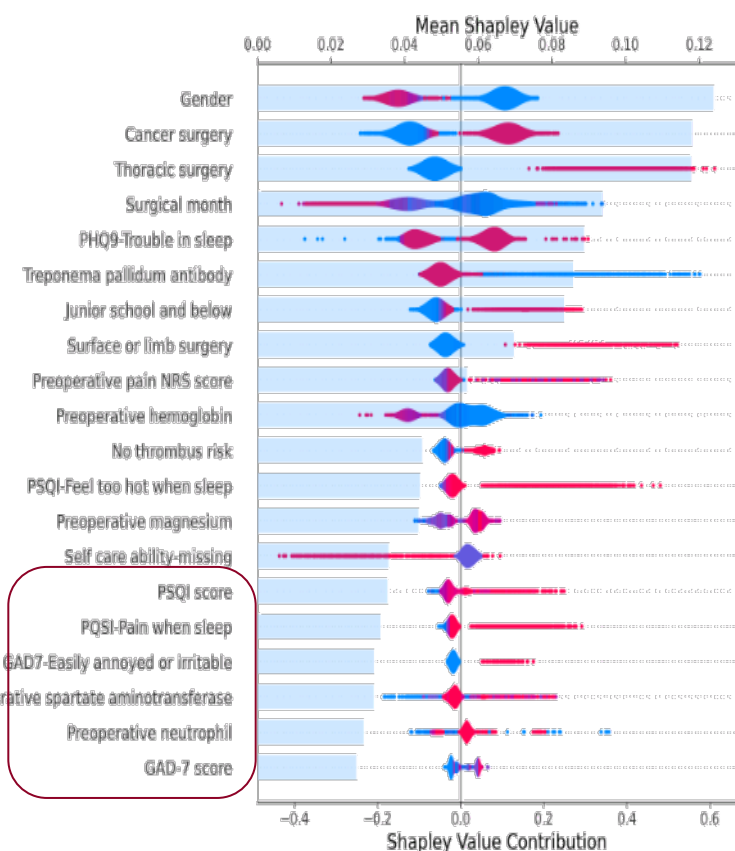
result - model performance (results of external validity)



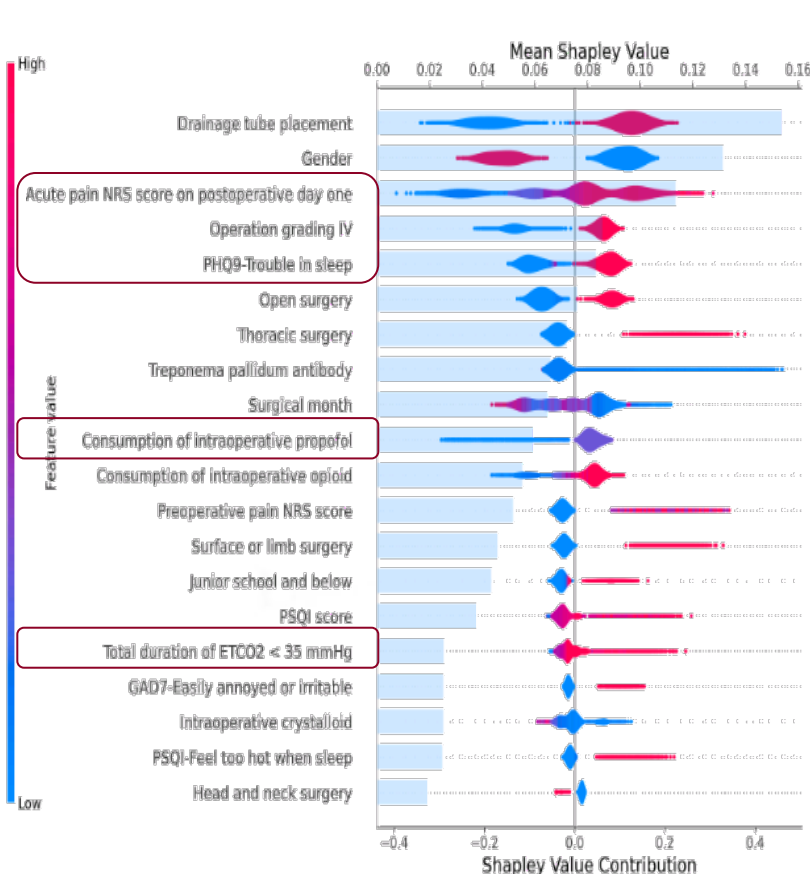
Model	AUROC	AUPRC	Sensitivity	Specificity	PPV	NPV	Accuracy	F1 score
Preoperative model	0.678 (0.637-0.718)	0.076 (0.038-0.046)	0.583 (0.506-0.660)	0.633 (0.619-0.647)	0.053 (0.043-0.065)	0.977 (0.971-0.983)	0.631 (0.617-0.646)	0.098 (0.080-0.117)
Postoperative model-Day 1	0.707 (0.670-0.743)	0.074 (0.035-0.043)	0.550 (0.470-0.629)	0.730 (0.717-0.744)	0.067 (0.054-0.082)	0.979 (0.973-0.983)	0.724 (0.711-0.737)	0.120 (0.097-0.144)
Postoperative model- Day 30	0.731 (0.693-0.770)	0.093 (0.070-0.129)	0.344 (0.268-0.420)	0.876 (0.866-0.886)	0.090 (0.066-0.114)	0.974 (0.969-0.979)	0.858 (0.848-0.869)	0.142 (0.107-0.178)



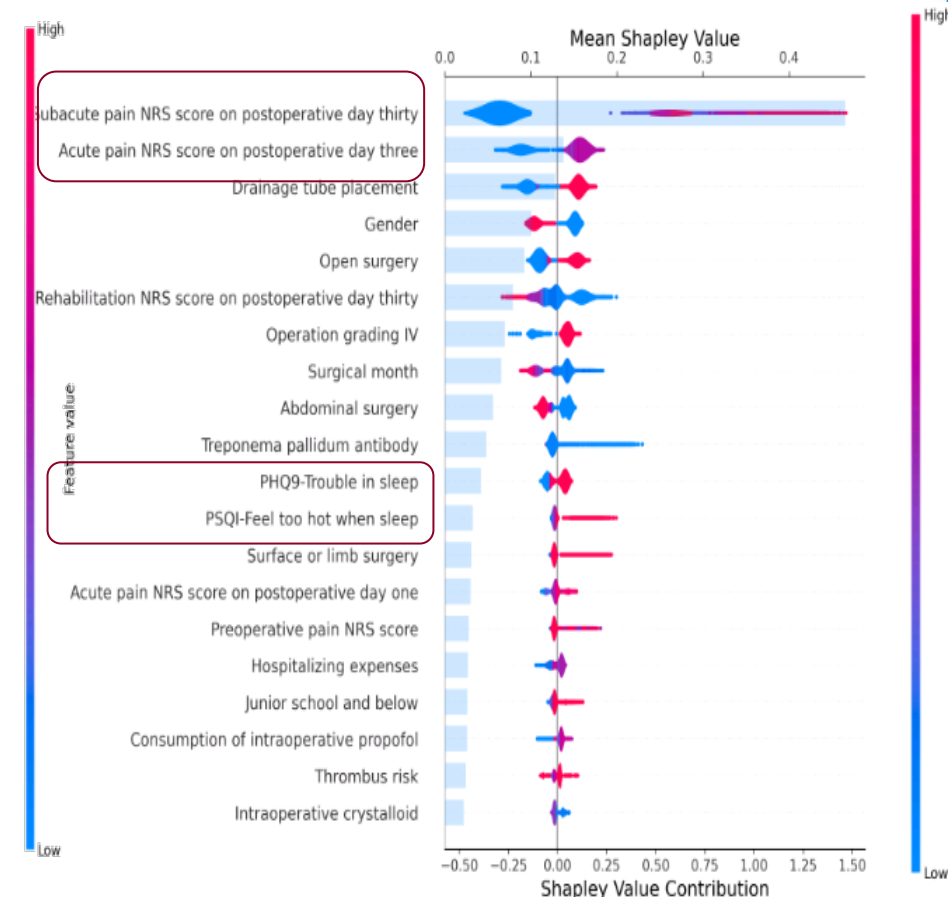
Result - Model explanation



TOP20 features of preoperative model



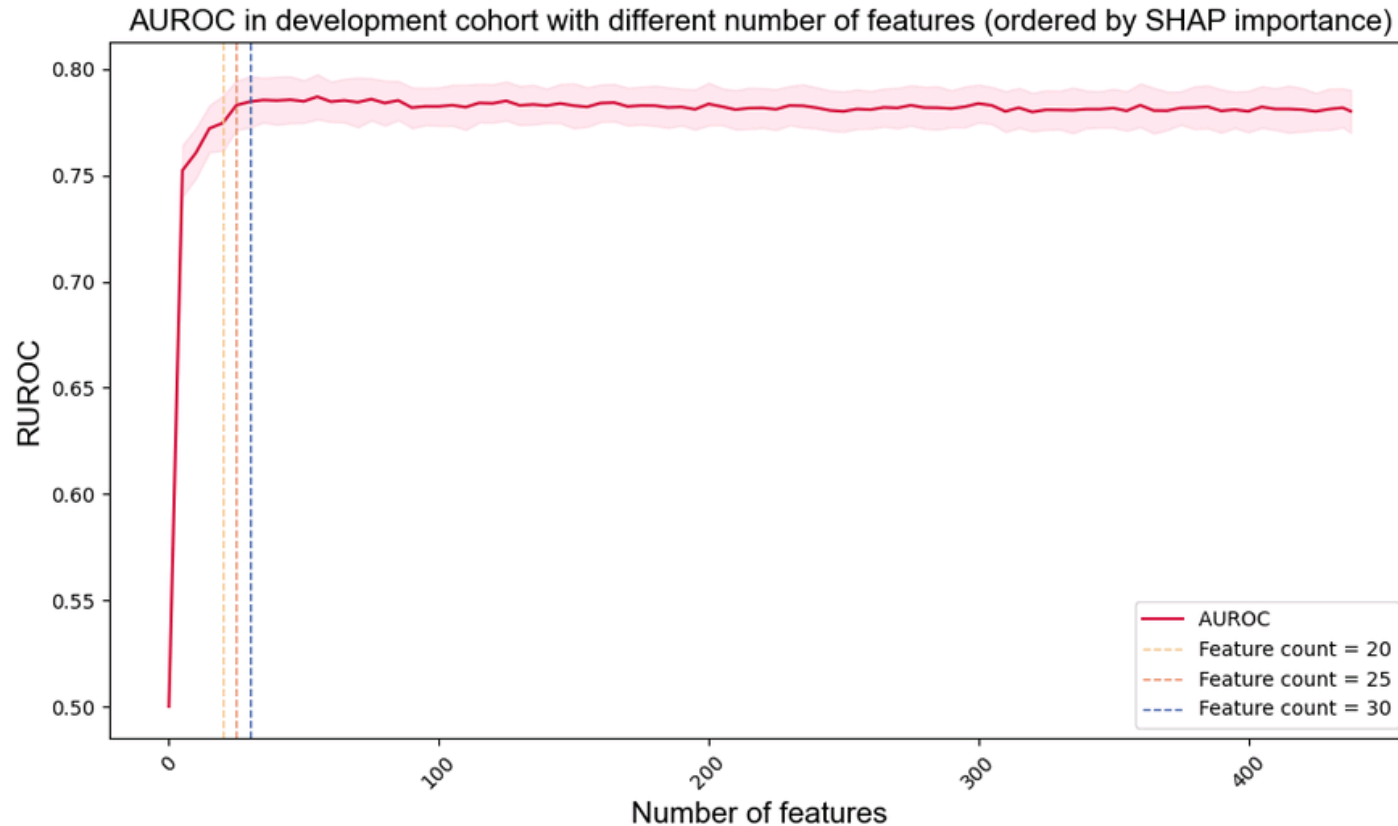
TOP20 features of postoperative model (Day 1)



TOP20 features of postoperative model (Day 30)



Result - Model simplification



- the model achieved optimal performance with the fewest features when the number of features reached 25

Feature count	AUROC	P-value*
TOP20	0.775	0.00183
TOP25	0.783	0.48588
TOP30	0.785	-

*corrected paired t-test, compared with TOP30



[illegible]

(<https://cpspcsac-b6phpoq23gzrgxq9njzjm.streamlit.app/>)



Implications:

- ❖ CPSP can be predicted **early and accurately**
- ❖ Psychological & pain-management factors are critical targets
- ❖ A model incorporating up to 25 key features achieved satisfactory predictive performance, which is ready for integration into clinical workflow



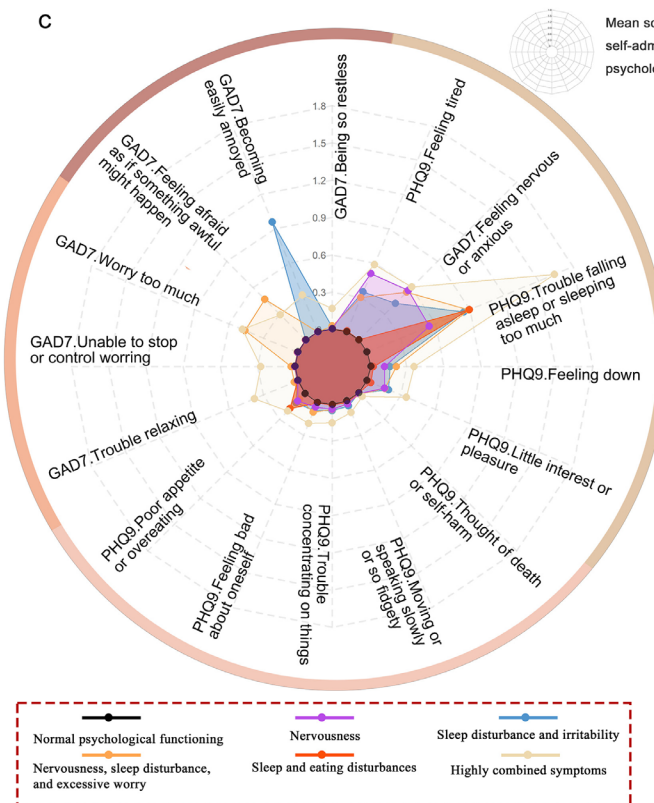
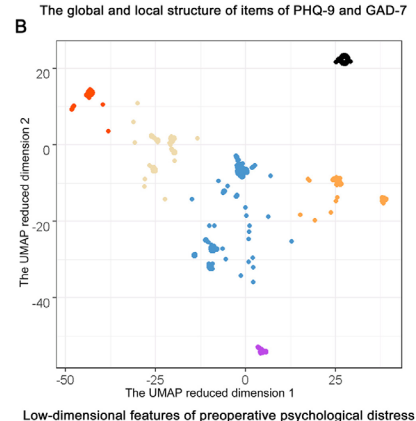
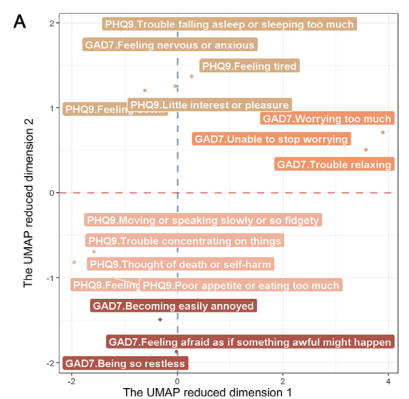


Project 4: The impact of intraoperative xxxx use on CPSP: a target trial emulation analysis and a clinical randomization trial (ongoing)

STEP1: Associations identified from the cohort

Associations between pre-operative psychological distress and chronic postsurgical pain (CPSP), *British Journal of Anesthesia*, 2023

STEP2: Machine learning-based identification of preoperative psychological distress and its association with surgery-related outcomes, *Depression and Anxiety* 2025



Intraoperative anesthesia	Postoperative length of stay, days, β with 95% CI ^b	Nausea/ Vomiting, β with 95% CI ^b	Postoperative pain ^e , β with 95% CI ^b			
			Pain during resting		pain during movement	
			Ref	Ref	Ref	Ref
Ref	Ref	Ref	Ref	Ref	Ref	Ref
(1.03, 1.59)	0.39 (0.11, 0.67)	0.05 (-0.01, 0.12) -0.01 (-0.04, 0.03)	-0.03 (-0.11, 0.05) -0.01 (-0.07, 0.04)	0.10 (0.00, 0.21) 0.13 (0.04, 0.23)		
(0.77, 1.71)	0.12 (-0.38, 0.62)	0.11 (-0.01, 0.23) 0.04 (-0.02, 0.11)	0.14 (0.00, 0.28) 0.20 (0.10, 0.29)	0.43 (0.24, 0.62) 0.47 (0.29, 0.64)		
(0.99, 1.52)	0.27 (0.00, 0.55)	0.08 (0.01, 0.15) 0.02 (-0.02, 0.05)	0.10 (0.02, 0.18) 0.04 (-0.01, 0.10)	0.27 (0.17, 0.38) 0.23 (0.13, 0.32)		
(0.88, 1.52)	0.30 (-0.04, 0.63)	0.12 (0.04, 0.20) 0.04 (-0.01, 0.08)	0.33 (0.24, 0.43) 0.10 (0.04, 0.17)	0.59 (0.46, 0.72) 0.45 (0.33, 0.57)		
(0.95, 1.37)	0.27 (0.04, 0.49)	0.12 (0.07, 0.18) 0.05 (0.02, 0.08)	0.20 (0.13, 0.26) 0.14 (0.09, 0.18)	0.39 (0.31, 0.48) 0.38 (0.30, 0.45)		
Ref	Ref	Ref	Ref	Ref	Ref	Ref
(0.55, 1.69)	0.48 (-0.21, 1.17)	0.29 (0.12, 0.46) 0.12 (0.02, 0.21)	0.44 (0.24, 0.63) 0.39 (0.25, 0.52)	0.57 (0.30, 0.83) 0.55 (0.31, 0.79)		
	0.5 1 1.5	-0.5 0 0.5	-0.5 0 0.5	-0.5 0 0.5	-0.5 0 0.5	-0.5 0 0.5
	1 day after surgery		3 days after surgery			



Project 4: The impact of intraoperative xxxx use on CPSP: a target trial emulation analysis and a clinical randomization trial (ongoing)

STEP3: Research question: Among patients identified with abnormal psychological status, can the use of anesthetic agents with antidepressant effects reduce CPSP ?

- a target trial emulation analysis based on cohort data**





14,972 Participants in the CSAC
from July 2020 to April 2025 at West China
Hospital

2,014 Excluded
8 withdraw
1,899 missing data on anesthesia
information
101 with missing data on surgery
6 with complication before surgery

12,958 Participants for analysis

9,033 with psychological distress risk
• 188 with **intraoperative xxx**
• 8,845 with other intraoperative
anesthetics/

3,925 with normal psychological
functioning
• 75 with intraoperative xxx
• 3,850 with other intraoperative
anesthetics



Methods: Target trial emulation framework

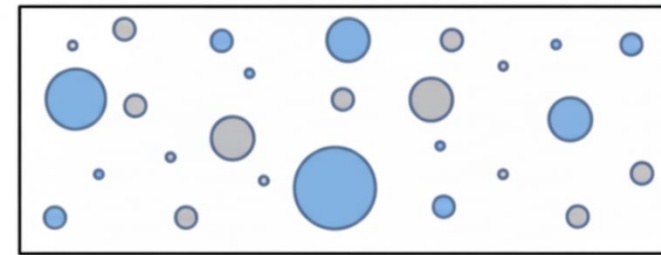
Randomization is simulated by propensity score matching (PSM):

- **Model :** **treatment** ~ age, sex, education, occupation, BMI, smoking status, dirking status, Charlson comorbidity index (CCI), inpatient diagnosis, ASA grade, site of surgery, type of surgery, surgical wound classification, preoperative antibiotic use, and age *inpatient diagnosis
- **Matching Methods:** Greedy nearest neighbor matching
- **Ratio:**1:20

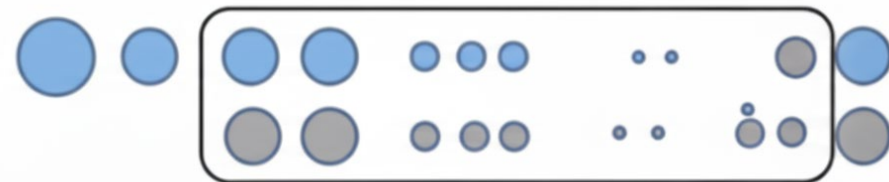
Probability of treatment

$$P(\text{treatment}) = f(\beta_0 + \beta_1 \text{Age} + \beta_2 \text{Sex} + \dots) \Rightarrow$$

Propensity Score



before matching

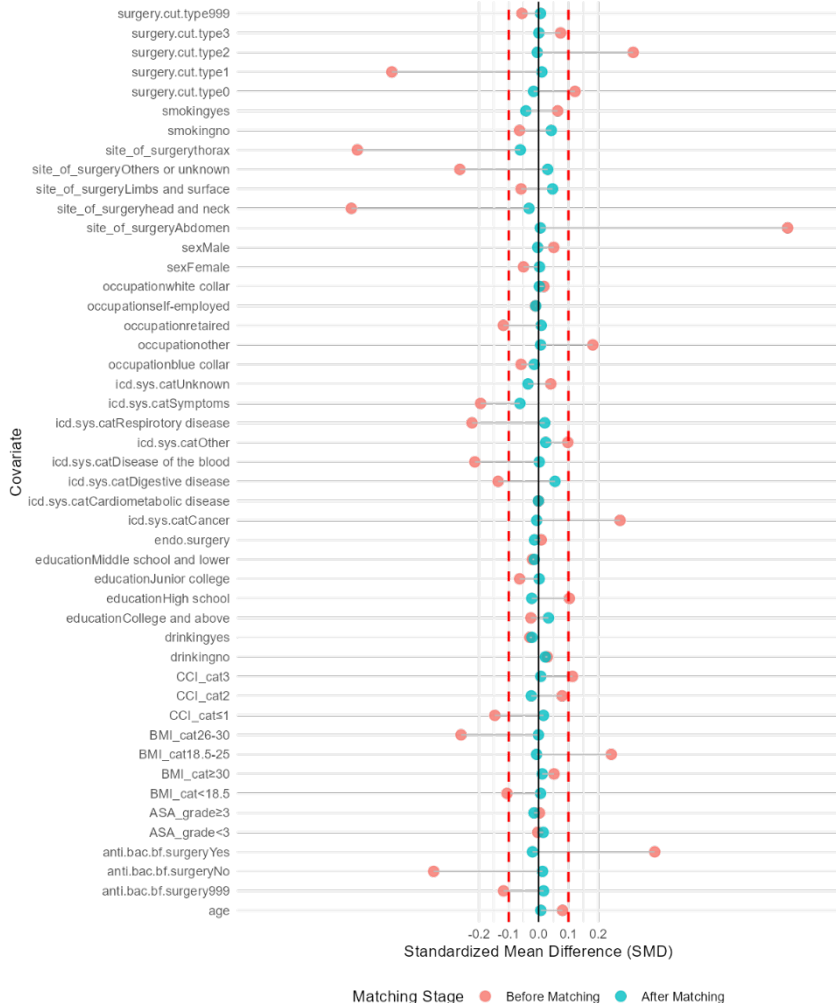


after matching

- Standardized mean difference (SMD) between intraoperative xxxxx/xxx-free individuals before/after matching by PSM (1:20)

Individuals with ML-identified psychological distress pattern

Standardized Mean Differences Before and After Matching



Unbalance

Balance

Unbalance

SMD
<10%

Individuals without ML-identified psychological distress pattern

Standardized Mean Differences Before and After Matching





- **Conditional logistic regression :**

Modle1: Outcome ~ treatment+strata (subclass)

Modle2: Outcome ~ treatment+strata (subclass)+Intraoperative anesthetic drugs (opiates, muscle relaxant, and other sedatives) and intraoperative antibiotic administration

Pain	Individuals with ML-identified psychological distress pattern				Individuals with ML-identified psychological distress pattern			
	Events in exposed group	Events in unexposed group	Odds ratio (95%CI)		Events in exposed group	Events in unexposed group	Odds ratio (95%CI)	
			Modle 1	Modle 2			Modle 1	Modle 2
3 day	146 (77.66%)	2284 (74.4%)	1.09 (0.91, 1.30)	0.99 (0.82, 1.20)	45 (60%)	862 (69.91%)	0.76 (0.56, 1.03)	0.76 (0.56, 1.03)
1 month	68 (36.17%)	1213 (39.51%)	0.99 (0.76, 1.29)	0.95 (0.71, 1.25)	23 (30.67%)	360 (29.2%)	1.03 (0.67, 1.58)	0.98 (0.63, 1.51)
3 month	25 (13.3%)	402 (13.09%)	1.06 (0.69, 1.65)	0.98 (0.61, 1.59)	6 (8%)	100 (8.11%)	0.93 (0.40, 2.15)	0.89 (0.37, 2.12)
6 month	6 (3.19%)	218 (7.1%)	0.42 (0.18, 0.98)	0.37 (0.15, 0.91)	2 (2.67%)	44 (3.57%)	0.63 (0.15, 2.66)	0.82 (0.18, 3.72)
12 month	5 (2.66%)	134 (4.36%)	0.60 (0.24, 1.52)	0.50 (0.19, 1.36)	1 (1.33%)	35 (2.84%)	0.47 (0.06, 3.47)	0.56 (0.07, 4.62)



Project 4: The impact of intraoperative xxxx use on CPSP: a target trial emulation analysis and a clinical randomization trial (ongoing)

STEP3: Research question: Among patients identified with abnormal psychological status, can the use of anesthetic agents with antidepressant effects reduce the incidence of CPSP ?

- **a target trial emulation analysis based on cohort data**
- **a multicenter RCT**
 - Screens high-risk patients using our ML model
 - Optimizes sample size and drug protocols from real-world data
 - Is now in active enrollment

This is a data-driven precision intervention, moving from observation to causality.



Across three integrated lines of evidence



Focus	Contribution
Psychological risk	Identify high-risk population
Genetic factors	Reveal biological pathways---further targets for drug development
Prediction & intervention	Translate findings into clinical tools

Advance **personalized pain management**

Acknowledgement



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Faculty of Medicine, University of
Iceland, Iceland



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Head of Department of Computer Science
Chair of Computer Science 5 (Pattern
Recognition)



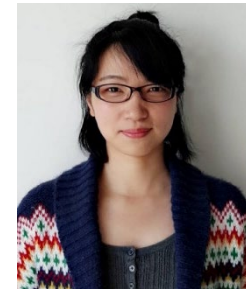
Prof. Qian Li
Department of Anesthesia,
West China Hospital, China



Prof. Bowen Ke
Department of Anesthesia, National-Local Joint
Engineering Research Centre of Translational
Medicine of Anesthesiologist, West China
Hospital, China



Prof. Xingdong Chen
Fudan University



Prof. Dan Wu
School of Public Health,
Nanjing Medical University,
Nanjing, China



— 四川大学 —
华西医院
WEST CHINA HOSPITAL, SICHUAN UNIVERSITY



終

感謝
華西醫院

Thank you for listening!



Joy Lab

@JoyLab14169974

A team dedicated to patient cohort&database construction and epidemiological research

keywords: stress, traumatic events, PTSD, lifestyle, disease network

📄 Medical & Health 📍 Chengdu, Sichuan, China 🕒 Born April 1, 1994

📅 Joined July 2022

Twitter: @JoyLab14169974

Email: songhuan@wchscu.cn