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Development and Validation of a Predictive Depression Model in Cancer Survivors Using CHARLS Data

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Abstract

Background: Depression significantly impacts the recovery and quality of life of cancer survivors. This study developed and validated a prognostic model to assess depression risk using data from the China Health and Retirement Longitudinal Study (CHARLS) and five external medical centers.

Methods: Data from 574 cancer survivors in the CHARLS dataset were analyzed, with 216 diagnosed with depression. An additional cohort of 503 cancer patients from five medical centers served as the external validation group. Predictive factors included demographic characteristics, lifestyle habits, and medical history. Least Absolute Shrinkage and Selection Operator (LASSO) regression was used to refine the variables, and multivariate logistic regression identified significant predictors. Model performance was evaluated using the C-index, calibration curves, Hosmer-Lemeshow test, Decision Curve Analysis (DCA), and Clinical Impact Curve (CIC).

Results: Five independent predictors of depression were identified: Rural residency, self-reported health, arthritis, memory efficiency, and life satisfaction. The model demonstrated excellent discrimination in the CHARLS cohort (C-index 0.854; 95% CI: 0.821-0.887), test group (C-index 0.902; 95% CI: 0.784-0.915), and external validation group (C-index 0.827; 95% CI: 0.762-0.892). The Hosmer-Lemeshow test yielded a value of 0.910. Calibration curves, DCA, and CIC analyses further confirmed its predictive accuracy and clinical relevance.

Conclusion: The developed model is a precise and clinically significant tool for predicting depression risk among cancer survivors. It enables early identification of high-risk individuals, facilitating timely and appropriate interventions.

Keywords: Depression; Cancer; Prediction model; Nomogram; CHARLS

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Introduction

Cancer survivors represent a rapidly growing global population, thanks to the rapid advancements in medical technology that have significantly increased patient survival rates [1]. However, the post-treatment recovery process presents many challenges, particularly in the realm of mental health [2]. The most common issues are adjustment disorders, with anxiety and depression being particularly prevalent [3]. The incidence of anxiety and depression among cancer patients shows considerable variability across different studies, with rates ranging from 24.8% to 42.7% [4]. This significant variability may be related to various factors, including ongoing physical discomfort, complex treatment experiences, and changes in quality of life [5]. Additionally, different types of cancer and treatment methods may also lead to variations in psychological stress [6].

Early studies suggest that cancer patients who had experienced depression or anxiety before diagnosis are at a higher risk of psychological stress [7]. Research identifies several risk factors associated with higher levels of depression among cancer patients, including social isolation, pain, and financial stress [8]. In primary care, depression is often severely underestimated and sometimes even misdiagnosed [9]. Moreover, there is often a discrepancy between healthcare providers' assessments of anxiety and depression in cancer patients and the patients' self-assessments [10].

Due to the lack of specialized training among non-specialist clinicians and nurses in identifying psychological stress in cancer patients, there is an urgent need to develop simple and practical diagnostic methods.

The incidence of depression among cancer survivors is high, posing a significant threat to their health [11]. Therefore, identifying potential high-risk groups for depression and implementing timely interventions is crucial for improving their quality of life and long-term survival [12]. To this end, we have developed a predictive model aimed at identifying patients likely to be depressed. This model is designed to enhance the early identification of patients at high psychological risk, thereby facilitating the implementation of personalized psychological interventions and optimizing overall treatment plans. The integration of psychological assessment tools in clinical practice underscores the central role of psychological evaluations in cancer management [13]. This study explores the potential for predicting levels of anxiety and depression in cancer patients, to identify those at risk early on, so that timely psychological interventions can be provided. We tested the predictive model in a diverse sample of cancer patients, aiming to identify the main psychological factors affecting cancer adaptation and to optimize prediction and intervention outcomes.

Methods

Research design and data sources

This study is based on data from the China Health and Retirement Longitudinal Study (CHARLS), which is publicly available at http://charls.pku.edu.cn. CHARLS employs a multi-stage clustered sampling method and has recruited 10,257 households encompassing 17,708 participants across 28 provinces in mainland China since 2011 [14]. Data collection began with a baseline survey in 2011-2012 and has continued biennially with face-to-face computer-assisted personal interviews, culminating in five waves of data collection completed in 2013-2014 (second wave), 2015-2016 (third wave), 2018 (fourth wave), and 2020 (fifth wave) [15]. This study has been approved by the Biomedical Ethics Review Committee of Peking University (IRB00001052-11015), and informed consent has been obtained from all participants. All research methods were conducted in strict accordance with the ethical guidelines of the Declaration of Helsinki.

The analysis incorporated data from the years 2011, 2013, 2015, 2018, and 2020, totaling 96,628 survey results. After excluding samples with missing core variables and responses of "don't know" or "refuse to answer," we obtained 28,037 samples. By further excluding 27,462 non-cancer patients, the study retained 575 valid samples of cancer survivors. Additionally, our external validation cohort was sourced from five medical centers located in various regions of China, including the Northeast, Northwest, Southeast, Southwest, and Central areas. Data collection for the external validation cohort of cancer survivors took place from September 2021 to March 2024. This diverse distribution and timing ensure a broad representation of the population, enhancing the generalizability of our findings across different geographical and cultural contexts within the country.

Data collection

Sociodemographic factors: Participants' age, gender, and residence (urban *vs.* rural) were recorded. The highest level of educational attainment was documented, and marital status was categorized as married, single, divorced, or widowed. Data on personal or household income were collected, and insurance status was assessed to determine the type and extent of health insurance coverage each participant had.

Behavioral factors: Behavioral attributes were closely examined, starting with smoking history, classified as 'ever smoked' or 'never smoked'. Drinking history was similarly categorized as 'ever drink' or 'never drink'. The study also assessed participants' engagement in social activities and their exercise habits, focusing on the frequency and intensity of physical activity.

Health status: Participants provided information on various chronic diseases, including hypertension, heart disease, stroke, dyslipidemia, digestive diseases, mental illnesses, arthritis, kidney disease, liver disease, and lung disease. Self-perceived health status was evaluated, with participants rating their health from 'very healthy' to 'very unhealthy'. The Activity of Daily Living (ADL) scale was used to measure functional independence, with higher scores indicating greater dependency.

Mental health factors: The CESD-10 scale was used to assess symptoms of depression, with scores ranging from 0 to 30, where a score of 10 or above typically indicates significant depressive symptoms. Sleep quality was evaluated to understand sleep patterns and disturbances. Life satisfaction was measured to gauge overall contentment with life, and social participation was assessed to determine the level of involvement in community or social activities.

Cognitive function assessment: Cognitive abilities were evaluated using various tests. Visual-spatial skills were assessed by having participants redraw two overlapping pentagons, with accuracy noted as correct or incorrect. Memory capacity was evaluated through the immediate and delayed recall of ten words, awarding points for each correctly recalled word. Orientation and attention were measured using tasks such as identifying the current date and performing serial subtractions, with a maximum possible score of ten.

Statistical methods

Continuous variables were summarized using the mean ± Standard Deviation (SD) or the median with Interquartile Range (IQR), as appropriate. Group comparisons for these variables were conducted using a t-test or Mann-Whitney U test based on the distribution. Categorical variables were expressed as frequencies (percentages) and analyzed using Chi-square tests for group differences. To develop and evaluate the nomogram, the dataset was randomly divided into a training set, constituting 70% of the participants, and a validation set, comprising the remaining 30%. The training set was employed to pinpoint the most pertinent predictors *via* the LASSO regression method. Key predictors identified were then analyzed using multivariate logistic regression to determine independent predictors, adopting a p-value threshold of <0.05 for inclusion.

The nomogram's effectiveness was gauged using the Receiver Operating Characteristic (ROC) curve, with the Area under the Curve (AUC) statistic as the indicator of predictive precision. The calibration of the model was checked using the Hosmer–Lemeshow test and depicted through calibration plots. Furthermore, the clinical utility of the nomogram was examined via clinical Decision Curve Analysis (DCA) [16], and Clinical Impact Curve (CIC) [17], and the optimum threshold for clinical use was determined by identifying the highest Youden index. These validation steps, including evaluations of discriminative capacity and model calibration, were also applied to the validation set. All statistical procedures were performed using R software, version 4.3.1.

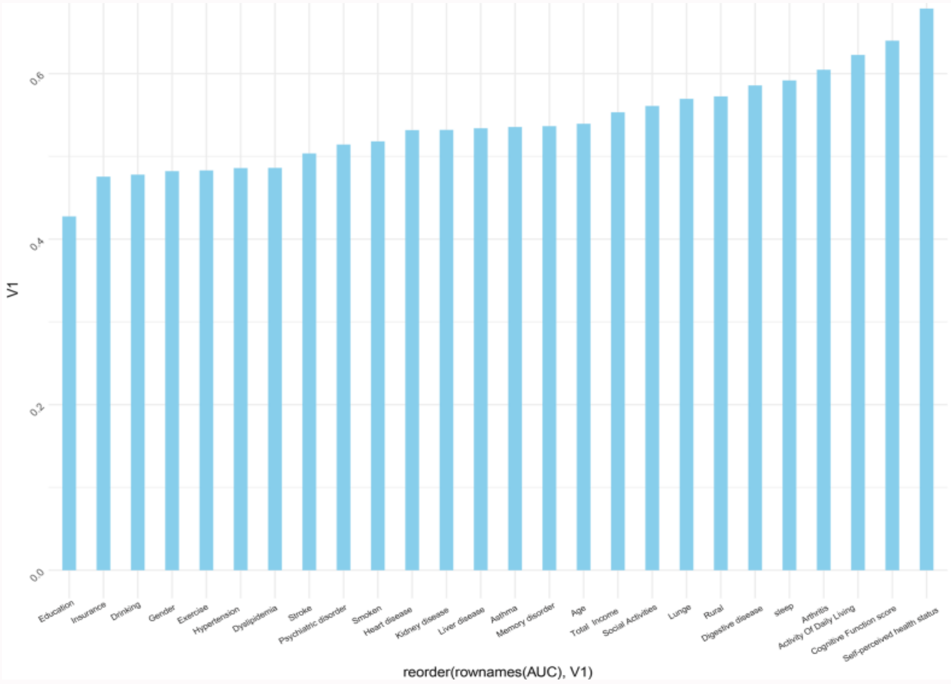

Figure 1: AUC Values for Health and Economic Predictors. This figure presents the Area under Curve (AUC) for several predictors, illustrating their diagnostic accuracy in a predictive model.

Results

Baseline clinical characteristics

In this study, we differentiated subjects into two groups based on depression status to evaluate their baseline characteristics. The non-depression group consisted of 358 participants with a mean age of 63.01 ± 9.44 years, including 152 males (42.5%) and 206 females (57.5%). The depression group included 216 participants, averaging 61.63 ± 9.00 years in age, with a nearly equal gender distribution of 84 males (38.9%) and 132 females (61.1%).

Our comparative analysis, as detailed in Supplementary Table 1, underscored significant distinctions in health indicators between the groups. Pathological features such as the prevalence of liver disease were markedly different. Lifestyle factors like alcohol consumption, smoking, and exercise habits also varied significantly, indicating behavioral patterns that may influence overall health outcomes. Besides, differences in total income and cognitive scores were notable, reflecting the physiological and socio-economic changes associated with varying health conditions.

Association of candidate predictive variables with depression

An initial analysis was carried out to ascertain the AUC values for each potential predictor, subsequently arranging these values in descending order as illustrated in Figure 1. Following the examination of these outcomes, it was observed that the AUC values for all assessed variables, except for education, insurance, drinking, gender, exercise, hypertension, and dyslipidemia, exceeded 0.5. Given that the correlations among variables were deemed to be within acceptable ranges, a multifactor analysis was initiated to identify the ultimate predictors.

The LASSO regression method pinpointed 14 variables with significant coefficients in the training set, specifically sleep quality, rural, self-perceived health, lunge, arthritis, digestive disease, memory disorder, life satisfaction, social activities, education, insurance, age, cognitive function, activity of daily living dependence, and sedentary lifestyle (Figure 2). Further analysis through multiple logistic regression confirmed six variables as independent predictors of depression, yielding the following results: Rural (Odds Ratio [OR]: 1.957, 95% Confidence Interval [CI]: 1.136–3.371, P=0.016), self-perceived health (OR: 0.649, 95% CI: 0.477–0.884, P=0.006), memory disorder (OR: 5.508, 95% CI: 1.637–18.540, P=0.006), arthritis (OR: 2.209, 95% CI: 1.268–3.848, P=0.005), life satisfaction (OR: 0.243, 95% CI: 0.156–0.380, P=0.001) and cognitive function (OR: 0.912, 95% CI: 0.834–0.996, P=0.041). These identified factors were integrated into the construction of the nomogram (Figure 3A). To refine the model, logistic regression was employed to identify and retain only the six most impactful variables, resulting in a streamlined version of the simple model (Figure 3B).

Prediction of depression in the development and validation groups

The efficacy of the nomogram was evaluated using ROC curve analysis across several cohorts. In the training group, the AUC was 0.847 (95% CI: 0.808-0.886), illustrated in Figure 4A. For the test group, the AUC improved to 0.902 (95% CI: 0.784-0.915), as shown in Figure 4B. The development cohort, using a reduced model, achieved an AUC of 0.854 (95% CI: 0.821-0.887), detailed in Figure 4C. Additionally, external validation demonstrated a consistent performance with an AUC of 0.827 (95% CI: 0.762-0.892), presented in Figure 4D, along with the corresponding calibration curve. This additional validation reinforces the nomogram's accuracy in forecasting depression, underlining its prospective value in clinical environments. These outcomes highlight the nomogram model's excellent capacity for discrimination and its predictive accuracy. At the maximum Youden index, the optimal cut-off value in the training set was 0.55. Calibration curves for both cohorts showed that the model's

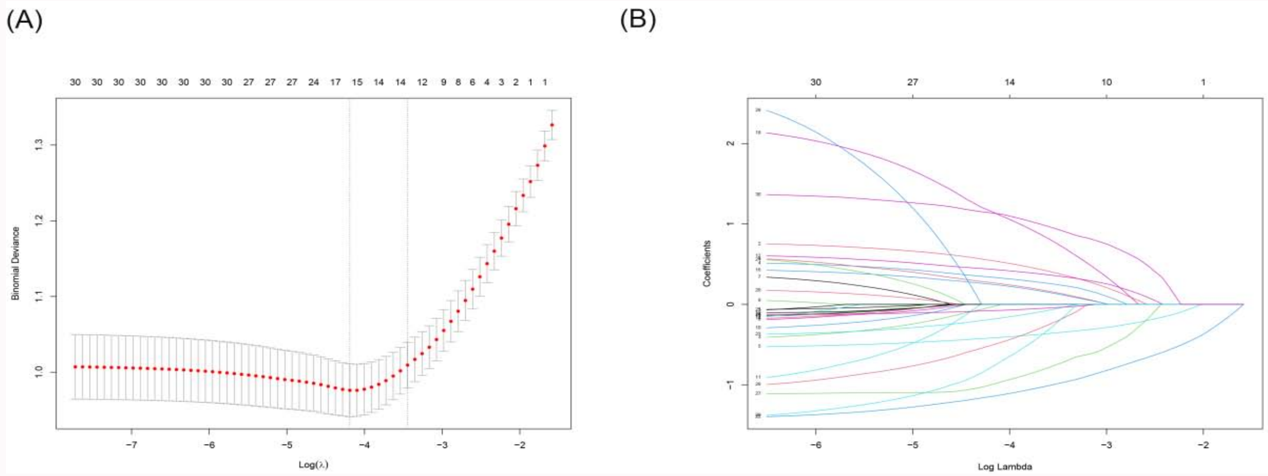

Figure 2: LASSO Regression for Feature Selection. This figure illustrates feature selection using LASSO regression in two parts: (A) showcases the coefficient profiles against varying logarithmic lambda values, identifying non-zero coefficients at the optimal lambda as key features; (B) presents the selection of the optimal lambda *via* 10-fold cross-validation, marked by the minimum criterion plus one standard error. This method effectively highlights the most relevant demographic and clinical predictors for the model.

predicted probabilities align closely with actual outcomes, forming an approximate 45-degree angle. This alignment was further supported by the Hosmer-Lemeshow test, which indicated no significant lack of fit, with p-values of 0.910 in the training cohort. These results indicate a strong agreement between the model's predictions and observed realities, underscoring its reliability in estimating the risk of depression (Figure 5A-5C). DCA (Figure 5D, 5E) and CIC (Figure 5F) revealed that the model provides substantial net benefits in the detection of depression risk within both sets, affirming its clinical value.

Discussion

Despite the existence of predictive models for depression in specific cancer patient subgroups, a comprehensive tool for accurately identifying at-risk individuals among broader cancer survivor populations remains undeveloped. Addressing this gap, our study leveraged data from the CHARLS collected in 2011, 2013, 2015, 2018, and 2020 to develop a nomogram. This model is designed to accurately predict the likelihood of depression among cancer survivors. While this method may sacrifice some degree of precision, it significantly enhances the utility of the model by making it applicable for initial depression screening across diverse cancer survivor groups.

This study found that cancer patients living in rural areas are more prone to depression compared to urban residents [18]. This may be due to the relative scarcity of medical resources in rural areas, the difficulty in accessing medical services, and the less developed social and psychological support systems compared to those in cities, all of which could exacerbate the psychological stress of patients [19,20]. Additionally, cultural factors and a lack of health education might also impact the mental health status of rural residents. Therefore, providing more mental health resources and support for rural cancer patients is particularly crucial [21].

Additionally, our research identified self-assessed health status as a key predictive factor for depression [22,23]. Survivors who hold negative views of their own health show a high sensitivity to depressive symptoms. This association may stem from a heightened focus on the adverse physical consequences of cancer treatment, such as ongoing pain and fatigue, which severely impact the quality of life [24,25]. Conversely, a positive view of health is associated with lower rates of depression, highlighting the importance of psychological interventions that address not only physical symptoms but also enhance health perception and coping strategies [26]. This finding underscores the significance of psychological attitude in managing emotional health within chronic disease management [27]. Implementing active psychological interventions, such as cognitive-behavioral therapy, may help improve patients' psychological states and thereby reduce the risk of depression [28]. Moreover, the study indicates that arthritis is associated with an increased risk of depression among cancer patients. Long-term pain and restricted activity may not only affect physical health but also negatively impact mental states [29]. This finding suggests that healthcare providers should pay attention to joint health and pain management while treating cancer, in order to reduce psychological stress and improve quality of life.

This study shows that life satisfaction is significantly correlated with the depressive states of cancer patients, indicating that high life satisfaction can significantly reduce the risk of depression. Life satisfaction may be influenced by a variety of factors, including social relationships, economic status, and a sense of personal achievement [30]. Therefore, improving the life satisfaction of cancer patients, such as through enhanced social support and psychological counselling services, may be an effective way to prevent and treat depression. These results not only enhance our understanding of the risk factors for depression among cancer patients but also provide important guidance for clinical practice and public health strategies, especially in terms of how to holistically consider biomedical and socio-psychological factors to optimize the overall health management of cancer patients [8].

A robust predictive model provides a scientific basis for implementing targeted interventions that can significantly improve patient outcomes. For example, Aarathi et al. applied digital cognitive-behavioral therapy interventions, effectively reducing depressive symptoms, and demonstrating the potential of precise interventions [31]. Similarly, Meenakshi et al. proposed a model-based strategy to manage personalized physical activity programs, which not only alleviated depressive symptoms but also improved overall physical

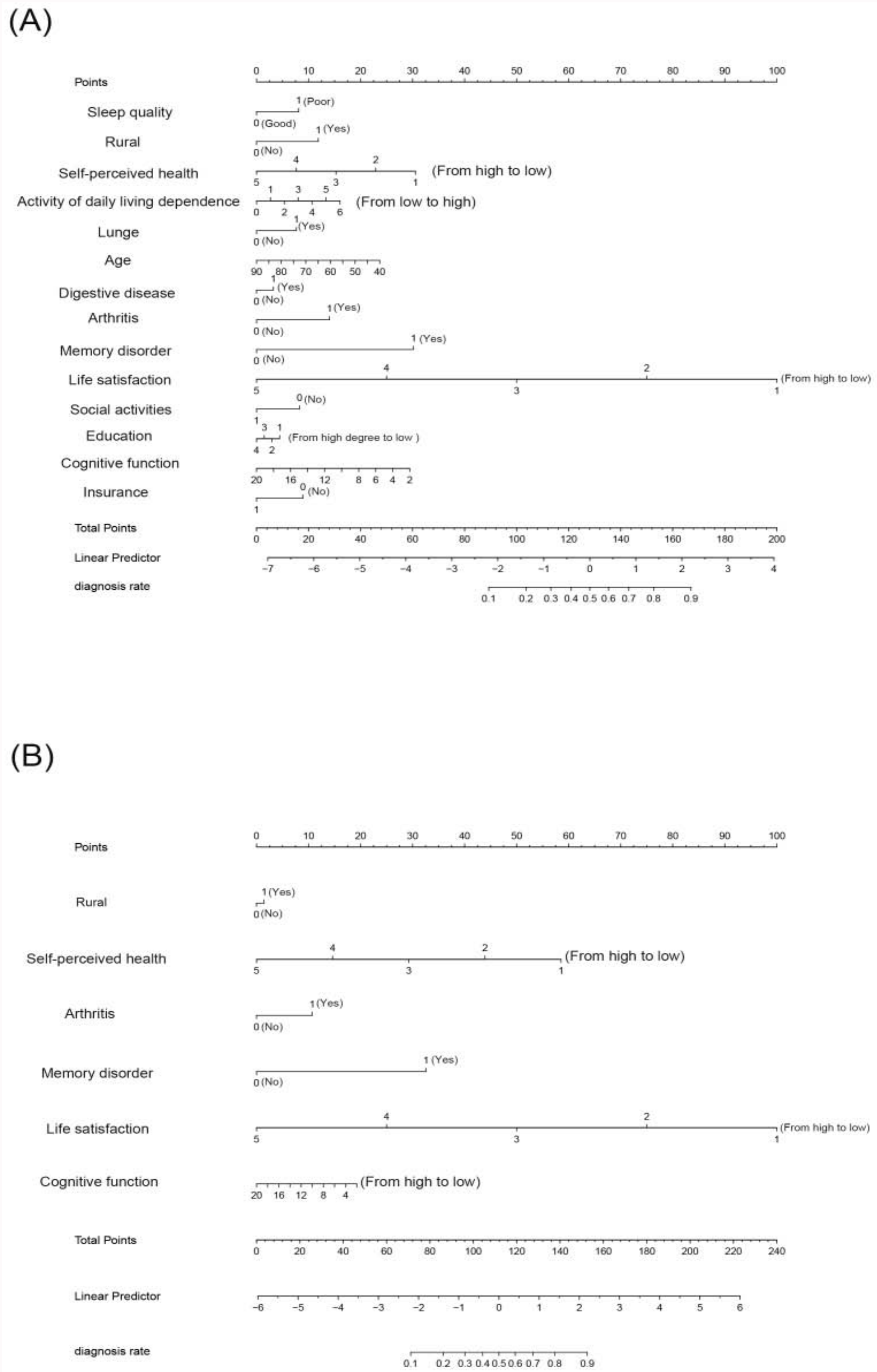

Figure 3: Nomograms for Predicting Depression Probability. This figure showcases two nomograms for estimating depression risk in a development group: (A) the full model, utilizing an extensive range of predictors, and (B) the simplified model, focusing on key factors for a quicker assessment. Both models aim to provide an accessible means for calculating individual depression likelihood.

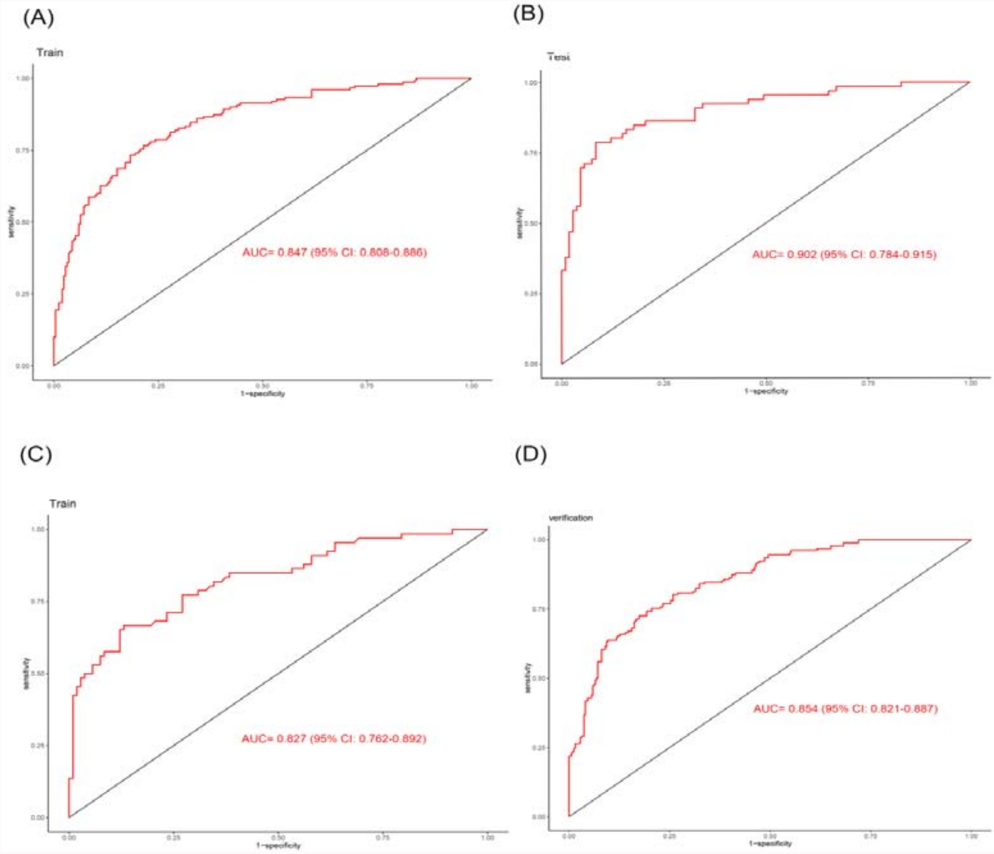

Figure 4: ROC Curves for Depression Prediction. This figure illustrates the evaluation of depression prediction models in fracture patients, featuring ROC curves for the training, test, and external validation dataset (A-D).

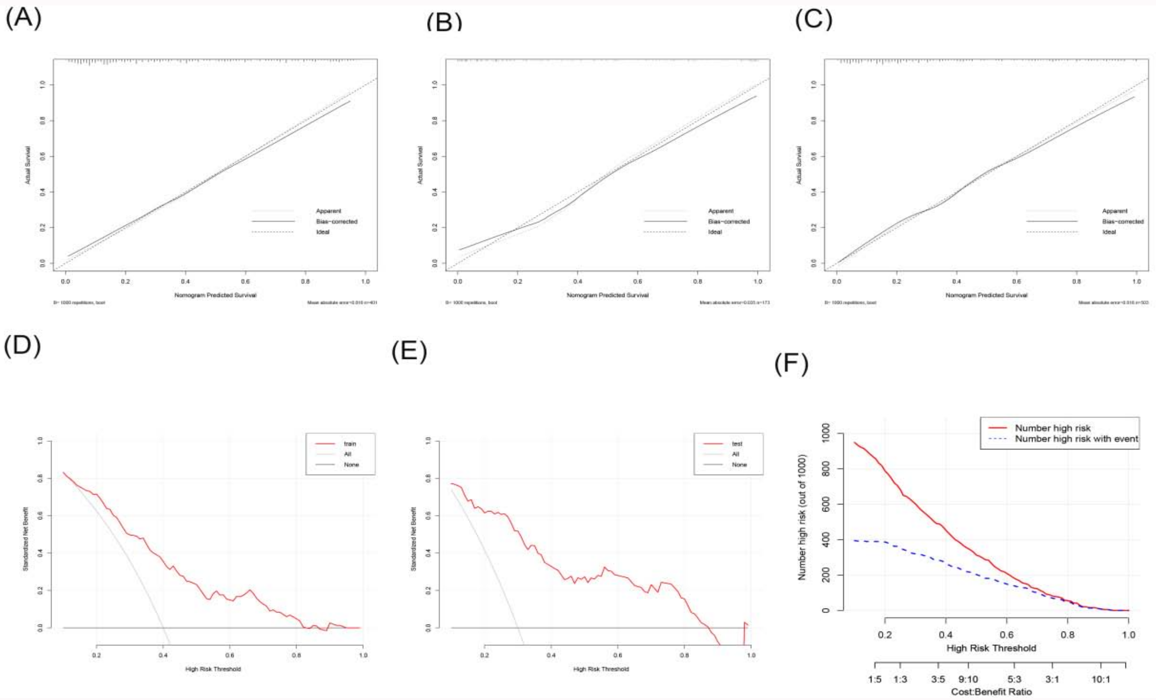

Figure 5: Nomogram Calibration Curves. This figure displays calibration curves for the nomogram's depression predictions in the training set (A), test set (B), and external verification (C), measuring the accuracy of predicted probabilities against actual outcomes. (D) and (E): Clinical Decision Curve Analysis (DCA). The x-axis represents the range of threshold probabilities, while the y-axis shows the net benefit calculated relative to the standard strategies of treating all or none. (F): This panel illustrates the Clinical Impact Curve (CIC), showing the number of patients who would be positively diagnosed by the model across varying threshold probabilities (x-axis) and how many of these are true positive cases (y-axis).

function [32]. These examples highlight the transformative impact of data-driven interventions. As models incorporate data from a broader population, their predictive accuracy is expected to improve. This enhancement will enable more precise interventions, potentially more effectively mitigating the risk of depression among cancer survivors.

This study has several limitations. Firstly, the nomogram developed is based on data exclusively from China, raising concerns about its applicability to other regions or countries. Further validation using international datasets is necessary to confirm its external validity. Secondly, the study employs a retrospective design without long-term follow-up of cancer survivors, which may restrict our understanding of the disease progression dynamics and limit the depth of the model's predictive capabilities. Additionally, the specific severity of cancer in the patient cohort was not accounted for, potentially introducing bias into the findings. Future research should incorporate long-term follow-up data to refine and enhance the accuracy of the current predictive model. These steps are crucial for ensuring the model's relevance and utility in broader clinical settings.

Conclusion

This study utilizes CHARLS data and multicenter data to develop a nomogram that serves as an effective tool for predicting depression risk among cancer survivors. The model exhibits strong clinical predictive capabilities, enabling the accurate identification of those at high risk for depression.

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References

1. Santucci C, Carioli G, Bertuccio P, Malvezzi M, Pastorino U, Boffetta P, et al. Progress in cancer mortality, incidence, and survival: A global overview. Eur J Cancer Prev. 2020;29(5):367-81.

2. Caruso R, Breitbart W. Mental health care in oncology. Contemporary perspective on the psychosocial burden of cancer and evidence-based interventions. Epidemiol Psychiatr Sci. 2020;29:e86.

3. O'Donnell ML, Agathos JA, Metcalf O, Gibson K, Lau W. Adjustment disorder: Current developments and future directions. Int J Environ Res Public Health. 2019;16(14):2537.

4. Naser AY, Hameed AN, Mustafa N, Alwafi H, Dahmash EZ, Alyami HS, et al. Depression and anxiety in patients with cancer: A cross-sectional study. Front Psychol. 2021;12:585534.

5. Wilmer MT, Anderson K, Reynolds M. Correlates of quality of life in anxiety disorders: Review of recent research. Curr Psychiatry Rep. 2021;23(11):77.

6. Urruticoechea A, Alemany R, Balart J, Villanueva A, Viñals F, Capellá G. Recent advances in cancer therapy: An overview. Curr Pharm Des. 2010;16(1):3-10.

7. Niedzwiedz CL, Knifton L, Robb KA, Katikireddi SV, Smith DJ. Depression and anxiety among people living with and beyond cancer: A growing clinical and research priority. BMC Cancer. 2019;19(1):943.

8. Riedl D, Schüßler G. Factors associated with and risk factors for depression in cancer patients - A systematic literature review. Transl Oncol. 2022;16:101328.

9. Fekadu A, Demissie M, Birhane R, Medhin G, Bitew T, Hailemariam M, et al. Under detection of depression in primary care settings in low and middle-income countries: A systematic review and meta-analysis. Syst Rev. 2022;11(1):21.

10. Kennedy BM, Rehman M, Johnson WD, Magee MB, Leonard R, Katzmarzyk PT. Healthcare providers versus patients' understanding of health beliefs and values. Patient Exp J. 2017;4(3):29-37.

11. Wang Y-H, Li J-Q, Shi J-F, Que JY, Liu JJ, Lappin JM, et al. Depression and anxiety in relation to cancer incidence and mortality: A systematic review and meta-analysis of cohort studies. Mol Psychiatry. 2020;25(7):1487-99.

12. McLaughlin KA. The public health impact of major depression: A call for interdisciplinary prevention efforts. Prev Sci. 2011;12(4):361-71.

13. Bornstein RF. Evidence-based psychological assessment. J Pers Assess. 2017;99(4):435-45.

14. Li X, Zhang W, Zhang W, Tao K, Ni W, Wang K, et al. Level of physical activity among middle-aged and older Chinese people: evidence from the China health and retirement longitudinal study. BMC Public Health. 2020;20(1):1682.

15. Zhao Y, Hu Y, Smith JP, Strauss J, Yang G. Cohort profile: The China Health and Retirement Longitudinal Study (CHARLS). Int J Epidemiol. 2014;43(1):61-8.

16. Van Calster B, Wynants L, Verbeek JFM, Verbakel JY, Christodoulou E, Vickers AJ, et al. Reporting and interpreting decision curve analysis: A guide for investigators. Eur Urol. 2018;74(6):796-804.

17. Vignon P, Pegot B, Dalmay F, et al. Acceleration of the learning curve for mastering basic critical care echocardiography using computerized simulation. Intensive Care Med. 2018;44(7):1097-105.

18. Joensen BM, Nielsen S, Róin Á. Barriers to quality of care for cancer patients in rural areas: A study from the Faroe Islands. J Multidiscip Healthc. 2020;13:63-70.

19. Gizaw Z, Astale T, Kassie GM. What improves access to primary healthcare services in rural communities? A systematic review. BMC Prim Care. 2022;23(1):313.

20. Chen X, Orom H, Hay JL, Waters EA, Schofield E, Li Y, et al. Differences in rural and urban health information access and use. J Rural Health. 2019;35(3):405-17.

21. Troy D, Anderson J, Jessiman PE, Albers PN, Williams JW, Sheard S, et al. What is the impact of structural and cultural factors and interventions within educational settings on promoting positive mental health and preventing poor mental health: A systematic review. BMC Public Health. 2022;22(1):524.

22. Paul P, Nguemdjo U, Kovtun N, Ventelou B. Does self-assessed health reflect the true health state? Int J Environ Res Public Health. 2021;18(21):11153.

23. Sokoya T, Zhou Y, Diaz S, Law T, Himawan L, Lekey F, et al. Health indicators as measures of individual health status and their public perspectives: Cross-sectional survey study. J Med Internet Res. 2022;24(6):e38099.

24. Wade M, Wright L, Finegold KE. The effects of early life adversity on children's mental health and cognitive functioning. Transl Psychiatry. 2022;12(1):244.

25. Monnat SM, Chandler RF. Long term physical health consequences of adverse childhood experiences. Sociol Q. 2015;56(4):723-52.

26. Hautekiet P, Saenen ND, Martens DS, Debay M, der Heyden JV, Nawrot TS, et al. A healthy lifestyle is positively associated with mental health and well-being and core markers in ageing. BMC Med. 2022;20(1):328.

27. Bradshaw J, Siddiqui N, Greenfield D, Sharma A. Kindness, listening, and connection: Patient and clinician key requirements for emotional support in chronic and complex care. J Patient Exp. 2022;9:23743735221092627.

28. Ojala B, Nygård CH, Huhtala H, Bohle P, Nikkari ST. A cognitive behavioral intervention program to improve psychological well-being. Int

J Environ Res Public Health. 2018;16(1):80.

29. Geneen LJ, Moore RA, Clarke C, Martin D, Colvin LA, Smith BH. Physical activity and exercise for chronic pain in adults: An overview of Cochrane reviews. Cochrane Database Syst Rev. 2017;4(4):Cd011279.

30. Kim ES, Delaney SW, Tay L, Chen Y, Diener ED, Vanderweele TJ. Life satisfaction and subsequent physical, behavioral, and psychosocial health in older adults. Milbank Q. 2021;99(1):209-39.

31. Venkatesan A, Rahimi L, Kaur M, Mosunic C. Digital cognitive behavior therapy intervention for depression and anxiety: Retrospective study. JMIR Ment Health. 2020;7(8):e21304.

32. Dauwan M, Begemann MJH, Slot MIE, Lee EHM, Scheltens P, Sommer IEC. Physical exercise improves quality of life, depressive symptoms, and cognition across chronic brain disorders: A transdiagnostic systematic review and meta-analysis of randomized controlled trials. J Neurol. 2021;268(4):1222-46.