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ORIGINAL RESEARCH

# Predictive Scores for Identifying Chronic Opioid Dependence After General Anesthesia Surgery

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**Purpose:** To address the prevalence and risk factors of postoperative chronic opioid dependence, focusing on the development of a predictive scoring system to identify high-risk populations.

**Methods:** We analyzed data from the Taiwan Health Insurance Research Database spanning January 2016 to December 2018, encompassing adults undergoing major elective surgeries with general anesthesia. Patient demographics, surgical details, comorbidities, and preoperative medication use were scrutinized. Wu and Zhang's scores, a predictive system, were developed through a stepwise multivariate model, incorporating factors significantly linked to chronic opioid dependence. Internal validation was executed using bootstrap sampling.

**Results:** Among 111,069 patients, 1.6% developed chronic opioid dependence postoperatively. Significant risk factors included age, gender, surgical type, anesthesia duration, preoperative opioid use, and comorbidities. Wu and Zhang's scores demonstrated good predictive accuracy (AUC=0.83), with risk categories (low, moderate, high) showing varying susceptibility (0.7%, 1.4%, 3.5%, respectively). Internal validation confirmed the model's stability and potential applicability to external populations.

**Conclusion:** This study provides a comprehensive understanding of postoperative chronic opioid dependence and introduces an effective predictive scoring system. The identified risk factors and risk stratification allow for early detection and targeted interventions, aligning with the broader initiative to enhance patient outcomes, minimize societal burdens, and contribute to the nuanced management of postoperative pain.

**Keywords:** chronic opioid dependence, postoperative care, predictive scores, general anesthesia, surgical risk stratification

## Introduction

Chronic pain, persisting for over six months, is a pervasive issue affecting approximately 30% of patients in developed countries.[1] The Centers for Disease Control and Prevention's (CDC) 2023 analysis in the United States highlighted that 20.9% of adults experienced chronic pain, with 6.9% facing high-impact chronic pain, significantly impacting daily activities.[2] Various demographic factors, disabilities, and specific health conditions contribute to higher prevalence rates.[2] Chronic Postsurgical Pain (CPSP) contributes significantly to chronic pain cases, affecting 10–50% of surgical patients.[3,4] The economic burden of CPSP is substantial, adding to the costs associated with chronic pain, including



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direct medical expenses and lost productivity.[5] Moreover, CPSP poses challenges in pain management, often leading to prolonged opioid use and associated risks.[6] Tailored prevention and management strategies for CPSP become crucial in mitigating its broader implications on public health, the economy, and individual well-being.

The presentation of patients at risk for developing CPSP is diverse, encompassing both surgical and patient-related risk factors.[7–12] Factors contributing to CPSP risk include surgical complexity, nerve damage, psychosocial aspects, and genetics.[7–14] Risk reduction strategies, such as psychotherapies, modifying or avoiding surgery, and careful anesthetic management, aim to alleviate the incidence of CPSP.[8,15–19] Coordinated perioperative care and follow-up are crucial for addressing and managing CPSP comprehensively.[20,21] Long-term opioid use, often resulting from CPSP,[6,7] extends beyond pain management, leading to dependence, tolerance, and various side effects.[22–26] Persistence of opioid use is associated with specific risk factors, and the practice implications emphasize judicious prescription, risk factor screening, and comprehensive discussions with patients.[27–29] Considering the potential implications of postoperative chronic opioid dependence, such as inducing dementia, elevating cancer risk, and increasing cancer mortality,[22–26] prioritizing the high-risk group becomes imperative. The multifaceted interplay between CPSP and chronic opioid dependence underscores the need for nuanced approaches to enhance patient outcomes and minimize societal burdens in postoperative pain management.

Creating predictive scores for postoperative chronic opioid use is vital for early detection of high-risk populations, facilitating timely intervention, and implementing non-opioid analgesics or alternative pain control methods such as psychotherapies. This proactive approach aims to prevent the development of chronic opioid dependence, thereby mitigating potential individual, social, family, and national economic burdens. By addressing this pressing issue, we strive to enhance patient outcomes, minimize societal burdens, and contribute to a more comprehensive understanding of postoperative pain dynamics.

# Patients and Methods

## Study Population

This investigation utilized the extensive dataset from the Taiwan National Health Insurance (NHI) Research Database (NHIRD), covering the period from January 2008 to December 2018, with follow-up extending until December 31, 2020. The NHIRD, boasting a considerable cohort of approximately 27.38 million beneficiaries, serves as a robust repository of registration records and unaltered claims data. This database is a formidable resource due to its inclusion of comprehensive details, such as patient identification numbers, birthdates, gender, and diagnoses coded according to the International Classification of Diseases, Ninth and Tenth Revision, Clinical Modification (ICD-9-CM and ICD-10-CM). Additionally, it captures treatment specifics, financial outlays, dates of hospitalization commencement and cessation, and even mortality dates.[30] All these datasets, encrypted within the NHIRD archives, were meticulously interconnected using patient identification numbers, providing a comprehensive and panoramic view of the healthcare landscape.

## Inclusion and Exclusion Criteria for Patient Selection

In our investigation, we included individuals aged 18 years or older who underwent significant inpatient elective surgery necessitating general anesthesia and required hospitalization for more than one day between 2008 and 2018 in Taiwan.[24] The selected surgical types included spine surgery, open thoracic surgery, knee or hip surgery, mastectomy, or abdominal surgery, including laparoscopic surgery, specifically chosen for their association with a higher incidence of persistent postoperative pain.[31–35] The index date was defined as the surgical date.

Chronic postsurgical pain is defined as pain that persists for at least three months following a surgical procedure.[36] In our study, we define Chronic Opioid Dependence based on the use of opioids, as detailed in Supplemental Table 1, which captures opioids use data from the NHIRD for at least three months post-surgery.

Patients were deemed ineligible if their surgery was minor and did not require general anesthesia, if they were younger than 18 years old, or if they had a history of cancer that might induce cancer pain. Additionally, patients with a diagnosis of chronic pain, long-term analgesic use (> 28 cumulative Defined Daily Dose before the index date), or multiple surgical histories were excluded. Ensuring that all enrolled patients were undergoing their first surgery under general anesthesia aimed to distinguish Chronic Opioid Dependence from the effects of previous multiple surgeries. Patients with incomplete baseline information, as detailed in Supplemental Table 2, were also excluded from our study. In our study, we also excluded patients with known psychiatric diseases, such as schizophrenia, post-traumatic stress disorder (PTSD), substance use disorders, personality disorders, obsessive-compulsive disorder (OCD), and attention-deficit/hyperactivity disorder (ADHD), were excluded from the study to avoid confounding factors. However, depression and anxiety were included and analyzed as risk factors in our study.

## Variables

Demographic characteristics and clinical parameters underwent thorough evaluation, encompassing a range of factors such as age, sex, income levels, urbanization, types of surgery, American Society of Anesthesiologists (ASA) physical status, duration of anesthesia (in hours), levels of the hospital, preoperative opioid use within 7 days, preoperative non-opioid analgesic use within 7 days, coexisting comorbidities associated with chronic pain, and CCI (Charlson Comorbidity Index) scores (as depicted in Supplemental Table 2).

## Evaluating Postoperative Chronic Opioid Dependence with Wu and Zhang's Scoring

The Wu and Zhang Predictive Scoring System was used to calculate cumulative risk scores by consolidating key risk factors. In our analysis, detailed in Table 1, we assessed the predictive efficiency of this scoring system for postoperative

**Table 1** Assessment of Chronic Opioid Dependence Beyond 90 Days Postoperatively Using Wu and Zhang's Predictive Scores in Patients Undergoing General Anesthesia Surgery

| Wu and Zhang's Predictive Scoring System | Number of No Chronic Opioid Dependence | Number of Chronic Opioid Dependence | Chronic Opioid Dependence Incidence |
|---|---|---|---|
| 1 | 239 | 0 | 0.0% |
| 2 | 5912 | 32 | 0.5% |
| 3 | 11,351 | 51 | 0.5% |
| 4 | 13,006 | 106 | 0.8% |
| 5 | 15,053 | 133 | 0.9% |
| 6 | 15,312 | 167 | 1.1% |
| 7 | 12,110 | 183 | 1.5% |
| 8 | 8977 | 153 | 1.7% |
| 9 | 7040 | 169 | 2.4% |
| 10 | 5455 | 134 | 2.4% |
| 11 | 4450 | 153 | 3.3% |
| 12 | 3420 | 130 | 3.7% |
| 13 | 2625 | 114 | 4.2% |
| 14 | 1694 | 79 | 4.5% |
| 15 | 1077 | 58 | 5.1% |
| 16 | 696 | 58 | 7.7% |

(*Continued*)

**Table 1** (Continued).

| Wu and Zhang's Predictive Scoring System | Number of No Chronic Opioid Dependence | Number of Chronic Opioid Dependence | Chronic Opioid Dependence Incidence |
|---|---|---|---|
| 17 | 394 | 31 | 7.3% |
| 18 | 233 | 24 | 9.3% |
| 19 | 116 | 20 | 14.7% |
| 20 | 52 | 8 | 13.3% |
| 21 | 25 | 4 | 13.8% |
| 22 | 10 | 2 | 16.7% |
| 23 | 6 | 1 | 14.3% |
| 24 | 2 | 1 | 33.3% |
| 25 | 1 | 1 | 50.0% |
| 26 | 0 | 1 | 100.0% |

chronic opioid dependence. This evaluation involved a rigorous analysis to determine the correlation between cumulative risk scores and the risk of developing postoperative chronic opioid dependence.

## Area Under the Curve of Wu and Zhang's Predictive Scores for Postoperative Chronic Opioid Dependence

The area under the ROC curve (AUC) was utilized to evaluate the predictive ability of Wu and Zhang's scoring system for postoperative chronic opioid dependence. The AUC serves as a comprehensive metric for assessing the overall discriminatory power of the predictive model, providing insights into its accuracy in distinguishing between patients with and without chronic opioid dependence following surgery.

## Validating Wu and Zhang's Predictive Scores for Postoperative Chronic Opioid Dependence

To validate Wu and Zhang's Predictive Scores, we conducted ROC analysis using a bootstrap sample. The AUC was calculated to assess the overlap with the original predictive scores. Additionally, the DeLong test was performed to evaluate the statistical significance of the overlap. This internal validation process helps determine the potential applicability of the predictive model to other external populations.

## Risk Stratification with Wu and Zhang's Predictive Scoring Systems for Postoperative Chronic Opioid Dependence

Patients were categorized into three distinct groups based on risk scores generated from Wu and Zhang's predictive scoring system: low-risk (score 1–5), moderate-risk (score 6–8), and high-risk (score ≥9). These risk groups were then analyzed to evaluate variations in the risk of developing postoperative chronic opioid dependence within one year. Statistical analysis was performed to assess the significance of these differences.

## Statistical Analysis

We performed all statistical analyses using SAS for Windows (version 9.4; SAS Institute, Cary, NC, USA), with statistical significance set at $P < 0.05$. Crucial demographic parameters, including gender and age, were stratified and categorized accordingly, with patient age determined at the index date. The primary variables of interest included age, sex, income levels, urbanization, surgical types, ASA physical status, anesthesia duration (hours), hospital levels, preoperative opioid use within 7 days, preoperative non-opioid analgesic use within 7 days, coexisting comorbidities related to chronic pain, and CCI scores, as outlined in Supplemental Table 2. To assess group differences, chi-square tests and *t*-tests were utilized. *T*-tests evaluated dependent quantitative variables concerning independent categorical variables with two groups, while chi-square tests assessed associations between two categorical variables.

Significant factors were identified to construct Wu and Zhang's Predictive Scoring System for Chronic Opioid Dependence beyond 90 Days Postoperatively in Patients Following General Anesthesia Surgery. The forward stepwise selection method was employed to choose factors significantly predicting Chronic Opioid Dependence beyond 90 Days Postoperatively ($P < 0.05$; Table 2). Factors with a coefficient of >0 or an adjusted hazard ratio (aHR) of >1 were selected as risk factors, with points added based on the aHR.[37] Nonsignificant factors were eliminated using a modified forward selection technique in the stepwise method. Duplicate entry and removal approaches were used for forward selection and backward elimination, applying the "minimum F-to-enter" criterion. The model with the lowest Akaike information criterion (AIC) estimated Chronic Opioid Dependence beyond 90 Days Postoperatively.[38] Patients were categorized into three risk groups based on their scores, predicting higher risk for those with moderate to high risk scores. Receiver operating characteristic (ROC) curves were created for each score, and areas under the ROC curves were determined.

We utilized bootstrap sampling,[39] a resampling technique treating the original sample as the population, and samples were drawn repeatedly with replacement. Bootstrap resampling enhances model assessment credibility by deriving distributions for performance metrics.[40] This process evaluates the model's stability and generalization capacity across scenarios. The DeLong test rigorously compared diagnostic test performance, assessing differences in ROC curve areas between Bootstrap validation and Wu and Zhang's predictive scoring system.[39] Kaplan-Meier analysis evaluated Chronic

**Table 2** Stepwise Multivariate Cox Proportional Hazards Model for Chronic Opioid Dependence Beyond 90 Days Postoperatively in Patients Following General Anesthesia Surgery

| Factor | aHR* | 95% CI | | *P* value | Assigned points |
|---|---|---|---|---|---|
| **Age > 60 years-old** | 1.48 | 1.35 | 1.84 | <0.0001 | 1 |
| **Male** | 1.34 | 1.04 | 1.71 | 0.0212 | 1 |
| **Rural residents** | 1.45 | 1.21 | 1.99 | 0.0006 | 1 |
| **Knee or hip surgery** | 1.42 | 1.21 | 1.96 | <0.0001 | 1 |
| **Open thoracic surgery** | 1.27 | 1.43 | 3.16 | <0.0001 | 1 |
| **ASA scores=3** | 1.44 | 1.26 | 2.43 | 0.0364 | 1 |
| **ASA scores=4** | 2.34 | 1.46 | 3.75 | 0.0154 | 2 |
| **Anesthesia duration >2 hours** | 3.18 | 2.68 | 4.84 | <0.0001 | 3 |
| **Preoperative Opioid Use Within 7 Days** | 6.02 | 3.18 | 11.38 | <0.0001 | 6 |
| **Preoperative Non-Opioid Analgesic Use Within 7 Days** | 1.43 | 1.04 | 2.03 | 0.0302 | 1 |
| **Depression** | 2.39 | 1.14 | 3.70 | 0.0011 | 2 |
| **Anxiety** | 2.45 | 1.18 | 2.22 | 0.0179 | 2 |
| **Pressure Ulcer** | 1.47 | 1.57 | 6.40 | 0.0013 | 1 |
| **Diabetes** | 1.51 | 1.07 | 2.10 | 0.0202 | 2 |
| **CCI≥1** | 1.29 | 1.12 | 1.48 | 0.0005 | 1 |

**Abbreviations**: ASA, American Society of Anesthesiologists; CCI, Charlson Comorbidity Index; HR, Hazard Ratio; aHR, Adjusted Hazard Ratio; CI, Confidence Interval.

Opioid Dependence beyond 90 Days postoperatively using Wu and Zhang's predictive scoring system, with the Log rank test determining differences among risk groups. A two-tailed P value of <0.05 indicated statistical significance.

# Results

## Demographics of Postoperative Chronic Opioid Dependence

In this study, we conducted a comprehensive comparison of demographic characteristics between patients who experienced chronic opioid dependence beyond 90 days postoperatively and those without such dependence following surgery under general anesthesia. Among the 111,069 patients included, 1812 (1.6%) developed postoperative chronic opioid dependence, while 109,257 did not. Postoperative chronic opioid dependence was associated with older age, a higher proportion of male patients, lower income levels, rural residence, knee and hip surgery, spine surgery, open thoracic surgery, higher ASA scores, longer anesthesia duration (hours), surgeries in medical centers, preoperative opioid use within 7 days, preoperative non-opioid analgesic use within 7 days, and various comorbidities (including depression, anxiety, dysthymic disorder, peripheral vascular diseases, osteoporosis, gout, headache, rheumatoid arthritis, pressure ulcer, chronic obstructive pulmonary disease, acute respiratory distress, diabetes, hypertension, and hyperlipidemia). Additionally, patients with postoperative chronic opioid dependence exhibited higher CCI scores compared to those without chronic opioid dependence among individuals undergoing elective General Anesthesia Surgery (Supplemental Table 2).

## Postoperative Predictors of Chronic Opioid Dependence in General Anesthesia Surgery

Table 2 displays the significant factors identified through the stepwise method in the multivariate model for variable selection. Each risk factor received a score based on its adjusted hazard ratio (aHR). In the multivariate Cox proportional hazards model for postoperative chronic opioid dependence in elective general anesthesia surgery patients, the following factors emerged as significant independent contributors to chronic opioid dependence beyond 90 days postoperatively, along with their respective aHRs and assigned scores: age > 60 years-old (aHR: 1.48, score: 1), male (aHR: 1.34, score: 1), rural residents (aHR: 1.45, score: 1), knee or hip surgery (aHR: 1.42, score: 1), open thoracic surgery (aHR: 1.27, score: 1), ASA scores=3 (aHR: 1.44, score: 1), ASA scores=4 (aHR: 2.34, score: 2), anesthesia duration >2 hours (aHR: 3.18, score: 3), preoperative opioid use within 7 days (aHR: 6.02, score: 6), preoperative non-opioid analgesic use within 7 days (aHR: 1.42, score: 1), depression (aHR: 2.39, score: 2), anxiety (aHR: 2.45, score: 2), pressure ulcer (aHR: 1.47, score: 1), diabetes (aHR: 1.51, score: 2), and CCI ≥ 1 (aHR: 1.29, score: 1). These factors significantly enhance the predictive accuracy of chronic opioid dependence.

## Evaluating Postoperative Chronic Opioid Dependence with Wu and Zhang's Scoring

The risk of postoperative chronic opioid dependence varies across distinct score ranges: [score: 1–5, 0.7%], [score: 6–8, 1.4%], and [score: ≥9, 3.5%]. These risk categories, precisely delineated to represent varying degrees of susceptibility, include the following: low-risk (score 1–5), moderate risk (score 6–8), and high risk (score ≥9), as clarified in Table 3.

**Table 3** Chronic Opioid Dependence Assessment Beyond 90 Days Postoperatively Utilizing Wu and Zhang's Predictive Scores

| Wu and Zhang's Predictive Scoring System | Risk Group | Patients Following General Anesthesia Surgery, N (%) | Chronic Opioid Dependence Among Patients Following General Anesthesia Surgery, N (%) |
|---|---|---|---|
| **Score** | | | |
| **1–5** | **Low** | 45,883 (41.3%) | 322 (0.7%) |
| **6–8** | **Moderate** | 36,902 (33.2%) | 503 (1.4%) |
| **9–26** | **High** | 28,284 (25.5%) | 987 (3.5%) |

**Abbreviation**: N, Numbers.

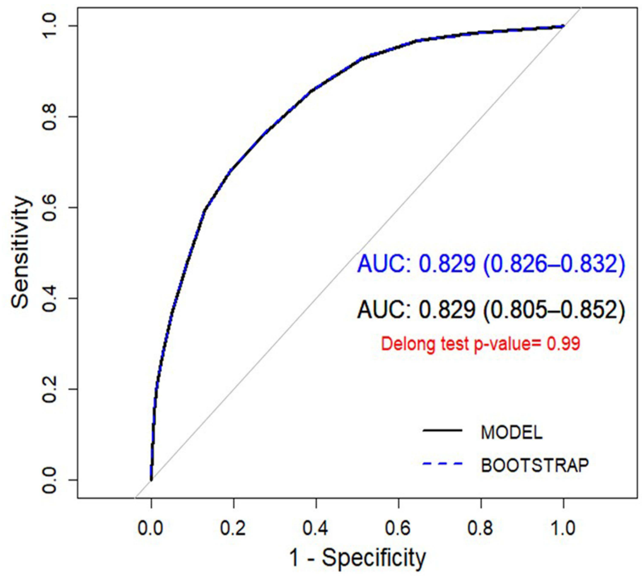


**Figure 1** ROC Curves: Areas Under the Curve for Wu and Zhang's Predictive Scores with Bootstrap Validation in Chronic Opioid Dependence Beyond 90 Days Postoperatively in Patients Undergoing General Anesthesia Surgery.
**Notes**: Wu and Zhang's predictive score exhibited substantial concordance with the BOOTSTRAP validation model, and the DeLong test revealed no statistically significant difference (p = 0.99).
**Abbreviation**: AUC, Area Under the Curve.

This categorization of risk groups enables us to identify surgical patients more prone to developing postoperative chronic opioid dependence.

## Area Under the Curve of Wu and Zhang's Predictive Scores for Postoperative Chronic Opioid Dependence

This AUC value of 0.83 indicates a good predictive ability of the scoring system for distinguishing between patients with and without chronic opioid dependence following surgery. The AUC is a comprehensive metric that assesses the overall discriminatory power of a predictive model. In this context, an AUC of 0.83 signifies a high level of accuracy in terms of sensitivity and specificity, implying that Wu and Zhang's predictive scores exhibit robust performance in identifying individuals at risk of postoperative chronic opioid dependence.

## Validating Wu and Zhang's Predictive Scores for Postoperative Chronic Opioid Dependence

Using this bootstrap sample, we conducted ROC analysis,[39] and the AUC closely overlapped with Wu and Zhang's predictive scores. Additionally, we performed the DeLong test, resulting in a p-value of 0.99, indicating substantial overlap (Figure 1).[39] This internal validation was further compared, suggesting that the predictive model trained on this sample might have potential applicability to other external populations if the differences between the two sets of results are minimal.

## Risk Stratification with Wu and Zhang's Predictive Scoring Systems for Postoperative Chronic Opioid Dependence

These risk groups demonstrated substantial variations in 1-year postoperative chronic opioid dependence risk (low-risk: 0.7%, moderate-risk: 1.4%, and high-risk: 3.5%). Statistical analysis affirmed the significance of these differences (Log rank test P < 0.001), as illustrated in Figure 2.

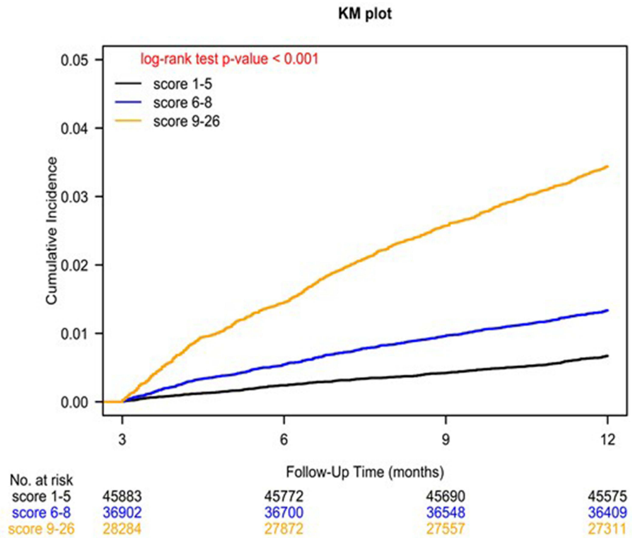


**Figure 2** Kaplan–Meier Cumulative Incidence Curves for Chronic Opioid Dependence Beyond 90 Days Postoperatively in Patients Undergoing General Anesthesia Surgery Stratified by Wu and Zhang's Predictive Scores Risk Groups.

## Discussion

Given the significant sequela associated with postoperative chronic opioid dependence, stemming from CPSP,[5,22–26] it becomes imperative to identify high-risk populations promptly. Timely identification of individuals at risk of chronic opioid dependence enables targeted interventions, including the utilization of non-opioid analgesics, psychotherapies, modifying or avoiding surgery, meticulous anesthetic management, and considering minimally invasive surgical approaches.[8,15–19] The primary objective of our study is to mitigate the risk of chronic opioid dependence and its subsequent repercussions. Through a concentrated emphasis on risk identification and preemptive measures, our study not only advances patient care but also contributes to the overarching endeavor of cultivating a healthcare paradigm that prioritizes individual well-being, minimizes societal burdens, and advocates for more efficacious and sustainable post-operative outcomes. Our study represents a groundbreaking initiative, standing out as the first to leverage a comprehensive dataset from the largest surgical population to craft innovative predictive scores for postoperative chronic opioid dependence (Table 3). The model's remarkable accuracy, reflected in an AUC of 0.83 (Figure 1), underscores its robust predictive capabilities. Importantly, we have identified and weighted specific risk factors contributing to postoperative chronic opioid dependence, providing a nuanced understanding of its etiology (Table 2 and Table 3). Furthermore, the Wu and Zhang's predictive scores encompass easily assessable risk factors, obviating the necessity for interventions or blood tests, relying solely on patient-reported comorbidities, demographics, and medication usage. This tool is convenient, easily accessible, and exhibits high accuracy in predicting postoperative chronic opioid dependence. This unique combination of risk factors and predictive scores empowers clinicians with the precision to identify high-risk individuals. For example, an elderly (> 60 years old) diabetic patient with ASA scores 3, a history of preoperative opioid use within 7 days, and facing hip surgery emerges as a high-risk subgroup (The Wu and Zhang's predictive score 10, high-risk group). Armed with this insight, timely interventions like non-opioid analgesics, psychotherapies, modified surgery or avoidance, careful anesthetic management, and minimally invasive surgical approaches can mitigate the risk of chronic opioid dependence.[8,15–19] This approach not only ensures early intervention for high-risk patients but also underscores the transformative potential of personalized and proactive postoperative care.

Complications arising from chronic opioid dependence are diverse, significantly impacting an individual's health.[41–44] Long-term opioid use leads to tolerance, necessitating higher doses for pain relief and elevating the risk of side effects, including constipation, sleep disturbances, hormonal imbalances, and respiratory depression.[45] Immunological repercussions, including heightened cancer risk and reduced cancer survival due to immunosuppression, also increase susceptibility to infections.[22–26,46] Neurologically, opioid-induced hyperalgesia may elevate pain sensitivity over time.[47]

Psychologically, chronic opioid dependence could contribute to mood disorders such as depression and anxiety, imposing a substantial burden on public health and potentially increasing the risk of dementia.[26,48] Societal repercussions include strain on healthcare systems, increased economic burdens associated with addiction treatment, and social challenges, including stigma and isolation.[49] The risk of opioid overdose, accidental injuries, and involvement in criminal activities further complicates the scenario.[50] To mitigate postoperative chronic opioid dependence linked to CPSP, a tailored, multifaceted approach is essential.[8,15–19] Timely identification and management of postoperative pain using Wu and Zhang's scores (Table 3 and Figure 1), coupled with psychosocial screening and risk assessments, enable personalized interventions. Optimization of anesthetic techniques, coordinated care, restricted opioid prescriptions, and postoperative follow-ups form a comprehensive strategy, addressing the complex factors leading to postoperative chronic opioid dependence.[8,15–19] Recognizing potential consequences such as elevated cancer risk, dementia, depression, anxiety, and increased mortality, the prioritization of the high-risk group through the utilization of Wu and Zhang's scores for the development of postoperative opioid dependence is essential for early detection and effective risk reduction.

The factors identified, along with their corresponding aHRs and assigned scores, offer a comprehensive understanding of the complex interplay influencing long-term opioid use following surgery (Table 1). Consistent with prior literature, advancing age emerges as a significant factor, with individuals over 60 years old exhibiting a higher risk of chronic opioid dependence.[36,51] Male gender, rural residence, knee or hip surgery, and open thoracic surgery also contribute to increased risk, aligning with existing evidence on the impact of demographic and procedural factors on postoperative opioid use.[31–36,51] The ASA scores serve as a reliable predictor, with ASA scores of 3 and 4 indicating a higher likelihood of chronic opioid dependence.[36,51] Anesthesia duration exceeding 2 hours is identified as a significant factor, emphasizing the role of surgical complexity and duration in influencing long-term opioid use.[28] Preoperative opioid use within 7 days is a potent predictor, underlining the impact of preexisting opioid use patterns on postoperative outcomes.[28] Interestingly, preoperative non-opioid analgesic use within 7 days also contributes to the risk, shedding light on the multifaceted nature of analgesic consumption before surgery.[28] Psychosocial factors, including depression and anxiety, emerge as strong contributors to chronic opioid dependence, reinforcing the interconnectedness of mental health and pain outcomes.[22,23,25,26,36,51,52] Other health-related factors such as pressure ulcer, diabetes, and CCI scores ≥ 1 further underscore the intricate relationship between overall health status and postoperative opioid dependence.[22,23,25,26,36,51,52] The Wu and Zhang's scoring system assigned to each factor reflects their relative impact on chronic opioid dependence (Table 1), offering a quantifiable tool for risk stratification. This nuanced approach enables healthcare providers to identify high-risk individuals and tailor interventions accordingly, paving the way for more personalized and effective postoperative pain management. The study contributes valuable insights into both consistent and novel risk factors, enriching the existing knowledge base and providing a foundation for targeted interventions to mitigate the risk of chronic opioid dependence in elective general anesthesia surgery patients.

The study's strength lies in its innovative and comprehensive approach to investigating the prevalence and risk factors of postoperative chronic opioid dependence, particularly within the Asian population. Wu and Zhang's predictive model, with an AUC of 0.83, serves as a valuable tool for risk stratification by easily assessing and capturing patients' demographics. The study benefits from Taiwan's stringent regulatory framework for opioids, ensuring controlled accessibility and meticulous documentation. This process guarantees a precise diagnosis of postoperative chronic opioid dependence, supported by the strict control and monitoring of opioid distribution in Taiwan. The regulatory environment enhances the reliability of the study's findings on prevalence and risk factors following elective surgery. Including previously unexplored Asian data fills a significant gap in the literature, revealing a 1.6% incidence of chronic opioid dependence after elective surgery under general anesthesia in this demographic. Identification of independent risk factors, including age, gender, surgical procedures, comorbidities, and preoperative opioid use, contributes valuable insights for tailored interventions. Recognizing a high-risk group exceeding a 3.5% risk underscores the study's relevance and its potential to inform targeted public health interventions. These strengths position the study as a significant contribution to the field, impacting clinical practice, public health, and inspiring further research endeavors.

Despite its valuable contributions, this study has several limitations that merit consideration. Firstly, the generalizability of the findings may be restricted by the predominantly Asian population, limiting the extrapolation of results to more diverse demographic groups. Additionally, the absence of data from other geographic regions may impede a comprehensive understanding of global patterns in postoperative chronic opioid dependence. While the predictive model demonstrated commendable accuracy, the study lacked external validation, potentially impacting the model's applicability to other settings. Moreover, the dosage of intraoperative opioid administration is not available in the NHIRD. Therefore, we could not determine whether a higher intraoperative opioid dosage leads to a greater need for opioids in the postoperative period, and consequently to chronic pain. Lastly, the data collection occurred over the period from 2016–2018, potentially rendering the information less reflective of current surgical practices and trends. Changes in healthcare practices over time could influence the relevance of the findings in the contemporary landscape. Despite these limitations, the study serves as a crucial starting point for further investigations into postoperative chronic opioid dependence and highlights areas for refinement and expansion in future research.

## Conclusions

Our study found that 1.6% of patients developed chronic opioid dependence beyond 90 days postoperatively. Using Wu and Zhang's predictive scores, we identified significant risk factors contributing to this condition, including age, gender, type of surgery, and preoperative opioid use. These findings highlight the importance of early identification and targeted interventions to mitigate the risk of chronic postoperative pain and opioid dependence in surgical patients.

## Abbreviations

AUC, Area Under the Curve; CDC, Centers for Disease Control and Prevention; CPSP, Chronic Postsurgical Pain; NHI, National Health Insurance; NHIRD, National Health Insurance Research Database; ICD-9-CM, International Classification of Diseases, Ninth Revision, Clinical Modification; ICD-10-CM, International Classification of Diseases, Tenth Revision, Clinical Modification; ASA, American Society of Anesthesiologists; CCI, Charlson Comorbidity Index; HR, Hazard Ratio; aHR, Adjusted Hazard Ratio; AIC, Akaike Information Criterion; SD, Standard Deviation; IQR, Interquartile Range; NTD, New Taiwan Dollar; N, Numbers; Q1, First Quartile; Q3, Third Quartile; CI, Confidence Interval.

## Data Sharing Statement

The datasets supporting the study conclusions are included within this manuscript and its additional files.

## Ethics Approval and Consent

The study protocols were reviewed and approved by the Institutional Review Board of Tzu-Chi Medical Foundation (IRB109-015-B). Lotung Poh-Ai Hospital does not have its own Institutional Review Board (IRB); therefore, we commissioned the IRB of Tzu-Chi Medical Foundation to review our human trials. All our clinical trials undergo regular audits by the Tzu-Chi Medical Foundation IRB, complying with human research regulations and AAHRPP accreditation standards.

## Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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## Disclosure

Mingyang Sun and Wan-Ming Chen are co-first authors for this study. The authors have no potential conflicts of interest to declare in this work.

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