



2025 生物统计学术会议

论文汇编



中国·重庆 2025年7月18-20日
Chongqing, China July 18-20, 2025



A Variable Transformation Framework for Multi-Group Global Tests of Restricted Mean Survival Time and Restricted Mean Time Lost

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【Abstract】 Background: Restricted mean survival time (RMST) quantifies survival benefits in single-endpoint analysis, while restricted mean time lost (RMTL) measures event-related time loss in competing risks settings. Both provide clinically intuitive interpretations of treatment effects without relying on proportional hazards assumptions or parametric distributions. While existing RMST/RMTL methods focus primarily on two-group comparisons, multi-arm trials are common in practice. However, asymptotic approaches for these metrics suffer from inflated type I error in small samples, limiting their reliability.

Objective: This study aims to address these limitations by developing a global test framework for multi-group comparisons of RMST and extending it to RMTL in the presence of competing risks. The proposed method seeks to provide robust statistical inference while maintaining clinical interpretability across diverse sample sizes.

Methods: We introduce a global test framework utilizing variable transformation methods—including log, complementary log-log (clog-log), arcsine square root, and logit transformations—to enable multi-group comparisons of RMST and RMTL. Monte-Carlo simulations were conducted to evaluate type I error and power under various scenarios, and two illustrative examples were provided.

Results: Simulations demonstrated that transformed RMST and RMTL global tests effectively controlled type I error across small samples and high censoring rates, while improving power compared to untransformed methods. For single-endpoint analysis, the RMST arcsine square root transformation is recommended. In competing risks settings, RMTL logit transformation is preferred when the event of interest occurs more frequently than competing events, whereas clog-log transformation performs better when competing events dominate.

Conclusions: The proposed transformation-based global tests offer researchers a flexible, assumption-free tool to compare treatment effects across multiple groups

with enhanced reliability and interpretability. Additionally, an R package "compRM" was developed to implement the proposed methods.

Funding: This work was supported by the National Natural Science Foundation of China (grant numbers 82473723) and the Guangdong Basic and Applied Basic Research Foundation (grant number 2024A1515011402).

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Adherence to the Healthy Low-Carbohydrate Diet and incident depression and anxiety

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Abstract

Background

The study aimed to explore the prospective associations between adherence to the Healthy Low-Carbohydrate Diet (HLCD) and incident depression, anxiety, and their comorbidity, as well as the mediating role of inflammation in the associations.

Methods

This cohort study included 173,207 participants from the UK Biobank. Cox proportional models were used to investigate the associations between the HLCD score and the three outcomes. Restricted cubic splines were used to explore non-linear associations. Mediation analyses were conducted to assess the role of inflammation in the associations.

Results

Compared with the lowest HLCD score group (0 – 6), the third (13 – 18), fifth (25 – 30), and second (7 – 12) groups exhibited the lowest risks of depression (hazard ratio: 0.705, 95% confidence interval: 0.626 – 0.793), anxiety (HR: 0.791, 95% CI: 0.688 – 0.909), and comorbidity (HR: 0.673, 95% CI: 0.555 – 0.816), respectively. Restricted cubic spline revealed nonlinear associations between the HLCD score and risks of all three outcomes (all P for non-linearity < 0.05). The mediation analyses indicated that White blood cell count, C-reactive protein, and the Low-grade chronic inflammation score played significant but weak mediating roles in the associations.

Conclusions

The prospective study showed that high adherence to the HLCD reduced risks of depression, anxiety, and comorbidity, highlighting that an appropriately improved diet

may lead to better psychological health improvements. The indirect effects of inflammatory indicators were relatively small, suggesting weak mediation.

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Advancing Invasive Pulmonary Nodules Screening: A Deep Learning Model for Classifying SLN, MDN and GNN in CT Scans

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Abstract

Background Lung cancer remains the foremost cause of cancer-related mortality globally, with its low survival rate primarily attributed to the fact that only 15% of all diagnosed lung cancers are detected at an early stage. The National Lung Screening Trial (NLST) and the Dutch–Belgian lung-cancer screening trial (NELSON) have demonstrated the efficacy of low-dose computed tomography (LDCT) in diminishing lung cancer mortality by 20% and 24%, respectively, leading to increased use of CT and LDCT for screening. However, this has also escalated the detection of indeterminate pulmonary nodules, emphasizing the need for accurate management to avoid overdiagnosis and resource wastage.

Purpose To evaluate the ability of CT images to identify imaging features of early lung nodules (less than 10 mm in diameter) and to screen deep learning algorithms for to indicate the possibilities of deterioration of the pulmonary nodules.

Methods A SqueezeNet model was developed and evaluated for early pulmonary nodules imaging classification. 901 cases (6089 images), including 557 patients with solid nodules (SLN, 4,775 images), 53 patients with mixed-density lung nodules (MDN, 291 images), and 169 patients with ground-glass nodules (GGN, 1,023 images) were retrospectively analyzed. The patients were first divided into a training set and a test set in a ratio of 8:2, and the model through tenfold cross-validation. We used six deep learning models, including MobileNet and SqueezeNet, for early diagnosis and

screening of SLD, MDN, and GGN. Accuracy, Kappa, F1-score, and Recall were utilized to evaluate the accuracy of multi-classification models. After classifying the CT images of lung nodules into the low-risk group (SLN) and high-risk group (MDN&GGN), a binary classification model was constructed. AUC, accuracy, sensitivity, and specificity were used to assess the level of binary classification models.

Results In the construction of the three classification models for the nature of lung nodules, SqueezeNet performed the best and its accuracy reached 88.67(86.21,91.13) and best in terms of Kappa value, F1-score, and recall. 0.6223, 0.8635, and 86.70% respectively. While in the binary classification model of low-risk group (SLN) and high-risk group (MDN&GGN), SqueezeNet and InceptionV3 models reached 0.87%. AUC, accuracy, sensitivity, and specificity of the former model were higher than those of the latter model, which were 0.8706, 88.69%, 79.21 and 82.30%.

Conclusion The application of deep learning algorithms can help radiologists identify features such as early solidity, mixed density, and ground-glass shadows of lung nodules from CT images and perform malignancy risk grouping.

Funding: This study was supported by the National Natural Science Foundation of China (grant number 82173617 and 82373683) and Beijing Medical Science and Technology Promotion Center (grant number KCZX-KT-002)

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Aflatoxin B1 exposure and the risk of liver cancer: a dose-response meta-analysis

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Abstract: Background: Aflatoxins (AFs) have been classified as Group 1 carcinogens by the International Agency for Research on Cancer (IARC). Among them, the relationship between AFB1 exposure and liver cancer risk has been widely investigated. However, the exact dose-response relationship remains unclear. This meta-analysis aims to quantitatively assess this association.

Objectives: Published studies reporting on the association between AFB1 exposure and liver cancer risk were systematically reviewed. Data were extracted based on predefined criteria and quantitatively synthesized to evaluate the association and potential dose-response relationship.

Methods: CNKI, PubMed, and Web of Science databases were searched for population-based studies published up to February 2025 that investigated the association between AFB1 exposure and the risk of liver cancer. Data extraction and the Newcastle-Ottawa Quality Assessment Scale (NOS) assessments were performed in duplicate. Studies were included if they adopted a case-control design, reported AFB1 as the exposure of interest and liver cancer as the outcome, and provided odds ratios (ORs) with 95% confidence intervals (CIs). A one-stage dose-response analysis assessed the associations between AFB1 exposure and the risk of liver cancer.

Results: After screening 2701 references, 8 case-control studies were included, involving 9450 participants and 2595 cases. All studies meeting the inclusion criteria were included, except for one with a NOS score below 6. The high exposure level of AFB1 was associated with an increased risk of liver cancer compared with the lowest exposure level of AFB1 (RR= 2.94, 95% CI: 1.28-6.78), with high heterogeneity ($I^2=89.17\%$, $P < 0.0001$). Exclusion of two studies with relatively high influence in sensitivity analysis resulted in a markedly lower heterogeneity with a RR of 1.87 (95% CI: 1.41-2.51, $I^2=0\%$, $P=0.46$). Subgroup analysis revealed statistically significant differences in the association between AFB1 exposure and liver cancer risk by region and study design. The dose-response analysis showed a piecewise linear relationship between AFB1 exposure and the risk of liver cancer. The OR for liver cancer was 1.02 (95% CI: 1.01-1.03) at an exposure level of 1 ng/kg bw/day.

Conclusion: This meta-analysis confirmed a positive association between AFB1

exposure and the risk of liver cancer, with evidence of a dose-response relationship. The results highlight the need for effective measures to reduce AFB1 exposure in the population.

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An online machine learning system for predicting RDKF in middle-aged and older adults: results from the China Health and Retirement Longitudinal Study

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Abstract

Background: Chronic kidney disease (CKD) progression can be mitigated through early detection of rapid decline in kidney function (RDKF), yet effective community-based screening systems are lacking.

Objective: We developed and validated an interpretable, machine learning-based prediction system to identify individuals at high risk of RDKF in middle-aged and older populations.

Methods: Using data from 5,012 participants in the China Health and Retirement Longitudinal Study (CHARLS, 2011–2015), we defined RDKF as an annualized estimated glomerular filtration rate (eGFR) decline ≥ 4 mL/min/1.73 m². The cohort was randomly divided into training (70%) and testing (30%) sets. Key predictors were selected using the Boruta algorithm, and six machine learning models—logistic regression, random forest, support vector machine (SVM), XGBoost, CatBoost, and LightGBM—were trained with 5-fold cross-validation. Model performance was evaluated using the area under the ROC curve (AUC), Brier score, calibration, and decision curve analysis. The optimal model was deployed as an interactive web system with SHAP-based interpretability.

Results: Over four years, 7.2% (n=361) of participants developed RDKF. Sixteen predictors, including lipid profiles, glycemic markers, and blood pressure, were selected. The SVM model demonstrated the best performance (AUC = 0.706, 95% CI: 0.652–0.760), with a Brier score of 0.063, strong calibration, and clinical utility across risk thresholds of 10–30%. The publicly accessible system supports individual and batch predictions with personalized risk explanations.

Conclusions: Our machine learning-based system provides a practical solution for predicting RDKF risk in public health servicest, enabling early intervention and

resource prioritization. Further validation is needed to assess its generalizability across diverse populations.

Funding: This work was supported by the Hainan Provincial Natural Science Foundation of China (no. 822QN323) and the Startup Foundation for Advanced Talents of Hainan Medical University (no. XRC202114).

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Analyzing Public Perception of Mpox on TikTok in China: A Topic Modeling Approach Based on LDA

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[Abstract] Objective: Mpox has re-emerged as a global public health concern. With the growing reliance on social media for health information, understanding public perception through these platforms is essential for epidemic control. Methods: We collected TikTok data related to "Mpox" from April 1, 2022, to March 31, 2025, using the Aisou Jisou system. Search Index trends and Target Group Index (TGI) were analyzed by time, gender, age group, and province. Latent Dirichlet Allocation (LDA) was applied to extract latent topics from associated search terms and comments. Topic evolution was further analyzed during four peak months of public interest to track changes in discourse. Results: Four major search peaks were identified, coinciding with key events such as the WHO's mpox declarations and domestic case surges. Younger users, particularly those aged 18-23, showed the highest levels of engagement; Beijing, Tianjin, and Jilin reported the highest regional TGI. LDA modeling identified eight primary topics, including transmission and prevention, vaccine-related concerns, symptom recognition, case discovery, and misinformation. Public concerns shifted over time from general disease knowledge to stigmatization, vaccine distrust, and conspiracy theories. Sankey diagrams revealed how public attention migrated across topics at different stages of the epidemic. Conclusions: TikTok provides real-time insight into public perception during mpox outbreaks but also amplifies misinformation and stigmatizing narratives. Public health authorities should leverage such platforms for timely communication while addressing false information and social bias. Tailored strategies are needed to improve health literacy, reduce stigma, and support outbreak preparedness and response.

Keywords: Mpox; TikTok; LDA; Public perception; Health communication; China

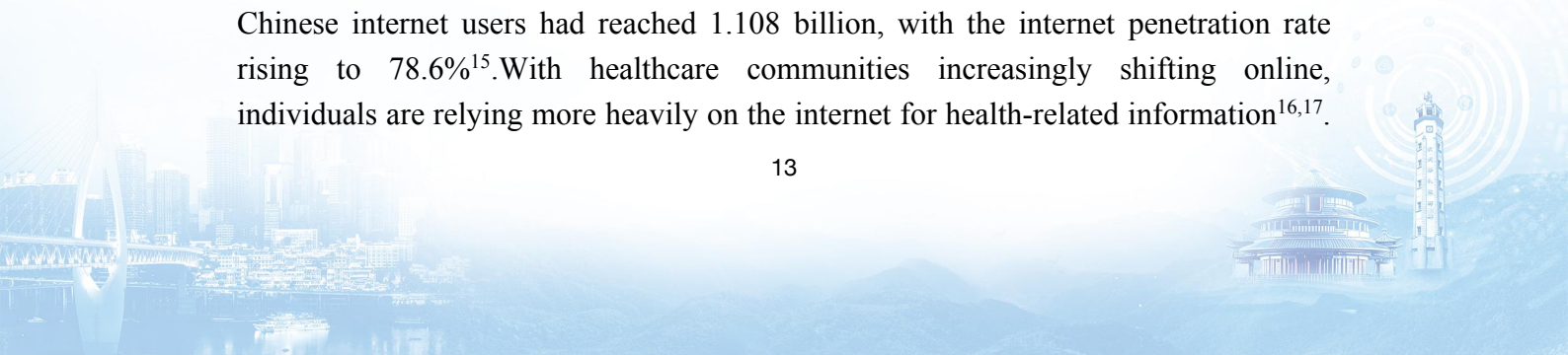
Introduction

Mpox, formerly known as monkeypox, is an emerging zoonotic disease caused by the

mpox virus (MPXV). The virus was first identified in monkeys in 1958 and has since been detected in various animal species. In 1970, the first human case was reported in the Republic of the Congo in Central Africa. Since then, MPXV has primarily spread within Central and West Africa through animal-to-animal (mainly rodents and non-human primates), animal-to-human, and human-to-human transmission pathways¹. In recent years, globalization has significantly contributed to the cross-border spread of mpox, leading to outbreaks in multiple countries. In May 2022, mpox had spread to 110 countries, prompting the World Health Organization (WHO) to declare it a Public Health Emergency of International Concern (PHEIC) in July 2022. This declaration was lifted in May 2023 as global case numbers declined². However, on August 14, 2024, the WHO again declared a PHEIC due to an outbreak in the Democratic Republic of the Congo, attributed to a previously unreported subtype, clade Ib, which is associated with more severe disease outcomes^{3,4}. As of February 28, 2025, 131 countries have reported a total of 134,034 confirmed cases and 291 deaths globally. Notably, men who have sex with men (MSM) account for 86.6% of cases reported in the past 12 months⁵.

The first imported case of mpox in mainland China was confirmed on September 16, 2022, in Chongqing⁶. By February 28, 2025, a total of 2,849 cases had been identified across the country, with 549 reported in the past year⁵. Although China has reported fewer cases compared to high-prevalence regions globally, its large population necessitates continued preparedness for the public health challenges posed by potential mpox outbreaks. Previous studies have identified several key risk factors for mpox infection in non-endemic countries, including having multiple sexual partners, close physical contact, MSM status, contact with confirmed cases, and younger age groups. Vaccination has been shown to be protective⁷. In China, however, cultural stigma, legal constraints, and the large but often hidden MSM population present significant challenges to identifying high-risk individuals⁸⁻¹⁰. Additionally, limited public knowledge about mpox has fueled fear and hindered the adoption of protective behaviors^{11,12}. Therefore, understanding public concerns and formulating targeted health education strategies based on these concerns is essential for effective outbreak prevention and control¹³.

The development of social media platforms is an inevitable trend in the digital era. As of February 2025, approximately 5.24 billion people—63.9% of the global population—were active on social media¹⁴. In China, according to the 55th "Statistical Report on China's Internet Development" released by the China Internet Network Information Center (CNNIC) in January 2025, as of December 2024, the number of Chinese internet users had reached 1.108 billion, with the internet penetration rate rising to 78.6%¹⁵. With healthcare communities increasingly shifting online, individuals are relying more heavily on the internet for health-related information^{16,17}.



User interactions on social media platforms, such as comments and shares, also reflect public concern and attitudes toward health emergencies to a certain extent^{18,19}. TikTok, known for its personalized content delivery and algorithm-based recommendations, has gained immense popularity in China and ranks among the top platforms in terms of user activity²⁰. According to a report by third-party research agency QuestMobile, as of December 2024, the combined number of unique active users of TikTok and its lite version reached 978 million, making it a key channel for information dissemination²¹. Despite TikTok's potential for health information delivery, concerns remain regarding the accuracy and reliability of its content. Some users may spread misinformation or incomplete content, which could trigger unnecessary public panic^{22–24}.

In this context, this study aims to employ Latent Dirichlet Allocation (LDA) to analyze mpox-related content on TikTok. LDA is an unsupervised Bayesian statistical model widely used in text mining and natural language processing. It represents each document as a mixture of topics, and each topic as a probability distribution over words^{25,26}. By analyzing mpox-related discussions and comments on TikTok using LDA, we aim to gain insights into public awareness, information-seeking behaviors, and perceptions of preventive measures. The findings will provide a scientific basis for developing precise health communication strategies and intervention measures. Furthermore, LDA can identify knowledge gaps and hotspots in public discourse on TikTok, offering valuable insights not only for mpox prevention but also for studying public concerns about other diseases. This approach allows for the optimization of health communication content and strategies, ultimately improving public health literacy and preparedness.

Methods

Data Sources

The data used in this study were obtained from the "Aisou Jisou(艾搜即搜)" Index Analysis System (<https://cdc.indexsta.cnaxc.com/#!/douyin/relate-word-search-item/index>), which provides TikTok-related data. The system has obtained a Chinese software copyright registration number from the National Copyright Administration of China, with the registration number being 14092309. The keyword used for data extraction was mpox. The starting point was set to onemonth prior to the first reported mpox case in the non-endemic United Kingdom in May 2022, and the endpoint was set to two months after the confirmation of the first clade Ib case by the Chinese Center for Disease Control and Prevention in January 2025. The total duration was three years,

covering the period from April 1, 2022, to March 31, 2025.

Retrieved data included: Search Index, Associated Search Terms, Target Group Index (TGI) stratified by gender, age group, and provinces in mainland China. The Search Index is a proprietary metric developed by TikTok to assess the popularity of specific keywords. It is derived by weighting the search volume of the keyword and its related content. It should be noted that the Search Index does not reflect the exact search volume. The TGI reflects the relative strength or weakness of the consumption behavior of a specific user demographic for a given keyword, as compared to the overall platform user base²⁷. A TGI value greater than 100 indicates that the proportion of users with a given profile tag who are engaging with this keyword exceeds the platform average. (Figure 1)

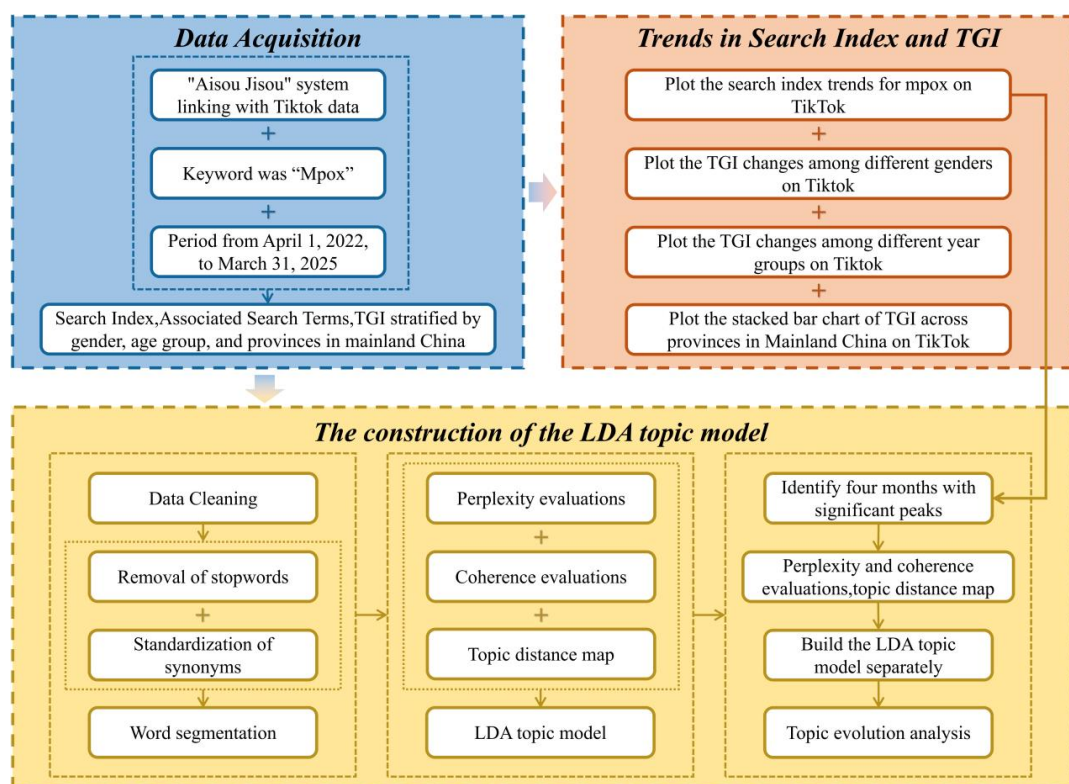


Figure1 Methodological flowchart.

Data Cleaning

Before conducting the LDA analysis, data preprocessing was performed to ensure accuracy and quality. This included: Removal of stopwords (e.g., modal particles, meaningless symbols), Standardization of synonyms (e.g., different expressions for the same country or disease abbreviations), Phrase merging (e.g., combining multi-word terms into single tokens), Word segmentation. These steps aimed to reduce noise and improve the semantic clarity of the dataset for topic modeling.

Statistical Analysis

Descriptive analysis of the Search Index was conducted using the Aisou Jisou system. LDA analysis and related procedures, including data preprocessing, word segmentation, perplexity and coherence evaluation, topic modeling, and visualization, were conducted using Python 3.12.0. The following third-party libraries were employed: "matplotlib", "numpy", "jieba", "scipy", "gensim", "pandas", "pyLDAvis", "openpyxl", and "pyecharts".

The number of topics is a critical parameter in LDA modeling. Both excessively few and overly many topics may hinder the model's interpretability. "Perplexity" and "coherence" scores were used to evaluate model performance. Lower perplexity indicates better predictive performance on unseen data, while higher coherence implies more semantically meaningful and interpretable topics^{28,29}.

We evaluated models with topic numbers ranging from 1 to 15. For each model, we identified the top 30 words per topic based on their conditional probability $P(w|z)$, which represents the probability of word "w" appearing given topic "z". Topic distance and overlap were visualized using the "pyLDAvis" tool. A non-overlapping distribution of terms across topics was used as an additional criterion for model selection. For peak months of public attention-identified based on Search Index spikes-separate LDA analyses were conducted. Topic evolution was tracked over time to reveal the temporal transition of thematic focus.

Results

Trends in Search Index and TGI

From April 1, 2022, to March 31, 2025, the Search Index for "Mpox" on TikTok in China showed four significant peaks, corresponding to May 2022, July 2023, August 2024, and February 2025 (Figure 2). These spikes aligned with major epidemic events both globally and domestically.



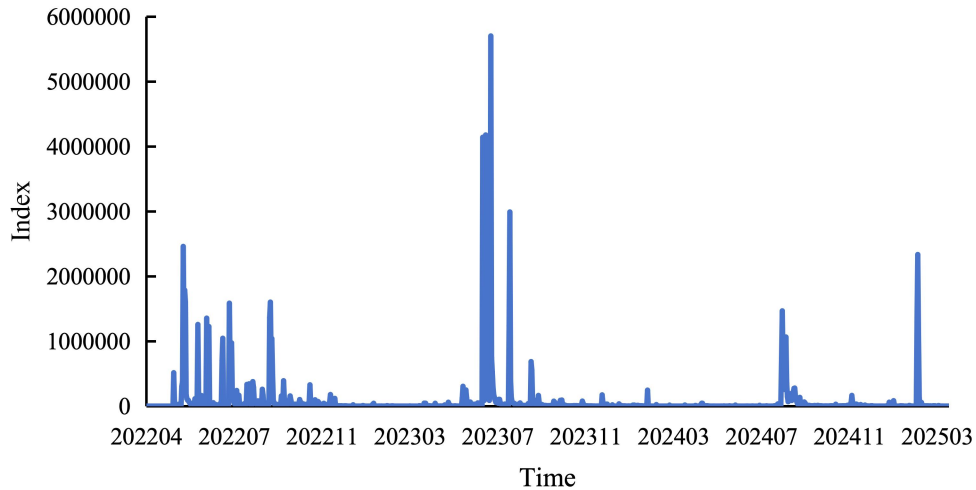


Figure2 Monkeypox search index trends on TikTok.

TGI analysis revealed fluctuating engagement across genders without a clear long-term bias; however, male users maintained higher TGI values for extended periods as the outbreak progressed. In terms of age, younger users consistently demonstrated higher TGI, with the 18-23 age group exhibiting the highest and most volatile engagement, peaking in late 2024; the 24-30 group followed with moderate but stable attention; while older groups (31-40, 41-50, and 51+) showed lower and more stable engagement. Spatially, provinces such as Beijing, Tianjin, and Jilin recorded the highest cumulative TGI; individual months also showed sharp increases in regions like Gansu (December 2023) and Tianjin (March 2025), possibly reflecting localized outbreaks or viral content amplification (Figures 3-5).

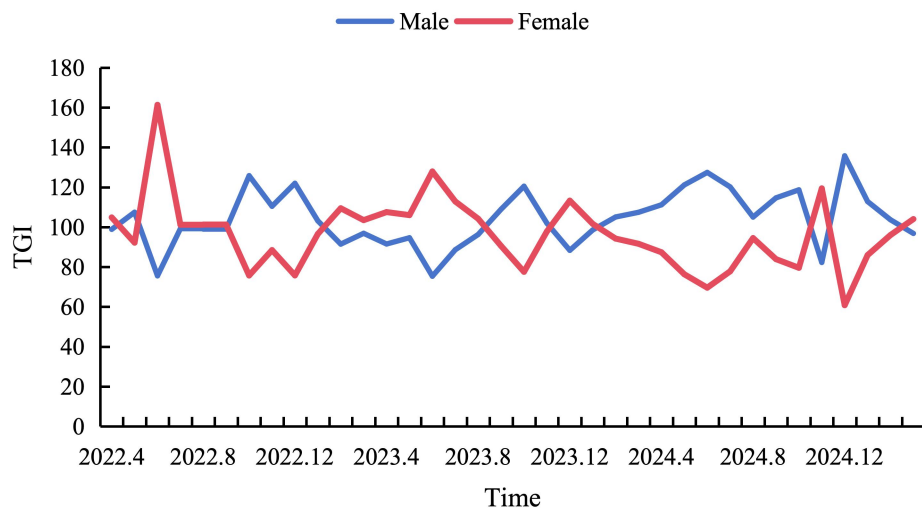


Figure3 TGI changes among different genders on Tiktok.

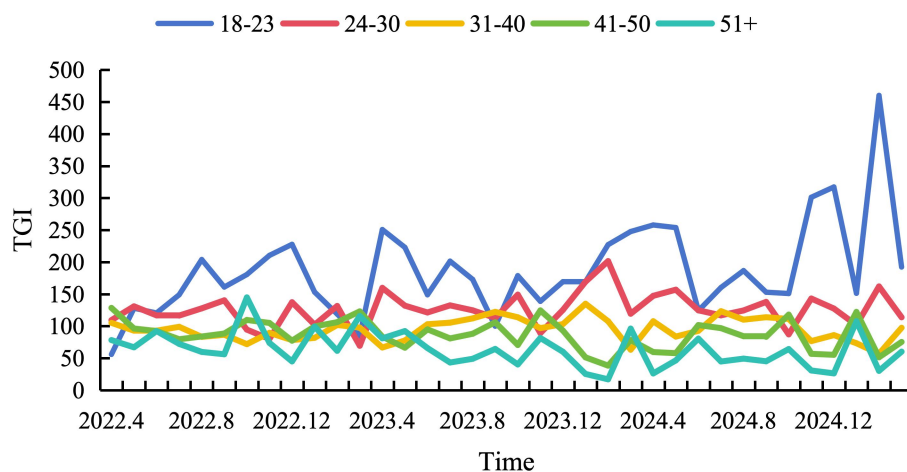


Figure4 TGI changes among different year groups on Tiktok.

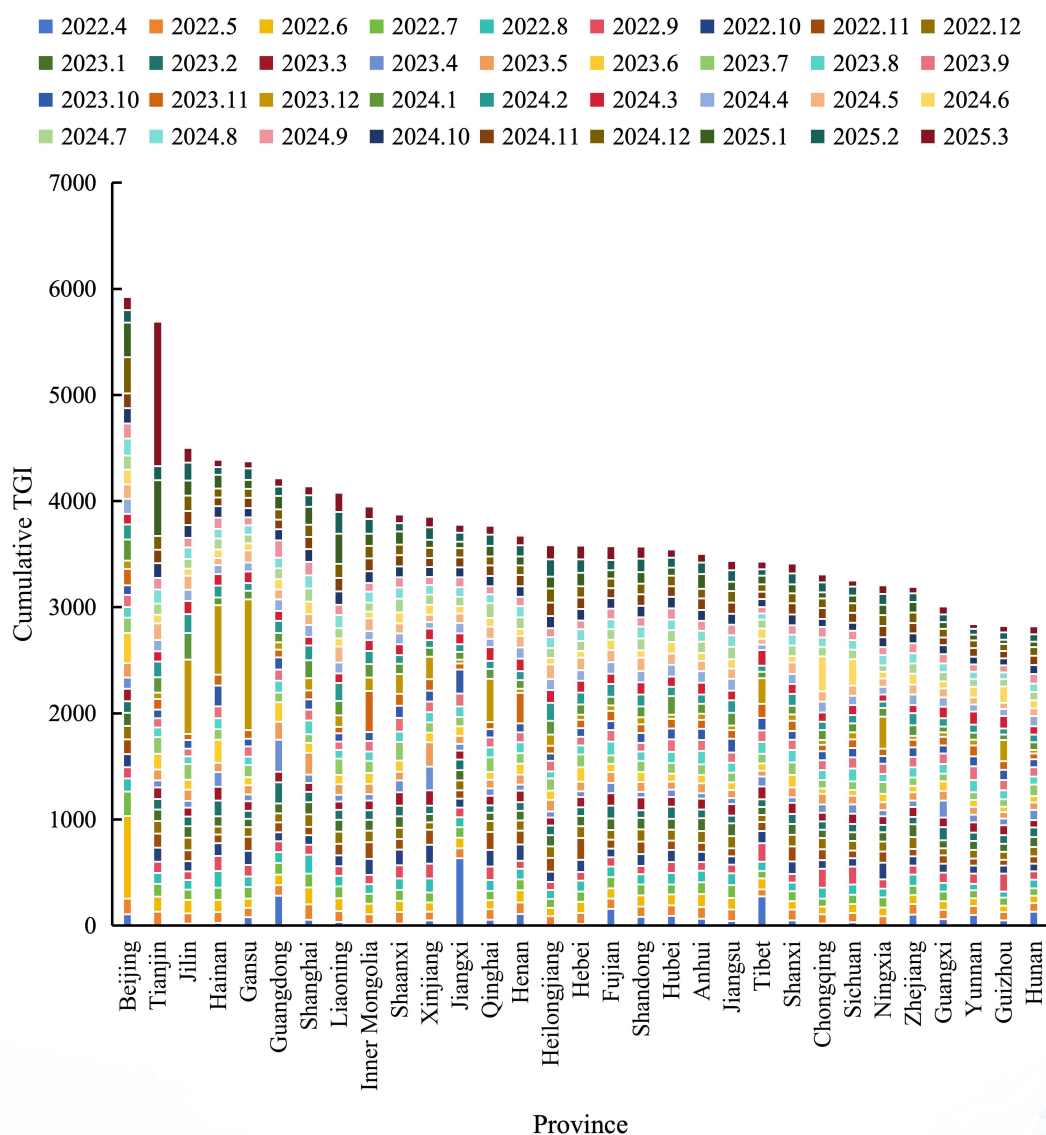


Figure5 Stacked bar chart of TGI across provinces in Mainland China on TikTok.

LDA Topic Modeling Results

LDA modeling, based on perplexity and coherence evaluations (Figure 6A, 6B), determined the optimal number of topics as eight. Topic distance mapping showed minimal overlap (Figure 7).

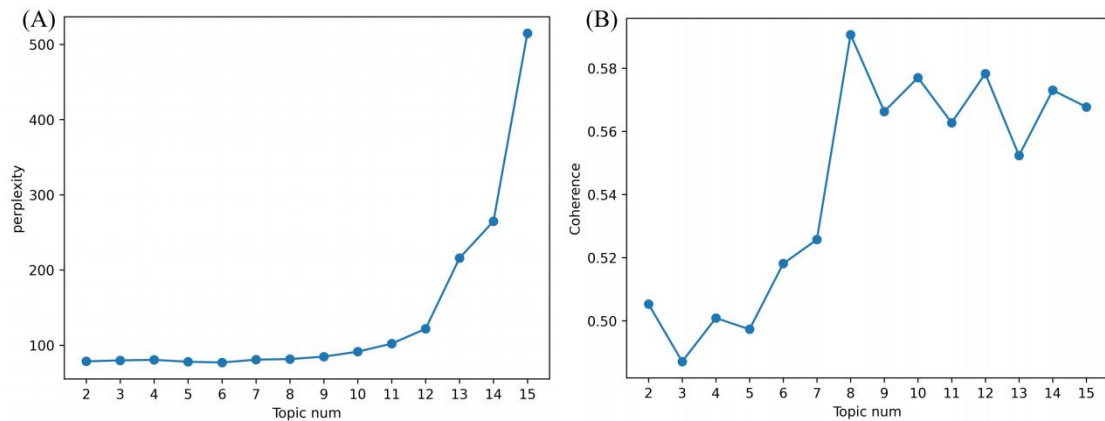


Figure6 Perplexity and coherence scores for different topic counts.(A)Perplexity scores for different topic counts;(B)Coherence scores for different topic counts.

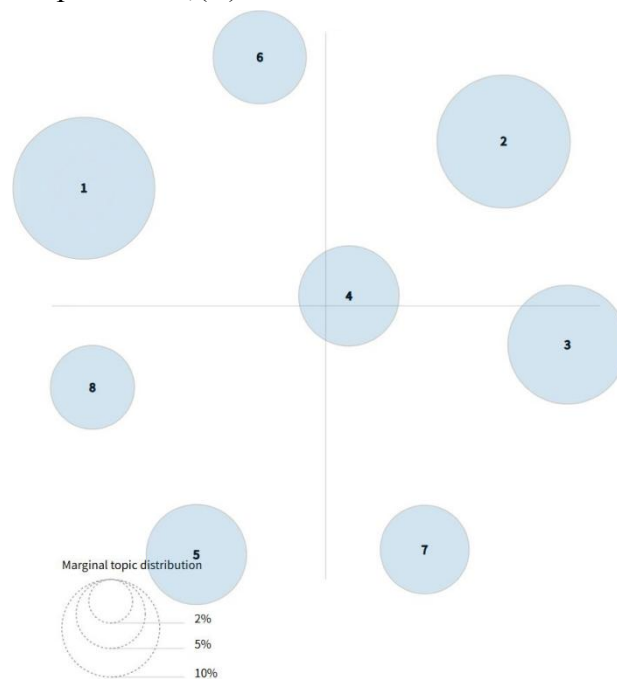


Figure7 The inter-topic distance map for 8 topics.

Table 1 presents the top 30 keywords ranked by $P(w|z)$ for each topic, along with their term frequencies.

Table1 The word frequency and top 30 associated words of $P(w|z)$ for 8 topics.

Topic	Top 30 related words (word frequency, $P(w z)$)
#1	patients (637, 0.239), rash (259, 0.152), Mpox (606, 0.141), virus-infected persons

- (178, 0.072), Sichuan (197, 0.067), infected persons (128, 0.067), prevention (310, 0.064), Beijing (171, 0.061), Shenyang (77, <0.05), Shanghai (116, <0.05), rumor-busting (80, <0.05), WHO (78, <0.05), official (63, <0.05), disease (25, <0.05), fever (11, <0.05), Qiantan (16, <0.05), stage (8, <0.05), cooked meat (1, <0.05), threat (4, <0.05), monkey (1, <0.05), Fanfan (1, <0.05), claiming power (1, <0.05), girlfriend (1, <0.05), suspected infection (1, <0.05), outbreak (20, <0.05), get mpox (3, <0.05), US (1, <0.05), hundreds of cases (12, <0.05), pox family (1, <0.05), like (1, <0.05)
- #2 Latest news (0.318, 1240), dense (0.115, 469), phobia (0.115, 471), honeycomb (0.092, 274), holes (0.09, 292), detection (0.071, 333), test kit (0.05, 140), CDC (<0.05, 196), growth (<0.05, 77), serious (<0.05, 100), experts (<0.05, 112), interpretation (<0.05, 63), Heilongjiang (<0.05, 44), transmission method (<0.05, 257), need (<0.05, 37), how long (<0.05, 12), condition (<0.05, 31), Fanfan (<0.05, 1), like (<0.05, 1), swallow (<0.05, 34), face (<0.05, 4), emphasize (<0.05, 43), form (<0.05, 1), spreader (<0.05, 1), Mpox (<0.05, 3), outbreak (<0.05, 20), know (<0.05, 2), hope (<0.05, 43), US (<0.05, 1), world (<0.05, 1)
- #3 Chickenpox (0.227, 545), difference (0.172, 314), AIDS (0.138, 257), treatment (0.138, 328), recovery (0.056, 186), Changsha (0.051, 128), medicine (0.05, 73), Henan (<0.05, 84), effective (<0.05, 93), distinguish (<0.05, 36), fever (<0.05, 102), protection (<0.05, 133), method (<0.05, 127), effect (<0.05, 16), Mpox (<0.05, 3), US (<0.05, 1), formation (<0.05, 1), spreader (<0.05, 1), Like (<0.05, 1), Emphasize (<0.05, 43), Worldly (<0.05, 1), Face (<0.05, 4), Hope (<0.05, 43), Stay away (<0.05, 65), Swallow (<0.05, 34), Property (<0.05, 43), Fanfan (<0.05, 1), Outbreak (<0.05, 20), Know (<0.05, 2), Suspect (<0.05, 1)
- #4 Red dot (0.416, 331), outbreak (0.229, 337), droplet (0.062, 102), WHO (0.06, 325), organization (0.057, 262), sexual transmission (<0.05, 35), prevention (<0.05, 47), hands and feet (<0.05, 22), transmission speed (<0.05, 40), warning (<0.05, 23), highest level (<0.05, 24), cooked meat (<0.05, 1), smiling face (<0.05, 1), people (<0.05, 1), life-threatening (<0.05, 1), smallpox (<0.05, 1), claiming power (<0.05, 1), knowing (<0.05, 2), Special monkey (<0.05, 1), threat (<0.05, 4), Fanfan (<0.05, 1), best (<0.05, 6), suspected infection (<0.05, 1), outbreak (<0.05, 20), Mpox (<0.05, 3), US (<0.05, 1), formation (<0.05, 1), like (<0.05, 1), girlfriend (<0.05, 1), rice cooker (<0.05, 1)
- #5 Infectious (0.167, 614), New (0.133, 481), First case (0.106, 685), Confirmed (0.1, 648), Cases (0.093, 2678), Disfigurement (0.072, 326), Preventive measures (0.064,

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- 177), Mainland (< 0.05, 191), AIDS (< 0.05, 382), Symptoms (< 0.05, 93), Warts (< 0.05, 44), Reports (< 0.05, 163), Holes (< 0.05, 30), Terror (< 0.05, 33), Congo (< 0.05, 114), Monkeys (< 0.05, 64), Golden monkeys (< 0.05, 45), Palm (< 0.05, 32), Guangxi (< 0.05, 21), plague (< 0.05, 35), clinical trial (< 0.05, 32), small hole (< 0.05, 51), epidemic (< 0.05, 18), disease can be cured (< 0.05, 12), US (< 0.05, 1), know (< 0.05, 2), like (< 0.05, 1), form (< 0.05, 1), suspected infection (< 0.05, 1), outbreak (< 0.05, 20)
- #6 infection (0.145, 1300), male (0.111, 446), vaccine (0.095, 845), poxvirus (0.089, 769), COVID (0.088, 507), easy (0.065, 150), USA (0.053, 652), virus (< 0.05, 321), smallpox (< 0.05, 202), vaccination (< 0.05, 96), male (< 0.05, 248), hole (< 0.05, 139), inclusion (< 0.05, 71), female (< 0.05, 47), isolation (< 0.05, 105), Mpox (< 0.05, 606), full hands (< 0.05, 51), ointment (< 0.05, 44), is there (< 0.05, 47), can prevent (< 0.05, 41), location (< 0.05, 26), event (< 0.05, 60), proceed (< 0.05, 33), UK (< 0.05, 81), public health (< 0.05, 53), severe (< 0.05, 12), cowpox (< 0.05, 38), outbreak (< 0.05, 20), US (< 0.05, 1), formation (< 0.05, 1)
- #7 Cases (0.181, 2678), Discovery (0.169, 1402), Chongqing (0.13, 707), Infectiousness (0.106, 342), Homosexuality (0.063, 126), Importation (0.052, 377), Gay (0.051, 120), Death (< 0.05, 292), Foot (< 0.05, 86), Strong (< 0.05, 84), Variation (< 0.05, 311), Not Strong (< 0.05, 70), Ratio (< 0.05, 90), Infectiousness (< 0.05, 614), Disease Energy (< 0.05, 73), Honeycomb (< 0.05, 45), Pathway (< 0.05, 123), Hong Kong (< 0.05, 111), nausea (< 0.05, 30), hollow (< 0.05, 22), Zhengzhou (< 0.05, 55), case (< 0.05, 39), US (< 0.05, 1), Mpox (< 0.05, 3), outbreak (< 0.05, 20), suspected infection (< 0.05, 1), formation (< 0.05, 1), like (< 0.05, 1), Fan Fan (< 0.05, 1), girlfriend (< 0.05, 1)
- #8 Symptoms (0.297, 1022), Appearance (0.175, 937), Mode of transmission (0.102, 257), Number of people (0.075, 282), Infectious disease (0.074, 263), Class B (< 0.05, 123), Statistics (< 0.05, 136), STD (< 0.05, 72), Infection (< 0.05, 1300), Meaning (< 0.05, 51), Class A (< 0.05, 49), Belong to (< 0.05, 69), Cases (< 0.05, 2678), Male (< 0.05, 16), Specific medicine (< 0.05, 89), True portrayal (< 0.05, 18), Mpox (< 0.05, 3), Deadly (< 0.05, 1), outbreak (< 0.05, 20), US (< 0.05, 1), smiling face (< 0.05, 1), like (< 0.05, 1), know (< 0.05, 2), worldly affairs (< 0.05, 1), face (< 0.05, 4), single move (< 0.05, 1), people (< 0.05, 1), suspected infection (< 0.05, 1), formation (< 0.05, 1), lesson (< 0.05, 1)
-

We've finalized 8 themes based on keyword associations and source text, and labeled them accordingly. Table 2 also includes specific examples for each theme.

Table2 Topic labels and examples.

Topic	Example
# 1 Mpox Transmission and Prevention	"Mpox outbreak in the Democratic Republic of the Congo", "Will mpox break out in China?", " Will mpox spread widely?"
# 2 Epidemic Monitoring and Control Measures	"The latest news on mpox from the China Center for Disease Control", "Mpox detection kit", "How to buy mpox detection kit"
# 3 Disease Treatment and Prevention Strategies	"Effective treatment for mpox", "How does TCM prevent and treat mpox", "What does recovery from mpox look like"
# 4 Epidemic Transmission and Prevention Measures	"Mpox is transmitted between men and men", "Is mpox more easily transmitted between homosexuals", "Isn't mpox only common among homosexuals?"
# 5 Epidemic Transmission Characteristics and Control	"Which is more contagious, mpox or COVID-19?", "Is mpox contagious without showing symptoms?", "Is mpox still contagious after recovery?"
# 6 Vaccination and Infection Prevention	"Domestic mpox vaccination", "Does China have mpox vaccine", "Adding HIV to mpox vaccine"
# 7 Case Detection and Transmission Research	"First case of new mpox variant found in France", "First case of new mpox variant confirmed in the United States", "Cities in China where mpox cases found"
# 8 Symptom Presentation and Transmission Modes	"Are the symptoms of mpox and AIDS similar?", "Mpox symptoms pictures", "What are the symptoms of mpox disease?"

Topic labels and interpretations are as follows:

1. "Mpox Transmission and Prevention": Focused on transmission routes, case distribution, and preventive measures. Keywords such as "patients," "Mpox," and "prevention" emphasize geographic spread and control strategies, with frequent references to locations like "Sichuan" and "Beijing."
2. "Epidemic Monitoring and Control Measures": Centered on detection methods, diagnostic kits, and public health interventions. Keywords like "detection," "test kit," and "CDC" highlight the role of real-time monitoring and institutional response.
3. "Disease Treatment and Prevention Strategies": Involved topics such as treatment, recovery, and preventive interventions. Terms like "treatment," "recovery," and "medicine" suggested a broad discourse on disease management, with comparisons to

other diseases like chickenpox and AIDS.

4. "Epidemic Transmission and Prevention Measures": Emphasized specific routes of transmission (e.g., sexual transmission) and corresponding warnings. Keywords suggested a focus on visualized transmission data and international guidance.

5. "Epidemic Transmission Characteristics and Control": Addressed the dynamic nature of transmission and its severity. Keywords like "infectious," "first case," and "preventive measures" emphasized the urgency of outbreak control.

6. "Vaccination and Infection Prevention": Focused on vaccine efficacy and viral mechanisms. Keywords such as "vaccine," "infection," and "poxvirus," along with references to "COVID" and "smallpox," highlighted vaccine applications across pathogens.

7. "Case Detection and Transmission Research": Related to the identification and study of cases and transmission pathways. Keywords like "cases," "discovery," and "pathway" reflected attention on early surveillance and viral spread.

8. "Symptom Presentation and Transmission Modes": Concentrated on clinical symptoms and transmission mechanisms. Keywords like "symptoms," "mode of transmission," and "infectious disease" indicated a focus on symptomatology and statistical tracking.

Topic Evolution During Search Peaks

To explore public interest during peak search months, we conducted separate LDA modeling for the four significant peaks months: May 2022, July 2023, August 2024, and February 2025. Perplexity and coherence metrics were recalculated for each period to determine the optimal number of topics: 2, 6, 4, and 5 topics, respectively (Figure 8). Topic distances were also examined, and no keyword overlaps were found (Figure 9).

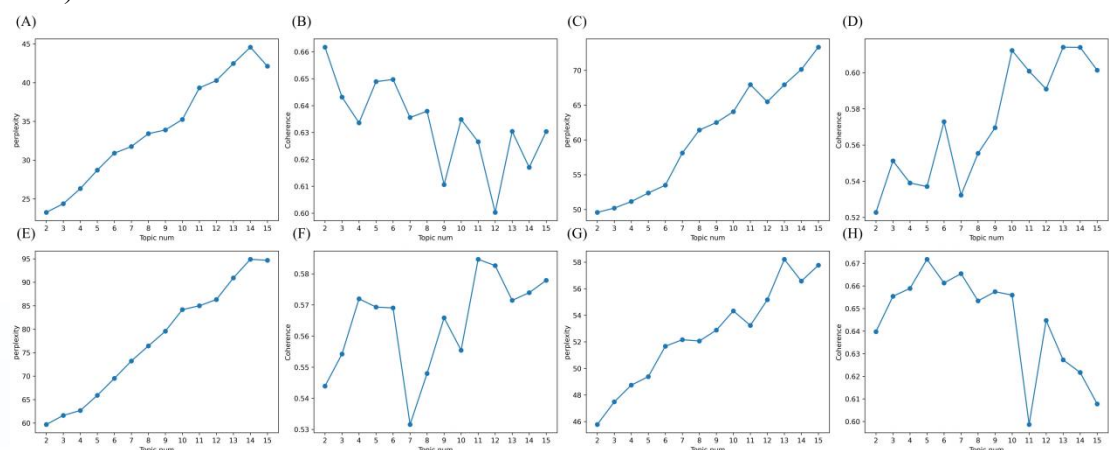


Figure8 Perplexity and coherence scores for different topic counts across different search Index peak periods.(A)Perplexity scores for different topic counts in May 2022;(B)Coherence scores for different topic counts in May 2022;(C)Perplexity scores for different topic counts in July 2023;(D)Coherence scores for different topic counts in July 2023;(E)Perplexity scores for different topic counts in August 2024;(F)Coherence scores for different topic counts in August 2024;(G)Perplexity scores for different topic counts in February 2025;(H)Coherence scores for different topic counts in February 2025.

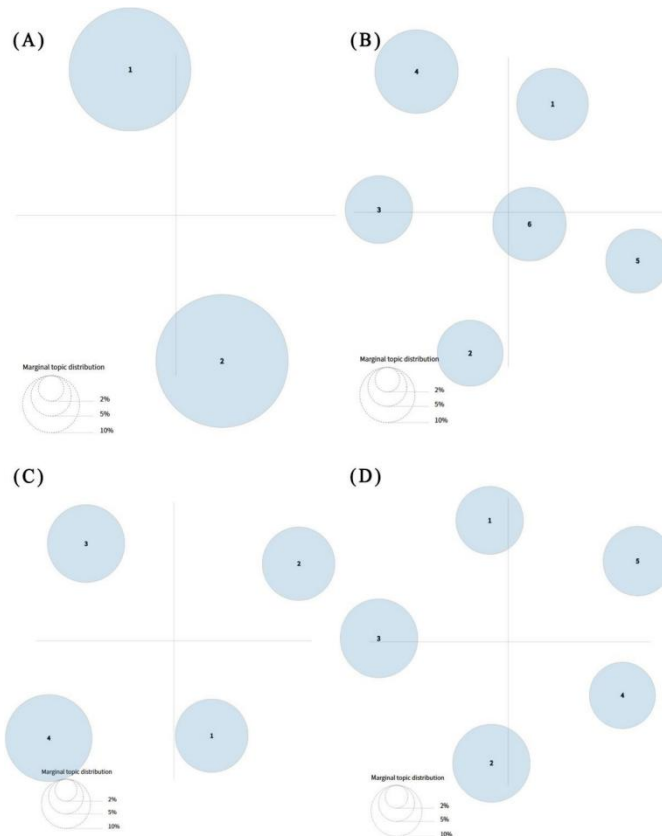


Figure9 The inter-topic distance map for different topic counts across different search Index peak periods.(A)The inter-topic distance map in May 2022;(B)The inter-topic distance map in July 2023;(C)The inter-topic distance map in August 2024;(D)The inter-topic distance map in February 2025.

Table 3 presents the top 30 keywords for each selected topic during the four peak periods of public interest. In May 2022, users primarily focused on gaining a general understanding of mpox, including its transmission routes, prevention methods, and global outbreak status. By July 2023, public attention had shifted toward real-time news updates, clinical features such as incubation periods, the impact on specific groups such as transgender individuals, and newly reported domestic cases. In August 2024, search content reflected growing concern over visual representations of the disease, availability of medical supplies, research on transmission mechanisms, and

discussions surrounding vaccine effectiveness and procedures. By February 2025, attention turned to China's latest outbreak situation, updated prevention strategies, the launch of mpox vaccine clinical trials, and widespread media coverage. To visualize how public concerns transitioned across these periods, we conducted topic evolution analysis using Sankey diagrams (Figure 10), which illustrated the thematic shifts in user interest in response to changing epidemic dynamics. The thicker the lines connecting different time points, the stronger the link between the topics. For instance, the topic of Mpox Disease Treatment and Prevention Strategies in July 2023 was influenced by Mpox Transmission and Prevention and Global Mpox Epidemic Monitoring and Control in May 2022. It then shifted to Mpox Outbreak Characteristics and Control in China and Mpox Symptom Presentation and Transmission Modes in August 2024, and further to Mpox Case Detection and Transmission, News Updates on Mpox Prevention, Mpox Infection and Treatment in China, and Mpox Transmission Characteristics in February 2025. This shows how mpox - related topics evolved from May 2022 to February 2025, shifting from global monitoring and prevention to regional control and practical applications, with a focus on mpox case management and vaccine - based prevention in China.

Table3 The top 30 associated words of $P(w|z)$ across different search Index peak periods.

Time	Topic	Top 30 related words
2022.5	#1 Mpox Transmission and Prevention	virus,symptom,patient,confirm,outbreak,smallpox,infection,russia,develop,picture,report,kit,country,rare,worldwide,canada,test,disease,congo,european,ebola,human,confirms,united,china,contagious,detection,people,131,guangzhou
	#2 Global Mpox Epidemic Monitoring and Control	confirm,smallpox,virus,country,symptom,outbreak,china,infection,death,report,patient,congo,resemble,confirms,ebola,contagious,skin,expert,black,spread,people,shanghai,democratic,future,republic,suspect,threat,prevent,dafeng>alert
2023.7	#1 News Updates on Mpox Transmission and Prevention	spread,late,news,changsha,outbreak,beijing,chongqing,transvestite,rumor,transmission,district,hunan,china,male,epidemic,qinghai,city,guangdong,copy,god,ban,Tiktok,province,artist,mainland,june,prevention,guangzhou,shanghai,characteristic
	#2 Mpox Disease Treatment and Prevention Strategies	symptom,outbreak,difference,picture,late,cure,chickenpox,guangzhou,china,infect,people,data,large-scale,treat,news,ordinary,concept,hospital,day,congo,smallpox,stock,covid-19,shenyang,democratic,republic,quarantine,zhejiang,shenzhen,l

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	#3 Mpox Infection Characteristics and Incubation Periods	country,infection,period,incubation,contagious,monkey,virus,s,pox,copy,Tiktok,mainland,spread,travel,measure,rash,china,xining,press,qinghai,gay,transvestite,people,infect,prevention,test,god,sister,artist,confirm,whuan
	#4 Mpox Scars and Transmission Among Transgender	scar,spread,transvestite,leave,ban,artist,mainland,god,cure,souldn,recovery,people,red,spot,iron,Mpoxvirus,scary,transgender,television,kill,bureau,broadcasting,tiktok,copy,picture,infection,symptom,susceptible,search,graphic
	#5 Mpox Patients and Reports in China	disease,china,patient,report,infect,woman,infectious,confirm,province,rumor,106,shanghai,whuan,june,vaccine,smallpox,detect,hubei,mainland,contact,harbin,shandong,people,tianjin,level,sichuan,jiangsu,covid-19,refute,close
	#6 Contagious Mpox Epidemic Transmission and Prevention	contagious,china,news,late,shenyang,outbreak,travel,virus,tianjin,covid-19,disease,shandong,control,disfigure,prevention,leave,infection,chongqing,recover,chickenpox,guangdong,province,liaoning,patient,department,detect,confirm,cdc,beijing,changsha
2024.8	#1 Mpox Pictures, Medical Stocks, and Transmission Routes	picture,infection,stock,transmit,confirm,virus,news,late,red,concept,health,treatment,spot,patient,city,shandong,africa,vaccine,emergency,hole,guangdong,international,symptom,list,china,distribute,medicine,declare,surge,kit
	#2 Mpox Vaccination and Infection Prevention	spread,vaccine,epidemic,virus,people,death,increase,proportion,outbreak,infect,wave,sharp,gate,bill,female,hiv,africa,2024,teenager,late,transmit,china,male,taiyuan,add,shaanxi,update,smallpox,pox,report
	#3 Mpox Outbreak Characteristics and Control in China	china,outbreak,country,hole,late,news,company,chongqing,2024,spread,monkey,vaccine,list,zhejiang,african,stock,scar,report,pox,concept,recovery,specific,sweden,urumqi,surge,kit,patient,leave,heilongjiang,drug
	#4 Mpox Symptom Presentation and Transmission Modes	outbreak,symptom,picture,health,spread,emergency,news,late,cure,measure,international,shandong,public>alert,disease,prevention,stock,period,africa,heal,concern,qingdao,concept,

organization,country,accord,global,issue,level,african

2025.2	#1	Global Transmission and Prevention	Mpox	2025,class,suspend,shenzhen,pandemic,patient,country,spre ad,hunan,changsha,tryphobia,xinjiang,male,heilongjiang,i nfect,wuhan,monkey,outbreak,harbin,hole,covid-19,sympto m,disease,treat,incubation,period,variant,test,guiyang,epide mic
	#2	Mpox Detection and Transmission	Case and	spread,outbreak,vaccine,symptom,confirm,china,country,hiv ,changchun,chickenpox,jilin,epidemic,kong,hong,city,contin ue,disfigurement,health,measure,protection,medicine,specifi c,fujian,people,protect,shandong,rash,child,jiangxi,distribute
	#3	News Updates on Mpox Prevention		news,late,outbreak,shandong,jinan,china,guangzhou,chongq ing,district,stock,concept,baiyun,virus,transmit,foundation,g ate,henan,people,kill,hebei,honeycomb,leader,sichuan,vacci ne,break,zhengzhou,tianjin,guangxi,city,anhui
	#4	Mpox Infection and Treatment in China		infection,china,cure,virus,outbreak,contagious,picture,statist ic,infect,report,hubei,scar,symptom,beijing,shaanxi,smallpo x,leave,covid-19,mongolia,people,recovery,patient,period,h ole,2025,red,syphilis,global,gansu,stage
	#5	Mpox Transmission Characteristics		picture,outbreak,symptom,country,dalian,shanxi,spot,red,tai yuan,prevent,cluster,zhejiang,treatment,difference,shenyang ,rate,chickenpox,liaoning,shijiazhuang,discover,report,subcl ade,transmission,large-scale,update,sichuan,require,late,new s,virus

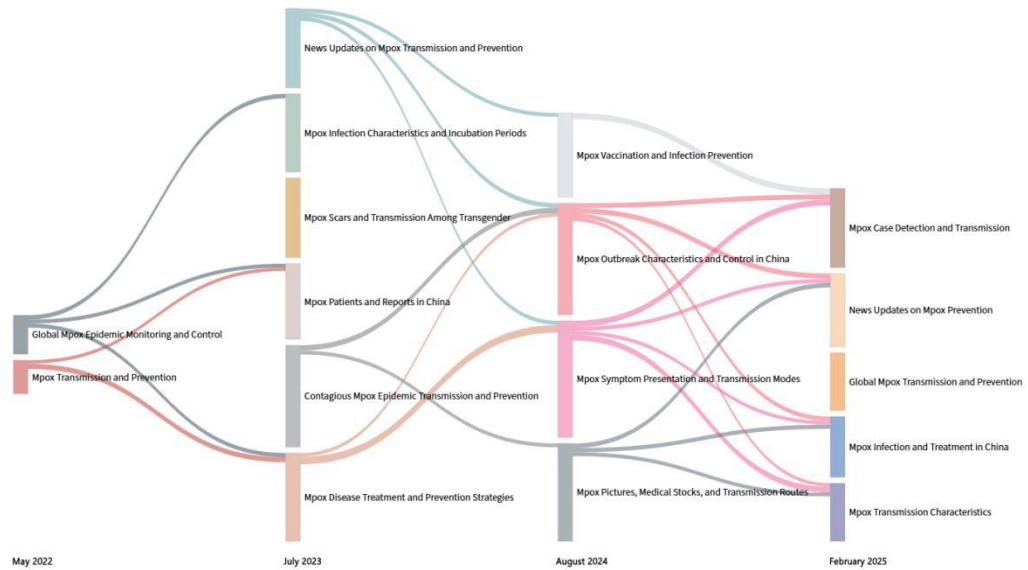


Figure10 The evolution of topics across different search Index peak periods.

Discussion

In this study, we analyzed the trends in the mpox-related Search Index on TikTok in China between April 1, 2022, and March 31, 2025. Four significant peaks were identified in May 2022, July 2023, August 2024, and February 2025. These surges corresponded closely to key global and national public health events. Specifically, in May 2022, the WHO announced the beginning of a global mpox outbreak³⁰; in July 2023, the Chinese CDC reported 106 newly confirmed mpox cases in June, marking the first update since the initial imported case in Chongqing in 2022³¹; in August 2024, the WHO declared the mpox outbreak in the Democratic Republic of the Congo a PHEIC³; and in January 2025, the Mpox Ib variant was detected in China. Then, in February 2025, multiple major Chinese media outlets reposted the latest WHO outbreak report, drawing significant public attention. These findings suggest that public concern regarding mpox on TikTok is highly sensitive to the progression and reporting of the epidemic.

TGI trend analysis by gender and age revealed important demographic insights. Although monthly gender-based TGI values fluctuated, no consistent gender bias was observed. However, male TGI values remained higher for longer periods as the outbreak evolved, potentially due to the predominance of male patients in China. Notably, age-based differences were more pronounced: younger users had higher TGI, with the 18-23 age group showing the most significant engagement and volatility, peaking in late 2024. The 24-30 age group followed with a more stable pattern. In contrast, TGI among users aged 31-50 were relatively low with minimal fluctuation, and those aged 51 and older exhibited the lowest and most stable TGI values. These differences may be attributed to younger users' more frequent engagement with social

media platforms and their greater curiosity and concern regarding emerging health threats. These findings highlight the need for age-targeted health communication strategies. For instance, older adults, who may have limited social media exposure, might benefit more from offline interventions aimed at improving mpox awareness.

Geographically, provinces such as Beijing, Tianjin, and Jilin exhibited the highest cumulative TGI values, which could reflect better healthcare infrastructure, more efficient information dissemination, and higher public health literacy. In some months, individual provinces such as Gansu (December 2023) and Tianjin (March 2025) showed sudden TGI spikes. These may have been triggered by local outbreak reports or intensified media coverage. For example, in December 2023, several widely circulated TikTok videos highlighted Gansu in bold text when discussing new mpox cases(<https://v.douyin.com/uByzrZCnEOo/>). Similarly, in March 2025, a viral post featuring a Weibo screenshot of a mpox case in Tianjin's Jing'an district gained extensive traction on TikTok(<https://v.douyin.com/qFSpuCGFMuw/>). These cases suggest that leveraging influential individuals or visual emphasis in digital communication can enhance the visibility and spread of health-related content.

By selecting eight topics based on perplexity and coherence scores, we were able to comprehensively capture the thematic structure of mpox-related discussions on TikTok. These topics spanned transmission, prevention, surveillance, treatment, vaccination, case studies, and symptomatology—indicating diverse public interests and concerns. However, certain associated keywords reflected ongoing public confusion and challenges in epidemic prevention. Previous studies on COVID-19 have demonstrated that misinformation, rumors, and conspiracy theories can spread widely on social media, potentially inciting public fear and misunderstanding^{32,33}. In our study, Topic 1 included search terms like "monkeypox spread by U.S. planes(<https://v.douyin.com/RNdlePuEhas/>)" and "virus developed by American and Jewish capital(<https://v.douyin.com/MA4Fm5K1yng/>)," which may incite xenophobic sentiment and public panic. In Topic 6, terms such as "Why is the mpox vaccine not being promoted?" and "Adding HIV to the mpox vaccine" revealed mistrust that may undermine vaccination efforts, particularly among high-risk populations^{10,34}. Concerns about vaccine side effects could also reduce vaccine uptake among vulnerable groups.

Stigmatization of certain populations emerged as another prominent issue. Topic 4 featured queries such as "Mpox is transmitted between men and men" and "Isn't mpox only common among homosexuals?"—statements that perpetuate harmful stereotypes. Such discourse not only marginalizes affected groups but may also lead to self-concealment of cases and reduce vigilance among the general public, ultimately hampering disease control efforts^{9,35}. Furthermore, the presence of fundamental knowledge gaps was evident. Queries such as "What's the difference between mpox and chickenpox?", "Can mpox be cured?", and "Is mpox still contagious after

recovery?" suggest a general lack of understanding. Alarming, previous studies have shown that even some sexual health professionals had limited knowledge about mpox³⁶. Therefore, enhancing public health literacy and empowering individuals to distinguish accurate from false information are essential to promoting risk awareness and responsible health behaviors.

Public concerns also shifted at different stages of the outbreak. In May 2022, when mpox first attracted public attention, searches focused on basic disease knowledge and global outbreak status (e.g., "What kind of disease is mpox?", "Mpox symptoms look like smallpox", "Which countries have outbreaks?"). These trends align with prior findings that individuals seek real-time information during health emergencies via social media platforms^{37,38}. While platforms like TikTok facilitate timely information dissemination, they may also host misleading content. One COVID-19 study reported that 27% of TikTok videos in the early phase contained incorrect or incomplete information³⁹. Thus, content regulation by authorities is essential.

As public understanding of mpox improved and the outbreak evolved, public interest shifted⁴⁰. In July 2023, keywords such as "expert interpretation of transmission," and "CDC's mpox infection risk analysis" reflected the growing presence of professionals in content creation. However, stigmatizing discourse also intensified, including inflammatory posts targeting transgender individuals or referencing celebrities associated with LGBTQ+ communities^{39,41} (e.g., "Ban transgender performers spreading mpox," "Jolin Tsai's fans got mpox"—Tsai being a pop icon known for LGBTQ+ support).

In August 2024, following the WHO's renewed declaration of a PHEIC, public discourse once again shifted, with growing expressions of fear—consistent with previous research showing increased fear-related posts during global health emergencies^{42,43}. Keywords such as "photos of mpox pustules," "disfigurement after recovery," and "Bill Gates injecting HIV into mpox" exemplify this trend. In February 2025, the release of WHO's latest mpox report and wide media dissemination reignited public interest, with a focus on domestic developments such as cluster outbreaks, case statistics, and clinical trials of mpox vaccines in China.

Overall, the evolution of mpox-related search content on TikTok closely paralleled the epidemic's progression and public information needs at various stages. This indicates TikTok's potential utility for real-time health surveillance and the importance of adapting health education strategies to the public's changing concerns. Simultaneously, efforts must be made by public health professionals and policymakers to counter misinformation, stigmatization, and fear-mongering that may obstruct effective disease prevention and control.

Nevertheless, this study has several limitations. First, due to technical constraints, we

were unable to retrieve all mpox-related TikTok content or conduct more granular analyses of user subgroups. Second, our data were limited to associated search terms, preventing deeper analysis of the content behind those searches. Third, some internal algorithms (e.g., TGI calculation) used by TikTok are not fully transparent, which may affect data accuracy. Finally, although we implemented comprehensive data cleaning, certain context-specific or emerging expressions might have been mistakenly removed or overlooked by the filtering system.

Conclusions

This study analyzed TikTok data on mpox in China using LDA modeling, revealing that public attention closely followed epidemic developments and varied by age and region. Eight major topics were identified, ranging from transmission and prevention to misinformation and stigmatization. The findings highlight the dual role of social media as both an information source and a potential vector for misinformation. Targeted health communication strategies and strengthened platform governance are essential to improve public awareness, reduce stigma, and support effective epidemic response.

基金资助: 无

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Assessing the Impact of Extreme Climate on City Cardiovascular Disease in China: A Spatial and Causal Analysis

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Background: Global climate change has intensified the frequency and severity of extreme weather events, posing substantial challenges to public health and particularly exacerbating the burden of cardiovascular diseases (CVD). China's rapidly aging population and urbanization process have further amplified climate-related health risks. While previous studies have focused on associations between extreme climate exposure and CVD mortality, critical gaps remain in understanding how the proportion of extreme weather events affects urban cardiovascular disease prevalence and in establishing causal evidence between individual-level extreme climate exposure and cardiovascular disease risk.

Objective: First, this study applies spatial analysis to explore and quantify the impacts of extreme climate events on cardiovascular disease prevalence across various prefecture-level cities in China. Second, it employs causal inference methods to examine how individual exposure to extreme climate conditions affects cardiovascular disease risk, while also identifying vulnerable population groups. The findings aim to provide empirical evidence for healthcare institutions to develop targeted prevention strategies and care interventions.

Methods: This study employed a repeated cross-sectional design for spatial analysis and a longitudinal cohort design for causal inference. Spatial analysis techniques included global spatial autocorrelation and local spatial autocorrelation. Multiscale geographically and temporally weighted regression was used to examine extreme climate impacts on urban cardiovascular disease prevalence. Dynamic double machine learning (DML) to quantify causal effects of individual-level extreme weather exposure on cardiovascular disease risk while analyzing heterogeneous factors including age, BMI, and air pollution.

Results: Spatial autocorrelation identified persistent CVD hot spots in northeastern industrial cities and cold spots in southern coastal cities. Extreme climate events exhibited significant spatial clustering (Moran's $I = 0.414-0.433$). Regression

analysis revealed that each unit increase in extreme climate proportion elevated urban CVD prevalence by 0.623-0.625 units, with impact intensity decreasing from southwest to northeast and strengthening annually. Socioeconomic factors showed dual effects: medical facility availability reduced CVD risk, while GDP growth and population density exacerbated it. Dynamic DML confirmed that extreme climate exposure directly increased individual cardiovascular disease risk ($ATE = 0.254$). Heterogeneity analysis indicated that BMI and PM2.5 elevation amplified cardiovascular risks during extreme weather exposure. . Protective effects emerged from retirement, higher education levels, and expanded urban green spaces.

Conclusions: Extreme climate events exacerbate cardiovascular risks in middle-aged and elderly populations through physiological stress and chronic damage, with impacts mediated by regional development disparities and individual vulnerability. We recommend prioritizing "meteorological-medical" joint warning systems in climate-vulnerable regions, developing targeted interventions for high-risk groups, and addressing health inequalities through cross-regional coordination of medical resources.

Funding

This work is supported by the National Key R&D Program (NO.2022YFC3603004), the Ministry of Civil Affairs Project (NO.2024MZY009), and the Scientific Research Foundation of State Key Laboratory of Vaccines for Infectious Diseases , Xiang An Biomedicine Laboratory (NO.2023XAKJ0101032).

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Assessing the policy effects of China's medical consumables pricing reform on percutaneous endoscopic lumbar discectomy: A regression discontinuity design integrating a mixed-methods framework

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Abstract

Background: To reduce the cost and alleviate the financial burden on patients, the Chinese government launched a nationwide medical consumables reform of county-level public hospitals. The key components of the reform were the zero markup consumable policy (ZMCP), and centralized volume-based procurement policy (CVBP) of high-value consumables.

Objectives: This paper employs a mixed-methods design and combines real-world data from hospitals to assess the impact of this policy in China on percutaneous endoscopic lumbar discectomy (PELD) patients.

Methods: Two phased mixed-methods study: 1) a regression discontinuity design (RDD) to evaluate variations in medicine expenditure, and therapeutic outcomes underwent percutaneous endoscopic lumbar discectomy (PELD) patients between January 2018 and June 2024; 2) semi-structured interviews with key stakeholders (hospital administrators, clinicians and patients) to examine policy implementation challenges and make policy recommendations.

Results: Regression discontinuity design (RDD) analysis of 1,099 percutaneous endoscopic lumbar discectomy (PELD) patients revealed that after the volume-based procurement (CVBP) reform significantly reduced total hospitalization costs, with medical consumables expenditures decreasing by 43% and 86% in the post-policy cohort compared to pre-reform levels. From the interviews stakeholder perceptions of medical consumables reforms were captured by three themes: clinical decision-making adaptations, hospital economic sustainability challenges, and patient decision-making behaviors.

Conclusion: The reforms in medical consumables pricing and procurement have effectively reduced the cost of consumables for inpatients undergoing PELD. The analysis of RDD revealed that the ZMCP policy had a limited effect on the level and trend of total hospitalization expenses. However, the implementation of the CVBP policy for orthopedic spine medical consumables led to a significant reduction in medical consumables expenses. The study found that the medical consumables policy's three impacts: clinical decision-making adaptations, hospital economic sustainability challenges, and patient decision-making behaviors. These findings contribute to the broader discourse on medical policy reform by demonstrating how reimbursement adjustments influence healthcare delivery at multiple levels.

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Assessing the risk of cardiovascular events and falls in hypertensive patients after initiating ACEi versus ARB monotherapy or two-drug combination therapy: A target trial emulation

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【 Abstract 】 Background: Angiotensin-converting enzyme inhibitor (ACEi) and angiotensin-receptor blocker (ARB) were recommended as first-line agents for the treatment of hypertension, the preferred initial treatment is a two-drug combinations of an ACEi or ARB with a calcium channel blocker (CCB) or a thiazide/thiazide-like diuretic (T/TLDiuretic) for most patients in recent guidelines. However, harms from antihypertensive treatment occur immediately (eg, dizziness, fall), and benefits for cardiovascular event reduction emerge over time. Nevertheless, evidence on their monotherapy or two-drug combination therapy benefits in reducing cardiovascular and the risk for fall-related events during actual use is limited.

Objective: To compare the benefits in reducing cardiovascular and the risk for fall-related events of ACEi and ARB monotherapy or two-drug combination therapy in the real-world.

Methods: The design was an observational study that attempts to emulate a target trial. All data were collected from the UK Biobank database. Participants were adults aged 40 years or older with hypertension who newly initiated the specified treatment strategies, without receiving prescriptions for both studied drugs at baseline or within 180 days before baseline, and without having a history of cardiovascular events prior to baseline. The treatment strategies involved the initiation of ACEi monotherapy versus ARB monotherapy, or two-drug combination therapy (ACEi+T/TLDiuretic versus ARB+T/TLDiuretic, and ACEi+CCB versus ARB+CCB). The primary outcomes were cardiovascular events and falls. The secondary outcome was fall-related adverse effects. Cox proportional hazards regressions were used after inverse probability of treatment weighting. 3 subgroup analyses and 2 sensitivity

analyses were conducted to explore potential heterogeneity and increase the robustness of results.

Results: A total of 15809 patients were identified, including 9686 for new ACEi (8859) or ARB (827) monotherapy users, 2977 new ACEi+T/TLDiuretic (2241) or ARB+T/TLDiuretic (736) users, and 3146 new ACEi+CCB (2454) or ARB+CCB (692) users. ARB monotherapy initiators had higher hazard of cardiovascular events than ACEi monotherapy initiators (HR, 1.14 [95% CI, 1.01 to 1.29]). Compared with ACEi+CCB initiators, ARB+CCB initiators had higher hazard of fall-related adverse effects (HR, 1.29 [95% CI, 1.01 to 1.64]). ARB+T/TLDiuretic initiators had lower hazard of falls than ACEi+T/TLDiuretic initiators among female who had history of falls (HR, 0.49 [95% CI, 0.27 to 0.89]). Results were similar across subgroup and sensitivity analyses.

Conclusion: Compared to ACEi monotherapy or two-drug combination therapy, ARB monotherapy or two-drug combination therapy showed higher cardiovascular risk. Additionally, ARB+CCB initiators had higher risk of fall-related adverse effects than ACEi+CCB initiators.

Funding Source: None.

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Association between depressive symptoms and cognitive decline: mediating effect of plasma p-tau181

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【 Abstract 】 Background: Depressive symptoms are increasingly recognized not only as a frequent comorbidity but also as a potential risk factor for cognitive impairment. However, the biological mechanisms linking depression to accelerated cognitive decline remain incompletely understood.

Objectives: This study aims to explore the relationship between depressive symptoms and cognitive decline and to evaluate the mediating effect of plasma p-tau181.

Methods: This study included 1658 dementia-free community residents recruited in 2009 – 2011 from the Shanghai Aging Study. At baseline, we assayed plasma p-tau181 and assessed depressive symptoms using the Center for Epidemiologic Studies Depression scale (CES-D). Cox proportional hazards regression models were performed to estimate the risks of incident dementia and Alzheimer's disease (AD), adjusting for age, sex, education, APOE ϵ 4. Generalized additive models (GAMs) were applied to estimate the nonlinear relationship of depressive symptoms and p-tau181 on the annual decline rate of Mini-Mental State Examination (MMSE) scores. Finally, a mediation analysis was conducted to evaluate the mediating role of plasma p-tau181.

Results: Older adults with depression had higher risks of dementia and AD (HR [95%CI] = 1.63 [1.12, 2.38], $p = 0.011$) and AD (HR [95%CI] = 1.77 [1.15, 2.73], $p = 0.009$). GAM found that baseline plasma p-tau181 significantly influenced the annual decline rate of MMSE ($p < 0.001$), indicating a strong non-linear relationship. Mediation analysis revealed that plasma p-tau181 had significant mediating effects on the relationship between depressive symptoms and cognitive decline ($\beta = 0.011$, 95%CI: 0.004, 0.020, $p = 0.009$), but the direct effect of depressive symptoms on cognitive decline was not significant ($\beta = 0.037$, 95%CI: -0.014, 0.088, $p = 0.119$).

Conclusion: Plasma p-tau181 mediates depression-cognitive decline linkage, highlighting its non-linear role as a critical biomarker for early intervention in

neurodegenerative process.

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Association between long-term burden of sarcopenia and cardiorespiratory multimorbidity

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Abstract

Background: Sarcopenia, the progressive loss of muscle mass and function, is a common condition in older adults and has been linked to both cardiovascular disease (CVD) and chronic respiratory diseases (CRD). However, the association between long-term changes of sarcopenia and cardiorespiratory multimorbidity remains underexplored.

Objective: This study aims to investigate how changes in sarcopenia burden over time relate to cardiorespiratory multimorbidity in Chinese adults.

Methods: Data from the China Health and Retirement Longitudinal Study (CHARLS) were used, including 5,186 participants aged 45 and older. Sarcopenia was assessed using criteria for muscle mass, strength, and physical performance. Sarcopenia trajectories were identified using group-based trajectory modeling, and associations with cardiorespiratory multimorbidity (CVD and CRD) were assessed using multivariable-adjusted logistic regression models.

Results: The study included 5,186 participants with mean age of 58.2 ± 8.4 years. A total of 301 (5.8%) participants experienced cardiorespiratory multimorbidity. Four distinct sarcopenia trajectory groups were identified: persistently low, moderate-to-low, low-to-high, and persistently high burden. Compared to the reference (persistently low group), the low-to-high trajectory of sarcopenia burden had the strongest association with cardiorespiratory multimorbidity (OR: 2.64, 95% CI: 1.73–4.04), followed by the persistently high group (OR: 2.05, 95% CI: 1.46–2.89) and moderate-to-low group (OR: 1.90; 95% CI: 1.38–2.60).

Conclusions: Changes in sarcopenia burden are significantly associated with cardiorespiratory multimorbidity, with a rapid increase in sarcopenia burden (low-to-high trajectory) being particularly detrimental. Monitoring sarcopenia

progression and early intervention may be crucial in preventing cardiorespiratory multimorbidity. Further research is needed to explore underlying mechanisms and evaluate interventions.

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Association between Metabolic Score for Visceral Fat (METS-VF) and risk of incident diabetes mellitus among middle-aged and older Chinese population

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[Abstract]Background: The association between Metabolic Score for Visceral Fat (METS-VF) and incident diabetes mellitus has been documented but remained controversial.

Purpose: The purpose of this study is to explore the association between METS-VF and risk of incident diabetes mellitus among middle-aged and older Chinese population.

Methods: A total of 7,988 participants (median age: 58 years) from China Health and Retirement Longitudinal Study (CHARLS) were included in the analyses. We analyzed the association between METS-VF and risk of incident diabetes mellitus, using the Cox proportional hazards models to assess hazard ratios (HRs) and 95% confidence intervals (CIs). Subgroup analyses of the association were also carried out, stratified by age and sex. Furthermore, sensitivity analyses were conducted to evaluate the robustness of the obtained results.

Results: A total of 734 participants were diagnosed with diabetes mellitus during 30,468 person-years of follow-up. After adjustment for potential confounders, the HRs (95% CIs) of diabetes mellitus for Q2, Q3, and Q4 was 1.17 (0.89–1.53), 1.80 (1.39–2.32), and 2.58 (2.01–3.31), respectively. Meanwhile, the corresponding HRs (95% CIs) for diabetes mellitus with per SD unit increase in Q4 were 1.35 (1.23–1.49) for METS-VF. Subgroup analysis still indicated a statistically significant association in women. Sensitivity analyses were consistent with the preliminary analysis.

Conclusions: Higher METS-VF was associated with increased risk of incident diabetes mellitus among middle-aged and older Chinese population, as a potential tool for monitoring and guiding primary prevention strategies.

Funding: This study was supported by Doctoral Scientific Research Foundation of Henan University of Chinese Medicine (grant no. 2022HZYBS03).

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Association Between PM_{2.5} Components Exposure and Dyslipidemia and the Mediating Role of DNA Methylation

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【 Abstract 】 Background: Dyslipidemia is a major risk factor for atherosclerotic cardiovascular disease. While fine particulate matter (PM_{2.5}) represents a leading environmental threat to human health, the health effects of its specific components on lipid metabolism and the potential epigenetic mechanisms involved remain unclear.

Objective: This study aimed to investigate the causal relationship between exposure to PM_{2.5} and its chemical components and dyslipidemia, and to explore the mediating role of DNA methylation in these associations.

Methods: A prospective panel study was conducted among 59 university students in Guangzhou, China, with six rounds of follow-up. Individual exposure to PM_{2.5} components, lipid profiles (ApoA, ApoB, LDL, HDL, ApoA/ApoB ratio, TC, and TG), and DNA methylation levels were measured. Linear mixed-effects (LME) models were used to evaluate associations between PM_{2.5} components and lipid parameters, with participant ID as a random effect. Mediation analysis based on a causal framework was used to identify methylation sites involved.

Results: Among the lipid biomarkers, ApoA, ApoB, ApoA/ApoB, and LDL were the most sensitive to PM_{2.5} component exposures. Exposure to ions (F⁻, Mg²⁺) and metals (Cu, As) was associated with elevated LDL-C and ApoB and reduced ApoA/ApoB ratio, while Zn, K, and Se showed protective effects. Notably, Mg²⁺ exposure effects on HDL-C were partially mediated by methylation at ABCG1 (cg06500161) and ACADS (cg21721566, cg24768164), with mediation proportions up to 41.6% (95% CI: 0.014, 0.819) and 30.0% (95% CI: 0.028, 0.573). For the Mg–HDL association, cg06500161 mediated 41.6% of the effect (95% CI: 0.014, 0.819).

Conclusion: This study identified key PM_{2.5} components linked to adverse lipid profiles and revealed DNA methylation as a potential epigenetic mediator. The findings provide insight into the biological mechanisms underlying environmental exposure and dyslipidemia risk.

Funding: National Natural Science Foundation of China (82204162); Basic and Applied Basic Research Foundation of Guangdong Province (2022A1515010823, 2025A1515012021)

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Association of pre-pregnancy psychological stress with fecundability: a population-based cohort study

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ABSTRACT

Background: Many women reported experiencing considerable psychological stress prior to conception, which may have impaired their ability to conceive successfully. Evidence regarding the effects of pre-pregnancy stress in both spouses on fecundability remains inconsistent, and the association with time-to-pregnancy (TTP) lacks validation in large population-based cohorts.

Objective: This study aims to explore the relationship between pre-pregnancy psychological stress in couples and TTP.

Methods: Utilizing the National Free Pre-pregnancy Checkups Project, this study included 831,663 couples planned to conceive, who were enrolled between January 1, 2014, and December 31, 2019 in Guangdong Province, China.

Perceived psychological stress of wives or husbands was assessed from two domains: work/life-related stress, and economic stress. The stress was measured with a 5-point Likert-type scale, and then it was divided into two levels in the final analysis.

Multivariable-adjusted Cox proportional hazards regression models were adopted to assess the association between stress status and TTP with hazard ratios (HRs) and 95% confidence interval [CI].

Results: Of 831,663 couples, 274,859 (33.05%) women had successfully conceived at the end of 1 year of follow-up. In the main effects model, a higher work/life-related stress level in both wives and husbands, and a higher economic stress level in husbands were all shown to be related to higher HRs of fecundability (i.e., shorter TTP), with adjusted HRs of 1.12 (95% CI: 1.11 – 1.14), 1.10 (95% CI: 1.08 – 1.12),

and 1.09 (95% CI: 1.07 – 1.10), respectively, while a higher economic stress level of wives was shown to be related to lower HRs of fecundability (i.e., longer TTP), with adjusted HRs of 0.76 (95% CI: 0.75 – 0.77). However, the results reversed in the interaction model and stress of couples showed interactive effect on fecundability. Compared with non-stressed couples, couples with higher work/life-related stress level and economic stress level were likely to have lower fecundability, with adjusted HRs of 0.69 (95% CI: 0.67 – 0.70), and 0.89 (95% CI: 0.86 – 0.91)], respectively. Compared with participants aged ≥ 40 years, both wives and husbands in younger age groups were likely to have significantly higher fecundability, with the youngest group having the highest fecundability. The adjusted HRs were 3.17 (95% CI: 3.02 – 3.32) for wives, and 1.30 (95% CI: 1.26 – 1.34) for husbands, respectively. Regarding body mass index categories, wives with obesity, overweight, or underweight all showed reduced fecundability compared to those with normal weight, with adjusted HRs of 0.70 (95% CI: 0.68 – 0.73), 0.87 (95% CI: 0.86 – 0.89) and 0.95 (95% CI: 0.94 – 0.96), respectively.

Conclusion: These findings identify that pre-pregnancy psychological stress in both spouses might have interactive effect on fecundability, which highlights the importance of paying attention to the psychological stresses of both wives and husbands.

Funding: This study was supported by Guangdong Province Medical Research Funding (B2023416).

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Association of TyG Index and TG/HDL-C Ratio with Trajectories of Depressive Symptoms: Evidence from the China Health and Retirement Longitudinal Study

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Abstract:

Background: Depression is a prevalent mental disorder among middle-aged and older adults, contributing significantly to the global disease burden with substantial economic costs. Evidence suggests that insulin resistance (IR) is associated with increased depressive symptoms. While cross-sectional studies have linked higher triglyceride-glucose (TyG) index and triglyceride to high-density lipoprotein cholesterol (TG/HDL-C) ratio to depressive symptoms, their longitudinal associations with the heterogeneous trajectories of depressive symptoms remain unexplored.

Objectives: To explore whether the TyG index and the TG/HDL-C ratio are associated with the trajectories of depressive symptoms.

Methods: In this longitudinal study, 4215 participants aged 45 years and older were recruited from the China Health and Retirement Longitudinal Study from 2011 to 2018. The trajectories of depressive symptoms, measured by the 10-item Center for Epidemiologic Studies Depression Scale (CESD-10), were identified using group-based trajectory modeling. Multinomial logistic models and restricted cubic spline analysis were used to investigate the relationships between the TyG index and the TG/HDL-C ratio and the trajectories of depressive symptoms. Stratified analyses were conducted based on sex, age, place of residence, and body mass index (BMI).

Results: Five distinct trajectories of depressive symptoms characterized by stable low, stable moderate, decreasing, increasing, and stable high were identified during a follow-up of 7 years. Associations of the TyG index and TG/HDL-C ratio with trajectories of depressive symptoms are not entirely consistent. After adjusting for covariates, a higher TyG index at baseline was associated with lower odds of being on the decreasing trajectory of depressive symptoms ($OR_{ad} = 0.61$, 95% CI: 0.40-0.92) compared to the stable low trajectory, and restricted cubic spline analysis revealed a

negative linear relationship between the TyG index and the likelihood of the decreasing trajectory of depressive symptoms. However, the relationship between the TG/HDL-C ratio and the decreasing trajectory of depressive symptoms was no longer statistically significant when all confounders were controlled ($OR_{ad} = 0.72$, 95% CI: 0.50–1.04). Additionally, this negative association between the TyG index and decreasing trajectory of depressive symptoms was observed among 45-64-year-old individuals, female participants, those living in rural areas, and those with a normal BMI.

Limitations: This study was conducted in a middle-aged and older population in China, and extrapolation to other regions and populations requires further confirmation.

Conclusions: Compared to the TG/HDL-C ratio, the TyG index may be a better predictor for trajectories of depressive symptoms in middle-aged and older adults. Considering that the pathology of depression progresses long term, our findings may have utility for identifying available and reliable markers for the development of depression.

Keywords: trajectory; depressive symptoms; triglyceride-glucose (TyG) index; TG/HDL-C ratio; longitudinal study

Funding: This research was funded by the Natural Science Foundation of Guangdong Province for Distinguished Young Scholars (Grant number: 2022B1515020094), and the Science and Technology Program of Guangzhou (Grant number: 2024A04J6551).



Association of visceral fat accumulation with cardiovascular disease and all-cause mortality in UK Biobank: the role of Cardiovascular-Kidney-Metabolic syndrome

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【Abstract】 Background: Body roundness index (BRI), as a more comprehensive indicator of visceral obesity, has been linked with cardiovascular disease (CVD) and all-cause mortality. The American Heart Association has recently introduced the concept of Cardiovascular-Kidney-Metabolic (CKM) syndrome, which emphasizes the link between metabolic, kidney, and CVD, yet the associations of BRI and CKM syndrome with CVD and mortality remain unclear.

Objective: To assess associations of the BRI with CVD and mortality, evaluate CKM's modifying role, and examine their interaction or joint effects on health outcomes..

Methods: This cohort study included 358, 981 participants from UK Biobank recruited between March 2006 and December 2010, followed until the occurrence of CVD, death, or last available date, which came first. The exposure was the participants' BRI, calculated using height and waist circumference, with inflection point determined by two-piecewise Cox models. Primary outcomes were CVD and all-cause mortality, obtained through self-reports and linkage to registries. Cox proportional hazards regression using age as time scale and restricted cubic spline (RCS) analyses were performed to assess the associations of BRI with CVD and mortality.

Results: During a median follow-up of 14.2 and 14.1 years, 4 9331 (13.7%) CVD and 24352 (6.8%) deaths occurred. BRI shows a positive linear association with CVD with the risk increased by 26% (HR, 1.26, 95% CI: 1.25-1.27), and a J-shaped curve for mortality, with an inflection point of 3.53. The predictive capabilities of BRI

outperformed traditional obesity indicators (all $p < 0.001$ for AUC differences). CKM syndrome mediated 27.7% and 29.2% of the association of BRI with CVD and mortality, respectively. The overall associations were attenuated in the early CKM stage compared with other stages (P for interaction: <0.001 for CVD; 0.003 for mortality). Significant joint and additive interaction was observed (Relative Excess Risk due to Interaction, 0.45; 95% CI: 0.27-0.64). Compared with those with lower BRI and early CKM syndrome stage, those of higher BRI and advanced CKM stage (stage > 0) had a higher risk of CVD (HR, 2.02; 95% CI, 1.95-2.10), and all-cause mortality (HR, 1.36; 95% CI, 1.29-1.43).

Conclusions: This cohort study demonstrated that BRI serves as a more valuable predictor for CVD and mortality, with risks partly modified and mediated by CKM syndrome. Integrating BRI and CKM syndrome in risk assessment frameworks may enhance the accuracy of CVD and mortality risk stratification.

基金资助：本研究获国家自然科学基金（82373683）及首都卫生发展科研专项（首发2024-1G-4261）资助

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Association of waist to height ratio and its 2-year change with incident hypertension: a national prospective cohort study

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Abstract

Background: Existing evidence on the association of dynamic change in waist to height ratio (WHtR) with risk of incident hypertension is limited.

Objective: To investigate the association of WHtR and its 2-year change with risk of incident hypertension among middle-aged and older population in China.

Methods: The present study included 7,849 participants aged ≥ 45 years from the China Health and Retirement Longitudinal Study (CHARLS). Cox proportional-hazard models were used to estimate hazard ratios (HRs) and 95% confidence intervals (CIs) for the association of WHtR and its 2-year change in WHtR with risk of hypertension. Subgroup and sensitivity analyses were conducted to explore the association of WHtR and its 2-year change with incident hypertension by sex and age.

Results: The association of WHtR and its 2-year change with incident hypertension was significant (per SD unit increase: HR = 1.14, 95% CI: 1.08–1.21 for WHtR, HR = 1.19, 95% CI: 1.05–1.34 for WHtR change). The significant association remained consistent in subgroup analyses by sex and age. Compared with participants who were not abdominally obese at both baseline and follow-up, those who were abdominally obese at follow-up exhibited a greater risk of hypertension.

Conclusions: Increased WHtR and 2-year WHtR change were positively associated with risk of incident hypertension. The current study suggests that WHtR may serve as a non-invasive indicator for interventions aiming to reduction risk of hypertension in Chinese middle-aged and older population.

Keywords: waist to height ratio; hypertension; epidemiology; perspective cohort study

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Associations of sleep pattern and genetic risk with risk of incident schizophrenia: A prospective cohort study of 300,034 participants

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Background

Schizophrenia is a serious psychiatric disorder characterized by a combination of positive symptoms, negative symptoms and cognitive dysfunction. Schizophrenia severely impairs the daily lives of patients and causes a huge social and economic burden. However, the cause of schizophrenia is unknown, and several studies have shown that its onset may be influenced by environmental factors, genetic factors, and gene-environment interactions. This study used a combination of five sleep behaviors: sleep duration, chronotype, insomnia, daytime napping, and getting up in the morning to investigate the association between sleep patterns and the risk of schizophrenia and explore whether sleep patterns can alter the relationship between genetic susceptibility and the risk of schizophrenia.

Objective

To investigate the associations of sleep behaviors with the risk of schizophrenia, and explore the interplay between genetic and sleep pattern in the development of schizophrenia.

Methods

We included participants who were free of schizophrenia at baseline based on the UK Biobank. Cox proportional hazard regression models were used to evaluate the associations of five sleep behaviors with the risk of schizophrenia. Then, we generated a healthy sleep behaviors score, classified the sleep patterns into three categories based on the scores and assessed its association with the risk of schizophrenia. The schizophrenia polygenic risk score (PRS) was categorized into high, intermediate, and low-risk groups using PRS tertiles. We finally explored the interactions of sleep patterns and genetic susceptibility on both multiplicative and

additive scales.

Results

During the 13.73 years follow-up, 237 individuals developed schizophrenia. We found that long sleep duration, evening chronotype, napping during the day, getting up in the morning difficultly were independently associated with an increased risk of schizophrenia. Comparing those with healthy sleep pattern to those with unhealthy sleep pattern participants, the HR of developing schizophrenia was 2.64 (95 % CI, 1.78-3.92). Similarly, individuals with a high PRS had a risk of 3.97 (95 % CI, 2.68-5.87) compared to those with a low PRS. Notably, individuals with both high PRS and unhealthy sleep pattern had a significantly higher risk of schizophrenia (HR = 9.44, 95 % CI, 4.21-21.18) compared to those with a low PRS and a healthy sleep pattern. Additionally, there are no statistically significant multiplicative or additive interaction was found.

Conclusions

Our findings suggest that long sleep duration, evening chronotype, napping during the day, getting up in the morning difficultly were independently associated with an increased risk of schizophrenia. A healthy sleep pattern and low genetic risk were associated with a reduced risk of developing schizophrenia.



Automated Sparse Feature Selection in High-Dimensional Proteomics Data via 1-bit Compressed Sensing and K-Medoids Clustering

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【Abstract】

Background: High-dimensional proteomics data present significant challenges in biomarker discovery due to technical noise, feature redundancy, and multicollinearity. Current feature selection methods, such as filter, wrapper, and embedded approaches, often struggle with instability, suboptimal sparsity, and computational inefficiency. These limitations hinder precise identification of biologically relevant biomarkers and compromise clinical applicability.

Objective: We introduce Soft-Thresholded Compressed Sensing (ST-CS), a hybrid framework combining 1-bit compressed sensing (CS) with K-Medoids clustering to address these challenges. The aim is to automate feature selection, improve classification accuracy, and enhance interpretability for high-dimensional proteomic analyses.

Methods: ST-CS operates through three key innovations: ① A dual-regularized optimization framework combining ℓ_1 -norm (sparsity) and ℓ_2 -norm (stability) constraints to recover sparse coefficients; ② K-Medoids clustering on coefficient magnitudes to partition biomarkers from noise, replacing manual thresholding dynamically; ③ Dimensionality reduction via parsimonious classifiers using selected features. The method was rigorously evaluated against Hard-Thresholded CS (HT-CS), LASSO, and SPLSDA using simulated datasets (varying signal-to-noise ratios (SNR) and sample sizes) and real-world proteomic data from the Clinical Proteomic Tumor Analysis Consortium (CPTAC).

Results: In simulations, ST-CS achieved superior specificity (>99.8%) and precision (>90% at $n > 100$), reducing false discovery rates (FDR) by 20–50% compared to HT-CS. It maintained balanced sensitivity (>80%) and outperformed all methods in F1 scores and Matthews Correlation Coefficients (MCC). Classification performance, measured by AUC, consistently surpassed benchmarks across SNR levels (e.g., 86.88% vs. HT-CS: 86.58%, LASSO: 85.91%, SPLSDA: 85.12% at SNR=100, $n=200$). Applied to CPTAC datasets, ST-CS demonstrated dual strengths in sparsity

and accuracy. For intrahepatic cholangiocarcinoma (PDC000356), it matched HT-CS's AUC (97.47%). Still, it used 57% fewer features (37 vs. 86). In glioblastoma (PDC000446), ST-CS achieved higher AUC (72.71% vs. HT-CS: 72.15%) with 30 features, half the number required by HT-CS. For ovarian serous cystadenocarcinoma (PDC000362), ST-CS attained the highest AUC (75.86%) while retaining only 24 biomarkers. Biological validation confirmed the relevance of selected features to disease mechanisms, such as peroxisome metabolism in cholangiocarcinoma and purine ribonucleotide pathways in glioblastoma.

Conclusion: ST-CS offers a practical solution to improve feature selection in proteomic studies by automating threshold determination and balancing sparsity with stability. Its integration of clustering and compressed sensing provides a scalable framework for biomarker discovery, reducing false positives while maintaining interpretability. The method's adaptability to diverse omics data suggests broader applicability in precision medicine.

Funding: This research was supported by grants from the National Natural Science Foundation of China (NSFC) (Grant Number 82173614).

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BHCAox-HS-GG: Bayesian heredity-constrained Cox proportional hazards model with a novel regularized horseshoe prior for detecting gene-gene interactions

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Abstract:

Gene-gene ($G \times G$) interactions are critical for elucidating disease etiology and prognostic factors. Incorporating them into prognostic models enhances predictive accuracy and opens new avenues for personalized cancer therapy. Effect heredity, which accounts for the dependency between main effects and their interactions, has been widely adopted in interaction detection studies. The Bayesian framework offers enhanced flexibility in modeling these relationships. However, the effect heredity has not yet been applied to Bayesian Cox proportional hazards model for detecting $G \times G$ interactions for censored survival outcomes. In this study, we proposed Bayesian heredity-constrained Cox proportional hazards (BHCox) model with a novel regularized horseshoe (HS) prior that incorporate effect heredity to detect $G \times G$ interactions. The no-U-turn sampler (NUTS) algorithm, which has been implemented in the R package brms, was used to fit the proposed model. Extensive simulations were performed to evaluate and compare our proposed approach with other alternative models. The simulation studies illustrated that BHCox-HS-GG model outperform other alternative models. We applied the BHCox-HS-GG model to real-world data from early-stage non-small cell lung cancer (NSCLC) patients and identified biologically plausible $G \times G$ interactions associated with prognosis. In summary, BHCox-HS-GG provides a powerful tool for detecting interactions in high-dimensional censored survival data, with important implications for prognostic biomarker research.

Key words: Bayesian Cox proportional hazards model, gene-gene interaction, effect heredity, regularized horseshoe prior

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Biological Age Acceleration Associated with the Progression Trajectory of Cardio-Renal–Metabolic Multimorbidity: A Prospective Cohort Study

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[Abstract] Objectives: Previous studies have confirmed that biological age (BA) acceleration is associated with single cardio-renal–metabolic diseases (CRMDs), typically including type 2 diabetes mellitus, cardiovascular disease, and chronic kidney disease. However, its association with progression to cardio-renal – metabolic multimorbidity (CRMM, coexistence of ≥ 2 CRMDs) and subsequent mortality remains unexplored. **Methods:** Using the multi-state model, we analyzed 278,927 UK Biobank participants free of CRMDs at baseline to investigate the association between BA acceleration—measured by phenotypic age (PhenoAge) and Klemera–Doubal method age (KDMAge)—and CRMM progression trajectory, from health to the first CRMD and then to CRMM and death. BA acceleration was the residual from regressing BA on chronological age; positive values indicated a biologically older individual. **Results:** PhenoAge acceleration showed stronger associations than KDMAge acceleration. Per the 1-SD increase in PhenoAge acceleration; HRs (95% CIs) were observed at 1.18 (1.17–1.19) for baseline to first CRMD; 1.24 (1.22–1.26) for first CRMD to CRMM; 1.25 (1.22–1.27) for baseline to death; 1.13 (1.11–1.15) for first CRMD to death; and 1.09 (1.06–1.12) for CRMM to death. Biologically older individuals by PhenoAge acceleration showed greater reductions in CRMD-free and total life expectancy than those by KDMAge acceleration. Age, socioeconomic status, education, smoking status, alcohol consumption, physical activity, and diet-modified risks for specific transitions. **Conclusions:** BA acceleration, particularly PhenoAge acceleration, relates to higher CRMM progression risk and shorter life expectancy. Combining BA acceleration with

sociodemographic or lifestyle factors improves risk identification for specific transitions. BA acceleration offers the potential to guide CRMM prevention across its entire progression.

Funding: This study was supported by grants from the Program of Natural Science Fund of China (Serial Number: 82373683) and Capital's Funds for Health Improvement and Research (CFH 2024-1G-4261).

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Causal Discovery in Observational Medical Research: A Scoping Review

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[Abstract]Background: Observational data, while ubiquitous in medical research, inherently face challenges in establishing causal relationships. Machine learning-driven causal discovery algorithms present promising pathways to infer causal structures from observational data. Current literature predominantly focuses on theoretical methodological developments, with limited systematic assessment of real-world medical applications and insufficient clarity on algorithm suitability across clinical contexts.

Objective: To systematically synthesize the landscape of causal discovery methods applied to observational medical research, analyzing methodological approaches, application domains, and implementation challenges, thereby providing a framework for scientifically robust causal inference in medicine.

Methods: Following Arksey and O'Malley's framework and PRISMA-ScR guidelines, we systematically searched Scopus, Web of Science, PubMed, MEDLINE, Embase, and CINAHL from inception to May 2025. Included studies applied causal discovery algorithms to real-world observational medical data. Exclusions comprised purely theoretical/methodological papers and studies using experimental data without real-world causal discovery. Descriptive analysis synthesized study characteristics, algorithm types, and application domains across four core themes.

Results: Of 4,844 identified publications, 81(81/4,844, 1.67%) met the inclusion criteria. Analysis yielded four themes::1) Methodological Classification and Innovation: Constraint-based methods (e.g., PC, FCI algorithms) predominated (60.5%, 49/81). 2) Disease Mechanisms and Application Domains : Neuropsychiatric disorders were the primary focus (46.9%, 38/81), notably schizophrenia (n=10), PTSD (n=8), and ASD/ADHD (n=7). 3) Public Health & Health Systems: Key applications included health behavior interventions (n=26), pandemic management (n=12), and healthcare service optimization (n=10). 4) Challenges and Future

Directions: Major barriers were unmeasured confounding (61.7%) and data quality issues (49.4%). Key priorities were multimodal data integration (37.0%) and clinical translation tool development (23.5%).

Conclusions: Causal discovery algorithms are increasingly applied in medical research, yet clinical translation is hindered by the absence of validation frameworks and persistent confounding. Future efforts must prioritize developing rigorous evaluation standards, enhancing multimodal data integration, and fostering interdisciplinary collaboration across medicine, statistics, and computer science to drive methodological innovation and practical implementation.

Funding: This study was funded by the National Natural Science Foundation of China (82360667, 82160645), the Natural Science Foundation of Jiangxi Province (20212BAB206091), the Graduate Innovation Special Fund (YC2024-S167) and the Research and Training Fund of Nanchang University (2024).

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Characterization of influenza epidemics in the post-pandemic era and its dynamic relationship with SARS-CoV-2 and Meteorological factors

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Abstract:

Background: The COVID-19 pandemic has changed the epidemic pattern of respiratory infectious diseases such as influenza. In the post-pandemic era, the rebound of influenza activity and the co-circulation of multiple pathogens have received widespread attention. This study aims to reveal the epidemic characteristics, dynamic interactions between influenza and SARS-CoV-2 in the post-pandemic era.

Methods: Firstly, we collected the surveillance data of influenza and SARS-CoV-2 in Mainland China from 2022 to 2025. Then, we employed wavelet analysis to explore the epidemic patterns and their interrelationships between the influenza and SARS-CoV-2 at multiple periodic scales, and analyzed the effects of meteorological factors. **Results:** Influenza gradually returned to its typical winter–spring seasonal pattern, while SARS-CoV-2 exhibited biannual short-period fluctuations. Wavelet coherence analysis showed a negative correlation between influenza positivity and SARS-CoV-2, with influenza positivity leading by approximately 7 to 18 weeks.

Meteorological factors played a notable role in driving influenza transmission. The heightened influenza activity was associated with the elevated temperatures (1.8 weeks ahead) and increased precipitation (1.6 weeks ahead) in early 2023 and summer 2024, respectively. In addition, The PWC analysis revealed a notable independent and direct association between influenza and SARS-CoV-2 positive rates.

Conclusions: Influenza and SARS-CoV-2 demonstrated a dynamic, alternating epidemic relationship in the post-pandemic era, with meteorological factors exerting a dynamic influence. These findings provide valuable evidence to inform targeted prevention and control strategies for both viruses in the context of long-term co-circulation.

Funding

This work was supported by the National Natural Science Foundation of China (82103947) and Science and Technology Program of Guangzhou, China (202206080003, 2024A04J4623).

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Combined effects of ambient air pollution exposure and biological aging on incident liver diseases: A large prospective cohort study

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[Abstract] Background: Both ambient air pollution exposure and biological aging are associated with incident liver diseases, but previous studies mainly focused on single-factor associations.

Objective: This study aimed to assess the combined effects of air pollutants exposure and biological aging on liver diseases incidence and investigate the potential mediating role of biological aging.

Methods: A total of 418,576 participants from the UK Biobank were analyzed. Annual mean concentrations of PM_{2.5}, PM₁₀, PM_{2.5-10}, NO₂, and NO for 2010 were estimated, and a weighted air pollution score was generated. Biological ages were assessed using the Klemera-Doubal method biological age (KDM-BA) and phenotypic age (PhenoAge). Cox proportional hazard regression models were employed to evaluate associations of air pollutants exposure and biological aging with incident liver diseases. Quantile g-computation method was used to investigate the joint effects of air pollutant mixtures. Mediation analyses were used to explore the role of biological aging.

Results: Over a median follow-up of 13.57 years, 7,991 (1.91%) participants developed liver diseases. Exposure to all individual air pollutants and biological aging were associated with higher liver diseases risk. Both the air pollution score and the mixture of air pollutants were associated with incident liver diseases, with NO₂ driving the positive effect primarily at 42.31%. Participants with higher levels of air pollutants exposure and biologically older status had a higher risk. Furthermore, the mediated proportion of accelerated biological aging was 1.9% to 7.7% for air pollution-associated liver diseases.

Conclusions: Ambient air pollution exposure may increase liver diseases risk, partly

mediated by biological aging. Slowing the aging process could be a key to reducing the impact of air pollution on liver diseases.

Funding: This study was supported by the Beijing Natural Science Foundation [grant number 7232233] and the National Natural Science Foundation [grant number 81773511].

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Developing predictive models for COVID-19 positive tests based on the XGBoost and Random Forest algorithms with Internet search data

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Abstract

Background: Although strategies for COVID-19 have shifted towards normalized measures globally, establishing predictive models based on Internet search data remains crucial for swiftly controlling and preventing future outbreaks. **Objective:**

This study aims to utilize Internet search data for early epidemic surveillance and warning. **Methods:** We collected the daily number of COVID-19 positive tests and the daily Baidu Search Index (BSI) of COVID-19 related keywords. First, we screened keywords with a maximum correlation coefficient exceeding 0.9 by time-lagged correlation analysis. Then, we used the original and lagged BSI to construct XGBoost and Random Forest (RF) models for short-term prediction of the COVID-19, respectively. Next, we selected top 5 important predictors according to the importance gain in XGBoost model and constructed a comprehensive search index (CSI) weighted by the importance gain. Finally, we used the distributed lagged nonlinear model (DLNM) to evaluate the relationship between the CSI and the number of COVID-19 positive tests. **Results:** We identified 20 keywords had a maximum correlation coefficient exceeding 0.9 with lag days of 1-10 days. Then, we found that the predictive performance of the XGBoost models was better than that of

the RF models. And XGBoost models using lagged BSI (compared to original BSI) had a better predictive performance for forecasting 3 days, with an RMSE of 803.85 and a MAPE of 9.96%. Finally, we observed that the CSI was statistically associated with the number of COVID-19 positive tests, with the maximum relative risks (RR) at lags of 0, 3, 5, and 7 days being 2.18 (95%CI 1.60-2.97), 1.94 (95%CI 1.10-3.43), 1.86 (95%CI 1.01-3.44), and 2.03 (95%CI 1.00-4.11), respectively. **Conclusions:** The XGBoost model with the lagged BSI can predict COVID-19 epidemics, which make it a powerful addition to the traditional surveillance systems.

Funding

This work was supported by the National Natural Science Foundation of China (82103947) and Science and Technology Program of Guangzhou, China (202206080003, 2024A04J4623).

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Effect of air pollution on burden of chronic obstructive pulmonary disease: a modeling study from the Global Burden of Disease Study 2023

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【Abstract】

Background: Chronic obstructive pulmonary disease (COPD) is one of the most prevalent disease. Air pollution is strongly associated with the pathogenesis and progression of COPD, imposing a disproportionate burden of morbidity and mortality. Comprehensive estimation of the attributable burden and long-term trend of air pollution on COPD is critical for targeted interventions and strategic adjustments.

Objective: This study aimed to assess the degree of exposure to overall and specific type of air pollution and evaluate COPD burden attributable to air pollution in terms of deaths, years lived with disability (YLDs) and disability-adjusted life years (DALYs) and stratified by sex, age, and location.

Methods: Based on data from the Global Burden of Disease Study 2023, overall and three specific types of air pollution, including ambient particulate matter pollution (APMP) and household air pollution from solid fuels (HAP) and ambient ozone pollution (AOP), were included. The non-fatal burden was estimated using DisMod MR-2.1, a Bayesian meta-regression model, while the fatal burden was quantified by the Cause of Death Ensemble model (CODEm). Several multi-step modelling strategy, including linear regression, spatiotemporal regression, and Gaussian process regression (ST-GPR) were used to assess the degree of exposure to air pollution. The relative risk and population attributable fraction were calculated using meta-regression-Bayesian, regularised, trimmed (MR-BRT) to obtain attributable burden of COPD.

Results: The age-standardized summary exposure value for air pollution has decreased from 46.5% (29.6 to 69.3) in 1990 to 35.9% (22.2 to 57.4) in 2023 worldwide. In 2023, there were 1.56 million (1.20 to 1.97) deaths, 5.13 million (3.91 to 6.41) YLDs, and 33.42 million (26.60 to 41.16) DALYs from COPD attributable to overall air pollution, with an increase of 38.6% (7.4 to 93.9), 59.1% (46.5 to 72.8) and 27% (0.8 to 70), respectively. Almost half of COPD deaths, YLDs and DALYs

can be accounted for air pollution. However, the age-standardized COPD death, YLD and DALY rates attributable to air pollution presented decreasing trend during 1990 to 2023. Specifically, there were 16.48 (12.44 to 20.56), 12.83 (9.19 to 17.84), and 8.50 (1.90 to 14.80) million COPD DALYs attributable to APMP, HAP and AOP, respectively. Compared with high sociodemographic index countries, low sociodemographic index countries had almost ten-times higher age-standardized attributable COPD death, YLD, and DALY rates. Males had higher age-standardized attributable DALY rate than females.

Conclusions: The absolute disease burden of COPD linked to air pollution have risen substantially. These trends are exacerbated by socioeconomic disparities, with low-resource regions and vulnerable populations bearing disproportionate risks. To mitigate this growing crisis, policymakers must prioritize integrated strategies that simultaneously target ambient and household pollution sources, especially for low- and middle-income countries.

Funding: This research was supported by grants from the National Natural Science Foundation of China (NSFC) (Grant Number 82173614).

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Effects of long-term air pollution and green space exposure on mortality in ischemic stroke patients: A prospective cohort analysis

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[Abstract]Background: Ambient air pollution is a leading cause of cardiovascular mortality and a critical environmental risk factor for stroke incidence and prognosis. Conversely, green space exposure offers cardiovascular benefits through multiple pathways. While prior studies suggest green space is associated with reduced mortality in ischemic stroke patients, most focus on single environmental factors, lacking comprehensive evaluation of the interplay between air pollution and green space, particularly regarding long-term outcomes. This prospective cohort study assessed the combined effects of multiple air pollutants and green space exposure on all-cause and cardiovascular mortality in ischemic stroke patients. We further investigated the mediating role of air pollutants in the green space-mortality relationship, aiming to provide a robust scientific foundation for evidence-based environmental interventions.

Objective: To evaluate the impact of long-term exposure to air pollution and green space on all-cause mortality and cardiovascular and cerebrovascular mortality among patients with ischemic stroke.

Methods: Between April 2019 and March 2021, 2,815 eligible ischemic stroke patients were enrolled and followed until December 2023. Long-term exposure to air pollutants ($PM_{2.5}$, PM_{10} , NO_2 , SO_2 , CO , O_3) and green space (quantified by the 250-m resolution Normalized Difference Vegetation Index, NDVI, derived from Sentinel-2 satellite data) was estimated using geocoded residential addresses, based on average monthly exposure during follow-up. Associations with mortality were analyzed using Cox proportional hazards models. Causal mediation analysis quantified the proportion of NDVI's protective effect mediated by air pollutants. Subgroup analyses explored potential effect modifiers.

Results: During a median follow-up of 42.1 months (116,918 person-months), 339

deaths occurred (221 cardiovascular). After adjusting for confounders, exposure to each $10 \mu\text{g}/\text{m}^3$ increase in $\text{PM}_{2.5}$ (HR for all-cause mortality: 3.61, 95% CI: 2.69–4.83; cardiovascular mortality: 4.24, 95% CI: 2.94–6.11), PM_{10} (HR: 1.62, 95% CI: 1.44–1.83; cardiovascular HR: 1.71, 95% CI: 1.47–1.98), NO_2 (HR: 1.90, 95% CI: 1.60–2.25; cardiovascular HR: 2.03, 95% CI: 1.64–2.50), and O_3 (HR: 2.37, 95% CI: 1.67–3.35; cardiovascular HR: 2.39, 95% CI: 1.55–3.68), each $1 \text{ mg}/\text{m}^3$ increase in SO_2 (HR: 1.63, 95% CI: 1.44–1.84; cardiovascular HR: 1.79, 95% CI: 1.55–2.08), and each $0.1 \text{ mg}/\text{m}^3$ increase in CO (HR: 1.64, 95% CI: 1.39–1.94; cardiovascular HR: 1.72, 95% CI: 1.40–2.11) was associated with elevated mortality risk. Conversely, each quartile increase in the NDVI was linked to reduced risks of all-cause mortality (HR: 0.70, 95% CI: 0.64–0.76) and cardiovascular mortality (HR: 0.67, 95% CI: 0.60–0.75). Mediation analysis revealed that reductions in $\text{PM}_{2.5}$ (36.91%), SO_2 (35.90%), and O_3 (42.59%) significantly contributed to the protective effect of green space (NDVI) on all-cause mortality.

Conclusion: Long-term green space exposure significantly mitigates mortality risk associated with chronic air pollution in ischemic stroke patients. These findings underscore the critical role of synergistic environmental interventions in improving stroke prognosis and inform future therapeutic and public health strategies.

Funding: This study was funded by the National Natural Science Foundation of China (82360667, 82160645), the Natural Science Foundation of Jiangxi Province (20212BAB206091), the Graduate Innovation Special Fund (YC2024-S167) and the Research and Training Fund of Nanchang University (2024).

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Elevated Cardiovascular Risk Associated with Hormone Replacement Therapy (HRT): A Comprehensive Analysis of Reproductive Factors and Atherosclerotic cardiovascular disease(ASCVD)

Outcomes in the UK Biobank Cohort

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ABSTRACT

Background: Atherosclerotic cardiovascular disease (ASCVD) poses a significant public health challenge for women, with risk increasing during menopausal transition. While hormone replacement therapy (HRT) has been explored as a potential intervention following post-menopausal estrogen decline, its cardiovascular effects remain controversial. Despite extensive research giving rise to the "timing hypothesis", gaps persist in understanding HRT's cardiovascular safety across reproductive stages, particularly regarding interactions between reproductive characteristics (menarche age, menopause age, menopausal status) and ASCVD risk.

Objective: To elucidate the relationship between HRT and ASCVD risk, thereby establishing an empirical foundation for personalized therapeutic approaches in women's cardiovascular health.

Methods: Utilizing data from 170,250 UK Biobank participants, we conducted a comprehensive analysis stratified by menarche age (early <12, normal 12 – 13, late >13 years), menopause age (premature <40, normal 40 – 55, late >55 years), and age groups (≤ 45 , 45 – 50, 50 – 55, 55 – 60, 60 – 65, ≥ 65 years). Perimenopause was defined as the interval from irregular menstruation onset to 12 months post-final menstrual period. Given the observed heterogeneity in ASCVD risk across reproductive parameters, we implemented stratified Cox proportional hazards models. Mediation analysis assessed the longitudinal effects of baseline sex hormones,

inflammatory markers, and lipid profiles. A competing risk model provided sensitivity analysis. Statistical analyses were performed using R software (version 4.2.2), with significance defined as two-sided $P < 0.05$.

Results: HRT use was associated with a significantly elevated ASCVD risk (adjusted HR = 1.13, 95%CI: 1.08-1.18, $P < 0.001$), with a particularly pronounced effect on ischemic stroke (adjusted HR = 1.14, 95%CI: 1.09-1.19, $P < 0.001$). Women with late menarche demonstrated increased ASCVD risk (adjusted HR = 1.15, 95%CI: 1.08-1.24, $P < 0.001$), while those with late menopause showed a hazard ratio of 1.25 (95%CI: 1.01-1.54, $P = 0.040$). The most substantial risk elevation occurred during perimenopause, with attenuated effects in premenopause. Notably, women ≤ 45 years exhibited the highest risk increase, with HRT users showing a 77% elevated ASCVD risk (adjusted HR = 1.77, 95%CI: 1.12-2.79, $P < 0.001$).

Conclusions: Our findings demonstrate a significant association between HRT use and increased ASCVD incidence, with no evidence of mediating effects. The heightened risk among women with late menarche, late menopause, or perimenopausal status underscores the critical role of reproductive characteristics in risk stratification. These results have important implications for clinical decision-making regarding HRT administration and highlight the need for personalized risk assessment in women's cardiovascular care.

Funding: This work was supported by National Natural Science Foundation of China (Grant Number: 82103944), Chinese National Key Research and Development Program of China (Grant Number: 2017YFC0907200, 2017YF0907201), and the Science and Technology Resources Open Sharing Platform of the Shaanxi Province (Grant Number: 2023-CX-PT-47).

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Global and China Burden of Ischemic Cardiocerebrovascular Diseases Attributable to Low Temperature from 1990 to 2050: Trends and Predictions

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【Abstract】Background: Ischemic cardiocerebrovascular diseases (ICVDs), including ischemic heart disease (IHD) and ischemic stroke (IS), are leading causes of global morbidity and mortality. Low temperature exacerbates cardiovascular risks through physiological mechanisms like increased blood pressure and platelet activation, disproportionately affecting vulnerable populations such as the elderly and those with pre-existing conditions. Despite evidence of climate-related health impacts, comprehensive analyses of long-term trends and future projections for low-temperature-attributable ICVD burden remain limited, especially in rapidly aging nations like China (15.6% aged ≥ 65 years in 2024). This study aims to fill this gap by integrating socioeconomic and demographic factors, providing evidence for region-specific prevention strategies.

Objective: To analyze the global and China burden of ischemic heart disease (IHD) and ischemic stroke (IS) attributable to low temperature, along with its trends and predictions, in order to provide data support for targeted prevention and treatment strategies.

Methods: Based on the 2021 Global Burden of Disease (GBD2021) database, we analyzed the trends of age-standardized mortality rates (ASMRs) and age-standardized disability-adjusted life years (ASDRs) from 1990 to 2021 for IHD and IS attributable to low temperature globally and in China. The estimated annual percentage change (EAPC) was calculated using linear regression models, and the correlation between the Human Development Index (HDI) and the Socio-Demographic Index (SDI) with these rates was assessed. The burden of disease was predicted for the years 2022–2050 using an Autoregressive Integrated Moving Average (ARIMA) model.

Results: Compared to 1990, the global burden of IHD and IS attributable to low temperature decreased in 2021, with EAPC of -1.73% (95% CI: -1.85%, -1.60%) for

ASDR in IHD and -2.64% (-2.77%, -2.50%) for IS. In China, the burden of IHD increased, with an EAPC of 0.32% (0.01%, 0.64%), while the burden of IS decreased, with an EAPC of -0.92% (-1.14%, -0.69%). The burden of IHD and IS decreased across all SDI quintiles during this period, with a greater reduction observed in females compared to males. In 2021, the IHD burden attributable to low temperature in China became higher than the global average, compared to being lower in 1990. Globally and in China, the burden of IHD was higher than that of IS, with a generally higher burden in males compared to females. The elderly population, particularly those over 95 years old, bore the heaviest burden. Pearson correlation analysis showed that countries with higher ASMR and ASDR exhibited an upward trend in disease burden ($r > 0$, $p < 0.01$). Moreover, HDI and SDI were significantly negatively correlated with disease burden ($r < 0$, $p < 0.01$). The ARIMA predictive analysis indicated that the burden of IHD and IS attributable to low temperature will continue to decrease globally and in China from 2022 to 2050.

Conclusion: The burden of ischemic cardiocerebrovascular diseases attributable to low temperature will decline globally and in China from 1990 to 2050. Males will bear a heavier burden than females, and the elderly population will face a higher disease burden. Future prevention and treatment strategies should focus on high-risk groups.

Funding: This project was supported by the National Natural Science Foundation of China (Grant No. 82173626).

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Global temporal trends of Mosquito-borne diseases among all age: Age-period-cohort analysis 2021

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【 Abstract 】 Background: Mosquito-borne infectious diseases pose a huge challenge to global health and to the prevention of infectious diseases in all countries. These conditions have severely affected the health of citizens of countries and highlighted problems related to socio-economic development and access to and efficiency of health care. Previous studies have been geographically limited and lack comprehensive global analysis. The Global Burden of Disease, Injuries and Risk Factors Study (GBD) is a comprehensive and up-to-date global epidemiological study that enables us to conduct global, regional and national burden of disease studies to identify potential hazards.

Objective: To provide scientific evidence for optimizing resource allocation, paying attention to the population with a high burden of mosquito-borne infectious diseases, and reducing the disease burden.

Methods: This study uses the 2021 Global Burden of Disease, Injury, and Risk Factor Study (GBD) system to assess trends in the global, regional, and national disease burden of malaria and dengue over a 30-year period from 1992-2021. Calculate the estimated annual percent change (EAPC) of the age-standardized rates of malaria and dengue by age and socio-demographic index (SDI) to quantify temporal trends. Spearman correlation analysis was used to examine the correlation between age-standardized rates and SDI. An APC model was established to assess age, period, and cohort effects.

Results: Compared to 1992, the global burden of malaria showed a downward trend in 2021 and an upward trend in dengue fever. The disease burden is higher in people under 30 years of age and in the elderly population aged 60-80 years, with the highest malaria burden observed in low SDI regions and the highest dengue burden in low and medium SDI regions. When studying the association of SDI with malaria and dengue incidence and DALYs, the burden of malaria and dengue fever was negatively correlated with SDI in 1992 and 2021, and the disease burden of malaria was more correlated with SDI.

Analysis of the effects of APC showed that the age-cohort effects of malaria and dengue fever were completely inconsistent, with older adults having a higher risk of dengue fever. Malaria, on the other hand, is more prevalent in children, and the risk decreases with age. The age cohort showed a reduced risk of malaria incidence and an increased risk of dengue fever.

Conclusions: Mosquito-borne infectious diseases pose a major challenge to global public health. Different mosquito-borne transmission routes and different disease burden trends are different, the increasing trend of dengue fever prevalence is a cause for concern, health inequalities are still prominent, and public health interventions need to be continued in countries with intermediate and high development levels. Global collaboration and data sharing are essential to facilitate life-cycle management models for the study and treatment of mosquito-borne infectious diseases, as well as to promote global health.

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Group sequential methods of restricted mean survival time

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Abstract

Objective: The proportional hazards (PH) assumption is often violated in clinical trials. If the most commonly used Log-rank test is used for trial design in non-proportional hazard (NPH) cases, it will result in power loss or inflation, and the effect measures hazard ratio will become difficult to interpret. To circumvent the issue caused by the NPH for trial design and to make the effect measures easy to interpret and communicate, two simulation-free methods about restricted mean survival time group sequential (GS-RMST) design were introduced in this study: the independent increment GS-RMST (GS-RMSTi) design and the non-independent increment GS-RMST (GS-RMSTn) design.

Methods: For the above two designs, we used the counting process and Martingale central limit theorem to derive the corresponding analytic expression of the variance-covariance matrix. The calculations of the stopping boundaries and sample size are given by non-binding method for both methods.

Results: Simulation studies showed that both designs can achieve the corresponding nominal type I error and nominal power. The GS-RMSTn simulation studies show that the Max-Combo test group sequential (GS-MC) design is robust in different NPH scenarios. GS-MC is suitable for discovering whether there is a treatment effect difference. However, it does not have a corresponding easy-to-interpret effect measure indicating effect difference magnitude.

Conclusion: GS-RMST performs well in both PH and NPH scenarios, and it can obtain time-scale effect measures that are easy to understand by both physicians and patients. In summary, if the PH assumption is expected to be violated, the GS-RMSTi design is recommended when the trial is only interested in the effect of a treatment or

intervention within a specific period; for a trial focused on sustained effect, we recommend trying the GS-RMSTn design.

Keywords: Restricted mean survival time, group sequential design, non-proportional hazards, survival analysis

FOUNDING INFORMATION: This work was supported by the National Natural Science Foundation of China (82473723) and the Guangdong Basic and Applied Basic Research Foundation (2024A1515011402).

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Identifying Suicide Risk Trajectories and Their Predictive Values for Subsequent Suicide Attempts among Crisis Hotline Callers in China

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【 Abstract 】 Background: Identifying suicide risk and predicting subsequent attempts are crucial for crisis hotline callers. However, it could be time-consuming to assess the risk using the traditional psychological scales during the call. Self-reported suicide scores are a time-varying subjective measure that reflects the feelings of callers at the moment, which can be quickly assessed. Whether this indicator could be utilized for risk assessment and future suicide prediction remains unclear.

Aim: This longitudinal study aims to identify suicide risk trajectories based on self-reported suicide scores and investigate their predictive values for subsequent suicide attempts (SAs) among crisis hotline callers with suicidality.

Methods: We collected data from the Guangzhou Psychological Crisis Hotline from January 1, 2023, to December 31, 2024. Callers who reported suicidality (attempts, ideation, and plan) were included and followed up on the 1st, 7th, 15th, and 30th day after the initial call. Latent class mixed models were applied to identify trajectories of self-reported suicide risk scores during the follow-up. The XGBoost model, adding trajectory class as a covariate, was constructed to predict subsequent suicide attempts. SHapley Additive exPlanation (SHAP) values were calculated to estimate the contribution of each predictor. Cox Hazard Ratio model was built to evaluate the association between key variables and subsequent SAs.

Findings: Among 1235 eligible participants (average age 23.32 ± 7.53 years old, and 58.1% female), 75.8% reported suicide ideation and 8.7% reported SAs before. A total of 127 (10.2%) participants had subsequent SA(s) during the follow-up. The 3-group model built with quadratic time effect was chosen as the optimal LCMM, which identified participants into the constant high-risk group (30.0%), the gradual decline group (12.0%), and the rapid decline group (58.0%). Participants who called at dawn (aOR 0.64, 95%CI 0.42-0.98, $P=0.008$), night (aOR 0.57, 95%CI 0.37-0.86, $P=0.040$), and summer (aOR 0.50, 95%CI 0.31-0.83, $P=0.007$), had relationship

query (aOR 0.40, 95% CI 0.20-0.78, $P=0.007$) and suicide ideation (aOR 0.48, 95% CI 0.29-0.79, $P=0.004$) were less likely to be classified to the constant high-risk group. The trajectory class had the highest SHAP values for SA prediction, followed by age, mental disorder history, and call duration. We found an 81% lower possibility of subsequent SAs for participants in the rapid decline group (HR 0.19, 95% CI 0.12 - 0.30, $P<0.001$), compared to the constant high-risk group. Age (HR 0.94, 95% CI 0.90-0.98, $P=0.004$), winter callers (HR 0.57, 95% CI 0.36-0.89, $P=0.013$), and suicide ideation history (HR 0.50, 95% CI 0.29-0.87, $P = 0.014$) was protective factors, however, those with depression had an increased risk to have subsequent SAs (HR 2.64, 95% CI 1.39-3.37, $P=0.001$).

Conclusions: Self-reported suicide risk scores can serve as a reliable referencing measure for identifying suicide risk and predicting future attempts for crisis hotline callers. We suggest that extra attention is required for callers with constantly high scores, younger age, and history of depression and SA, as well as those calling in winter to prevent subsequent SAs.

Funding: The National Natural Science Foundation of China (No.82401811); Guangdong Basic and Applied Basic Research Foundation (Grand no. 2024A1515220104, 2022A1515110694);

Science and Technology Program of Guangzhou (No.2024A04J10000, 2024A03J0223, 2024A03J0295, 2023A03J0854, 2023A04J1869, 20251A011047, 20252A011018);

Guangzhou Municipal Key Discipline in Medicine (2025-2027);

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Impact of Black Carbon Exposure on Length of Hospital Stay in Asthma Patients: A Retrospective Cohort Study in Yulin, China

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【Abstract】Background: Asthma prevalence in China has reached 4.2% among adults, yet control remains suboptimal. While PM_{2.5} exposure is established as a key environmental risk factor for asthma exacerbation, most studies focus on total PM_{2.5} concentrations and outpatient visits rather than examining specific PM_{2.5} components and their impact on hospitalization outcomes. Since PM_{2.5} health effects may depend on chemical composition, particularly components like black carbon (BC), there is a critical need to investigate how individual constituents affect asthma severity as measured by hospital length of stay.

Objective: To evaluate the association between short-term exposure to PM_{2.5} and its components—particularly black carbon (BC)—and the length of hospital stay among asthma patients, and to explore whether variations of BC exposure on additional asthma exacerbations.

Methods: A retrospective cohort study was conducted using data from asthma patients in Yulin, China, from 2018 to 2023. Air pollution data, including PM_{2.5} components, were collected, and general linear models (GLM) and restricted cubic spline (RCS) analyses were employed to evaluate the associations between BC exposure and hospital stay length. The study also examined the effects of BC across different age groups and seasons.

Results: A significant association between BC exposure and longer hospital stays was identified, with each 1.00 µg/m³ increase in BC concentration leading to an additional

0.45 days of hospitalization at lag9. Age-specific analysis revealed that children and middle-aged individuals were more vulnerable to BC exposure, while elderly patients showed no significant effects. Seasonal analysis indicated that the impact of BC was more pronounced during the non-pollen season, with BC exposure during this period contributing to longer hospital stays.

Conclusions: BC, a key component of PM_{2.5}, was significantly associated with prolonged hospital stays in asthma patients, particularly among younger populations. The findings highlight the need for targeted public health interventions to reduce BC emissions and protect vulnerable groups. Future research should focus on large-scale prospective studies to further explore the health risks of particulate matter exposure and develop effective strategies to mitigate asthma exacerbations.

Funding Statement: This work was supported by National Natural Science Foundation of China (Grant Number: 82103944), Chinese National Key Research and Development Program of China (Grant Number: 2017YFC0907200, 2017YF0907201), and the Science and Technology Resources Open Sharing Platform of the Shaanxi Province (Grant Number: 2023-CX-PT-47).

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Impact of the Urban-Rural Resident Basic Medical Insurance on Self- Rated Health of Older Adults in China: Evidence from the CLHLS

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【Abstract】Background: Urban-Rural Resident Basic Medical Insurance (URRBMI) has played a pivotal role in mitigating healthcare resource disparities between urban and rural areas in China since 2016. While existing studies have extensively investigated the impact of URRBMI on healthcare utilization, limited research has focused on its association with the self- rated health (SRH) of the elderly population. This study to address this research gap by rigorously assessing the effects of URRBMI on SRH of the elderly population.

Methods: We selected 1,911 individuals aged 65 and older from the Chinese Longitudinal Healthy Longevity Study (CLHLS) in 2014 and 2018. Propensity scores (PS) were estimated using a logit model, and individuals with similar PS in both groups were matched in a 1:2 ratio based on the nearest neighbor matching method. The difference-in-differences (DID) approach was applied to evaluate the implementation effect of URRBMI on the SRH of the elderly population.

Results: Following propensity score matching (PSM), no significant differences in covariates were detected between the intervention and control groups ($P > 0.05$), satisfying the common support and balancing assumptions, thereby confirming successful matching. The DID analysis demonstrated that the URRBMI policy was associated with a 0.188-unit improvement in SRH scores among older adults ($P = 0.037$). Robustness checks using kernel matching further corroborated the reliability of the DID estimates.

Conclusion: The URRBMI has a significant positive impact on the SRH of older adults. The governments should further expand URRBMI's effectiveness and leverage its advantages to the fullest extent possible to safeguard this population's health.

This work was supported by the National Natural Science Foundation of China (Grant No. 82003560), Shandong Natural Science Foundation (Grant No. ZR2020MH340).

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Inflammation-mediated lipid metabolism in endocrine autoimmune diseases: a genetic distance based PRS approach integrating HLA region

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【Abstract】

Background : Endocrine autoimmune diseases (AID) exhibit special polygenic characteristics in human leucocyte antigen (HLA) region. Current understanding of their association with lipid metabolism remains constrained by imprecise polygenic risk score (PRS) modeling.

Aim: Advanced analytical approaches are needed to elucidate the inflammatory mechanisms bridging genetic susceptibility and metabolic dysregulation.

Methods : We proposed a genetic distance based clumping gPRS to account for linkage disequilibrium in HLA region. gPRS and pathway gPRS were constructed for individuals diagnosed with type I diabetes (T1D), Graves disease (GD), Hashimoto thyroiditis (HT) and Addison ' s disease (AD) in UK Biobank. Latent correlation between PRS and phenotypes were explored utilizing Kendall ' s tau test, two traits LDSC regression and gene annotation.

Results : Lipid metabolism address an important function through immune and inflammatory biomarkers across multiple traits. Males with low genetic risk tend to have lower high density lipoprotein cholesterol components, while the correlation presented the opposite in females. Higher genetic susceptibility in AID are associated with the elevation of cholesterol components in low-density lipoprotein, triglycerides in low density lipoprotein and very-low-density lipoprotein were associated with the increase of genetic risks across all traits. Moreover, polyunsaturated fatty acids including omega-3 and omega-6 decreased with higher PRS in males and females, while monounsaturated fatty acids exhibited an increasing trend.

Conclusion : Our study constructed a three-tier validation framework that bridges methodological innovation, biological exploration, and genome wide validation, highlighting inflammation mediated lipid metabolism as a potential pathogenic mechanism in endocrine AID, offering valuable insights into commonality for future

comprehensive investigations.

This project was supported by grants from the National Natural Science Foundation of China (82173628), the Youth Fund Project of Hubei Provincial Department of Science and Technology (Grant No. 2024AFB027).

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Investigation of the Potential Causal Effect and Mediation Pathways between Prenatal Greenness Exposure and the Risk of Gestational Diabetes Mellitus

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【Abstract】 Background: Growing evidence links greenness exposure to reduced gestational diabetes mellitus (GDM) risk, though findings are inconsistent. The role of air pollutants in this relationship remains unclear.

Objective: This study examined the link between maternal greenness exposure during pregnancy and GDM risk, focusing on the potential mediating effects of O_3 , dew point temperature, and $PM_{2.5}$ and its components.

Methods: We included 183 cases and 732 controls using data from the Guangdong Registry of Congenital Heart Disease. Residential greenness exposure was measured using the Normalized Difference Vegetation Index (NDVI). Inverse probability weighting (IPW) was applied to evaluate the association between greenness and GDM risk using three weighted models: general linear models, generalized estimating equations, and extreme gradient boosting. Multiple mediation analysis was performed to assess the mediating effects of air pollutants and dew point temperature.

Results: Greenness exposure during pregnancy was significantly associated with reduced GDM risk, with ORs ranging from 0.62 to 0.73 across multiple models. IPW-based models consistently showed stronger protective effects compared to traditional logistic regression. The protective effect was more pronounced within 250m and 500m buffers than within 1000m. Mediation analysis indicated that the effect of greenness on GDM was primarily mediated through reduced $PM_{2.5}$ exposure. Among $PM_{2.5}$ components, NO_3^- had the strongest mediating effect, contributing to a 41.3–43.1% reduction in GDM risk. In contrast, greenness exposure was associated with increased GDM risk via NH_4^+ (e.g., a 39.6% increase at 500m) and elevated dew point temperature (e.g., a 13.2% increase at 1000m).

Conclusions: This increased residential greenness may reduce the risk of GDM in pregnant women by improving air quality and regulating local climate conditions. These findings highlight the potential of optimizing greenness distribution as a cost-effective strategy to enhance maternal health outcomes.

Funding: National Natural Science Foundation of China (82204162); Basic and Applied Basic Research Foundation of Guangdong Province (2022A1515010823, 2025A1515012021)

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Knowledge Graphs Reveal Multi-Target Mechanisms and Herbal Substitution Strategies in Huanglian Wendan Decoction for Palpitation Treatment

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ABSTRACT

Research Background: Traditional Chinese Medicine (TCM) has garnered global attention for its therapeutic efficacy and favorable safety profile, yet the sustainability of its herbal resources faces unprecedented challenges. Overharvesting and habitat loss have driven the depletion of wild medicinal species, necessitating scientifically validated substitution strategies to preserve therapeutic integrity. Early substitution paradigms relied on phylogenetic relatedness as a proxy for bioequivalence, but modern approaches demand integrative frameworks that harmonize ecological, chemical, and pharmacological data. A critical barrier persists: the absence of robust clinical validation for substituted herbs risks compromising TCM's empirical legacy. To address this, we propose a pharmacological proximity analysis anchored in multi-layered knowledge graphs (TCM × KG), enabling systematic evaluation of herbal substitutions through compound similarity, target engagement, and pathway modulation. This study focuses on Xin Ji (palpitations, ICD-11: ME24.1), a cardiovascular condition marked by perceived irregular heart rhythms and anxiety. In TCM, palpitations arise from multifactorial imbalances — qi deficiency, yin insufficiency, or phlegm-fire disturbances — contrasting Western medicine's reliance on arrhythmia-suppressing drugs, which often incur adverse effects. Among TCM interventions, Huanglian Wendan Decoction (HLWDD) stands out for its dual capacity to regulate heart function and minimize side effects. First documented in the Qing Dynasty, HLWDD combines Coptis, Pinellia, Poria, and other herbs to clear heat, resolve phlegm, and stabilize cardiac rhythm. Despite its clinical prominence, HLWDD's mechanistic basis remains enigmatic, hindering its integration into precision medicine paradigms.

Objective: Traditional Chinese Medicine (TCM) formulations like Huanglian Wendan Decoction (HLWDD) exhibit multi-target therapeutic effects, but their mechanistic complexity and substitution strategies remain underexplored. This study integrates knowledge graphs, network pharmacology, and molecular docking to systematically decode HLWDD's anti-palpitation mechanisms and evaluate herbal substitution viability.

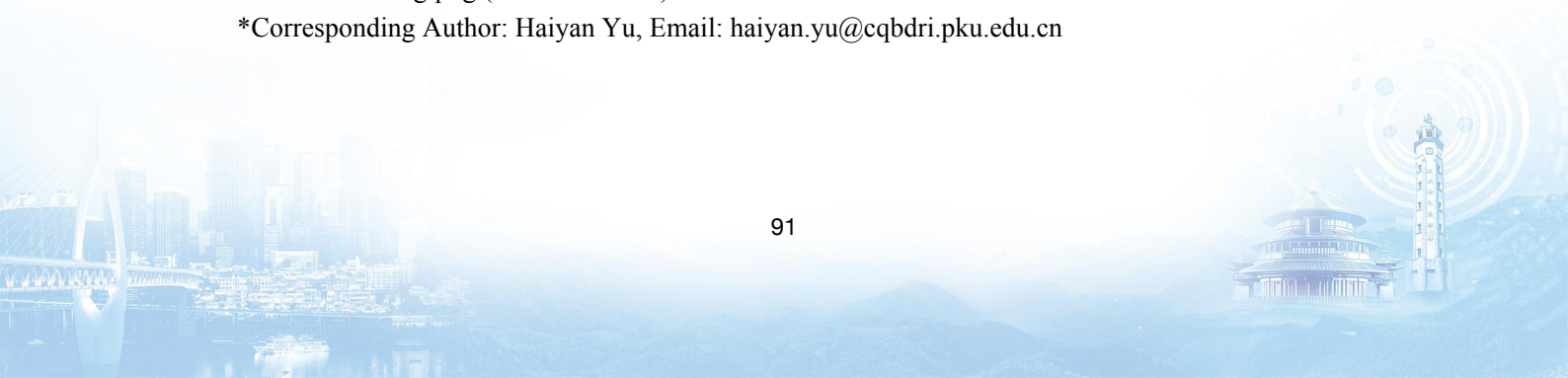
Methods: Multi-layered TCM knowledge graphs (TCM $\times$ KG) were constructed to map HLWDD's bioactive components, disease targets, and pathway interactions. Network pharmacology identified 105 active compounds and their shared targets with palpitation-related genes (via GeneCards). Protein-protein interaction (PPI) networks, Gene Ontology (GO), and Kyoto Encyclopedia of Genes and Genomes (KEGG) analyses prioritized hub targets and pathways. Molecular docking validated ligand-receptor interactions, while knowledge graphs quantified substitution efficacy between Bupleurum (BU-CY) and Radix Ophiopogonis (RO-CY) for Cyperus in HLWDD.

Results: Quercetin, kaempferol, and naringenin emerged as HLWDD's core anti-palpitation compounds, synergistically modulating AKT1, TNF, and ALB—key hubs in cancer and MAPK signaling pathways. Molecular docking confirmed robust binding (energies < -20.92 kJ/mol) between HLWDD components and ALB/AKT1. Substitution analysis revealed BU-CY's superiority over RO-CY in compound similarity (89.2% vs. 82.4%), PPI target overlap (95.7% vs. 87.5%), and clinical docking compatibility (100% vs. 33.3%). While BU-CY enhanced calcium signaling (+0.07%), RO-CY upregulated cancer (+0.82%) and lipid pathways (+0.38%) but compromised MAPK activity.

Conclusion: HLWDD alleviates palpitations via multi-target regulation of cancer and MAPK pathways, with ALB as a pivotal mediator. Bupleurum is a clinically viable substitute for Cyperus, balancing pathway specificity and historical precedent, whereas RO-CY's niche effects warrant context-dependent use. Our integrative framework advances TCM modernization by bridging mechanistic insights with data-driven substitution protocols, offering a blueprint for precision herbal medicine.

Funding: This work was supported in part by the National Natural Science Foundation of China (No. 62272077, 82071492), Chongqing Municipal Education Commission (No. KJQN202200608), Chongqing Municipal Science and Technology Bureau (No. 2022TIAD-KPX0155, 2023DBXM008, CSTB2023NSCQ-MSX0073), and Bishan District Science and Technology Bureau of Chongqing (No. BSKJ0067).

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Lipid metabolism-related inflammatory indexes (LMIs) and risk of incident peripheral artery diseases (PAD) in patients with type 2 diabetes mellitus (T2DM): a multicohort study in elderly Chinese and the UK Biobank

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【Abstract】

Background: Lipid metabolism-related inflammatory indexes (LMIs) have been recognized as potential biomarkers for the risks of atherosclerosis and major adverse cardiovascular events (MACEs). Some evidence also indeed linked these indexes to the risk of PAD, yet the available data is scarce and predominantly confined to cross-sectional design.

Objectives: This study aims to explore the associations of LMIs, including neutrophil to high-density lipoprotein cholesterol ratio (NHR), monocyte to high-density lipoprotein cholesterol ratio (MHR), platelet to high-density lipoprotein cholesterol ratio (PHR), and lymphocyte to high-density lipoprotein cholesterol ratio (LHR), with the risk of peripheral artery disease (PAD) in elderly T2DM patients.

Methods: A total of 2837 participants aged ≥ 60 years with T2DM from the Jinshan Cohort (China) and 13542 participants from the UK Biobank (UK) were included in the primary analyses. According to the type of outcome variables, logistic regression models and Cox proportional-hazards models were used to estimate the risk of PAD associated with LMIs. The methods of generalized propensity score (GPS) and negative control exposure (NCE) were applied to control the potential confounding. The mediation effects of liver and kidney function-related indicators on associations between LMIs and incident PAD were also explored.

Results: The results from traditional regression models suggested positive associations of incident PAD with all four LMIIs. The ORs and 95% confidence intervals of PAD for one unit increase in NHR (10^9 mmol), MHR (10^8 mmol), PHR (10^{11} mmol) and LHR (10^9 mmol) were 1.24 (1.11 to 1.39), 1.22 (1.08 to 1.37), 1.69 (1.32 to 2.15) and 1.57 (1.22 to 2.01), respectively, in the Jinshan Cohort. While the HRs were 1.14 (1.10 to 1.18), 1.03 (1.01 to 1.04), 1.19 (1.09 to 1.29), 1.11 (1.07 to 1.14), respectively, in the UK Biobank. The estimated hazards of PAD with all four LMIIs were still robust in regression models weighted by GPS. The results of negative control exposure analyses revealed no statistically significant associations between any selected NCE and PAD, either in the Jinshan Cohort or the UK Biobank. On calibration using NCEs, the calibrated *P* values for the associations between LMIIs and the risk of incident PAD further indicated that the observed effect sizes were significant (all for $P < 0.05$). Estimated glomerular filtration rate (eGFR) mediated the relationships between LMIIs and PAD, with the proportions of mediating effect ranging from 10.03% to 20.80%.

Conclusions: Elevated levels of LMIIs, such as NHR, MHR, PHR and LHR, were associated with an increased risk of incident PAD among elderly diabetic patients. eGFR served as a mediating factor in the association between LMIIs and the occurrence of PAD.

Funding: This work was supported by the National Nature Science Foundation of China (82273733), Shanghai Shenkang Hospital Development Center Projects (SHDC2023CRS034), Basic Standard of Dataset for Diabetic Foot Disease Screening by the Shanghai Municipal Health Commission (2023WB06), and Development of Technical Standards for Hierarchical and Closed-Loop Prevention and Treatment of Diabetic Foot Disease by the Shanghai Science and Technology Commission (23DZ2203200).

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Long-Term Ambient Air Pollution, Physical Activity, and Premature Mortality Risk in a National Prospective Cohort

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[Abstract]Background: Premature mortality is a major global health challenge. Ambient air pollution is the top modifiable environmental risk factor for adult mortality, strongly linked to cardiovascular disease and early death. While most research focuses on particulate matter, little is known about how multiple pollutants interact with behavioral factors like physical activity (PA). Evidence is scarce on whether PA reduces or intensifies pollution's effects on premature mortality. This study examines PA's influence on air pollution-related premature mortality in China's middle-aged and older adults.

Objective: This study aimed to investigate the effects of long-term exposure to air pollutants and physical activity (PA) on premature mortality, and to further explore their potential interactions.

Methods: A total of 5,507 participants were enrolled from the China Health and Retirement Longitudinal Study (CHARLS) in 2013 and followed until 2020. Air pollutants concentrations, including fine particulate matter (PM_{2.5}), inhalable particulate matter (PM₁₀), ozone (O₃), nitrogen dioxide (NO₂), sulfur dioxide (SO₂), and carbon monoxide (CO), were obtained from the China High Air pollutants dataset (CHAP). Physical activity was quantified using the total metabolic equivalent (MET-minutes/week) for each participant. Premature mortality was defined in relation to the average life expectancy in 2020. Cox regression models were employed to examine the associations between air pollution exposure, physical activity, and premature mortality. Further analyses explored the mediating role of physical activity in the relationship between air pollution exposure and premature mortality, as well as interactions between air pollution and physical activity.

Results: In fully adjusted models, per 10 $\mu\text{g}/\text{m}^3$ increase in PM_{2.5} (HR:1.47, 95% CI:1.36-1.58), PM₁₀ (HR:1.23, 95% CI:1.19-1.28), NO₂ (HR:1.20, 95% CI:1.08-1.34), SO₂ (HR:2.04, 95% CI:1.84-2.26), and per 1 mg/m^3 increase in CO

(HR:4.78, 95% CI:3.31-6.90) were associated with elevated risks of premature mortality. High-level physical activity, compared to low-level physical activity, was associated with a reduced risk of premature mortality (HR: 0.60, 95% CI: 0.46-0.79). Physical activity played a modest mediating role in the link between air pollution exposure and premature mortality, with mediating proportions of 3.2% for NO₂ and 1.6% for CO.

Conclusion: Long-term exposure to air pollutants is associated with an increased risk of premature mortality, whereas high levels of physical activity can mitigate this risk, particularly in environments with high concentrations of air pollution

Funding: This study was funded by the National Natural Science Foundation of China (82360667, 82160645), the Natural Science Foundation of Jiangxi Province (20212BAB206091), the Graduate Innovation Special Fund (YC2024-S167) and the Research and Training Fund of Nanchang University (2024).

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Lower risk of atrial fibrillation associated with visible greenness within community life circle: findings from a population-based study

Authors

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Abstract

Objectives: Existing studies have found the health implications of greenness on cardiovascular health, but largely focus on greenspace rather than visible greenness. We aimed to investigate the relationship between visible greenness within the community life circle and atrial fibrillation (AF).

Methods: Our study included 11,539 permanent residents from a large prospective cohort in a megacity of southern China from 2015 to 2017. We generated 15-minute walking isochrone for each study participant as the community life circle and combined it with green view index (GVI) to estimate corresponding exposure to residential greenness. GVI was calculated utilizing street view images and a fully convolutional neural network tailored for evaluating urban environments. We combined logistic regression model and a doubly-robust approach to explore the relationship between GVI and AF. Mediation analyses were used to assess the mediating role of air pollution, body mass index (BMI) and exercise time on the relationship between GVI and AF.

Results: We found that each IQR increase in GVI exposure was associated with a

19.8% (95% CI: 4.2%, 32.3%) reduction in the risk of AF. The mediation effect of PM_{10} on the relationship between GVI and AF was also identified.

Conclusions: Higher visible greenness exposure within community life circle was associated with reduced risk of AF among urban residents. Visible greenness within urban community areas should be emphasized as a solution to promote cardiovascular health.

Keywords: Atrial fibrillation; Community life circle; Doubly robust estimation; Residential greenness; Street view

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MAVD: A new approach to microbial abundance data analysis through vector decomposition

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Funding information:

This research was funded by the National Natural Science Foundation of China (No. 82473698), the Central government-led local science and technology development special project (No. 2019L3006 and 2020L3009), the Fujian Provincial Financial Special Project (23SCZZX004), and the Natural Science Foundation of Fujian Province (No. 2021J01726 and 2021J01733).

Abstract

Background: Differential Abundance Analysis (DAA) is a vital statistical task in the analysis of microbiome data. Addressing the distinctive challenges inherent in microbiome abundance data, such as compositional effects, zero inflation, overdispersion, and high dimensionality, this study introduces the Microbial Abundance Data Vector Decomposition Model (MAVD).

Objective: Utilizing techniques like data standardization, normalization, and vector decomposition, MAVD adeptly tackles the data issues, aiming to identify highly reliable microbial biomarkers.

Methods: An integrative analysis was conducted on 13 current DAA methods to address the complexity of microbiome abundance data. The MAVD was constructed based on the concept of vector decomposition, employing R software for code integration, simplification, and optimization of the model construction process. A simulation-based study was performed within a semi-parametric simulation framework using the 'SimulateMSeq' function in R to generate simulated microbial abundance data. Performance evaluation of the MAVD model and other DAA methods was conducted using metrics such as precision, true positive rate, false positive rate, false discovery rate, F1 score, and model execution time. Empirical

validation was also conducted on fecal microbiota research related to colorectal cancer using two real-world colorectal cancer cases.

Results: The MAVD model, employing seven standardization and normalization steps, demonstrated excellent performance across varying effect sizes and sample sizes. It showed high true positive rates, precision, F1 scores, and low false discovery rates, outperforming other DAA models in both simulated and empirical validations.

Conclusion: The MAVD model exhibits stability, robustness, and flexibility in handling microbial abundance data, thereby enhancing the reliability and accuracy of microbiome research. MAVD is freely available at

<https://github.com/ZhifengLin-micro/MAVD>.

Maximum oxygen consumption and the risk of major adverse cardiovascular events and all-cause mortality: a prospective study from UK Biobank

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[Abstract]Background: Maximal oxygen consumption (VO₂max), defined as the maximum amount of oxygen a person can utilize during intense exercise involving large muscle groups, is considered the best standard for assessing cardiovascular fitness and cardiorespiratory capacity. However, the dose-response relationship between VO₂max and major adverse cardiovascular events (MACE) remains insufficiently characterized.

Objective: This study aims to investigate the dose-response relationship between VO₂max and MACE.

Methods: Participants with available VO₂max data from UK Biobank were included. The primary outcome was MACE, while secondary outcomes included all-cause mortality, MACE incidence and MACE mortality. The dose-response associations between VO₂max and outcomes were evaluated using restricted cubic splines and Cox proportional hazards models.

Results: A total of 49,996 eligible participants were included in this study. During a median follow-up period of 14.2 years, 2,854 MACE events and 3,425 all-cause death events occurred, with cumulative incidence rates of 4.12%, 4.94% per 1000 patient-year, respectively. Restricted cubic spline analyses showed that there was a significant trend between increased VO₂max values and reduced MACE risk, and a significant inverse linear relationship was observed (P for overall <0.001, P nonlinear = 0.070). Cox proportional hazards models revealed that each 5 unit increase of VO₂max were associated with 7% reduction in MACE risk [HR (95% CI): 0.93(0.89-0.97), P = 0.0012] and 13% reduction in all-cause mortality risk [HR (95% CI): 0.87(0.84-0.91), P < 0.0001].

Conclusions: This study demonstrates an inverse dose-response associations between VO₂max and risks of MACE and all-cause mortality. These findings highlight the potential of improving VO₂max through exercise as a key factor for preventing cardiovascular disease and reducing mortality.

基金资助: 本项目获国家自然科学基金资助 (82373687)

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Noninvasive Oxygenation Monitoring in Neonatal PPHN: Validation of OSI and SpO₂/FiO₂ Against Conventional Invasive Indices

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Abstract

Objective: This multicenter retrospective study evaluated the correlation between non-invasive oxygenation indices (Oxygen Saturation Index [OSI] and the ratio of peripheral oxygen saturation to the fraction of inspired oxygen [SpO₂/FiO₂, S/F]) and conventional invasive measures (Oxygenation Index [OI] and the ratio of arterial oxygen partial pressure to FiO₂ [PaO₂/FiO₂, P/F]) in neonates with persistent pulmonary hypertension (PPHN). The study aimed to validate non-invasive monitoring methods and establish clinically relevant thresholds for disease severity assessment.

Methods: We analyzed data from 377 PPHN neonates across five neonatal ICUs in China (2012-2021), including demographic characteristics, vital signs, and 2,717 paired arterial blood gas measurements. Oxygenation indices were calculated for each measurement. Statistical analysis included: Spearman's rank correlation (r) for assessing relationships. Bland-Altman analysis with 95% limits of agreement for method comparison. Intraclass correlation coefficients (ICC) for consistency evaluation. ROC curve analysis (using Youden's index) to determine optimal thresholds within the peripheral capillary oxygen saturation (SpO₂) 80-97% range.

Results: Spearman correlation analysis demonstrated significant positive correlations between oxygenation indices: OSI and OI ($r=0.926$, $p<0.001$), and between S/F and P/F ($r=0.853$, $p<0.001$). Within the optimal SpO₂ range (80-97%), Bland-Altman analysis revealed excellent agreement for both index pairs: OSI-OI showed a mean difference of 0.417 (95% LoA -1.82 to 2.65), while S/F-P/F demonstrated a mean difference of 0.053 (95% LoA -28.7 to 28.8). ROC curve analysis confirmed strong diagnostic performance (AUC 0.96-0.98), with established clinical thresholds: OSI values ranged from 5.05 (corresponding to OI=5) to 27.57 (OI=40), and S/F from 118.63 (P/F=100 mmHg/l) to 330.14 (P/F=400 mmHg/l).

Conclusion: This large-scale study validates OSI and S/F as reliable non-invasive alternatives for oxygenation assessment in PPHN neonates. The established thresholds within the SpO₂ 80-97% range provide clinically useful benchmarks for disease severity stratification and treatment monitoring, potentially reducing the need for invasive blood gas measurements in this vulnerable population.

Keywords: Persistent Pulmonary Hypertension of the Newborn (PPHN); Percutaneous Oxygen Saturation (SpO₂); Oxygen Saturation Index (OSI); SpO₂/FiO₂ Ratio (S/F); Bland–Altman Analysis

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Optimizing Vaccine Dose Combinations: A Novel Adaptive Interval Design for Early-Phase Trials

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Background: Recent advances in cancer therapeutic vaccines in combination with other treatments emerged as an efficient way to induce tumor regression, yet exploring optimal dose combination (OBDC) for concomitant therapies rather than simply adopting monotherapy dose optimization rely heavily on appropriate dosage determination. However, early-phase vaccination clinical trials encounter challenges due to various dose combinations and non-monotonic dose-response patterns within dose ranges. This dearth of tailored clinical trial designs poses a significant hurdle in cancer therapeutic vaccine development.

Purpose: To address this gap, we propose a novel two-dimensional dose-escalation framework tailored to cancer vaccines, enabling clear and practical dose decision-making. The primary objective of this design is to pinpoint the optimal biological dose combination, striking a delicate balance between efficacy and toxicity.

Methods: Our proposed design adopts a Bayesian interval design for dose-finding, making dose (de)escalation decisions while simultaneously considering efficacy and safety of all dose-combinations. Extensive simulation studies are conducted to evaluate the performance of our proposed design.

Results: Comparative analyses with commonly used existing early-phase vaccine dose-finding designs reveal that our proposed method excels in identifying the optimal toxicity-efficacy trade-off, offering simplicity and accuracy. Furthermore, extensive sensitivity analyses across various dose dimensions and cohort configurations confirm the robustness and efficiency of our approach. Our proposed early-phase vaccine clinical trial design offers a user-friendly approach for clinicians, with promising operating performance, particularly in terms of accuracy and robustness. The adoption of this methodology holds significant potential for advancing vaccine research and enhancing global health outcomes.

Conclusion: Our innovative Bayesian interval design represents a significant step forward in addressing the challenges inherent in early-phase vaccination clinical trials, promising improved accuracy and efficacy in combined vaccine dosage

determination.

Sponsored by the National Natural Science Foundation of China (Project Nos. 82404383, 82173620, 82373690).

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Personalized Intravenous Thrombolysis in Acute Mild Ischemic Stroke: Who Benefits Most?

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【Abstract】

Background: Acute mild ischemic stroke (AMIS) accounts for a substantial share of stroke cases but lacks clear treatment guidelines. Although intravenous thrombolysis (IVT) is a cornerstone therapy for ischemic stroke, its role in AMIS remains controversial due to uncertain benefits, potential bleeding risks, and unclear cost-effectiveness.

Objective: To assess the impact of IVT on functional outcomes and its cost-effectiveness in AMIS patients, with a focus on identifying subgroups most likely to benefit.

Methods: Data were obtained from the Specific Disease Quality Monitoring System, comprising 19,166 AMIS patients across 298 hospitals. The average treatment effect (ATE) of IVT on functional outcomes was estimated using Bayesian Additive Regression Trees with Random Effects (BART-RE) and Clustered Inverse Probability Weighting (IPW). Subgroup analyses were stratified by NIHSS score, age, sex, and TOAST classification. Cost-effectiveness was evaluated using Incremental Cost-Effectiveness Ratios (ICERs).

Results: Overall, IVT was associated with slightly worse functional outcomes (ATE = -0.035, 95% CI: -0.041 to -0.029). However, among patients with NIHSS scores of 3-5, IVT significantly improved outcomes (ATE = 0.017, 95% CI: 0.011 to 0.023), particularly in younger patients, males, those with cardioembolic stroke, and those who received early treatment. The most cost-effective subgroups were patients aged 18-44 years and those with cardioembolic stroke. Conversely, patients aged ≥ 75 years and those with small-artery occlusion showed limited clinical benefit and poor cost-effectiveness.

Conclusion: IVT demonstrates substantial benefits in selected AMIS subgroups — particularly those with NIHSS scores of 3-5, younger age, and cardioembolic etiology. These findings underscore the importance of a personalized approach to IVT in AMIS to enhance therapeutic efficacy, improve resource allocation, and achieve better clinical outcomes.

Funding: This research was supported by grants from the National Natural Science Foundation of China (NSFC) (Grant Number 82173614).

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Personalized Prediction of Parkinson's Disease Progression Using Longitudinal Data: Dynamic Prediction Models Based on Principal Component Analysis through Conditional Expectation

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[ABSTRACT] Background: Accurate and intuitive prediction of Parkinson's disease (PD) progression is essential for optimizing treatment strategies. Existing predictive models for PD progression have three primary limitations: (1) Most of them are static prediction models that rely solely on baseline data and ignore the impact of dynamic changes in disease or interventions during follow-up. (2) To minimize the impact of changes due to interventions during follow-up, model development often uses data solely from the OFF-medication state (with minimal efficacy), failing to address the clinical prediction needs of all early-stage PD patients. (3) Many models yield probabilistic outcomes, which lack sufficient clinical interpretability. The dynamic restricted mean survival times (RMST) model can utilize longitudinal data and provide intuitive time-scale predictions. However, existing dynamic RMST models use the last observation carried forward (LOCF) method to impute missing data, which assumes little change in covariates over time. This strong assumption limits its clinical applicability.

Objectives: Our study aims to develop an improved dynamic RMST model that relaxes the time-varying covariate constraints and provide more accurate, practical, and intuitive personalized disease progression predictions for all early-stage PD patients.

Methods: This study proposes a dynamic RMST model that imputes missing data using the principal components analysis through conditional expectation (PACE) method, without requiring the assumption that covariates exhibit less time variability. To comprehensively and accurately assess the model results from both time and risk perspectives, our study used the dynamic RMST model and dynamic Cox model to construct dynamic prediction models for PD progression, with the ON (significant efficacy) and OFF medication states measures as endpoints, respectively. The models' predictive performance was assessed through internal and internal-external validation.

Results: The proposed dynamic models for PD progression show significantly better predictive performance than static models using only baseline data. The dynamic

models identified the male sex and better cognitive function as protective factors, while older age and worsening motor symptoms were risk factors for progression. Autonomic dysfunction was a significant risk factor for PD progression only in the ON state. In the OFF state, treatment had no significant effect on PD progression.

Conclusion: The dynamic RMST model proposed in this study effectively relaxes the time-varying covariate assumption. Our dynamic prediction models apply to early-stage PD patients across different medication states. These models incorporate longitudinal measurements that change over time, offering more comprehensive, accurate, and easily interpretable personalized predictions of PD progression at various follow-up times based on the latest changes in the patient's condition. These provide strong support for precision medicine.

Funding: This work was supported by the National Natural Science Foundation of China (grant numbers 82473723) and the Guangdong Basic and Applied Basic Research Foundation (grant number 2024A1515011402).

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Physical Activity and Frailty in Benign Prostatic Hyperplasia Risk: A Longitudinal Trajectories and Mediation Pathways National Cohort Study

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Abstract

Background: Benign prostatic hyperplasia (BPH) is a prevalent urological disorder resulted in lower urinary tract symptoms and reduced quality of life. While age, androgen levels, and genetic predisposition are established risk factors, the roles of physical activity (PA) and frailty remain underexplored.

Aims: This study investigates longitudinal associations between PA, frailty trajectories, and BPH risk and examines potential mediating roles of frailty and body mass index (BMI).

Methods: Using data from the China Health and Retirement Longitudinal Study (CHARLS), 5,288 males without baseline BPH were included. Group-based trajectory modeling identified PA and frailty index (FI) trajectories. Cox proportional hazards models assessed associations between PA/FI trajectories and BPH risk. Mediation analysis evaluated the indirect effects of PA via frailty and BMI.

Results: Two PA trajectories were identified: a declining high-PA group (26.3%) and a lower-PA group (73.7%) with progressive decline. Frailty trajectories included a low-FI group (78.5%) and a high-FI group (21.5%), both worsening over time. Higher PA was inversely associated with BPH risk (adjusted HR=0.81, 95% CI: 0.66–0.98), while higher FI increased risk (HR=1.89, 95% CI: 1.60–2.23). Frailty mediated 9.45% (indirect HR=0.98, $p=0.035$) and BMI mediated 23.2% (indirect HR=0.94, $p<.001$) of PA's protective effect on BPH.

Conclusion: Higher PA and lower frailty are independently associated with reduced BPH risk. Frailty and BMI partially mediate PA's protective effect, suggesting that interventions targeting PA, frailty mitigation, and weight management may offer novel strategies for BPH prevention. These findings highlight the importance of longitudinal lifestyle and aging-related factors in BPH pathophysiology.

Funding: This work was supported by the National Natural Science Foundation of China [grant numbers 82173628].

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Poor Benefits of Treatment in Stroke Patients with Critical Time Delays: Stratified Efficacy Analysis by Delay Quartiles

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【Abstract】

Background: Stroke is a leading global cause of death and disability, with treatment timeliness being pivotal for outcomes. Although studies confirm the time-efficacy gradient in stroke care, the interplay between treatment delays, quality, and outcomes remains unclear.

Objective: This study aims to quantify the differences in the causal effects of improved treatment quality on patient prognosis across groups with varying degrees of delay.

Methods: The time delays were categorized into four distinct phases: pre-hospital delay, examination delay, thrombolysis delay, and total delay. Patients were stratified by quartiles of different delay time, with the first quartile representing the shortest delay duration. Potential confounders among delay, quality, and outcomes were identified through multivariate analysis. Multivariate logistic regression and doubly robust causal modeling evaluated the treatment delay-quality-outcome relationship.

Results: Prehospital delay demonstrated the longest duration and greatest variability (median: 270 min; IQR: 0-1321 min), whereas thrombolysis delay showed relatively concentrated distribution (median: 262 min; IQR: 29-538 min). Treatment quality demonstrated maximal protective effects in the shortest-delay quartiles across all delay categories (OR range: 0.414-0.530; all $P < 0.0001$), whereas no statistically significant benefits were observed in the highest-delay quartiles (OR range: 0.599-0.856; all $P > 0.05$). The doubly robust estimation demonstrated that treatment benefits progressively diminished with increasing total delay time, ultimately losing statistical significance, where the first quartile showed an ATE of -0.0015 (95% CI: -0.0018 to -0.0012; $P < 0.001$), the second quartile -0.0011 (95% CI: -0.0014 to -0.0008; $P < 0.001$), the third quartile -0.0002 (95% CI: -0.0005 to 0.0001; $P = 0.120$), and the fourth quartile -0.0002 (95% CI: -0.0006 to 0.0002; $P = 0.343$), a pattern consistently observed across all delay time categories.

Conclusion: The benefits of improved treatment quality in reducing mortality risk vary significantly based on delay duration, with the greatest effect observed in low-delay patients and markedly diminished benefits in high-delay cases. These findings highlight the need for targeted strategies to identify and prioritize high-delay, low-treatment-quality patient subgroups.

Funding: This research was supported by grants from the National Natural Science Foundation of China (NSFC) (Grant Number 82173614).

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Quasi-U-shaped Generalized Additive Model

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Abstract

Background: Incorporating shape constraints into models is widely recognized to enhance both accuracy and interpretability of results by leveraging epidemiologically plausible shape priors. However, existing shape-constraint methods cannot effectively account for the prior following a quasi-U shape—a composite pattern encompassing monotonic increase, monotonic decrease, and U-shaped curves, as exemplified by the exposure-response relationship between temperature and mortality.

Methods: In this work, we developed a new method called quasi-U-shaped generalized additive model (qUGAM) and theoretically demonstrate its advantages in integrating the quasi-U-shaped priors.

Results: Simulation studies showed that qUGAM significantly outperformed conventional generalized additive model (GAM) in estimating quasi-U-shaped exposure-response associations. Specifically, qUGAM achieved comparable or superior performance in root mean squared error (RMSE), relative RMSE, mean absolute error (MAE), relative MAE, 95%-confidence-interval coverage rate, and interpretability. These improvements were particularly pronounced at both ends of the exposure range with threshold effects and under a small sample size. A case study examining temperature-mortality associations further supported these findings.

Conclusion: Given the wide existence of quasi-U-shaped priors, qUGAM holds substantial potential for broad application across diverse scientific and public health practice.

Keywords: GAM, Exposure-response association, Quasi-U-shaped, qUGAM

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Funding: This work was supported by the Key Project of Young Doctor Program, Second Affiliated Hospital of the Army Medical University (2024YQB026).

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Research on the application of bayesian propensity score in multilevel data

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【Abstract】

Research Background: When focusing on evaluating the effects of certain factors in observational studies, Propensity Score (PS) is one of the options for balancing other confounding factors in addition to the study factors. Observational studies, however, often involve complex data structures, such as multilevel data with different levels of measurement error, and main effects that are influenced by measured and unmeasured confounding. Bayesian inference methods can be an important choice for causal inference due to their unique inference logic and ability to handle complex data structures. Among them, Bayesian Additive Regression Trees (BART) is a tree-based nonparametric integrated model that employs Bayesian regularization prior to prevent overfitting of the tree model, which further saves computational effort in cross-validation and avoids strong parametric assumptions. The tree-based approach is flexible enough to avoid biases in the estimation of target effects due to the selection of confounding variables or the mis-specification of covariates entering the model. The method is not only easy to implement but also has strong predictive power, and it is necessary to extend its application to PS estimation..

Aim: This study aims to explore the practical application strategies of the Bayesian propensity score method in observational studies containing multilevel data based on simulation studies and example data, and to compare it with the classical methods.

Methods: Simulation studies: Generate simulated data with different characteristics based on different simulated parameters. PS estimation of multilevel data using BART in combination with single-level, Fixed Effects (FE), and Random Effects (RE) models. Two PS weighting techniques, Stabilized Weights (SW) and Overlap Weights (OW), were used to estimate treatment effects. Model evaluation metrics included Absolute Standardized Mean Difference (ASMD), Relative Bias (RB), Root Mean Square Error (RSME), 95% Confidence Interval Coverage Rate (CICR) and computation time.

Example analysis: Based on the longitudinal data of China Health and Retirement Longitudinal Study (CHARLS) from 2011-2018, the study constructed the following models respectively models without considering PS and PS-weighted models to assess the effect of sleep quality on fall risk in older adults during the 8-year follow-up.

Results: Simulation studies: ① Intergroup balance indicator: the BART model combined with OW was better balanced than combined with SW intergroup covariates. And the balance was better when the number of clusters was small and the cluster size was large, but when the number of clusters was large and the cluster size was small, the balance deteriorates, especially for the control of covariate confounding at the unmeasured group level.

② Evaluation metrics for target efficacy estimation: The target efficacy estimated based on the BART model combined with OW had a smaller error value, more stable estimation, and higher confidence interval coverage than that estimated by combining SW. RB was relatively high for small sample sizes. With large sample sizes, BART and BART-RE had the smallest RB and higher 95% CICR coverage when the number of clusters was large and the cluster sizes were small, and this advantage was more pronounced with stronger degrees of unmeasured group-level confounding, and BART-RE performs optimally. The calculation time of BARTs method was significantly faster than that of GBM.

Example analysis: A total of 3,263 participants were enrolled in this study at baseline, with 50.26% of participants reported poor sleep quality, and 44.13% of participants, at 8 years of follow-up, reported the occurrence of falls. At univariate analysis, the *RR* value for sleep quality was 0.7121. Significant factors screened using multiple regression analysis, logistic stepwise regression, mixed-effects models were consistent. The different PS estimation methods combined with weighted methods resulted in covariates with ASMD values of less than 0.1. Target efficacy estimation based on samples balanced across groups of covariates, and the target effect estimates of the different methods ranged from 0.0524 to 0.0897 with *P*-values greater than 0.05.

Conclusions: In multilevel data, the BART model combined with OW, promoted intergroup balance, thereby enhancing the accuracy and validity of causal effect estimation, particularly in scenarios involving substantial sample sizes. The multilevel BART model demonstrated superior performance in comparison to its single-level model. Additionally, the BART-RE model exhibited superior performance in comparison to the BART-FE model. In scenarios where a substantial number of clusters exhibited modest group sizes, the BART-based methodologies, namely the single-level BART and the BART-RE, demonstrated superior performance. This enhancement in efficacy was more pronounced in instances of high-level unmeasured group-level confounding.

Funding: No

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Risk Factors and Influence Pathways of Psychological Resilience in College Students

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[Abstract]

Background: Healthcare professionals both domestically and internationally commonly experience varying degrees of mental health issues. As future healthcare workers, if medical students can enhance their psychological resilience, it will help them better cope with the pressures and challenges of their future work, thereby improving the overall mental health of healthcare personnel.

Methods: We constructed an Extreme Gradient Boosting (XGBoost) model using information on medical students' basic characteristics, family background, and health behaviors. In addition, we conducted an interpretive analysis of the model using Shapley additive explanations (SHAP). After identifying strong predictor variables, we also conducted a mediation effect analysis.

Results: The accuracy of the XGBoost prediction model is 0.806 (95%CI: 0.759–0.850), with an AUC value of 0.825 (95%CI:0.763–0.875), sensitivity of 0.551 (95%CI:0.431–0.662), specificity of 0.902 (95% confidence interval: 0.858–0.943), and F1 score of 0.608 (95%CI:0.495–0.693). Smartphone addiction and sleep disturbances are negatively correlated with psychological resilience in medical students, while perceived social support is positively correlated with it. Additionally, smartphone addiction and sleep disturbances can serve as either independent mediators or chain mediators between perceived social support and psychological resilience in medical students.

Conclusions: Machine learning prediction models can provide a simple, cost-effective screening tool for low psychological resilience in medical students. Additionally, improving peer and teacher-student relationships in schools can enhance their psychological resilience.

Short-term impact of PM_{2.5} constituents on the risk of anxiety disorders outpatient visits: A case-crossover study

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【Abstract】 Background: Fine particulate matter (PM_{2.5}) is considered as a potential risk factor for anxiety disorders (ADs). However, the specific constituents associated with ADs remain unclear.

Aims: We aimed to evaluate the association between short-term exposure to PM_{2.5} constituents, including black carbon (BC), organic matter (OM), sulfate (SO₄²⁻), nitrate (NO₃⁻), and ammonium (NH₄⁺), and ADs outpatient visits.

Methods: Patients data were extracted from the basic medical insurance system of a city in China from 2021 to 2023. Daily individual-level exposure to air pollutants was assessed using validated gridded datasets. We implemented a time-stratified case-crossover design and applied conditional logistic regression models to compare pollutant exposure levels between case days (hospital visit dates) and matched control days (same weekday, month, and year), thereby examining the association between air pollution exposure and anxiety disorder-related hospital visits.

Results: The study included 2,195 outpatient visits for ADs. BC and OM were identified as the primary harmful constituents of PM_{2.5} associated with outpatient visits for ADs. For each interquartile range (IQR) increase in concentrations, the highest odds ratios (ORs) were 1.15 (95% CI: 1.01, 1.30) for BC at lag07 day and 1.08 (1.01, 1.16) for OM at lag4 day. No significant associations were observed between SO₄²⁻, NO₃⁻, or NH₄⁺ and ADs. Subgroup analysis revealed a stronger association between PM_{2.5} constituents and outpatient visits for ADs in older adults (≥60 years).

Conclusions: Our study suggests that BC and OM might be important risk factors for ADs related health care-seeking behaviors, with more pronounced effects observed in older adults. Implementing stricter regulations on emissions of these key PM_{2.5} components could be an effective strategy to improve population mental health and optimize the allocation of limited mental health resources.

Funding: This research was funded by the National Natural Science Foundation of China (72074229) and Guangdong Basic and Applied Basic Research Foundation (2022B1515020094).

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Sleep Disturbance, Inflammatory Markers, and Perinatal Depression: Mediation Analysis in Chinese Pregnant Women

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Abstract:

Background: Perinatal depression (PND), a common complication during pregnancy and postpartum, adversely affects mothers and their offspring. Sleep disturbances are a key risk factor for PND, potentially mediated by inflammatory pathways. Although studies have explored pairwise associations between sleep disturbances, inflammatory markers, and depression, the interaction among the three remains unclear.

Objectives: This study examines whether inflammatory markers mediate the relationship between sleep disturbances and PND in pregnant women.

Methods: A prospective cohort study enrolled 711 pregnant women in Guangzhou, China (2023–2024). First-trimester data included depressive symptoms (Edinburgh Postnatal Depression Scale, EPDS), sleep disturbances (Pittsburgh Sleep Quality Index, PSQI), and inflammatory markers (neutrophil-to-lymphocyte ratio [NLR], monocyte-to-lymphocyte ratio [MLR], platelet-to-lymphocyte ratio [PLR]) derived from complete blood counts. Logistic regression models assessed associations with PND, and linear regression models evaluated associations between inflammatory markers and sleep disturbances, adjusting for sociodemographic characteristics, lifestyle factors, health conditions, and laboratory data. Mediation was evaluated using structural equation modeling with 1,000 bootstrap resamples.

Results: Women with PND or sleep disturbances exhibited higher PLR levels compared to those without ($p < 0.05$). Sleep disturbances were strongly associated with PND (adjusted odds ratio [aOR] = 4.70, 95% CI: 2.72–8.13). PLR was positively associated with PND (aOR = 4.90, 95% CI: 1.07–8.73) but negatively associated with sleep disturbances ($\beta = -0.026$, 95% CI: -0.037 to -0.014). PLR mediated 9.7% of the effect of sleep disturbances on PND ($P < 0.05$), while NLR and MLR showed no significant mediation.

Limitations: The study is limited to first-trimester data from a single region, requiring validation in diverse populations and later gestational stages.

Conclusions: Sleep disturbances and elevated PLR are associated with PND, with PLR partially mediating their relationship. These findings underscore inflammation's role in perinatal mental health, warranting further mechanistic and longitudinal studies.

Keywords: inflammation; mediation; perinatal depression; platelet-to-lymphocyte ratio; sleep disturbance

Funding: This research was funded by the Natural Science Foundation of Guangdong Province for Distinguished Young Scholars (Grant number: 2022B1515020094), and the Science and Technology Program of Guangzhou (Grant number: 2024A04J6551).

Statistical Challenges and Normalization Strategies in Zero-Inflated Microbiome Data: A Comprehensive Methodological Review

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Abstract:

High-throughput sequencing has revolutionized our understanding of the human microbiome and its impact on health and disease. However, the high dimensionality, sparsity, and zero inflation of microbiome data pose substantial analytical challenges.

This review provides a comprehensive overview of the statistical and computational methods developed to address the unique features of microbiome sequencing data. We focus on zero-inflated models, including Zero-Inflated Negative Binomial (ZINB) and Zero-Inflated Beta Regression (ZIBR), which explicitly model the excess of zeros and improve the robustness of differential abundance analysis. Normalization strategies such as GMPR, CSS, TMM, and RLE are systematically compared, highlighting their assumptions and applicability. We also discuss the performance and methodological underpinnings of commonly used differential analysis tools, including DESeq2, edgeR, ANCOM, and MaAsLin2. Emphasis is placed on the importance of appropriate data preprocessing and model selection to ensure valid biological interpretations. By synthesizing recent methodological advances and providing practical recommendations, this review aims to support researchers in navigating the complexity of microbiome data analysis, thereby enhancing the reproducibility and translational potential of microbiome research.

Keywords : Microbiome analysis; Zero-inflated data; Differential abundance; Normalization; Metagenomics; Statistical modeling; Compositional data; Sparse count data

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Funding information:

This research was funded by the National Natural Science Foundation of China (No. 82473698), the Central government-led local science and technology development special project (No. 2019L3006 and 2020L3009), the Fujian Provincial Financial Special Project (23SCZZX004), and the Natural Science Foundation of Fujian Province (No. 2021J01726 and 2021J01733).

The relationship between body roundness index and risk of cardiometabolic multimorbidity: the roles of accelerated biological aging

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Abstract

Objectives: To investigate the association between visceral fat accumulation and the risk of cardiometabolic multimorbidity (CMM) and the potential roles of accelerated biological aging in this relationship.

Methods: Using data from the UK Biobank, a nationwide cohort study was conducted using the available baseline body roundness index (BRI) measurement. Biological aging was assessed using the Kleméra–Doubal method for biological age and the phenotypic age algorithms. The association between the BRI and CMM was estimated using the Cox proportional hazards regression model, while the roles of biological aging were examined through interaction and mediation analyses.

Results: During a median follow-up of 14.52 years, 6156 cases of CMM were identified. A significant association was observed between the BRI and CMM. The hazard ratio (HR) for CMM was 3.72 (95% confidence interval [CI]: 3.35–4.13) for individuals in the highest quartile compared with those in the lowest quartile of the BRI. More importantly, the BRI (AUC, 0.701; 95% CI, 0.694–0.707) demonstrated superior predictive performance relative to body mass index (AUC, 0.657; 95% CI, 0.650–0.664). Furthermore, the BRI exhibited additive interactions with accelerated biological aging on the risk of CMM, and accelerated biological aging partially mediated the association between the BRI and CMM.

Conclusions: These findings provide evidence for the application of the BRI as a novel and readily accessible screening tool associated with CMM, suggesting that the effective management of visceral fat and bio-logical aging deceleration may hold

promise for reducing CMM risk.

Keywords: body roundness index; visceral obesity; cardiometabolic multimorbidity; accelerated biological aging

Funding: This work was supported by the National Natural Science Foundation of China (No. 82373683).

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Time-Aware Depressive Trajectory Modeling Based on Transformer: Dynamic Prediction of Secondary Risk in Elderly Mild Cognitive Impairment

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Abstract

Background: Mild cognitive impairment (MCI) is a transitional state between normal aging and dementia, with a high conversion rate to dementia. Depression significantly increases the risk of MCI in the elderly. However, existing clinical prediction models have limitations in dynamically assessing the risk of MCI secondary to depression.

Objective: This study aims to propose a Transformer-based temporal-aware depression trajectory modeling method to achieve precise quantitative assessment of secondary MCI risks and provide an interpretable tool for early warning of MCI secondary to geriatric depression.

Methods: Leveraging longitudinal data from 2,119 elderly depression patients in the China Health and Retirement Longitudinal Study (CHARLS) database, we constructed time-series samples through sliding window strategies and integrated multiple imputation with feature selection techniques to handle missing values and redundant information. The optimized Transformer architecture incorporates dynamic positional encoding, multi-head self-attention mechanisms, and gated feedforward networks to effectively capture long-term dependencies between depressive symptom fluctuations and cognitive decline.

Results: The model achieves 81.6% accuracy and an 85.1% AUC on the test set, significantly outperforming XGBoost (AUC 80.7%) and SVM (AUC 77.6%), with particularly outstanding performance in precision (89.2%) and specificity (84.1%). By establishing dynamic modeling, this research provides an interpretable tool for early warning of MCI secondary to geriatric depression, offering significant practical value for optimizing clinical intervention pathways and delaying cognitive deterioration.

Conclusion: This study provides novel evidence for the pathological association between depressive symptoms and secondary mild cognitive impairment (MCI), guiding future mechanistic research. The research demonstrates profound

multidimensional value across clinical practice, public health, technological outreach, and scientific understanding. The integration of multimodal data and enhanced model interpretability will further empower this framework as a core tool for early warning and intervention in psychiatric and neurodegenerative diseases.

Funding: The study was supported by Tianjin Municipal Education Commission Project (2022KJ143), Tianjin University of Traditional Chinese Medicine's "Chuying" Program (XJS2022102) and Tianjin College Students' Innovation and Entrepreneurship Training Program (Project Number: 202410063030).

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Trajectories of self-reported suicide risk with predictive and interpretive value for suicide attempts: Longitudinal evidence from crisis hotline callers in China

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【 Abstract 】 Background: Identifying suicide risk and predicting subsequent attempts are crucial for crisis hotline callers. However, it could be time-consuming to assess the risk using the traditional psychological scales during the call. Self-reported suicide scores are a time-varying subjective measure that reflects the feelings of callers at the moment, which can be quickly assessed. Whether this indicator could be utilized for risk assessment and future suicide prediction remains unclear.

Aim: This longitudinal study aims to identify suicide risk trajectories based on self-reported suicide scores and investigate their predictive values for subsequent suicide attempts (SAs) among crisis hotline callers with suicidality.

Methods: We collected data from the Guangzhou Psychological Crisis Hotline from January 1, 2023, to December 31, 2024. Callers who reported suicidality (attempts, ideation, and plan) were included and followed up on the 1st, 7th, 15th, and 30th day after the initial call. Latent class mixed models were applied to identify trajectories of self-reported suicide risk scores during the follow-up. The XGBoost model, adding trajectory class as a covariate, was constructed to predict subsequent suicide attempts. SHapley Additive exPlanation (SHAP) values were calculated to estimate the contribution of each predictor. Cox Hazard Ratio model was built to evaluate the association between key variables and subsequent SAs.

Findings: Among 1235 eligible participants (average age 23.32 ± 7.53 years old, and 58.1% female), 75.8% reported suicide ideation and 8.7% reported SAs before. A total of 127 (10.2%) participants had subsequent SA(s) during the follow-up. The 3-group model built with quadratic time effect was chosen as the optimal LCMM, which identified participants into the constant high-risk group (30.0%), the gradual decline group (12.0%), and the rapid decline group (58.0%). Participants who called

at dawn (aOR 0.64, 95% CI 0.42-0.98, $P=0.008$), night (aOR 0.57, 95% CI 0.37-0.86, $P=0.040$), and summer (aOR 0.50, 95% CI 0.31-0.83, $P=0.007$), had relationship query (aOR 0.40, 95% CI 0.20-0.78, $P=0.007$) and suicide ideation (aOR 0.48, 95% CI 0.29-0.79, $P=0.004$) were less likely to be classified to the constant high-risk group. The trajectory class had the highest SHAP values for SA prediction, followed by age, mental disorder history, and call duration. We found an 81% lower possibility of subsequent SAs for participants in the rapid decline group (HR 0.19, 95% CI 0.12 - 0.30, $P<0.001$), compared to the constant high-risk group. Age (HR 0.94, 95% CI 0.90-0.98, $P=0.004$), winter callers (HR 0.57, 95% CI 0.36-0.89, $P=0.013$), and suicide ideation history (HR 0.50, 95% CI 0.29-0.87, $P = 0.014$) was protective factors, however, those with depression had an increased risk to have subsequent SAs (HR 2.64, 95% CI 1.39-3.37, $P=0.001$).

Conclusions: Self-reported suicide risk scores can serve as a reliable referencing measure for identifying suicide risk and predicting future attempts for crisis hotline callers. We suggest that extra attention is required for callers with constantly high scores, younger age, and history of depression and SA, as well as those calling in winter to prevent subsequent SAs.

Funding: The National Natural Science Foundation of China (No.82401811); Guangdong Basic and Applied Basic Research Foundation (Grand no. 2024A1515220104, 2022A1515110694);

Science and Technology Program of Guangzhou (No.2024A04J10000, 2024A03J0223, 2024A03J0295, 2023A03J0854, 2023A04J1869, 20251A011047, 20252A011018);

Guangzhou Municipal Key Discipline in Medicine (2025-2027);

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Unveiling the Hidden Genetic Conundrum Linking Pulmonary Diseases and Neuropsychiatric Disorders: Novel Insights from Advanced Omics-based Analyses of the Lung-Brain Axis

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【Abstract】

Objective: This study seeks to elucidate the shared genetic underpinnings between these pulmonary diseases and neuropsychiatric disorders, focusing on common genomic loci, implicated genes, and biochemical pathways.

Methods: This study is a genome-wide pleiotropic association study that utilized genome-wide association summary statistics from publicly available data sources. Diverse bioinformatics and statistical genetics strategies were applied to sequentially investigate the pleiotropic associations from SNV, gene-level data, and biological pathways, with the aim to better understand the shared genetic etiology between 3 pulmonary diseases and 7 neuropsychiatric disorders.

Results: Significant genetic correlations and overlaps were observed among 20 of the 21 trait pairs. Pleiotropic analysis, using a composite null hypothesis, identified 3962 potentially pleiotropic SNVs across 20 trait pairs, along with 31 pleiotropic loci and 3 colocalized loci. Gene-based analysis revealed 103 unique candidate pleiotropic genes, which were notably enriched in LBA-related phenotypes and tissues. Pathway enrichment analysis highlighted key biological processes related to cell adhesion, synaptic structure and function, and immune cell differentiation. Several pleiotropic loci were also found to share causal variants with lung-related phenotypes. Mendelian randomization analysis demonstrated vertical pleiotropy across 8 trait pairs.

Conclusions: These findings indicate that pleiotropic genetic factors connecting pulmonary and neuropsychiatric diseases are widely distributed throughout the genome. This provides robust evidence for a shared genetic basis underlying the lung-brain axis and has important implications for the potential for developing targeted intervention and treatment that simultaneously address both diseases types.

Funding

This work was supported by National Key Research and Development Program (Grant No.2024YFA0918404), the National Natural Science Foundation of China (Grant No. 82003560), the National Natural Science Foundation of Shandong Province (Grant No. ZR2020MH340) and Key Research and Development Program of Shandong Province (Grant No. 2024TSGC0151).

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US-LEAF: A Cost-Effective Deep Learning Strategy Using Dense Ultrasound Monitoring for Precision Prediction of Breast Cancer Response to Neoadjuvant Chemotherapy

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Abstract

Background: Neoadjuvant chemotherapy (NAC) is a cornerstone of breast cancer treatment, enabling tumor downsizing, surgical optimization, and prognostic insights. However, 30–50% of patients show poor response to NAC, highlighting the critical need to identify non-responders early and avoid unnecessary treatment exposure. Current approaches, relying on static molecular biomarkers or sparse imaging modalities with single-timepoint or pre-post treatment delta analyses, fail to capture early dynamic tumor responses during the critical treatment phase.

Purpose: To develop a novel early dynamic ultrasound monitoring strategy for rapid and precise identification of breast cancer patients non-responsive to NAC.

Methods: We developed an early intensive ultrasound monitoring strategy integrating the Ultrasound-based Longitudinal Early Forecasting (US-LEAF) deep learning model. For 882 breast cancer patients undergoing NAC, baseline and cycle-specific (1–8) ultrasound scans were performed to capture serial tumor images, with clinical information and pathological markers collected. The strategy employed a time-aware framework to analyze longitudinal radiomic features (texture, vascularity, shape) extracted from images, using the Potential Improvement Value (PIV) to identify the optimal early timepoint for predicting non-response based on chemotherapy-induced microstructural changes.

Results: At the selected optimal prediction window, the third NAC cycle, the US-LEAF significantly outperformed static and delta radiomics, achieving an AUROC of 0.986 and a specificity of 98.1%—improvements of 23% and 18%, respectively. This high specificity enabled precise identification of non-responders when 60% of a complete NAC regimen remained. By modeling longitudinal feature trajectories, US-LEAF detected subtle, cycle-specific response patterns invisible to static or delta analyses, reliably differentiating patients who benefited from continued therapy from those requiring regimen adjustment.

Conclusion: The novel monitoring strategy with US-LEAF model addresses a critical unmet need by leveraging dense early-cycle ultrasound and longitudinal deep learning to achieve unprecedented specificity in identifying NAC non-responders at NAC3. Surpassing static and delta radiomics, it minimizes unnecessary treatment adjustments for responders while enabling timely intervention for non-responders, reducing exposure to ineffective chemotherapy and aligning with precision oncology principles. With its cost-effective (\$50–\$100 per scan) and non-invasive design, this strategy offers a practical, scalable tool to guide personalized NAC decisions, establishing a new paradigm for adaptive cancer therapy.

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1990–2021 年东亚地区结直肠癌疾病负担的变化趋势分析

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【摘要】研究背景：结直肠癌（CRC）是全球第三大常见恶性肿瘤和第二大癌症相关死亡原因，东亚地区发病和死亡人数约占全球 25%。然而，目前尚缺乏对东亚各国 CRC 发病、死亡和残疾调整生命年（DALYs）的长期趋势及其驱动因素的深入分析。

目的：本研究基于全球疾病负担研究（GBD）2021 数据，分析 1990–2021 年东亚五国（中国、日本、韩国、朝鲜和蒙古）CRC 的发病、死亡和 DALYs 变化趋势，探究其关键驱动因素，为制定公共卫生政策和筛查策略提供依据，助力东亚地区 CRC 防控。

方法：本研究基于 GBD2021 数据库，提取 1990–2021 年东亚五国的年龄和性别特异性 CRC 发病、死亡和 DALYs 数据。使用 Joinpoint 回归模型评估时间趋势变化特征，采用年龄-时期-队列模型解析年龄效应、时期效应及出生队列效应对 CRC 的独立影响，并借助分解分析剖析老龄化、人口增长和流行病学变化对 CRC 疾病负担改变的影响。所有分析依赖于 Joinpoint 回归程序（5.0.2 版本）和 R 软件（3.6.0 及 4.3.2 版本）。

结果：1990–2021 年，东亚五国 CRC 年龄标化发病率整体均呈上升趋势，韩国上升最快（男性 AAPC=2.18%；女性 AAPC=1.41%）。年龄标化死亡率和标化 DALY 率基本呈下降趋势，女性改善优于男性。然而，中国（AAPC=0.01%，95%CI: -0.23%, 0.24%）和蒙古（AAPC=0.50%，95%CI: 0.08%, 0.91%）男性死亡率未见下降。年龄-时期-队列效应显示，东亚五国 CRC 的发病、死亡和 DALYs 风险均随年龄增长而增加，在老年群体中达到峰值；时期效应呈线性上升趋势，在 2017–2021 年时期组达到最高相对风险；队列效应基本表现为先快后慢的下降趋势，年轻一代风险有所降低。分解分析表明，老龄化和人口增长是 CRC 负担加重的主要驱动因素，其中韩国受老龄化影响最大，蒙古和朝鲜由人口增长主导；而流行病学变化则在一定程度上减缓了死亡率和 DALYs 的上升态势。

结论：尽管过去 32 年间东亚地区在 CRC 预防与控制方面取得了进展，但在性别和国家层面仍存在显著差异。因此，为进一步减轻 CRC 疾病负担，东亚各国需实施因地制宜且个性化的策略，例如针对男性推广健康生活方式，在韩国加强老年医疗保健服务，以及调整策略以应对人口结构变化和不断演变的疾病模式。

基金资助：本项目获四川省科技厅重点研发项目（2024YFFK0348）和教育部人文社会科学研究规划基金项目（24YJAZH217）基金资助

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1990-2021 年全球抑郁障碍疾病负担趋势 及预测模型性能影响因素研究

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【摘要】

研究背景: 抑郁障碍作为全球性公共卫生挑战, 影响约 3.5 亿人口 (患病率 5%)。全球疾病负担 (GBD) 数据显示, 2021 年全球的抑郁障碍导致了 5633 万伤残调整寿命年 (DALYs), 其年龄标准化发病率 (ASIR)、患病率 (ASPR) 和 DALYs 呈持续上升趋势。COVID-19 大流行等因素可能加剧疾病负担, 但此类因素对预测模型的影响尚未系统评估。

目的: 量化分析 1990-2021 年全球 204 个国家抑郁障碍的 ASPR、ASIR 及 DALYs 演变特征, 评估 8 种时间序列机器学习模型对 2020-2021 年关键指标的预测效能, 探索 COVID-19 等因素对预测准确性的影响机制

方法: 本研究采用 GBD 2021 数据集, 涵盖 204 个国家抑郁障碍的 ASPR、ASIR 和 DALYs 指标。之后, 使用 1990-2019 年数据训练 8 种机器学习模型 (ARIMA/弹性网络/ETS/LSTM/Prophet/随机森林/SVR/XGBoost), 来预测 2020-2021 年的疾病负担指标, 并通过 MAE、RMSE、MAPE、SMAPE、 R^2 评估性能。构建多元线性回归模型来研究影响预测准确性的因素, 以预测误差 (绝对差 AD、相对差 ADP) 为因变量, 自变量包括社会人口指数 (SDI)、COVID-19 发病率、世界银行区域划分等, 采用偏回归平方和及标准化偏回归系数 (β) 评估影响因素的重要性。

结果: 抑郁障碍疾病负担的趋势研究显示, 2021 年全球大部分国家的 ASPR、ASIR 和 DALYs 指标呈上升趋势, 且不同地区疾病负担分布不均衡, ASPR 最高的国家为乌干达 (7769.97/10 万), 最低的为文莱 (1857.73/10 万), 格陵兰岛成为 ASIR (9885.55/10 万) 和 DALYs (1467.92) 双重高负担地区。此外, 模型预测结果显示, 随机森林的预测效果相对最佳, 但是所有模型均明显低估了 2020 年和 2021 年抑郁障碍的疾病负担, 提示可能存在其他因素影响预测准确性。影响因素研究结果显示 COVID-19 发病率、世界银行区域划分和 SDI 指数是影响预测准确性的因素。

结论: 本研究揭示了 COVID-19 大流行等指标对抑郁障碍时间序列预测模型预测性能的影响。当今抑郁障碍的全球疾病负担持续加重且存在明显区域分布特征, 而传统时间序列模型在发生突发公共卫生事件时会失去预测效能, 提示未来构建预测模型需考虑突发风险因素的影响。

基金赞助: 无

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1990-2021 年中国、日本和韩国脑卒中发病率与死亡率的时间趋势及至 2035 年预测

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【摘要】研究背景：脑卒中是全球主要慢性非传染性疾病之一，也是成人死亡和残疾的重要原因，具有高发病率、致残率、死亡率和复发率，且经济负担沉重。尽管近年全球年龄标准化发病率和死亡率有所降低，但因人口老龄化和生活方式变化，脑卒中病例和死亡绝对数仍在上升。东亚因人口多、风险因素集中，脑卒中负担更突出。

目的：本研究旨在利用全球疾病负担 (GBD) 2021 数据，系统分析 1990 至 2021 年期间中国、日本、韩国的脑卒中发病率和死亡率趋势，同时预测其到 2035 年的趋势，为优化脑卒中预防和控制政策提供科学依据。

方法：本研究基于 GBD2021 数据，分析了脑卒中粗发病率和死亡率及年龄标准化发病率和死亡率的时间趋势。通过 Joinpoint 回归模型分析时间趋势的变化特征，并使用年龄-时期-队列模型评估不同年龄组、时期和出生队列的发病和死亡风险，还采用贝叶斯年龄-时期-队列模型预测到 2035 年脑卒中发病和死亡的趋势。

结果：从 1990 年到 2021 年，中日韩三国男性和女性的脑卒中发病人数以及死亡人数明显增加，然而，中日韩两性的年龄标准化发病率和死亡率均呈下降趋势。Joinpoint 回归分析显示，中日韩三国，脑卒中 ASIR 下降速度由高到低依次为韩国 (AAPC=-3.58%)、日本 (AAPC=-1.55%)、中国 (AAPC=-0.37%)，ASMR 下降速度由高到低依次为韩国 (AAPC=-5.52%)、日本 (AAPC=-3.54%)、中国 (AAPC=-1.79%)。APC 模型分析显示，年龄和出生队列效应是脑卒中发病和死亡的关键因素。年龄越大的群体脑卒中发病和死亡风险越高，晚出生队列发病死亡风险呈下降趋势。预测表明，在未来 14 年里，中国和韩国的脑卒中 ASIR 和 ASMR 将保持稳定或下降，日本 ASMR 下降但 ASIR 上升。此外，三国男性发病率和死亡率均显著高于女性。

结论：脑卒中发病率和死亡率受人口老龄化及生活方式变化影响。尽管其年龄标化率有所下降，但因人口增长与老龄化，绝对病例数和死亡数仍在上升。在老龄化严重的国家，未来需加强脑卒中风险管控，聚焦高风险群体，持续优化医疗及

公共卫生措施，以应对这一健康挑战。

基金资助：本研究获四川省中枢神经系统药物重点实验室（资助编号：230035-01SZ）、四川省科技厅重点研发项目（资助编号：2024YFFK0348）和西南医科大学科研项目（资助编号：2021ZKMS002）资助。

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1990—2021 年中国女性宫颈癌发病与死亡趋势分析及预测

研究：与日本和韩国的比较

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【摘要】研究背景：宫颈癌是全球重大的公共卫生问题，也是女性第二大常见妇科恶性肿瘤。亚洲占全球宫颈癌新发病例和死亡病例的一半以上，主要源于其庞大的人口基数。在东亚地区，中国、日本和韩国虽然地理位置相近且种族及文化背景相似，但宫颈癌的发病率和死亡率差异显著，其潜在原因尚未明确。

目的：本研究基于全球疾病负担研究（GBD）2021 数据，分析 1990—2021 年中国、日本及全球宫颈癌发病率与死亡率的长期趋势，并预测到 2035 年各国宫颈癌的发病及死亡情况的变化，为各国制定宫颈癌的针对性防控策略提供科学依据，并支持加速消除宫颈癌的全球战略。

方法：从 GBD 数据库提取 1990—2021 年中日韩女性宫颈癌的发病与死亡数据，使用 Joinpoint 回归模型识别趋势转折点，并计算各国年度变化百分比（APC）和平均年度变化百分比（AAPC）；通过年龄-时期-队列模型分解年龄效应、时期效应和出生队列效应对各国发病率和死亡率的独立影响；采用贝叶斯年龄-时期-队列模型预测到 2035 年各国未来发病与死亡趋势。

结果：1990—2021 年，中国（AAPC = 0.44%；95% CI [0.16, 0.72]）和日本（AAPC = 0.44%；95% CI [0.14, 0.74]）女性宫颈癌的年龄标准化发病率（ASIR）整体上升，而韩国（AAPC = -1.75%）则保持下降；年龄标准化死亡率（ASMR）在中日韩三国均呈下降趋势，其中韩国降幅最大（AAPC = -3.50%）。年龄-时期-队列效应显示，中日韩三国女性宫颈癌的发病风险在中年人群中最高，而死亡风险在老年人群中达到峰值。时期效应表明，中国和日本的发病和死亡风险缓慢上升，而韩国则缓慢下降。队列效应表明，三国发病与死亡风险呈下降趋势。预测至 2035 年，韩国 ASIR 或小幅上升，中日 ASIR 下降，而三国 ASMR 均持续下降；但中国和韩国的新发病例及死亡人数预计逐年增加。

结论：近年来，韩国宫颈癌的 ASIR 有所下降，但在中国和日本有所上升。各地区 ASMR 均有所下降。年龄和出生队列是影响各国发病率和死亡率变化的主要因素。未来需结合各国特征优化宫颈癌的防控策略，重点加强 HPV 疫苗接种、筛查覆盖、健康教育和规范化治疗，以降低宫颈癌疾病负担。

基金资助：本项目获四川省科技计划重点研发项目（No. 2024YFFK0348）和泸州市科技局项目（No. 2023JYJ032）基金资助。

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1990-2023 年金砖国家老年人跌倒疾病负担 及其主要归因因素变化趋势研究

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【摘要】研究背景: 跌倒是老年人伤害和死亡的主要原因之一, 低骨矿物质密度 (LBMD) 和饮酒是显著增加其跌倒风险及其不良结局的关键危险因素。金砖国家 (BRICS) 作为超大型发展中国家, 在社会经济和卫生体系等方面差异显著, 开展对比研究有助于制定更有针对性的预防策略, 并为其他发展中国家提供参考。

目的: 分析 1990–2023 年金砖国家 60+ 岁跌倒疾病负担及其主要危险因素的变化趋势及归因模式的演变。

方法: 数据来源于 1990-2023 年全球疾病负担 (GBD) 数据库, 采用世界卫生组织 (WHO) 标准人口进行年龄标准化, 评估五国老年人群跌倒的年龄标化发病率 (ASIR) 和伤残调整寿命年 (ASDR)。通过 Joinpoint 回归分析归因疾病负担变化趋势, 分年龄段探讨 LBMD 与饮酒归因结构演变, 并采用多因素分解量化人口增长与老龄化及风险因素变化对跌倒疾病负担变动的贡献。

结果: 2023 年, 印度的跌倒 ASIR 和 ASDR 最高 (5756.31/10 万人、3551.57/10 万人), 中国次之, 南非最低。与 1990 年相比, 各国 ASDR 变化不一, 南非降幅最大。LBMD 归因 ASDR 占比最大, 随年龄增长上升, 女性较高; 反之, 饮酒归因占比随年龄下降, 男性较高。饮酒归因 ASDR 占比中, 俄罗斯和南非占比较高, 印度最低; LBMD 归因中印度最高, 南非最低。Joinpoint 回归显示, 俄罗斯饮酒归因 ASDR 在 2009-2018 年下降 (年度变化百分比 (APC) = -3.47%, $p = 0.02$), 但 1990-2023 年间整体仍上升 (平均年度变化百分比 (AAPC) = 0.67%, $P < 0.001$)。巴西饮酒归因 ASDR 持续上升, 中国男女趋势相反, 女性下降, 男性上升。中国 LBMD 归因 ASDR 在 2016-2022 年显著下降 (APC = -6.25%, $p < 0.001$), 后略有回升, 整体呈上升趋势 (AAPC = 0.43%, $p < 0.001$)。南非和印度两因素归因 ASDR 均显著下降。分解分析显示, 跌倒疾病负担的增长主要受人口增长与老龄化驱动, LBMD 和饮酒对 DALY 增长的贡献在俄罗斯和南非为负值, 提示两国防控初见成效。

结论: 印度和中国的老年人群跌倒负担水平较高, 南非降幅最大。LBMD 和饮酒为主要可干预因素, 呈现显著的年龄和性别差异。各国疾病负担差异较大, 提

示应针对本国风险特征，加强老年人跌倒防控策略，以应对人口老龄化带来的挑战。

基金资助：本研究获国家重点研发计划基金资助（2022YFC3603000）

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2014—2023 年武汉市急性心肌梗死发病趋势及年龄-时期-队列模型分析

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[摘要]研究背景: 急性心肌梗死 (acutemyocardial infarction, AMI)是在冠状动脉狭窄、硬化的基础上, 产生了一系列的生理、病理变化而导致心肌的缺血缺氧, 诱发心肌坏死等表现。AMI 起病急, 病情重且病死率高, 严重损害居民健康, 并且会造成巨大的社会经济负担。随着我国人口老龄化带来的生理年龄结构变化, AMI 的疾病负担将进一步加重。

目的: 分析 2014—2023 年武汉市 AMI 发病率及变化趋势, 为武汉市 AMI 防控提供科学依据。

方法: 收集武汉市心脑血管疾病监测系统 2014—2023 年 AMI 发病数据, 以 2010 年全国人口普查数据中的人口构成进行标化率的计算, 采用 Joinpoint 回归模型分析 AMI 发病率变化趋势, 计算年度变化百分比 (APC) 和平均年度变化百分比 (AAPC), 并应用年龄-时期-队列 (APC) 模型分析 AMI 发病风险的年龄、时期、出生队列效应。

结果: 2014—2023 年武汉市总体、男性、城市、农村 AMI 发病率、标化发病率整体均呈上升趋势 (发病率 AAPC 分别为 3.65%、5.05%、2.36%、7.24%, 标化发病率 AAPC 分别为 2.67%、4.30%、1.95%、5.70%, 均 $P < 0.05$), 农村上升趋势更加显著。年龄-时期-队列模型结果显示, 武汉市总体、男性、女性 AMI 发病风险的年龄效应均呈上升趋势; 武汉市总体、男性、女性 AMI 发病风险的时期效应均呈先下降后上升的趋势, 以 2017—2019 年为参照组, 武汉市总体和男性在 2020—2022 年发病风险最大, RR 值分别为 1.37 和 1.41, 女性在 2014—2016 年发病风险最大, RR 值为 1.25; 队列效应显示, 武汉市总体和男性 AMI 发病风险呈上升趋势, 均在 1990—1992 年达到峰值(RR 值分别为 6.71 和 8.46), 女性 AMI 发病风险差异无统计学意义。

结论: 2014—2023 年武汉市 AMI 发病率呈上升趋势, 年龄和出生队列效应对 AMI 发病风险的影响较大, 在对不同群体采取针对性干预措施的同时, 应重点关注男性和老年人群的防控。

基金资助: 本项目获武汉市卫健委、武汉市科技局课题 (WX23Z95) 基金资助

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2022-2035 年中国四种老年疾病死亡率趋势预测：

基于身体质量指数的多情景分析

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【摘要】研究背景：随着我国经济社会快速发展，居民超重肥胖问题日益凸显。高身体质量指数（BMI）与老年人多种健康风险显著相关，严重影响晚年生活质量。“体重管理年”将 BMI 管控纳入公共卫生优先干预领域。

目的：通过人群超重率（ $BMI \geq 25 \text{ kg/m}^2$ ）多情景设定，预测 2022-2035 年中国阿尔兹海默症（AD）、肺癌、糖尿病、跌倒四种老年疾病的死亡率趋势。

方法：从全球疾病负担 2021、世界卫生组织、世界银行等全球性数据中获取 ≥ 60 岁老年群体四种疾病死亡率、人群超重率、社会人口指数（SDI）等，构建全球性纵向数据库。以人口结构数估计年龄标化死亡率（ASMR）。采用广义加性混合模型（GAMM），以对数转换平均人口数作为权重，并控制 SDI 水平，量化全球范围内超重率对四种疾病 ASMR 的影响。以《世界肥胖地图 2024》中国人群超重率的年均增长率（2.8%），构建指数增长模型预测超重率的自然趋势，并设定改善/恶化趋势（自然趋势的基础上下降/上升 30%）。以构建的 GAMM 预测不同情景下中国四种疾病的 ASMR。

结果：共匹配形成 195 个国家/地区 1990-2021 年数据。GAMM 结果显示，超重率与 AD 的 ASMR 呈倒“U”型关系（峰值为 60%），与肺癌、糖尿病的 ASMR 均呈“J”型（拐点分别为 65%，60%），与跌倒的 ASMR 为正向非线性关系。2021 年中国全性别、男性和女性的超重率水平分别为 36.49%，41.42%和 30.99%。肺癌、AD、糖尿病、跌倒的 ASMR (/10 万) 分别为 252.58, 242.44, 61.50, 48.16。不同情景下的超重率均呈现上升趋势，男性自然趋势下增幅最大，至 2035 年可达 63.23%。自然趋势下，AD、肺癌的 ASMR 呈下降趋势，至 2035 年分别降至 237.73/10 万，225.61/10 万。相反，糖尿病、跌倒的 ASMR 呈上升趋势，至 2035 年分别 66.42/10 万、51.13/10 万。相较自然趋势，超重率改善情景下，跌倒的 ASMR 下降最为显著，降幅达 11.23%（自然趋势 51.12/10 万 vs 改善趋势 45.39/10 万）；相反，在恶化情景下，糖尿病的 ASMR 增幅最大，达 40.50%（自然趋势 66.42/10 万 vs 恶化趋势 93.33/10 万）。除 AD 外，2035 年男性群体肺癌、糖尿病和跌倒的 ASMR 均高于女性，以肺癌的性别差异最大，男性的 ASMR 高达 352.30/10 万，是女性的 2.54 倍。

结论：有效控制超重率的过快增长可有效降低四种老年疾病（尤其是跌倒）的 ASMR。反之，若不加以控制，糖尿病的 ASMR 将呈现显著大幅上升趋势，将进一步加剧我国老年人群的健康负担。

基金资助：本研究获国家重点研发计划基金资助（2022YFC3603000）

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2024 年武汉市居民伤害死亡及潜在寿命损失分析

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【摘要】研究背景: 伤害被世界卫生组织列为三大公共卫生问题之一。伤害具有高发、高致残率、高死亡率的特点, 给国家、家庭和个人带来了沉重的疾病负担和经济负担。

目的: 分析 2024 年武汉市伤害死亡流行特征和寿命损失情况, 为伤害防控提供数据支持。

方法: 利用武汉市死因监测系统采集的 2024 年武汉市居民伤害死亡数据, 采用描述性统计分析, 评估潜在寿命损失。

结果: 2024 年武汉市因伤害死亡率为 39.16/10 万, 标化死亡率为 41.15/10 万。意外跌落、其他意外伤害、道路交通事故、自杀及后遗症, 溺水是伤害前五位死因。0-4 岁主要伤害死亡原因为其他意外伤害, 5-14 岁年龄组、15-44 岁年龄组主要伤害死亡原因为自杀及后遗症、45-64 岁年龄组主要伤害死亡原因为道路交通事故, 65 岁及以上主要伤害死亡原因为意外跌落。自杀及后遗症造成的 PYLL 最高, 为 22365 人年, 他杀及后遗症的 AYLL 最高, 为 35.50 年, 自杀及后遗症的 PYLLR 最高, 为 1.624‰。

结论: 2024 年武汉市居民伤害死亡率较高, 疾病负担较重; 伤害防控工作需针对不同年龄、不同性别人群制定防控策略。

基金资助: 1、基于多维度数据整合的武汉市老年健康体检队列构建与精准健康风险预测研究, 本项目获中华预防医学会基金资助。

2、慢病综合防控示范区实施效果评价指标体系构建及实证研究, 本项获武汉市科技局基金资助, 项目编号 WX23Z95。

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2 岁内认知发育水平及发育轨迹与青少年多维健康结局的 关联研究

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摘要 目的: 探究陕西省农村地区婴幼儿期认知发育水平及认知发育轨迹与青春早期多维健康结局之间的关联。**方法:** 研究对象来自在陕西农村地区开展的一项出生队列研究。婴幼儿期的智力发育采用贝利婴幼儿量表第二版评价, 并采用亚组轨迹模型 (group-based trajectory model, GBTM) 分析婴幼儿期的智力发育轨迹。采用两种青少年多维健康结局, 一是基于体格指标 (身高体重、BMI 等)、血压、智力、睡眠和行为问题构建的健康综合得分; 二是利用潜在剖面分析确定的三种健康模式, 分别命名为代谢问题高风险组、行为问题高风险组、健康问题低风险组。采用广义估计方程 (GEE)、多元 logistic 回归模型分别探讨婴幼儿期时点认知发育及认知发育轨迹对青春早期健康综合得分、以及健康模式之间的关联, 并调整混杂因素的影响。**结果:** 共 602 名 10-14 岁儿童纳入分析, 其中男孩占比 61.1%。在控制了相关的协变量后发现 12 月龄、18 月龄、24 月龄时婴幼儿认知水平与青春早期健康综合得分呈正相关 (12 月龄: $\beta=0.16$, 95%CI:0.01-0.30; 18 月龄: $\beta=0.33$, 95%CI:0.08-0.58; 24 月龄: $\beta=0.25$, 95%CI:0.07-0.43); 共提取 4 种婴幼儿期认知发育轨迹, 分别命名为: 始终高于平均水平, 始终处于平均水平, 开始低于平均水平然后升高, 开始低于平均水平然后下降。相较于婴幼儿期智力发育始终高于平均水平的个体, 始终处于平均水平的婴幼儿在青春早期发生行为问题的几率是前者的 1.94 倍 (OR=1.94, 95%CI: 1.01-3.75)。**结论:** 婴幼儿时期的认知发育水平越高, 青春早期的综合健康水平越高; 认知发育轨迹水平越高, 越不易发生行为问题。关注 2 岁以内婴幼儿的认知发育情况, 有利于青少年身体健康, 减少行为问题发生的风险。

【关键词】 婴幼儿认知发育水平、认知发育轨迹、多维健康结局

52550 例病例和 1617173 例对照的罕见变异分析确定了肺癌中的非编码变异和基因

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目的: 本研究旨在鉴定和功能表征罕见的非编码种系变异和与肺癌易感性相关的基因。通过整合来自三个深度测序队列的 WGS 数据、来自五个大型基因型阵列研究的插补和多维功能分析——跨越表达数量性状位点 (eQTL)、转录组学和蛋白质组学分析, 以及 All of Us (AoU) 队列中的外部验证——我们试图找出新的非编码风险变异并阐明其机制作用, 最终目标是突出个性化早期预防的生物标志物。

方法: 使用 REGENIE 进行单变量关联分析, 使用经年龄、性别、吸烟状况和前十大遗传主成分调整的 Firth 逻辑回归; 条件分析采用 GCTA-COJO。罕见变异 (MAF<0.01) 采用严格的全基因组显著性阈值 $P \leq 5 \times 10^{-9}$ 进行荟萃分析。基于基因集水平, 使用 STAAR 分析个体水平数据, 使用 sumSTAAR 分析汇总数据, 使用聚集柯西关联检验进行多队列整合和 FDR 控制。功能优先级包括来自 GTEx 的肺组织 eQTL、差异表达、基于 PRS-CS 的预测表达关联以及 UKB 蛋白质组学项目中的蛋白质组学相关性分析。

结果: 单变异分析发现了四个新常见变异位点 (1q25.1、3p21.31、5q31.2、19p13.2) 和两个罕见变异: C22orf46 中的 rs763076863 和 WWOX 中的 rs1014871851。基因集分析确定了 50 个候选非编码基因。根据功能分析证据, 我们关注 CLEC12A-AS1, 并进一步通过链式中介模型证实 CLEC12A-AS1 通过对 CLEC12A 基因表达和蛋白质表达的影响间接影响肺癌的发展。

结论: 这项基于 WGS 和填补数据的综合研究阐明了罕见的非编码变异对肺癌易感性的贡献。通过整合稳健的功能注释和多组学验证, 我们将 CLEC12A-AS1 鉴定为新的生物标志物和潜在的治疗靶点。我们的发现强调了探索非编码基因组的重要性, 并阐明了从罕见变异发现到机制洞察的途径, 从而为肺癌的个性化早期预防策略奠定了基础。

关键词: 肺癌全基因组关联研究

GAMM 模型在海拔与睡眠及认知能力关联性研究中的应用

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【摘要】研究背景: 随着人口老龄化加剧, 中老年认知能力衰退成为重大公共卫生挑战。认知功能受多种因素影响, 除个体的社会人口学特征外, 环境因素也越来越受到关注。近年来, 有研究表明, 自然环境中的海拔高度可能通过影响睡眠结构、大脑供氧水平及神经调节机制, 进而对个体的认知能力产生影响。在我国地理环境复杂的背景下, 揭示海拔对认知健康的效应至关重要。然而, 传统线性模型在捕捉非线性趋势和数据层级结构方面存在局限, 难以揭示其变量之间的真实关系。广义加性混合模型 (generalized additive mixed models) 能通过光滑函数拟合非线性趋势, 并纳入随机效应处理层级结构, 更适于解析复杂关联。

目的: 本研究整合全国中老年人群调查数据, 探索海拔高度通过睡眠路径对认知功能的可能影响路径, 为高海拔地区的健康干预提供参考依据。

方法: 本研究基于“中国健康与养老追踪调查” (China Health and Retirement Longitudinal Study, CHARLS) 2020 年数据, 纳入符合标准的中老年人群共 13196 人。海拔信息来源于国家气象科学数据中心 (<https://data.cma.cn>), 通过省份变量与 CHARLS 样本进行匹配整合。提取个体层面睡眠时长、认知得分及社会人口学变量后, 采用 GAMM 模型分析海拔对睡眠的非线性影响, 并进一步探讨海拔与睡眠对认知能力的作用关系。

结果: GAMM 模型结果显示, 海拔与睡眠时长之间存在非线性关系 ($\text{edf}=6.375$, $F=9.028$, $p<0.001$), 在 1000 米以下睡眠时长较短, 在 1500 米左右达峰值后趋于下降。进一步分析发现, 海拔 ($\text{edf}=2.861$, $p<0.001$) 和睡眠时长 ($\text{edf}=4.597$, $p<0.001$) 均对认知能力产生影响, 且与年龄、性别、教育程度、抑郁状态等因素共同构成复杂交互关系。认知能力在睡眠 6 小时左右最佳, 过短或过长均不利。

结论: 海拔通过影响睡眠时长, 间接作用于中老年人群的认知水平。GAMM 模型有助于揭示其潜在的非线性作用机制, 为地区性认知障碍干预提供了理论依据。

基金项目: 本项目获四川省科学技术厅科研基金 (24NSFSC5345) 基金资助

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Random Stacking 算法及其在多组学数据整合中的应用

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【摘要】

研究背景: Stacking 是一种集成学习算法。其通过整合多个基础模型提升整体预测性能。然而, Stacking 因其算法依赖交叉验证, 在处理高维数据时存在预测高方差的问题。

目的: 针对 Stacking 在高维数据预测时存在的高方差问题。本研究提出 Stacking 的改进算法, 并评估其在临床与组学数据整合中的预测表现。

方法: 本研究提出 Random Stacking。该算法在 Stacking 的基础上, 通过随机样本抽样和随机特征, 引入更多随机化, 以期提升模型泛化能力。本研究将 Random Stacking 应用于临床数据与组学数据整合建模, 并利用一系列公开数据集和模拟数据, 将其与包括传统 Stacking 在内的多种方法进行比较, 同时分析预测误差的来源。此外, 针对 Random Stacking 计算复杂度高的问题, 本研究开发一种计算高效的 Random Stacking 变体 (Fast Random Stacking), 通过优化基学习器实现效率提升。

结果: 在不同条件下 (特征相关强度、特征数量、信噪比等) Random Stacking 在模型预测的准确性及稳健性上均优于传统 Stacking 及其他算法。其预测性能的提升归因于高维数据条件下对方差与偏差的双重降低。Fast Random Stacking 可以在保证预测性能的同时, 计算效率超越传统 Stacking。

结论: Random Stacking 表现出优良的预测精确度和稳健性, 弥补传统 Stacking 的不足, 是高维数据建模 (尤其是数据整合建模) 的理想选择。该方法为个性化预后模型的开发提供了新的技术路径。

基金资助: 本项目获得国家自然科学基金面上项目资助 (82373688)

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TCDFomer 在 2023 - 2025 年兵团流行性感冒疫情 预测分析中的应用

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【摘要】研究背景:

目的: 本研究旨在通过 TCDFomer 模型对 2023-2025 年兵团呼吸道传染病疫情进行预测分析, 以提前掌握疫情发展趋势, 为制定针对性防控策略提供科学依据, 从而有效降低疫情传播风险, 保障兵团居民的身体健康与生命安全。

方法: 数据来源于兵团疾病预防控制中心信息系统的 2023 年 1 月-2025 年 4 月 年流行性感冒的日发病数据。TCDFomer 是一种融合时序卷积 (Temporal Convolution) 和 Transformer 架构的深度学习模型。对收集到的数据进行完整性检查和预处理, 剔除缺失值和异常值后, 按照时间顺序将数据分为训练集 (60%)、验证集 (20%) 和测试集 (20%), 并进行标准化、归一化处理, 以消除不同变量间量纲和数量级差异带来的影响。此外本研究将其与多种经典预测模型进行了对比, 包括传统 ARIMA 模型、Prophet 模型、LSTM (长短期记忆网络) 模型, 采用均方误差 (MSE)、平均绝对误差 (MAE) 等指标对模型进行定量评估。本研究实验环境: GPU: 英伟达 RTX2080TI; CPU: 锐龙 7950X。研究设置初始学习率 0.0001。学习率下降策略采用指数阶梯下降策略。

结果: 共收集到 2023 年 1 月-2025 年 4 月 年流行性感冒日发病数据 724 条, 平均每天发病人数 21.73 人。经过 10 轮的训练, TCDFomer 在兵团 2023 年 1 月-2025 年 4 月流行性感冒数据的测试集上 MSE 为 0.89, MAE 为 0.65, 相比于 ARIMA 模型 (MSE: 1.29, MAE: 0.92)、SARIMA (MSE: 0.89, MAE: 0.67)、Prophet (MSE: 4.49, MAE: 1.90)、LSTM (MSE: 1.67, MAE: 0.92) 获得了最优的性能表现。

结论: TCDFomer 模型通过时序卷积捕获局部动态特征与 Transformer 捕捉全局依赖关系的协同机制, 有效提升了时间序列预测性能, 证实了多模态深度学习架构在传染病预测领域的应用潜力。研究结果为兵团呼吸道传染病防控提供了精准的预测工具, 有助于实现疫情早期预警与防控资源优化配置。未来可进一步整合气象、人口流动等多源数据, 并探索模型在其他新发传染病的适应性, 为构建智慧化公共卫生预警体系提供技术支撑。

基金资助：本项目获 2025 年兵团卫生科技计划项目基金资助 (BTKY250055)

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包含多阶段早期终止的 II/III 期推断无缝设计的条件点估计 以及区间估计方法研究

Conditional point estimation and confidence interval for the inferentially seamless phase II/III clinical trials involving multi-stage early stopping

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[Abstract] Background: To avoid the unnecessary resource expenditure resulting from the sample size overestimation in the inferentially seamless phase II/III designs, some researchers have proposed implementing multi-stage early stopping in phase III. However, there remains a paucity of research on appropriate methods for parameter estimation within these designs.

Purpose: This study proposes and evaluates five conditional point estimations and three confidence intervals for estimating the phase II selected treatment group, conditional on that the trial has continued to phase III.

Method: For point estimation, we propose the uniformly minimum variance conditional unbiased estimator (UMVCUE), the multiple iterations-based conditional bias-adjusted estimator (CBAE-MI), the single iteration-based conditional bias-adjusted estimator (CBAE-SI), and the conditional median unbiased estimators with the unselected treatment group effects be estimated by their maximum likelihood estimators (CMUE-MLE) or set as zero (CMUE-ZERO). For confidence intervals, we derive the Wald confidence interval based on the UMVCUE, as well as the sample space ordering confidence intervals derived from CMUE-MLE, and CMUE-ZERO.

Result: Simulation results reveal that the naive estimator exhibits substantial positive conditional bias and inadequate conditional interval coverage probability. In contrast, the proposed point and interval estimation methods consistently demonstrate superior statistical properties. Among the point estimators, UMCVUE, CBAE-SI, and CMUE-MLE yield approximately unbiased estimates across most simulation scenarios. While CBAE-SI and CMUE-MLE may achieve lower conditional root mean square error, UMVCUE exhibits greater robustness to variations in group selection and the timing of interim analyses. For the remaining two point estimation methods, the CMUE-ZERO partially mitigates the bias inherent in the naive estimator

but fails to eliminate it completely, whereas CBAE-MI tends to overcorrect, resulting in negatively biased estimates. Regarding the confidence interval, CMUE-ZERO-based interval offers improved conditional coverage relative to the naive Wald interval, though its coverage remains below the nominal 95% level. In contrast, the intervals derived from UMVCUE and CMUE-MLE demonstrate conservative coverage properties, with the former exhibiting narrower widths.

Conclusion: For the inferentially seamless phase II/III trials with multi-stage early stopping, the UMVCUE is recommended for point estimation due to its strong robustness across diverse trial design configurations. For interval estimation, confidence intervals based on UMVCUE and CMUE-MLE are preferable, despite their tendency to yield conservative coverage.

基金资助：本项目获国家自然科学基金资助（82273727）

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不同预处理策略和方法下的类不平衡数据模型性能优化研究

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【摘要】研究背景: 类别不平衡现象常见于科研实践, 传统的分类算法因多数类偏好导致敏感度系统性偏移, 显著损害模型性能 (AUC 下降可高达 32%), 这一现象在 COVID-19 重症预测、癌症早期筛查等应用中尤为突出, 但目前尚缺乏“标准”的数据预处理范式。

目的: 系统评估不同策略和方法在轻度 (1:10)、中度 (1:20)、重度 (1:50) 及极度 (1:100) 类别失衡场景下的模型优化效应。

方法: 基于 Python 3.12.9 和蒙特卡洛模拟, 构建基准数据集 ($n=50,000$; 病例/对照=1:1), 通过分层随机抽样生成四组失衡数据集, 采用以下四类数据划分策略获得试验数据: A (分层随机测试集+训练集过采样)、B (平衡测试集+训练集过采样)、C (训练集过采样+测试集欠采样)、D (全局过采样后分层随机划分)。采用 8 种重采样方法如随机过采样、随机欠采样、合成少数类过采样技术 (SMOTE)、SMOTE-Tomek、Borderline-SMOTE、基于支持向量机的 SMOTE (svmSMOTE)、基于 K 均值的 SMOTE (KMeans-SMOTE) 以及自适应合成采样 (ADASYN) 完成数据预处理, 通过多维度指标 (混淆矩阵、G-mean、平衡准确率、宏 F1、AUC) 评估模型性能的提升效果。

结果: 在轻、中、重和极度类别失衡下, 召回率较基准模型分别下降了 17.2%、29.0%、43.0% 和 52.7%。从策略角度来看, 策略 A 对模型性能有一定提升作用; 策略 B 与策略 C 在处理类不平衡时更能拟合实际数据分布, 预测表现相对稳定, 但策略 C 在样本利用效率方面存在一定损失; 策略 D 提升有限且过拟合风险较高。在 8 种重采样方法的比较中, ADASYN 在四种失衡数据中较基准数据的平均召回率变化分别为 2.4%、1.6%、0.8% 和 2.7%, 对于少数类阳性事件的识别能力最为优, 其次为 Borderline-SMOTE。SMOTE 与 SMOTE-Tomek 效果相近, 而 KMeansSMOTE 的稳定性较差。随着类别失衡比例加重, 各类过采样方法在提升模型性能的同时, 均明显增大模型的过拟合风险, 提示面对严重失衡数据, 控制模型的复杂度和合理选择重采样方法极为关键。

结论: 类不平衡数据不宜直接用于模型构建, 可使用“平衡测试集+训练集过采样”

策略与 ADASYN 方法以提升模型性能。本研究为疾病预测模型特别是罕见病诊断模型的性能优化提供了方法学框架。

基金资助：本项目获 2024 年浙江省大学生科技创新活动计划暨新苗人才计划基金资助 (2024R413C088)

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不同孕前体重指数下的妊娠期增重对妊娠结局的影响-基于 EHR 的出生队列研究

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【摘要】研究背景：妊娠期体重增长（Gestational Weight Gain, GWG）是反映孕妇营养状况与胎儿生长发育的重要指标。现行国家卫生行业标准《妊娠期妇女体重增长推荐值标准：WS/T 801-2022》虽提出分 BMI 水平的推荐增重值，但其科学性与适用性尚缺乏大样本人群的实证验证。

目的：探索不同孕前 BMI 水平下中国女性最佳妊娠增重总量及孕期各阶段的增重速率，并评估其与不良妊娠结局（Adverse Pregnancy Outcomes, APO）的关联。

方法：本研究基于宁波市 MATCHLESS 队列中 16.9 万余名单胎妊娠女性，使用 Z 评分标准化体重增长值，并构建中国人群特异性孕期体重增长参考曲线。暴露指标为总 GWG 的 z 分值及各孕期阶段的每周体重变化率。主要结局为 APO 复合指标，包括子痫前期、妊娠期糖尿病、早产、大于胎龄儿、小于胎龄儿及死产。采用具有 4 个节点的受限立方样条及多因素修正泊松回归模型，评估总 GWG 及各孕期增重变化率对应 APO 的调整相对风险，识别出最佳体重增长量及变化率。同时，将识别出的最佳体重增长水平与 WS 标准推荐的孕期体重增长值进行了比较。

结果：在这项前瞻性分析中，我们发现，体重不足、正常、超重和肥胖的女性最佳总 GWG 分别为 15.2 (13.4-17.1) kg、12.4 (10.6-13.8) kg、9.4 (5.7-11.5) kg 和 5.6 (≤ 9.8) kg。肥胖孕妇在孕期体重轻微增加甚至减重时，并未显著增加 APO 风险。在孕早期至孕中期早期，低体重及正常体重孕妇的最佳每周体重增长速率分别为 0.7kg/week 和 0.1kg/week，超重及肥胖孕妇表现出体重减少越多、风险越低；孕中期的最佳每周体重增长速率分别为 0.7 kg/week、0.5 kg/week、0.4 kg/week 和 0.4 kg/week；孕晚期的最佳增重速率则分别为 0.5 kg/week、0.5 kg/week、0.4 kg/week 和 0.4 kg/week。

结论：现行 WS 指南对低体重孕妇的推荐增重值可能偏低，而对于肥胖孕妇则可能存在过度干预的风险。此外，各 BMI 组在孕中期和孕晚期的最佳体重增长速率普遍高于 WS 推荐或在范围上限，表明当前指南对中后期体重增长的控制标准

可能存在偏紧，尤其是对低体重孕妇在孕中期的建议值明显偏低。

注册：本研究经宁波大学医学部伦理委员会批准（NBU-2023-240），并注册于 ClinicalTrials.gov（NCT06422130）。

基金资助：本研究获浙江省自然科学基金（ZCLY24H2601）、宁波大学"One-Health"交叉学科研究项目、国家自然科学基金（81602940）、宁波市医学重点学科建设项目（2022-F28）的资助。

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产出导向法应用于医学统计软件课程教学的研究

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【摘要】研究背景: R 语言因其免费开源、高效灵活的数据分析与可视化能力, 在医学研究中发挥重要作用, 已成为医学本科生重要的统计软件学习工具。然而, 传统教学模式通常以讲授为主, 互动不足, 学生学习积极性不高, 应用能力偏弱, 未能有效实现学以致用。产出导向法 (POA) 强调以产出驱动学习, 促进理论与实践的融合, 近年来在多学科教学改革中取得良好成效, 但在医学统计软件教学中的应用较少。

目的: 本研究旨在评估产出导向法在医学本科生《R 语言基础与应用》课程教学中的应用效果, 以提升学生的学习兴趣、主动性及知识应用能力。

方法: 2023-2024 学年秋季学期, 中山大学 47 名医学本科生选修了基于产出导向法的《R 语言基础与应用》课程。教学过程包括驱动环节 (布置产出任务, 如制作 R 语言功能包或绘制高质量图表)、促成环节 (结合实际科研案例教学, 鼓励学生自主学习与合作探讨) 及评价环节 (通过作品提交、小组互评与教师评价共同完成学习效果评价)。课程结束后采用匿名问卷调查 (李克特 5 级量表) 和编程作品综合考评的方式评估教学效果。

结果: 课程实施后, 学生整体满意度达到 97.5%, 其中教学内容和教学方式的满意度分别为 87.5% 和 97.5%。85.0% 的学生认为 POA 提升了学习兴趣和主动性, 95.0% 的学生认可 POA 促进了理论知识与实际应用的结合, 87.5% 的学生认为 POA 增强了创新和探索意识。所有学生均按要求完成编程作品, 61.7% 的学生成绩达到优秀水平。约 90% 的学生表示愿意推荐该课程给同学, 82.5% 的学生愿意未来继续参与 POA 相关课程。课前调查显示 79.24% 的学生对 R 语言基本或完全不了解, 而课后评价表明显著提升了学生的实际应用能力与满意度。

结论: 产出导向法应用于医学本科生《R 语言基础与应用》课程中显著提高了学生的学习兴趣、主动性和知识应用能力。POA 有效促进了理论知识与实践技能的融合, 提升了课程的整体教学效果。未来教学实践中应进一步优化任务难度分层设计, 加强团队合作的合理分工, 以持续增强学生的自主学习能力和创新能力。

基金资助: 本项目获中山大学本科教学质量与教学改革工程类项目 (51000-12220011) 基金资助。

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成年期亲密伴侣暴力对精神疾病与心血管疾病共病的影响

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目的：探讨成年期亲密伴侣暴力（IPV）与精神疾病 - 心血管疾病共病的关联，分析性别差异及暴露剂量效应，为共病预防提供流行病学证据。

方法：基于英国生物样本库（UK Biobank）的 156,941 名参与者数据，通过心理健康问卷识别 IPV 暴露组（44,268 人）与非暴露组（112,673 人）。采用修正泊松回归计算患病率相对风险（PR）及 95% 置信区间（CI），控制年龄、性别、社会人口学特征、生活方式及合并症等混杂因素，并进行性别分层和剂量反应分析。

结果：IPV 暴露组女性占比 70.6%，童年不良经历比例显著更高（47.1% vs. 25.8%， $P<0.001$ ），且吸烟率、精神疾病史比例更高（ $P<0.001$ ）。在共病风险方面，调整后模型显示 IPV 暴露组共病患病率显著高于非暴露组（2.2% vs. 1.6%），相对风险值（PR）为 1.40（95% CI: 1.29-1.52）。共病风险随 IPV 暴露数量增加呈梯度上升，并且性别分层显示女性共病风险增幅更大（PR=1.49 vs. 男性 1.32）。

结论：成年期 IPV 是精神疾病 - 心血管疾病共病的重要危险因素，其风险具有性别差异和剂量累积效应。性暴力及多重 IPV 暴露人群需重点关注，临床应加强共病筛查与创伤干预。研究为“创伤 - 精神疾病 - 心血管共病”路径提供了流行病学证据，临床应加强创伤史筛查及共病预防，未来需结合纵向数据验证因果机制。

关键词：心血管系统疾病

大学生心理压力来源及影响因素分析——以某高校在校大学生为例

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【摘要】背景：近些年，社会竞争愈加激烈，大学生的心理抗压能力将受到严峻的考验，人们对大学生心理健康问题的关注程度也越来越高。心理压力对大学生心理健康的危害是不容小觑的，必须时时注意其心理问题并缓解其心理压力。大学生正值青春年华、风华正茂，其精神状态与其长期的发展与进步有着密切的联系

目的：了解某高校在校大学生心理压力状况，找出影响大学生心理健康的主要压力来源，并分析大学生心理压力的影响因素。

方法：利用问卷星设计并发放问卷，调查某高校在校大学生性别、年级、专业、生源地等个人基本信息。以压力强度量表评估大学生压力，通过 t 检验和方差分析研究大学生各方面的心理压力，采用多元线性回归分析大学生心理压力影响因素。

结果：就业压力、学习压力、适应压力、经济压力是在校大学生感到压力的主要来源。单因素分析结果显示，性别、年级、专业对就业压力的影响；性别、专业对学习压力的影响；性别对适应压力的影响；性别、家庭是否贫困对经济压力的影响均有统计学意义 ($P < 0.05$)。多元线性回归分析显示，专业、性别 2 个因子进入就业压力模型；专业、性别 2 个因子进入学习压力模型；家庭是否贫困和性别 2 个因子进入经济压力模型，差异均有统计学意义 ($P < 0.05$)。

结论：某高校在校大学生心理压力的出现与学生性别、家庭是否贫困、专业等有着密切的联系，应通过对大学生进行心理疏导，减轻其心理负担，提高其心理素质。

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地理统计模型与 meta 分析在估算区域患病率中的比较：

模拟与实例研究

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【摘要】研究背景: 估算区域患病率对于反映疾病风险和提供干预参考至关重要。实际研究工作中通常由普查、抽样调查或是合并已有随机抽样数据估计区域患病风险, 其中常用的分析方法有 meta 分析和地理统计模型, 但目前尚缺乏基于不同情景下的方法比较研究。

目的: 比较 meta 分析和地理统计模型两种方法在不同情景下估算区域患病率的结果和性能差异。

方法: 通过设置不同的空间方差、空间范围来模拟患病率的不同空间特征, 以及不同的采样地点分布类型 (包括随机分布、空间不平衡分布、基于患病率的优先分布、点和面数据的随机分布) 两个方面模拟生成研究区域患病率及不同样本量。将所模拟的研究数据作为实际研究中样本, 分别应用地理统计模型和 meta 分析, 前者根据二项分布产生的平面分布代表患病率并通过积分嵌套拉普拉斯近似法在贝叶斯框架下进行参数估计区域患病率, 后者通过异质性检验判断数据异质性并据此选择固定效应模型或随机效应模型估计区域汇总患病率, 并比较不同方法结果的准确性、精确性和效率。最后, 以一个实例研究来展示这两种方法在实际应用中的结果。

结果: 在大多数情况下, 地理统计模型比 meta 分析具有更高的准确性。在准确性方面, 当空间方差增大或空间范围减小时, 或在不同采样位置分布类型下, 地理统计模型均优于 meta 分析。在精确性方面, 当给定足够的样本量时, 地理统计模型提高更多。meta 分析的效率高于地理统计模型。

结论: 我们的研究表明, 在大多数情况下, 地理统计模型比 meta 分析更可靠、更全面地估计了整个地区的患病率。未来, 有必要为缺乏专业知识的人员开发更高效、更易于使用的地理统计模型软件来估算区域患病率。

基金资助: 无

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Advances and Trends of Methodological Approaches to Dealing with Missing Data in Electronic Medical Records: A Bibliometric Analysis

电子病历中缺失数据处理方法的进展与趋势：文献计量学分析

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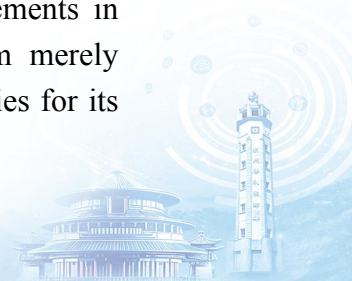
Background The rapid adoption of electronic health records (EHRs) has generated vast amounts of healthcare data; however, the problem of missing data remains a major challenge, potentially compromising the validity and generalizability of research findings.

Objective This study conducted a bibliometric analysis to explore research advances and trends in methodological approaches for handling missing data in EHRs.

Methods Using the Web of Science Core Collection database, we analyzed 1,270 publications from 1994 to 2025, employing CiteSpace software to visualize collaboration networks, keyword co-occurrence, and citation bursts.

Results A bibliometric analysis of 1,270 studies (1994–2025) revealed exponential growth in EHR missing data research, with 58.27% (n=740) published post-2020. The U.S. dominated contributions (679; 53.76%), followed by the UK and China. Harvard University led institutional output, while four institutions showed high collaborative centrality (≥ 0.1). Key disciplines included Computer Science & Interdisciplinary Applications (publication volume) and Health Care Sciences (centrality > 0.5). Keyword clustering identified 11 themes, with 25 keywords exhibiting citation bursts (2004–2025), reflecting evolving methodological and ethical priorities.

Conclusion This analysis reveals a significant growth in scholarly research addressing missing data in EHRs from 1994 to 2025, driven by advancements in imputation techniques and machine learning. The field has shifted from merely documenting missing data to actively developing sophisticated methodologies for its



resolution, underscoring the critical role of robust computational tools in improving EHR data quality and supporting evidence-based clinical decision-making.

Funding Research and Development Fund of Peking University People's Hospital (RDX2023-11, RDGS2024-05) and the National Natural Science Foundation of China (No. 81602939).

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儿童生长发育模式与青春早期健康问题的关联

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【摘要】研究背景: 近年来, 儿童和青少年肥胖的发病率显著上升, 青春期儿童的生长发育问题及其对后续健康状况的影响已越来越受到关注。

目的: 探讨儿童从出生至青春早期的 BMI 和身高发育轨迹与青春早期代谢和行为问题之间的关联, 为早期识别高风险儿童群体提供依据。

方法: 本研究基于 2002-2016 年在中国西部农村开展的孕期微量营养素干预随机对照试验所建立的出生队列, 分别在婴幼儿期 (12、24 月龄)、学龄早期 (6-10 岁)、青春早期 (10-14 岁) 完成随访并测量身高体重等数据。采用基于组的轨迹模型 (Group-Based Trajectory Model, GBTM) 构建出生到青春早期 BMI 和身高的发育轨迹。整合青春早期的行为问题得分、认知得分、肺活量、体质指数、心率、收缩压等指标, 利用熵权法求青春早期健康结局的综合得分, K-Means 聚类分析来识别青春早期健康问题模式。通过多因素线性回归和 Logistic 回归模型, 分析生长发育轨迹与青春早期健康结局的关联, 并控制相关混杂因素。

结果: 共有 1037 名儿童纳入分析, 其中男孩有 634 名 (61.1%)。GBTM 建立四类 BMI 轨迹: 正常组 (36.6%)、持续偏高组 (14.1%)、早期偏高组 (18.7%)、偏低组 (30.6%); 以及四类身高轨迹: 平均组 (12.3%)、偏高组 (14.1%)、快速增高组 (51.0%)、偏低组 (22.6%)。K-Means 聚类识别出三类健康模式: “代谢问题高风险组” (38.4%)、“健康问题低风险组” (44.9%) 和 “行为问题高风险组” (16.7%)。Logistic 回归显示: BMI 持续偏高组相较于正常组显著增加青春早期行为问题 ($OR=2.24$, 95%CI: 1.17 – 4.30) 与代谢问题 ($OR=3.66$, 95%CI: 2.19 – 6.12) 的风险; BMI 偏低组风险显著下降。身高快速增高组相较于平均身高组显著增加行为问题 ($OR=2.07$, 95%CI: 1.16 – 3.70) 与代谢问题 ($OR=2.39$, 95%CI: 1.48 – 3.86) 的风险。

结论: 儿童异常的 BMI 及身高发育轨迹可能预示青春早期健康问题, 早期识别具有这些异常发育轨迹的儿童, 并实施针对性干预, 可能有助于改善其长期健康结局。

基金资助: 国家自然科学基金 (82103867); 陕西省重点研发计划 (2024SF-YBXM-310)

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二甲双胍妊娠暴露对胎儿多系统畸形影响的性别特异性研究

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目的：妊娠期糖尿病的全球流行加剧了母体代谢紊乱及不良妊娠结局风险。相较于胰岛素治疗，二甲双胍在控制血糖方面具有显著的用药依从性和经济性优势，但其潜在的胎儿致畸风险仍存争议性。本研究旨在探究孕妇在孕期服用二甲双胍与胎儿多系统先天性畸形之间的因果关系，为 GDM 临床用药安全提供循证医学证据。

方法：本研究首先整合随机对照试验与队列研究证据进行 meta 分析，评估母体二甲双胍使用与胎儿先天畸形的关联强度；继而建立药物靶向孟德尔随机化模型，基于 eQTLGen 和 GTEx 数据库获取药物作用靶点的遗传工具变量，以芬兰 FinnGen 数据库中 11 个器官系统的 64 种先天畸形为结局指标进行因果推断；进一步采用多变量孟德尔随机化方法校正女性特异性混杂因素（包括体重指数、血压、血脂及血糖水平）；最终通过中介分析整合加拿大老龄化纵向研究的肠道代谢物数据，揭示潜在生物学通路。

结果：Meta 分析显示，与胰岛素治疗相比，二甲双胍对胎儿先天性畸形具有一定保护作用 ($RR=0.83$, $95\%CI\ 0.71-0.99$)。在筛选的 92 个二甲双胍靶点基因中，有 22 个基因与胎儿先天性畸形存在因果关联。中介分析显示未发现代谢通路介导作用。经 Bonferroni 校正及协变量调整后，有 7 个基因依然保持显著关联，其中 *NDUFS5*、*NDUFA2* 和 *ETFDH* 基因分别对循环系统、神经系统及其他系统先天性畸形具有特异性保护作用。

结论：本研究结合 meta 分析和药物靶向孟德尔随机化，为妊娠期使用二甲双胍的安全性提供了强有力的证据。研究结果减轻了先前对二甲双胍潜在致畸性的担忧，并为胎儿安全性提供了新见解。总体保护效应提示在妊娠期糖尿病管理中可谨慎使用二甲双胍。

关键词：胎儿先天性畸形

构建基于 PCA-TOPSIS 与多元权重集成的中国疾控体系科研能力评价方法

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【摘要】研究背景: 准确评估疾控体系科研能力是开展疾控科研能力提升工作的重要前提。实际评价过程中因评价指标类目多、范围广, 各级疾控填报缺项多等问题, 导致数据呈现高维稀疏特征, 评价指标数据分析存在指标冗余、权重偏差和数据噪声大等局限, 影响评价结果的科学性与稳定性。

目的: 针对疾控体系科研能力评估中高维稀疏数据的信息挖掘难题, 本研究创新构建整合主成分分析 (PCA)、逼近理想解排序 (TOPSIS) 与动态赋权集成的综合评价方法, 突破传统方法在降维去噪与权重优化中的局限。

方法: 调研于 2024 年 3 月至 4 月进行, 以中国大陆地区的省级、地市级疾控中心为研究对象, 通过电子问卷进行普查。疾控科研能力评价指标体系包含 4 个一级维度、15 个二级维度、34 个评价指标、177 个采集指标。针对采集指标数据稀疏、多缺项等问题, 采用主成分分析法 (Principal Component Analysis, PCA) 进行降维, 提取 34 项评价指标。基于 PCA 处理结果, 进一步引入 TOPSIS 法 (Technique for Order Preference by Similarity to Ideal Solution, TOPSIS) 对科研能力进行综合分析, 为增强评价结果的科学性与解释力, 分别结合三种权重方案: 1) 熵权法确定的客观权重; 2) Delphi 法获得的主观权重; 3) 主观与客观权重 1:1 比例加权形成的综合权重。最终构建“PCA + TOPSIS + 多元权重”的科研能力评价方法。计算各单位的 C_i 值作为综合得分并据此排序。此外, 基于综合权重分别对一级和二级维度开展综合评价, 进一步识别各单位在不同维度上的优势与短板。

结果: 共分析 31 所省级和 337 所地市级疾控中心的 2023 年科研能力数据。基于 3 种权重设定, TOPSIS 法计算的 C_i 值结果均显示: 东部地区疾控的科研能力整体排名优于中西部地区。TOPSIS 法结合综合权重计算的省级单位层面 C_i 值结果显示, 单位平均科研能力 C_i 值为 0.29, 上海市疾控居首 (C_i 值=0.49), 陕西省疾控末位 (C_i 值=0.16)。

结论: 构建基于 PCA-TOPSIS 与多元权重融合的科研能力评价方法, 能有效解决高维复杂数据信息挖掘问题, 实现疾控机构科研能力的科学排序, 为资源配置与政策制定提供依据, 具备较强实用性与推广价值。

基金资助：本项目获国家自然科学基金（资助号：82103944）、国家重点研发计划（项目编号：2017YFC0907200, 2017YFC0907201）、陕西省科技资源开放共享平台（资助号：2023-CX-PT-47）资助。

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贵州省某市心脑血管疾病的疾病负担及灰色预测模型分析

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【摘要】研究背景：心脑血管疾病已成为全球及我国城乡居民首要的死亡原因和主要的疾病负担来源。准确评估特定区域心脑血管疾病 (CCVDs, Cardiovascular and Cerebrovascular Diseases) 的疾病负担并预测其发展趋势, 对于制定针对性的区域的公共卫生策略、优化医疗资源配置及提升居民健康水平具有重要的意义。

目的：本研究旨在分析贵州省某市 CCVDs 的流行特征与疾病负担现状, 并运用灰色预测模型对其未来发展趋势进行预测。

方法：基于全球疾病负担 (GBD) 研究框架, 收集整理贵州省某市 2019 年至 2024 年官方统计年鉴、疾病预防控制中心关于 CCVDs 的死亡率、年龄标准化死亡率 (ASR)、早死损失寿命年 (YLL)、潜在减寿率 (PYLLR) 等数据。采用描述性统计方法分析不同性别、年龄组人群 CCVDs 的疾病负担指标, 并采用年度变化百分比 (APC) 评估其变化趋势。构建 GM(1,1) 灰色预测模型, 采用后验差比 (C 值) 和小误差概率 (P 值) 评估模型的拟合优度和预测精度, 对未来 6 年 CCVDs 的 ASR 进行预测。

结果：全市 CCVDs 粗死亡率从 2019 年呈波动上升趋势, 2023 年达峰值 (260.24/10 万), 2024 年回落至 233.33/10 万。男性粗死亡率始终高于女性 (2024 年: 256.92/10 万 vs. 208.42/10 万)。粗死亡率随年龄增长呈指数上升, ≥ 85 岁人群死亡率最高 (2019 年: 12861.96/10 万)。2019 年-2024 年 CCVDs 的 ASR 整体呈下降趋势 (APC = -5.41, $P < 0.05$)。男性 YLL (2024 年: 96,900 人年) 与 PYLLR (19.39‰) 显著高于女性 (39,800 人年与 6.76‰)。脑血管病是导致该市居民 CCVDs 疾病负担的主要病种 (2024 年: 142.64/10 万), 其次为缺血性心脏病 (56.41/10 万)。GM (1,1) 模型显示后验差比 $C=0.06$, 小误差概率 $P=83.33\%$, 精度良好, 预计 2025 年 ASR 为 262.86/10 万, 2030 年降至 192.37/10 万。

结论：贵州省某市 CCVDs 的粗死亡率呈现先上升后回落趋势, 尤其在男性人群中问题突出。脑血管病是主要的健康威胁。灰色预测模型显示到 2030 年 CCVDs 死亡风险将进一步下降。本研究可为该地区制定防控策略、优化卫生资源配置、加强高危人群筛查与管理提供一定的科学依据和数据支持。

基金资助: 本研究获台湾民主自治同盟中央委员会资金资助。

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机器学习与贝叶斯网络在阿尔茨海默病发病风险预测中的应用研究

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【摘要】研究背景: 轻度认知障碍(Mild Cognitive Impairment, MCI)是介于正常衰老与阿尔茨海默病(Alzheimer's Disease, AD)之间的过渡状态, 被广泛认为是 AD 的高危前期阶段。

目的: 筛选从轻度认知障碍发展到阿尔茨海默病的危险因素, 构建阿尔茨海默病发病风险贝叶斯网络模型, 为从轻度认知障碍发展到阿尔茨海默病的发病风险预测提供参考。

方法: 首先从阿尔茨海默病神经影像学计划(ADNI)数据库中纳入 342 例 MCI 患者和相关变量, 将所有患者按照 7:3 的比例随机划分为训练集和测试集, 然后在训练集分别构建随机森林和 XGBoost 模型, 利用测试集进行模型评估, 选取最优模型进行变量筛选, 最后基于最大最小爬山(MMHC)算法和极大似然估计构建贝叶斯网络模型。

结果: 本研究中, MCI 患者的 AD 发病率为 42.1%。基于随机森林模型进行变量重要性排序, 排名前 10 的变量为逻辑记忆延迟回忆总分(LDELTOTAL)、临床痴呆评定量表得分(CDRSB)、年龄、功能活动量表得分(FAQ)、简易精神状态量表得分(MMSCORE)、全脑体积(WholeBrain)、受教育年限、收缩压(VSBPSYS)、脑室体积(Ventricles)、体质量指数(BMI)。在测试集上, 随机森林模型受试者工作特征(ROC)曲线下面积(AUC)为 0.898, 模型准确性为 0.851, 灵敏度为 0.833, 特异度为 0.864, 约登指数为 0.698。贝叶斯网络模型分析结果显示, WholeBrain、LDELTOTAL 与 AD 的发病直接相关, 是 MCI 发展为 AD 的重要风险因素; 年龄、FAQ、CDRSB、受教育年限、MMSCORE 间接影响 MCI 到 AD 的发生风险。

结论: 当 MCI 患者出现全脑萎缩、记忆功能障碍、功能活动障碍、精神状态不良时, 其患 AD 的概率会大大增加。加强 MCI 患者的功能活动能力、关心和调整其精神状态, 可以降低 AD 发生的风险。贝叶斯网络模型可用于预测从 MCI 到 AD 的发病风险

基金资助: 本研究得到了国家自然科学基金(项目编号: 82003560)和山东省自然科学基金(项目编号: ZR2020MH340)的资助。

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基于 ARIMA 模型的某市中老年人群 HIV/AIDS 动态演变规律与预测性监测研究 (2014–2024)

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【摘要】研究背景：抗逆转录病毒疗法广泛应用后，HIV 感染者寿命延长，老龄化趋势明显。中国中老年新发病例持续上升，诊断延迟和并发慢病问题突出。某市为深度老龄化地区，老年人口占比高，且 HIV/AIDS 疫情负担沉重，使中老年防控压力加剧。开展该人群 HIV/AIDS 流行趋势的定量分析，有助于把握疫情动态、优化防控策略与资源配置，提升公共卫生应对效能。

目的：本研究旨在运用自回归积分滑动平均 (ARIMA) 模型，深入揭示某市 50 岁及以上人群 HIV/AIDS 疫情的动态演变特征与时间趋势，量化年度变化，识别关键转折点，并提供短期预测性洞见，从而为该老龄化区域制定精准的公共卫生干预措施提供定量依据。

方法：收集并分析 2014 年 1 月 1 日至 2024 年 12 月 31 日期间，某市报告的所有年龄 ≥ 50 岁的 HIV/AIDS 月度新发病例数据。遵循标准时间序列分析流程，构建季节性 ARIMA(SARIMA)模型，包括采用增强迪基-福勒 (ADF) 检验进行平稳性判断、差分处理、基于赤池信息准则 (AIC) 进行模型定阶、参数估计以及全面的模型诊断检验 (如 Ljung-Box 白噪声检验、残差分析)。使用 2024 年数据作为测试集对模型预测性能进行验证。最后，运用优化后的模型预测 2025–2027 年的发病趋势。

结果：研究期间共纳入 9337 例新报告病例。分析显示疫情呈现明显阶段性：2014–2019 年年均增长率达 37.45%；而在 2020–2022 年新冠疫情期间，年均下降率达 26.31%，2023 年略有回升。疫情表现出显著的季节性，每年 3–5 月为发病高峰，10–12 月为低谷。最优模型确定为 SARIMA(1,1,1)(2,0,0)[12]，该模型在训练集上拟合良好 (MAPE=22.12%, MASE=0.52)，并在测试集上展现出稳健的预测性能 (MAE=9.58 例, RMSE=13.12 例, MAPE=18.68%)。预测结果显示，2025–2027 年年新发病例数预计分别约为 593.4、592.7 和 576.3 例，将趋于稳定，但仍伴随显著的季节性波动。

结论：SARIMA(1,1,1)(2,0,0)[12]模型能够有效捕捉并预测某市 50 岁及以上人群 HIV/AIDS 的月度发病模式。该定量工具可为区域老龄化背景下的疫情动态监测与资源优化配置提供宝贵的决策支持。建议将本地化的时间序列模型纳入常规监

测体系，以强化循证防控策略。未来研究可通过引入外部协变量或融合机器学习方法，以提升中长期预测精度。

基金资助：无

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基于 GBDTM 模型 1990-2021 年全球 HIV/AIDS 的男女发病率变化模式研究

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【摘要】研究背景 艾滋病自发现四十年来, 经历了发现、扩散、增长、稳定四个时期, 其传播机制和特征发生了重大变化, 从主要以注射吸毒和男男同性性行为传播向一般人群扩散, 异性性行为传播占比不断上升, 男女性别发病比例从主要以男性为主逐渐趋于平衡。同时由于社会文化、经济发展、治疗与干预策略, 以及不同性别生理结构、性行为模式差异等原因, 造成了不同国家和地区发病率的发展变化趋势存在异质性, 而且不同性别的发病率存在关联同时, 又有其独特的规律。既往研究多从单一国家或全球角度对 HIV/AIDS 发病率进行长期趋势研究, 往往忽略了该异质性, 单一变量、单一轨迹分析常常难以揭示出不同群体 HIV/AIDS 的动态演变规律。因此, 在如何考虑不同国家地区异质性的同时, 考察男女发病率的协同变化模式仍有待研究。

目的 对全球不同性别 HIV/AIDS 标化发病率进行趋势描述基础上, 利用 GBDTM 识别不同国家及地区 HIV/AIDS 发病轨迹模式。

方法 利用全球疾病负担数据库, 收集 1990-2021 年全球 204 个国家及地区的 HIV/AIDS 发病率数据。采用 joinpoint 模型拟合标化发病率的整体趋势, 采用 GBDTM 模型中的限制性模型拟合不同性别标化发病率的协同变化联合轨迹模式。

结果 GBDTM 模型将男女标化发病率划分为四个联合轨迹组: 低水平上升组占 16.35%, 主要集中在中欧、东欧、中亚、北非和中东地区; 中低水平上升组占 34.14%, 集中在东南亚、东亚、大洋洲及高收入国家; 中高水平稳定组占 30.77%, 集中于拉丁美洲、加勒比海和部分高收入国家; 高水平下降组占 18.75%, 主要分布在撒哈拉以南的非洲地区。

结论 GBDTM 模型有效捕捉了不同性别发病率的动态关联, 并识别了四种发病轨迹模式, 与既往对 HIV/AIDS 发病率的认识基本一致, 说明该方法具有一定的合理性和可解释性, 并为进一步的传播机制研究和针对性防控策略的制定提供了理论基础。

基金项目: 重大传染病防控中央补助资金课题 (No: 223Z021)

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基于 Quarto 的多中心队列研究可重复性项目文档管理系统的构建与应用

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【摘要】研究背景：多中心队列研究作为流行病学重要研究方法，其文档管理质量直接影响研究效率和成果质量。随着研究规模扩大和数据复杂性增加，依赖人工操作和分散式存储的传统管理模式存在版本控制混乱、可重复性差、协作效率低等问题，难以满足智能化科研（AI for Science）转型对标准化、模块化、自动化管理的需求。Quarto 作为新一代科学出版系统，具备跨语言兼容、多格式生成、可重复性保障等技术优势，为解决多中心队列研究文档管理难题提供了新的技术路径。

目的：构建基于 Quarto 的多中心队列研究项目管理体系，实现可重复性科学研究、阶段任务管理和文档化编程的一体化管理，以满足智能化科研转型背景下对流行病学研究项目标准化、模块化和自动化管理的迫切需求。

方法：以 ACACIA 多中心队列研究为例，构建基于 Quarto 的三层技术架构。标准化层面上，研究采用 here 包统一目录结构，renv 包锁定环境版本，YAML 配置实现报告模板标准化。模块化层面上，构建可重复性研究模块（targets 包管理工作流依赖）、任务管理模块（YAML+purrr 实现批量处理）、文档化编程模块（集成 ggplot2、plotly 等实现交互可视化）。自动化层面上，通过 targets 自动执行分析，quarto 自动生成和发布报告，集成 Git 版本控制和 Docker 容器化技术确保多中心协作。

结果：基于 ACACIA 多中心队列研究的系统验证表明，该管理系统在三个关键维度取得显著效果。在自动化层面，构建覆盖 75% 核心工作流的全流程自动化体系，使重复分析计算时间缩短 75%（60 分钟→15 分钟），报告生成效率提升 73%（75 分钟→20 分钟）。在模块化层面，通过模块化设计实现 92% 代码复用率，批量处理使代码量减少 47.3%（12,452 行→6565 行），参数化配置使新增分析时间缩短 87.5%（96 小时→12 小时）。在标准化层面，renv 与 Docker 确保 100% 环境一致性和 88% 分析结果复现率，全分析链可在 5 分钟内完成溯源。

结论：基于 Quarto 的项目管理模式有效提升了流行病学研究效率和质量，技术架构成熟可靠，实施成本可控，适合在不同规模的流行病学研究项目中推广应用，为现代流行病学研究提供了标准化、自动化和可重复的管理解决方案。

基金资助：本项目获国家自然科学基金（资助号：82103944）、国家重点研发计划（项目编号：2017YFC0907200, 2017YFC0907201）、陕西省科技资源开放共享平台（资助号：2023-CX-PT-47）资助。

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基于 UK Biobank 的衰弱人群疾病轨迹与死亡风险研究

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【摘要】研究背景: 衰弱 (Frailty) 是老年人群中常见的一种综合征, 表现为应激后稳态恢复能力减弱, 显著增加多种疾病的风险。尽管衰弱可独立存在, 但与共病关系密切, 且衰弱人群中疾病的相互作用及时序演化机制尚不明确。近年来, 疾病轨迹分析为探索疾病的时间顺序提供了新方法, 结合共病网络分析, 可更系统地揭示疾病的动态演化特征与潜在机制。

目的: 整合疾病发生顺序与共病结构, 构建衰弱人群的疾病轨迹网络, 识别其关键疾病节点及其疾病发展路径, 揭示衰弱人群中疾病的演化规律, 为精准预防与干预策略提供理论支持。

方法: 本研究基于英国生物样本库 (UK Biobank), 在倾向性评分匹配后纳入 18,999 名衰弱个体及 94,995 名匹配对照。采用 PhencodeX 体系将诊断重新分类为 385 种疾病及 14 类死亡原因, 开展衰弱人群中的疾病轨迹分析与共病网络分析, 系统刻画衰弱人群疾病的演化路径。

结果: 研究对象中位年龄为 60 岁 (四分位数: 53 – 65 岁), 女性占 61.9%。在中位随访 14.9 年期间, 利用 Cox 回归进行全表型组关联研究, 发现衰弱人群在 147 种疾病及 6 种死亡原因上的风险显著升高。通过构建疾病对, 建立衰弱人群的时间序列疾病轨迹, 结合共病网络, 识别出衰弱人群的三个主要疾病集群: 肌肉骨骼疾病与精神障碍集群、呼吸系统疾病集群、心血管与代谢疾病集群。在死亡轨迹分析中, 心血管疾病、恶性肿瘤、呼吸系统疾病及神经系统疾病为主要死因结局, 慢性阻塞性肺疾病、缺血性心脏病和贫血等是终末期高发疾病。

结论: 衰弱人群面临多种疾病和死亡原因的高度风险, 这些疾病构成了多个干预靶点的疾病演化路径。疾病轨迹分析结合共病网络提供了揭示衰弱人群疾病演化链条, 为制定更具针对性的预防和治疗策略提供了理论依据。

基金资助: 本研究获浙江省自然科学基金 (ZCLY24H2601)、宁波大学"One-Health"交叉学科研究项目、国家自然科学基金 (81602940)、宁波市医学重点学科建设项目 (2022-F28) 的资助。

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基于百度指数的 ARIMAX 模型在北京市猴痘疫情预测预警应用研究

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【摘要】

研究背景: 猴痘是由猴痘病毒感染引起的新型人畜共患传染病, 2022 年来呈全球扩散态势, 由于猴痘病毒 Ib 新分支流行, 世卫组织于 2024 年 8 月再次宣布猴痘疫情构成“国际关注的突发公共卫生事件”, 防控形势严峻。当前, 网络搜索已成为公众获取健康信息的重要方式, 百度指数通过对关键词搜索、点击及分享行为的加权统计, 动态体现搜索趋势, 是反应传染病社会关注度的重要指标之一。已有多项研究基于百度指数对新冠、流感等传染病的流行趋势进行预测, 为早期预警提供科学依据。然而, 猴痘领域相关研究尚显不足, 且由于重点关注易感人群的特殊性, 探索互联网数据对猴痘早期预警预测具有重要现实意义。

目的: 分析 2023-2024 年北京市猴痘报告病例的流行特点, 构建基于百度指数的 ARIMAX 预测模型, 评估其预测预警应用效果。

方法: 通过《中国疾病预防控制中心信息系统》收集 2023-2024 年北京市猴痘报告病例数据, 采用时间序列分析流行趋势; 以“猴痘”为中心关键词, 检索与其高度相关的基础关键词, 通过互相关分析筛选与猴痘病例数具有时滞相关的关键词, 并应用偏最小二乘回归 (PLSR) 降维构建综合百度指数 (CBI)。引入 CBI 构建 ARIMAX 预测模型, 并评估模型性能。

结果: 北京市猴痘疫情在初期报告高峰后转为波动性下降, 逐步趋于低水平稳定流行。关键词“猴痘病毒”“猴痘病例”“猴痘疫苗”“天花疫苗”“如何预防猴痘”与病例数滞后 1 期呈现显著相关 ($P < 0.05$)。基于 PLSR 提取的 CBI 与滞后 1 期病例数相关性较高 ($r = 0.739$)。ARIMAX(2,0,2)模型在拟合阶段优于 ARIMA(2,0,2), 且 CBI 对病例数呈正向预测效应 ($\beta = 0.1802$, $P < 0.001$); 但测试集预测误差有所增大 ($MAE = 0.265$, $RMSE = 0.336$, $MASE = 0.508$)。

结论: 基于百度指数的 ARIMAX 模型拟合表现良好, 提示其在猴痘疫情早期预警中具应用潜力, 但短期预测效果尚不稳定。网络搜索数据可作为传统监测体系的补充工具, 为提升猴痘等新发传染病的主动响应能力提供新路径。

基金资助：本项目获创新疫苗质量评价和标准化研究资金资助（项目编号：2021-I2M-5-005）

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基于动力学模型的肥胖及慢性并发症流行趋势预测方法及干预措施效果评估

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【摘要】研究背景: 肥胖及其引发的心脑血管疾病 (CVD)、2 型糖尿病 (T2DM) 等慢性并发症已成为我国重大公共卫生挑战。动力学模型在传染病领域应用广泛, 但在其在慢性非传染性病领域应用较为缺乏。

目的: 本研究旨在构建肥胖及慢性并发症动力学模型, 探究动力学模型在慢性病流行趋势预测方法与干预措施的效果评估。

方法: 将肥胖人群划分为无并发症、仅患 CVD、仅患 T2DM 及共患 CVD 与 T2DM 四类仓室, 构建含人口自然死亡率、疾病发展速率及并发症相关额外死亡率等参数的微分方程组。模型参数通过整合权威统计年鉴、卫健委报告及经筛选的文献与公开数据库信息进行估计, 并使用 2017-2023 年数据校准模型。AI 健康管理及中医适宜技术干预措施通过降低无并发症肥胖人群患 CVD 和 T2DM 风险实施防控。通过运用校准后的模型, 分别对 2050 年无干预、AI 健康管理干预、中医适宜技术干预这三种情景下, 肥胖及其慢性并发症的流行趋势进行预测分析。

结果: 模拟结果显示, 动力学模型在不同情景模拟中表现稳定。基准情景预测: 2030 年仅患 CVD、仅患 T2DM 及两者共病的肥胖人群患病率较 2023 年基线分别增长约 6.9 倍、3.3 倍和 1.3 倍; 2050 年分别升至基线的约 13 倍、11 倍和 3 倍。干预效果显示: 较无干预情况, AI 健康管理干预措施情景下 2030 年仅患 CVD 和 T2DM 的肥胖患者患病率分别降低约 27.7% 和 24.2%, 2050 年分别降低约 7.9% 和 21.2%; 中医适宜技术干预措施情景下 2030 年两者分别降低约 18.5% 和 17.3%, 2050 年降低约 1.4% 和 12.6%。

结论: 本研究构建了肥胖慢性并发症动力学预测模型, 该模型可预测肥胖及慢性并发症的流行趋势并量化评估干预措施效果, 为慢性非传染性疾病动态模拟提供了一定的方法学参考。

基金资助: 本研究获台湾民主自治同盟中央委员会资金和人工智能科研学科跃升计划项目 (A1-W25-301-0414) 资助。

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基于多层知识图谱映射的中医处方中治疗不寐病的草药替代物 药理邻近性分析

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【摘要】研究背景: 中药方剂中草药替代对维持疗效至关重要, 但传统替代策略 (如形态学相似性) 缺乏临床等效性验证, 且现代方法存在活性成分表征不全等问题。不寐病在中医理论中与心肾不交等失衡相关, 亟需系统整合生物医学机制。天王补心丹等中药复方疗效显著, 但多组分协同机制不明, 阻碍标准化应用。

目的: 提出多层知识图谱框架 (TCM×KG), 以天王补心丹治疗不寐病为例, 阐明其多靶点作用机制, 量化评估中药替代方案的药理学邻近性。

方法: 构建三层知识图谱: 宏观层整合 216 种疾病临床指南 (3231 节点、2810 边), 建立“症状-诊断-治疗-方剂”关联; 中观层利用网络药理学筛选天王补心丹的活性成分, 通过 PPI 网络识别关键靶点; 微观层进行 GO/KEGG 富集分析和分子对接验证。比较天王补心丹的药物替代方案中, 药方北沙参替代麦冬和党参替代甘草这两种替代方案, 评估成分相似度、靶点重叠率、稳定性等 5 项指标。

结果: 北沙参替代麦冬在成分相似度 (89.80% vs 69.39%)、靶点稳定性 (93.93% vs 81.23%) 及临床等效性 (分子对接符合率 82% vs 79%) 上均优于党参替代甘草。KEGG 分析揭示天王补心丹通过神经活性配体-受体相互作用、cAMP 信号通路等 132 条通路调控睡眠, 其中北沙参替代麦冬显著提升 cAMP 通路覆盖 (+3.42%)。分子对接证实丹参酚 A/B 与核心靶点 (GAPDH、TNF、ALB、IL-1 β) 结合能均 $\leq$ -20.92 kJ/mol, 提示成分与靶点相互作用稳定。

结论: TCM×KG 框架首次实现从中医临床指南到分子通路的跨尺度整合, 为中药替代提供量化评估工具。丹参酚 A/B 等关键成分通过调节 TNF/IL-1 β 等靶点改善失眠。药理邻近性分析得出。在天王补心丹的药物替代方案中, 北沙参替代麦冬具较高临床替代潜力, 而党参替代甘草不推荐。

基金资助: 重庆市科学技术委员会 (项目编号: CSTB2022NSCQ-MSX0121)、重庆市教育委员会 (项目编号: KJZD-K202300501)、教育部 (项目编号: 23XJAZH004)、重庆市卫生健康委员会 (项目编号: 2024ZYZD004) 以及重庆市科学技术局 (项目编号: CSTB2023NSCQ-MSX0073)。

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基于多核学习与图卷积网络融合的 snoRNA-疾病关联预测 方法

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【摘要】研究背景: 核仁小 RNA (snoRNAs) 在人类疾病的发病机制中发挥着至关重要的作用。研究 snoRNA 与疾病的关联对于疾病诊断和治疗尤为重要, 特别是在阐明复杂的致病机制方面。

目的: 目前的方法依赖于成本高昂且耗时的实验, 并且缺乏有效的 snoRNA-疾病关联预测模型, 突显了对新型计算方法的迫切需求。

方法: 我们提出了一种新型的基于图卷积网络的多核学习 snoRNA-疾病关联预测方法 (GCNMKLSDA), 该方法使用图卷积网络提取多层特征并整合多个核矩阵, 最后采用双图正则化最小二乘法有效预测 snoRNA 与疾病之间的关联。

结果: 使用 MNDR v3.1 数据集, GCNMKLSDA 在五折交叉验证、全局留一法交叉验证 (LOOCV) 和局部 LOOCV 中分别取得了 87.98%、89.02%和 75.38%的 AUC 值。此外, 我们选择了三种典型疾病和三种代表性 snoRNA 进行外部验证。GCNMKLSDA 在揭示 snoRNA 与疾病之间潜在关联方面表现出色。

结论: 所有验证结果都证实了 GCNMKLSDA 在识别候选 snoRNA-疾病关联方面具有卓越能力。

关键词: snoRNA-疾病关联预测; 图卷积网络; 多核学习; 双拉普拉斯最小二乘法

基金资助: 本项目无基金资助。

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A Novel Graph Convolutional Network with Multi-Kernel Learning Approach for Predicting snoRNA-Disease Associations

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Abstract

Small nucleolar RNAs (snoRNAs) play crucial roles in the pathogenesis of human diseases. Investigating snoRNA-disease associations is highly important for disease diagnosis and treatment, particularly in elucidating complex pathogenic mechanisms. Current methods rely on costly and time-consuming experiments and lack effective predictive models for snoRNA-disease associations, highlighting the urgent need for novel computational approaches. We propose a novel Graph Convolutional Network-based Multi-Kernel Learning for SnoRNA-Disease Associations prediction (GCNMKLSDA), which uses graph convolutional networks to extract multilayer features, integrates multiple kernel matrices, and employs dual graph regularized least squares for effectively predicting associations between snoRNAs and diseases. Using the MNDR v3.1 dataset, GCNMKLSDA achieved high AUC scores of 87.98%, 89.02%, and 75.38% in five-fold cross validation, global leave-one-out cross validation (LOOCV), and local LOOCV, respectively. Furthermore, three typical diseases and three representative snoRNAs were selected for external validation. GCNMKLSDA demonstrated superior performance in revealing potential associations between snoRNAs and diseases. All the validation results confirmed that GCNMKLSDA has exceptional ability in identifying candidate snoRNA-disease associations.

Keywords

snoRNA-disease association prediction; graph convolutional network; multi-kernel learning; dual Laplacian least squares

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基于多模态深度学习的阿尔茨海默病辅助诊断模型研究

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【摘要】研究背景: 阿尔茨海默病(Alzheimer's disease, AD)是导致痴呆的主要原因, 已成为全球重大健康挑战。现有辅助诊断模型多采用单一模态数据且具有侵入性。本研究结合临床量表和非侵入性 MRI 数据, 构建安全可靠的多模态深度学习辅助诊断模型。

目的: 本研究针对 AD 多模态诊断问题, 构建基于 MRI 的 3D-ResNet 和 3D-DenseNet 模型, 结合 Grad-CAM 可视化注意力热图, 探究能够有效提取影像数据特征的模型结构, 再进一步利用跨模态特征交互模块, 实现影像数据与临床数据深度融合, 构建高精度的 AD 分类模型, 以期 AD 临床辅助诊疗提供可解释的、无创的便捷工具。

方法: 本研究数据来自 ADNI 数据库的 ADNI-2 和 ADNI-GO 队列中 3DMRI 影像数据与临床量表数据。影像数据基于 FSL 和 Python 软件进行预处理。单模态模型以四种 3D-ResNet 及两种 3D-DenseNet 模型为基础构架, 利用训练集训练模型、测试集完成超参数调整并进行模型构建, 基于验证集对不同模型最终性能评估选取最优模型, 并进行 Grad-CAM 可视化分析。多模态模型构建阶段, 将最优 3D-ResNet 模型提取的影像特征与多层感知机提取的临床特征融合, 经 Transformer 编码器的多头注意力机制捕获跨模态交互信息, 通过全连接层和 Softmax 层实现 NC/MCI/AD 三分类任务。模型评估采用 Accuracy、Precision 和 Sensitivity 等指标进行。

结果: 在构建的四个不同的 3D-ResNet 模型中, 3D-ResNet18 模型性能最优。在构建的 3D-DenseNet 模型中, 3D-DenseNet169 在整体性能上略优于 3D-DenseNet121, 其 Accuracy、Sensitivity 表现更佳, 但二者 Accuracy 均低于 3D-ResNet18 模型。对优势模型 3D-ResNet18 进行 Grad-CAM 发现模型主要关注大脑中部及后部的皮层区域。基于影像数据和临床量表数据构建的多模态模型的 Accuracy 为 0.9292, Sensitivity 为 0.9152, 优于单模态影像数据构建的模型。

结论: 本研究揭示, 较浅层的 3D-ResNet 模型通过简化残差块结构, 能够在降低计算复杂度的同时保持 AD 影像特征提取效能, 克服了深度网络的过拟合与梯度退化问题。Grad-CAM 可视化结果为模型决策提供了合理解释。基于 Transformer 的多模态融合机制能够通过动态权重分配, 很好的融合多模态数据特征, 充分利

用各模态特征之间的互补性,为 AD 的早期诊断和预测提供了高稳健性的解决方案。

关键词: 深度学习; 多模态; 阿尔茨海默病; Transformer; Grad-CAM

基金资助: 本项目获得国家自然科学基金(82003560)、山东省自然科学基金(ZR2020MH340, ZR2023MH313)、国家重点研发计划-合成生物学专项(2024YFA0918404)和山东省重点研发计划(2024TSGC0151)资助。

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基于多种族群测序的 C 反应蛋白全基因组关联研究

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目的：通过整合来自英国生物样本库 (UK Biobank, UKB) 和精准医学转录组计划 (Trans-Omics for Precision Medicine, TOPMed) 的全基因组测序 (WGS) 数据作为发现集，并在 All of Us (AoU) 队列中进行外部验证，本研究旨在为深入探索 C 反应蛋白及其多种族遗传基础提供更全面的框架。

方法：我们进行了一个多种族 seqGWAS 的 meta 分析，发现集包括 447,369 名欧洲人、10,389 名非洲人、9,685 名亚洲人和 9,200 名西班牙裔人，验证集包括 23,521 名欧洲人、7,160 名非洲人、771 名亚洲人和 5,178 名西班牙裔人。我们进行了条件分析、跨种族精细定位和功能富集分析。多基因优先得分 (PoPS) 和基因集分析被用来推测潜在的调控基因。

结果：我们识别了 113 个独立的关联信号 (发现集 $P \leq 5 \times 10^{-9}$, 验证集 $P \leq 0.05$)，其中包括 21 个位点通过了条件分析，且有 3 个信号是欧洲特异性的。跨种族精细定位分析在 95% 的可信集内识别了 19 个独立信号。功能注释显示，在血液组织、H3K27me3 组蛋白标记和外显子区域中存在显著富集。共涉及 151 个基因作为 CRP 水平的潜在调控因子，其中 55 个基因为首次报告。在这些基因中，有 17 个基因和 4 个蛋白质显示了与 CRP 相关疾病具有因果证据或强烈的共定位证据。

结论：我们的多种族 seqGWAS 研究为 CRP 的遗传决定因素提供了新的见解，深化了我们对 CRP 机制的理解，从而为未来的研究奠定基础，指导功能基因组学实验的开展。最终，这些知识将有助于指导针对一系列复杂疾病的干预措施，如心血管疾病、癌症和免疫介导的疾病，拓宽潜在治疗靶点的范围。

关键词：多种族 C 反应蛋白全基因组测序关联研究

基于多组学整合分析探索代谢功能异常相关脂肪性肝脏谱系疾病的潜在生物标志物

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研究背景: 代谢功能异常相关脂肪性肝病 (Metabolic dysfunction-associated steatotic liver disease, MASLD) 及其进展性疾病肝硬化 (cirrhosis) 与肝细胞癌 (Hepatocellular Carcinoma, HCC) 构成全球范围的重要公共健康负担。目前针对该类疾病缺乏有效的预防及治疗手段, 探索疾病早期生物标志物可为疾病的预测、治疗及靶向药物开发提供科学依据。

目的: 通过多组学数据整合分析, 识别影响 MASLD、cirrhosis 及 HCC 发病风险的因果效应蛋白, 并构建可用于早期疾病风险分层的生物标志物。

方法: 基于全基因组关联分析 (Genome-wide association study, GWAS) 数据进行 meta 分析识别更多 MASLD 谱系疾病的遗传关联位点, 并结合蛋白质组数据构建孟德尔随机化 (Mendelian randomization, MR) 模型识别与疾病具有因果效应的血浆蛋白。进一步, 结合转录组学数据进行两性状 (蛋白-疾病表型) 共定位及多性状 (基因表达水平-蛋白水平-疾病表型) 共定位分析, 探索共有因果驱动变异。依据因果证据强度将与疾病相关的蛋白水平划分证据等级。最后, 通过个体级别的蛋白质组与基因组数据构建用于肝脏谱系疾病的机器学习模型, 并对包含不同蛋白质组合面板的模型进行预测效果评价, 以获得最优的疾病预测模型。

结果: 与 MASLD 谱系疾病存在显著关联的蛋白质水平中, 1 个蛋白质水平同时具有多组学共定位证据, 10 种蛋白质水平与疾病存在两性状共定位证据, 12 种蛋白质水平在基于不同基因-蛋白组学研究中的 MR 研究中效应估计结果一致, 分别被归为一级、二级、三级证据强度标志物, 其余蛋白质水平被归为四级证据强度标志物。这些蛋白质在代谢调控、免疫反应、凝血过程等多个通路中发挥作用。预测模型结果显示, 基于潜在靶点的蛋白质组面板 Logistic 回归模型相比于全蛋白质组面板模型在预测 MASLD 和 cirrhosis 风险上具有更好的预测性能 (MASLD: AUC = 0.75 vs. 0.64; cirrhosis: 0.85 vs. 0.77, P value for Delong test < 0.05)。

结论: 通过构建基于多组学数据整合分析的研究框架绘制了 MASLD 谱系疾病的分子标志物关联图谱, 研究结果为肝病的病因流行病学研究提供理论基础, 并为疾病早期风险干预及靶向药物开发提供证据支持。

基金资助：本项目获深圳市医学研究专项资金项目（A2403060）及国家自然科学基金（82373692）资助

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基于机器学习的老年心力衰竭患者再入院风险预测模型及 风险分层

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目的: 心力衰竭再入院给患者和医疗保健系统带来巨大压力。尽管预测模型众多, 但很少有模型具有临床实用性或能够支持及时分层, 从而造成资源浪费。本研究开发并验证了一种可解释的工具, 供护士预测再入院风险并对患者进行分层, 从而能够采取有针对性的护理干预措施, 以降低再入院率。

方法: 本研究收集山西省长治市三级医院老年心力衰竭患者的电子健康记录和 6 个月随访数据。将患者按 7: 3 被随机分为训练集和验证集。使用递归特征消除算法选择关键变量构建预测模型。基于最优模型应用 SHAP 方法进行模型解释。根据约登指数寻找阶段阈值划分群体最后开发了一个在线预测工具。

结果: 在几种算法中, 随机森林模型表现最佳 ($AUC = 0.86$, 95% CI: $0.78 - 0.88$), 外部验证结果良好 ($AUC = 0.82$, 95% CI: $0.76 - 0.88$)。根据约登指数, 56% 的风险阈值可识别出高危患者。我们开发了在线工具 (<http://42.192.102.169/>), 帮助临床工作人员锁定高危个体, 以便加强随访和干预。

结论: 我们开发了一款基于机器学习的工具, 用于预测心力衰竭患者六个月内的再入院风险, 其效果优于传统的风险评分。这款在线工具能够及早识别高危人群, 从而提升高危患者的随访率。

关键词: Elderly; Heart failure; Readmission; Machine learning; Prediction models; SHAP

基于机器学习的育龄女性生育意愿的影响因素研究

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摘要: 研究背景: 面对持续下降的生育率, 建设生育友好型社会已刻不容缓然而, 现阶段在女性生育意愿的研究仍显不足, 缺乏对女性生育意愿影响因素的多维度的系统探索。

目的: 本研究旨在探讨在生育友好型社会目标框架下, 潍坊市育龄女性的生育意愿的现状。同时, 构建多维度生育意愿预测模型, 并从社会信息加工的角度, 探讨女性生育意愿的影响机制, 为提升女性生育意愿的策略提供理论支持。

方法: 通过文献分析法、专家咨询法以及小组讨论制定女性生育意愿的调查问卷; 利用问卷中潍坊市育龄女性的个体特征、行为特征、人际网络等多维度信息, 采用 RF-RFE、SVM-RFE、XGBoost-RFE、LASSO 四种机器学习算法筛选影响女性生育意愿的关键因素, 并结合 LR、RF、DT、SVM、XGBoost 五种算法构建二十个预测女性生育意愿的组合模型; 使用 Shapley 加性解释 (SHAP) 对模型进行解释性分析。

结果: 四种特征选择方法均筛选出的特征有孩子使人生完整的认同感、年龄、城市居住共几年、幸福美满的家庭须有孩子的认同感、兄弟姐妹数量、家庭氛围利于孩子及害怕无法负担生养孩子的费用。RF-RFE 结合 RF 算法构建的预测模型性能最佳, 准确度 (0.848, 95%CI: 0.786~0.903)、AUC 值 (0.903, 95%CI: 0.850~0.951)、灵敏度 (0.836, 95%CI: 0.750~0.915) 和特异度 (0.861, 95%CI: 0.786~0.946)。相关特征的 SHAP 值发现, 对潍坊市女性生育意愿影响最大的前四特征为孩子使人生完整的认同感、家庭氛围利于孩子、年龄及兄弟姐妹数量; SHAP 摘要图表示当女性对幸福美满的家庭须有孩子的认同感越高, 越有可能选择生育, 相比于愿意接受托育服务的女性, 不愿意接受托育的女性更有可能选择不生育。

结论: 机器学习预测模型可以为女性生育意愿的监测提供一种简单、经济有效的工具。本研究提示, 建立普惠托育服务分级体系、优化网络生育信息生态、强化家庭支持干预等, 有利于构建生育友好型社会。

基金资助: 本项目获医防融合视域下传染病医疗机构高质量发展路径研究问题、机制与策略基金资助 (YG2024A010)

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基于机器学习冠心病患者抑郁风险预测模型的建立及验证

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目的: 抑郁症是冠心病(Coronary Heart Disease, CHD)发生和预后的独立危险因素, 不仅加剧健康风险, 而且还增加了社会负担。本研究旨在评价现有冠心病患者抑郁预测模型的偏倚风险和适用性, 探索冠心病患者抑郁风险预测模型的重要影响因素, 以构建一个能够全面、准确评估冠心病患者抑郁风险的预测模型, 为医疗工作者在临床实践中提供决策支持。

方法: 筛选 2009 年至 2018 年美国国家健康与营养检查调查(NHANES)数据库中 ≥ 20 岁且患有冠心病的成年人。运用 SPSS 26.0 软件进行数据统计分析, 将冠心病患者按照 7: 3 的比例进行随机分配。采用 Lasso 回归分析训练组确定影响冠心病患者抑郁的风险因素, 构建随机森林(RF)、逻辑回归(LR)、极端梯度提升(XGBoost)、高斯朴素贝叶斯(GNB)及梯度提升决策树(GBDT)5 种模型并进行内外部验证。通过 ROC 曲线下面积(AUC)评估预测效能, 校准曲线评价校准度, 决策曲线评价临床实用性。

结果: 1.通过 Lasso 回归筛选出 12 个预测因素用于构建模型, 分别为性别、教育程度、吸烟、睡眠障碍、年龄、身体质量指数(BMI)、中性粒细胞(NE)、血小板计数(PLT)、淋巴细胞(LYM)、总胆固醇(TC)、动脉粥样硬化指数(AIP)及甘油三酯(TG); 2.基于随机森林(RF)所构建的冠心病患者抑郁风险预测模型表现最佳。模型具有较好的预测性能; 校准曲线显示具有较好的校准度, 临床决策曲线显示具有较好的临床实用性, 依据各指标综合判断模型具有较好的预测效果。

结论: 1.性别、教育程度、吸烟、睡眠障碍、年龄、身体质量指数(BMI)、中性粒细胞计数(NE)、血小板计数(PLT)、淋巴细胞计数(LYM)、总胆固醇(TC)、动脉粥样硬化指数(AIP)、甘油三酯(TG)。作为预测因素, 能更好的预测冠心病患者抑郁的发病风险。2.基于随机森林(RF)构建的冠心病患者抑郁风险预测模型具有较好的区分度、校准度和临床适用性, 对冠心病患者抑郁风险具有一定的预测价值, 有助于临床医生对冠心病患者抑郁的早期识别和干预。

关键词: 冠心病; 抑郁症; 预测模型

基于卷积神经网络的心律不齐分类研究

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【摘要】研究背景: 心律不齐是一类常见的心血管疾病，包括窦性心动过速、房颤、室性早搏等多种类型。流行病学研究表明，房颤的全球患病率已超过 1%，随年龄增长而显著增加；严重心律失常可导致卒中、心衰及猝死风险上升，给公共卫生和临床诊疗带来巨大挑战。传统人工读图既耗时又易受主观因素影响，迫切需要一种自动化、精准、高效的心律分类工具。

目的: 针对常见及少见的十余种心律类型，本研究提出一种基于 12 导联 ECG 数据的卷积神经网络混合模型，旨在实现心律失常的高效精准分类。通过融合多导联心电图特征，模型可捕捉单导联难以识别的细微病理改变。

方法: 我们提出了一种端到端的高阶深度学习框架：首先，多尺度 1D-CNN 层自动学习心电波形上 QRS 复合体与 P-T 波的局部时频特征，无需手动设计滤波器；随后，Transformer 自注意力机制跨越整个心电周期，捕获长程节律依赖；与此同时，并行引入 RR 间期计算出的 HRV 统计量，将生理学先验有机融合进网络。针对心律类别分布极度不平衡，我们在损失函数中引入 Class-Balanced Focal Loss，对 AT、SAAWR 等稀有心律进行动态加权，显著提升了弱势类别的召回稳定性。

结果: 高阶模型实现了 98.3% 的整体准确率、Macro-F1 = 0.96 和 Macro-AUC $\approx$ 0.995，且仅需 5–10 个 epoch 即可快速收敛，单次推理延迟低于 10 ms，充分展现了卓越的精度、效率与临床可部署性。

混淆矩阵中，模型对所有 11 类心律的正确分类率接近 98.34%，节律窦性心律 (SR) 99.04%，室上性心动过速 (SVT) 98.96%，房颤 (AF) 96.94%，房扑/房颤伴搏动 (AFIB) 96.33%，窦性心动过速 (ST) 98.40%。室性早搏 (SB) 95.27%，窦性心动减缓 (SA) 97.78% 中等样本量类别表现稳定。

准确率: 模型在测试集上达到 98.3% 的准确率意味着模型几乎能对所有心律类型给出正确判读，具备足够的鲁棒性和可靠性。

召回率: 模型在测试集上取得了 96.7% 的加权召回和 98.1% 的宏平均召回，反映出极低的整体漏检率和几乎无漏诊的高风险心律检测能力。

宏平均: 本模型的宏平均指标均高于 0.95，说明即使在类别极度不平衡的场景下，也能保持对每种心律的高水平检测和识别。

加权平均：指标接近 98%，完美契合模型在临床大规模心电监护中对高频、常见心律的“高精度”“高可靠”需求；同时结合 Macro 指标，可确保对少样本、边缘心律类别的均衡判别。

讨论：本研究构建了一种融合 1D-CNN、Transformer 与HRV 特征的高阶心律失常分类模型，精准识别 11 种心律类型，展现出优异的性能（准确率 98.34%，Macro-AUC $\approx$ 0.995）。模型结合局部时频提取与全局时序依赖建模，成功将视觉深度学习策略迁移至 ECG 信号分析中。通过多模态特征融合，不仅提升了诊断智能化水平，还为揭示心律异常机制与推动个体化治疗提供了技术支撑。

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基于联合模型分析 tau 蛋白沉积脑区 对轻度认知障碍向阿尔茨海默病转归的影响

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【摘要】研究背景: 阿尔茨海默病 (Alzheimer's disease, AD) 是老龄化社会的重大公共卫生挑战, 其早期预测和病理机制解析亟待突破。Tau 蛋白异常沉积是 AD 的核心病理特征, 但现有研究多聚焦于单一脑区的静态 tau 病理分析, 而 tau 蛋白在多脑区的动态沉积轨迹及其与疾病转归的关联尚未阐明。联合模型 (Joint Models) 通过整合纵向随访数据与生存数据, 可克服传统横断面研究的局限性, 为揭示 tau 病理的时空演化规律及其对 AD 进展的动态影响提供了方法框架。

目的: 构建联合模型探究轻度认知障碍 (mild cognitive impairment, MCI) 向 AD 转归的关键 tau 异常沉积脑区, 分析其沉积轨迹与 AD 发生的动态关联, 为 AD 早期预测提供理论依据。

方法: 利用阿尔茨海默病神经影像学倡议 (Alzheimer's Disease Neuroimaging Initiative, ADNI) 数据库的 tau-PET 影像数据, 首先通过纵向随机森林中的混合效应回归森林算法 (Mixed-effects regression random forest, MERF) 筛选重要性前 50 位的脑区, 然后采用惩罚广义估计方程 (penalized generalized estimating equations, PGEE) 二次降维, 最终基于关键脑区构建联合模型, 通过关联参数 α 评估 tau 蛋白的纵向随访数据和生存结局之间的关系。

结果: 对 165 个脑区进行两阶段降维筛选出 6 个关键脑区: 大脑白质、左侧大脑白质、右侧外侧眶额皮层、腹侧齿状核、杏仁核及苍白球。纵向子模型显示, 大脑白质、左侧大脑白质、右侧大脑皮层外侧眶额区、杏仁核的 SUVR 值随时间显著上升 ($P < 0.05$), 苍白球的 SUVR 值显著下降 ($P = 0.032$), 而腹侧齿状核的变化无统计学意义 ($P = 0.297$); 生存子模型显示, 大脑白质、左侧大脑白质、腹侧齿状核、杏仁核、苍白球的关联参数 α 有统计学意义 ($P < 0.05$), 其中杏仁核区域 tau 沉积效应最强且高度显著 ($\alpha = 7.098$, $P < 0.001$)。

结论: 本研究通过联合模型系统揭示 tau 病理的时空异质性: 大脑白质、左侧大脑白质、腹侧齿状核、杏仁核、苍白球的 tau 蛋白异常沉积是影响 MCI 向 AD 转变的关键脑区。杏仁核作为 AD 转归的核心驱动脑区, 其 tau 沉积呈现持续累积特征并与疾病风险呈强正相关。联合模型通过推断纵向监测指标对生存结局的影响, 能够系统揭示 tau 蛋白病理沉积的时空演化规律及其对 AD 转归的预测效应,

进而为构建 AD 生物标志物预测模型提供新的思路。

基金资助：本项目获 81803337、81872719、82003560 基金资助

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基于迁移学习和数据增强的社区老年肿瘤标志物水平的预测方法研究

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【摘要】

研究背景:碳水化合物抗原 125 (CA-125)、癌胚抗原 (CEA) 和前列腺特异性抗原 (PSA) 是多种癌症的重要血清肿瘤标志物。肿瘤标志物作为临床常用的辅助诊断和预后评估指标, 其水平变化与肿瘤的发生发展密切相关。

目的: 本研究旨在构建一种基于迁移学习与数据增强技术相结合的社区老年肿瘤标志物水平预测模型, 以提高社区老年人群肿瘤标志物水平的预测精度。

方法: 本研究选取了 2022 年上海市某社区卫生服务中心的 6,461 名 65 岁及以上老年人作为研究对象, 其中, CA-125 标志物预测模型构建纳入了 2,278 例有效样本, CEA 标志物预测模型构建纳入了 2,742 例有效样本, PSA 标志物预测模型构建纳入了 1,284 例有效样本。本研究采用条件生成对抗网络 (Conditional Generative Adversarial Network, c-GAN) 对原始 CEA 和 PSA 训练数据进行数据增强处理。在模型迁移学习方面, 以基于 CA-125 数据集训练的多层感知器 (Multilayer Perceptron, MLP) 模型作为源模型, 将该模型在 CA-125 任务上预训练所得的参数加载至新的模型实例中。为保留原始特征提取能力, 冻结模型首个全连接层 (即输入层), 仅对后续层参数进行微调, 以适配 CEA 与 PSA 目标任务的特征差异。随后, 利用增强后的 CEA 与 PSA 训练集对模型进行微调优化, 并开展性能评估。预测因子包括人口学、生理健康状况、生活方式等指标。模型评价指标主要为工作特征曲线下面积 (AUC), AUC 大于 0.7 表示模型具有较好的分类能力。

结果: 研究表明, 应用 c-GAN 数据增强和迁移学习后, CEA 预测模型的 AUC 提升了 25.43% (从 AUC=54.07%提升到 AUC=79.50%), PSA 预测模型的 AUC 提升了 20.32% (从 AUC=56.61%提升到 AUC=76.93%)。

结论: 本研究所提出的基于迁移学习与数据增强的组合模型可以显著提升社区老年肿瘤标志物水平的预测准确性。

基金资助: 本研究获人工智能科研学科跃升计划项目 (A1-W25-301-0414) 资助。

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基于倾向性评分匹配法探索体质指数与高尿酸血症的关联

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【摘要】研究背景: 近年来, 高尿酸血症 (Hyperuricemia, HUA) 与肥胖在我国均呈高发态势, 成为威胁公共健康的重要问题。大量证据表明超重/肥胖显著增加 HUA 风险, 且二者协同加剧代谢紊乱。然而, BMI 与 HUA 之间具体的关联机制尚未明确, 且既往观察性研究易受混杂因素干扰, 难以确立可靠因果关联。

目的: 本研究旨在利用倾向性评分匹配法 (PSM) 控制混杂因素, 探索体检人群体质指数 (BMI) 与高尿酸血症 (HUA) 的关联。

方法: 回顾选取 2023 年 1 月-12 月于甘肃省某三甲医院体检中心进行体检且重要变量完整的 1305 名体检者作为研究对象, 收集其人口学资料及相关生化指标。将研究对象分为正常 BMI 组 ($BMI < 24 \text{ kg/m}^2$) 和高 BMI 组 ($BMI \geq 24 \text{ kg/m}^2$), 采用倾向性评分匹配法 (PSM) 对两组进行 1:1 匹配, 均衡潜在混杂因素, 通过单因素和多因素 Logistic 回归分析 BMI 与高尿酸血症的关联, 采用限制性立方样条 (RCS) 分析二者之间的剂量-反应关系, 进一步对 BMI 各亚组进行分层分析。

结果: 经 PSM 控制组间协变量后, 成功匹配 343 对, 两组协变量均衡性良好 (SMD 均 < 0.1)。匹配前后高 BMI 组与正常 BMI 组高尿酸血症的患病率差异均有统计学意义 ($30.3\% \text{ vs } 10.7\%$, $\chi^2=72.245$, $P<0.001$; $20.1\% \text{ vs } 14.3\%$, $\chi^2=4.094$, $P=0.043$)。PSM 后多因素 Logistic 回归显示, 高 BMI 组患 HUA 的风险是正常 BMI 组的 1.781 倍 (95%CI: 1.078~2.736, $P=0.023$)。RCS 分析表明 BMI 与 HUA 患病风险呈正相关, BMI 越高, HUA 患病风险越高, 二者之间不存在显著的非线性关联 (非线性 $P=0.725$)。分层分析结果显示, $BMI \geq 26 \text{ kg/m}^2$ (Q4 组) 显著增加 HUA 风险, 尤其在男性、 ≤ 50 岁及无慢性病人群中风险显著升高 ($P<0.05$)。

结论: 高 BMI 是 HUA 的独立危险因素, 且关联性在特定人群中更为显著。PSM 有效控制了混杂偏倚, 在体检人群中关注 BMI 水平对于预防和控制 HUA 具有重要意义, 建议通过体重管理降低 HUA 患病风险, 以此降低代谢性疾病负担, 改善群体健康水平。

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基于去中心化临床试验的纵向剂量-反应关系贝叶斯整合学习方法

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目的：去中心化临床试验（DCTs）将试验活动扩展到传统研究中心之外，提高了可及性、便利性、效率及结果外推性。这种方法尤其适用于糖尿病和肥胖等慢性病研究，因为这些疾病需要更长的研究周期来评估药物疗效。然而，去中心化的数据收集可能增加数据变异性和潜在偏倚风险。本文提出了一种新颖的贝叶斯集成学习方法，用于分析结合中心化与去中心化数据收集的 II 期 DCT 纵向数据中的剂量-效应关系。

方法：本文推广了参数化指数衰减模型以处理混合数据来源，并采用贝叶斯 spike-and-slab 先验来解决去中心化测量带来的偏倚和不确定性。该模型实现了中心化与去中心化数据源的自适应信息整合。

结果：数值研究表明，该模型展现出优异的估计精度和稳定性，且敏感性分析验证了不同试验场景下的稳健性。

结论：本文提出的模型实现了跨剂量水平和中心化/去中心化测量数据的自适应信息整合，当去中心化数据收集不引入额外变异性或误差时，本方法可达到与传统临床试验相当的效率。

关键词：去中心化临床试验 剂量 - 反应关系 数据整合 II 期试验 spike-and-slab 先验

基于全国健康追踪调查数据的疾病风险贝叶斯伪似然时空模型构建及应用：以 CHARLS 数据高血压为例

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【摘要】研究背景：疾病风险地图能直观展示疾病风险的时空分布，指导资源优化和政策评估。全国健康追踪调查数据为疾病风险制图提供了潜在应用价值，但其具有复杂抽样设计和失访特征。需联合考虑时间维度的横断面代表性和空间维度的模型区域估计准确性提供可靠的估计。

目的：基于全国健康追踪调查的复杂抽样与失访特征，计算横断面权重，构建贝叶斯伪似然时空模型，评估其不同抽样设计、失访率及失访类型下估计患病率的效果，并与样本加权法及普通贝叶斯模型比较。

方法：针对全国健康追踪调查的复杂抽样与失访特征，采用逆概率加权方法计算横断面权重，利用贝叶斯伪似然估计调整似然函数，结合权重与时空信息，构建贝叶斯伪似然时空模型。基于人口普查与 CHARLS 数据模拟动态人群，设置不同抽样设计（简单随机与复杂抽样）、失访率（0%-30%）及失访类型（完全随机、随机及非随机失访），生成全国健康追踪数据，绘制疾病风险地图，评估贝叶斯伪似然时空模型效果，并与样本加权法及普通时空模型比较。收集 2011-2020 年 CHARLS 及省级数据，构建贝叶斯伪似然时空模型，绘制中国高血压风险地图，通过全局和局部空间自相关分析识别高风险区域，指导资源分配。

结果：贝叶斯伪似然时空模型在简单随机抽样无失访数据下，MAE、MSE、RMSE 显著低于样本加权估计法，与普通时空模型相近；在复杂抽样数据中，其偏差显著低于两者，估计效果更优。贝叶斯伪似然时空模型在不同场景下，估计效果稳定，其余两种方法的偏差受影响的程度和方式存在差异。基于贝叶斯伪似然时空模型，2011-2020 年中国 45 岁及以上人群高血压患病率上升，呈北高南低特征，华北最高，华南最低。2011 年患病率中位数 28.55%-51.48%，2020 年为 40.64%-57.77%。

结论：本研究针对全国健康追踪调查的复杂抽样与失访特征，构建贝叶斯伪似然时空模型，模拟验证其不同抽样与失访场景下估计偏差小且稳定，优于传统方法；应用于中国健康与养老追踪调查数据，扩展伪似然模型应用。

基金资助：本研究获国家自然科学基金-面上基金项目资助（82073665）

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基于时间序列数据的山西省空气污染与流感传播 因果关系识别研究

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【摘要】 研究背景: 空气污染对流感传播具有显著影响, 其作用机制表现为动态耦合性、非线性特征、时滞效应及多维交互作用等复杂特性。这些因素使得传统统计关联方法难以有效区分真实关联与虚假依赖关系。

目的: 基于山西省空气污染与流感相关数据, 从因果关系角度探究空气污染物对流感传播的影响机制, 为制定科学合理的流感防控政策提供理论依据。

方法: 本研究利用中国疾病预防控制中心监测信息系统中 2014~2019 年山西省 11 个地市每日新增流感病例数据, 并结合中国高分辨率高质量近地表大气污染物数据集中的 PM_{2.5}、PM₁₀、SO₂、NO₂、O₃ 和 CO 污染数据, 探究空气污染与流感传播的关系。具体方法如下: (1) 对各城市流感发病与空气污染的时间序列数据进行 ADF 单位根检验, 确保序列平稳性; (2) 运用 Granger 因果关系检验构建向量自回归模型, 定性分析污染物与流感发病之间的因果关系; (3) 在经验动态建模的框架下, 放宽对模型及数据分布的假设, 将观测的时间序列进行流行重构并映射到高维相空间中, 基于相空间中的重构轨迹和局部邻域的收敛行为, 构建收敛交叉映射模型 (convergent cross mapping, CCM) 推断因果关系。

结果: 2014~2019 年间, 山西省共计报告流感病例 54096 例。基于 Granger 因果检验, 太原市 SO₂、NO₂ 和 CO 与流感传播之间存在显著的因果关系 ($F=2.217$, $P=0.007$; $F=2.657$, $P<0.001$; $F=1.989$, $P=0.006$)。进一步的 meta 分析结果显示, 11 个地市的 Fisher P 值合并后, PM_{2.5}、PM₁₀、SO₂、NO₂ 和 CO 与流感传播之间均存在显著的因果关系 ($P<0.05$)。收敛交叉映射分析显示, 太原市 SO₂ 和 O₃ 对流感传播具有正向因果效应, 滞后期为 14~20 天, Mann-Kendall 趋势检验的 z 值分别为 4.369 和 4.482 ($P<0.05$)。除阳泉外, 其他 10 个城市的收敛交叉映射模型均显示 SO₂ 与流感之间的正向因果效应。

结论: 本研究表明山西省空气污染物与流感传播之间存在正向因果关系。基于时间序列数据的因果关系挖掘有助于流感预测时间窗的前移, 对更深层次阐释疾病传播的本质机制以及指导靶向干预策略制定具有重要的科学价值。

基金资助: 本项目获山西省基础研究计划青年项目资助 (202403021222225)

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基于睡眠质量解锁领悟社会支持对大学生心理韧性赋能效应的关键密码

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【摘要】研究背景 随着经济发展, 当代大学生面临着多重压力, 导致心理问题(如焦虑、抑郁)发生率与严重程度双增。心理韧性(弹性)作为应对逆境的积极特质可缓冲压力损害。领悟社会支持能显著增强心理韧性。此外, 作为基础健康指标的睡眠质量对维持免疫系统功能及心理健康至关重要, 深入探讨睡眠质量的作用机制很有必要。

目的 探讨睡眠质量在大学生领悟社会支持与心理韧性间的中介作用, 为提升大学生心理韧性提供实证依据。

方法 本研究以山东省某高校 843 名大学生为样本, 采用一般资料调查表、领悟社会支持量表、心理韧性量表简表及匹兹堡睡眠质量指数量表进行问卷调查。通过 SPSS 27.0 进行 t 检验、单因素方差分析和偏相关分析, 利用 AMOS 26.0 构建结构方程模型, 通过 Bootstrap 法进行中介效应检验。

结果 研究对象领悟社会支持总分为 (67.70 ± 12.06) 分, 心理韧性总分为 (72.20 ± 15.21) 分, 匹兹堡睡眠质量总分为 (4.08 ± 2.83) 分, 大学生领悟社会支持与心理韧性呈正相关 ($r=0.59, P<0.01$), 与睡眠质量呈负相关 ($r=-0.36, P<0.01$), 心理韧性与睡眠质量呈负相关 ($r=-0.42, P<0.01$)。根据结构方程模型显示, 领悟社会支持对心理韧性的总效应值为 0.63, 占总效应的 82.54%, 睡眠质量在领悟社会支持与心理韧性之间的中介效应值为 0.11, 占总效应的 17.46%。

结论 睡眠质量是大学生领悟社会支持影响心理韧性的显著中介变量, 建议高校心理健康工作体系将睡眠健康纳入心理韧性培养框架, 同时构建家庭-学校-社会协同支持网络, 通过多维度干预提升学生心理复原力与生活品质。

本项目获医防融合视域下传染病医疗机构高质量发展路径研究问题、机制与策略 (YG2024A010)

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基于特征加权非负矩阵分解的多组学数据整合肿瘤分子分型

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目的: 本文创新性地提出了一种基于特征加权非负矩阵分解的相似网络融合方法 (Feature Weighted Non-negative Matrix Factorization based similarity network fusion, FNMF-SNF), 通过增强信号特征, 弱化噪音特征, 进而提高分型准确性, 并在肾乳头状细胞癌 (Kidney Renal Papillary Cell Carcinoma, KIRP) 的多组学数据中进行实证验证, 旨在为个体化治疗策略提供新的理论依据与方法支持。

方法: FNMF-SNF 方法首先结合癌组织与癌旁组织的生物学差异信息, 为不同组学的特征基因赋予差异化权重, 以增强关键特征信号。在加权后的组学数据基础上, 分别采用 NMF 进行降维, 提取潜在结构并获得每个组学的低维表达矩阵。随后, 利用 SNF 方法对各组学低维表达矩阵进行整合, 以识别潜在的肿瘤分子分型。同时, 通过模拟研究和实际数据分析验证 FNMF-SNF 的性能, 同时, 构建了九种机器学习分类模型 (GA-fKPLS、Logistic 回归、LASSO、RF、SVM、NN、KNN 和 NB) 以评估其在 KIRP 亚型预测中的性能

结果: 模拟研究结果表明, FNMF-SNF 在不同噪声水平和信号比例下均展现出优异的性能, 归一化互信息 (Normalized Mutual Information, NMI) 值显著优于现有的多组学数据整合方法。在实际数据分析中, FNMF-SNF 能够有效识别出不同肿瘤的分子亚型, 并显著区分不同亚型患者的生存差异。基于分型结果, 进一步筛选出多个与预后相关的差异基因、通路活性及免疫细胞浸润特征、构建并验证了预后模型, 揭示了不同肿瘤亚型的分子生物学机制。

结论: 本文提出的 FNMF-SNF 方法在多组学数据整合分型中展现了较高的准确性, 能够有效识别肿瘤的分子亚型。这些方法为肿瘤患者的精准诊疗、精准预后判断以及早期干预提供了重要的依据。此外, 通过分型结果筛选出的潜在生物标志物和信号通路, 不仅为揭示肿瘤的分子机制提供了重要线索, 也为临床肿瘤精准治疗策略的制定提供了参考。

关键词: 多组学数据整合

基于西北自然人群队列探索睡眠行为与抑郁症的关联

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【摘要】

研究背景: 抑郁症是一种常见的慢性精神障碍, 严重影响个体的情绪状态和日常功能, 其发生发展受多重因素影响, 而睡眠行为发挥重要作用, 但目前西北地区缺乏数据支持证明二者之间的关联。

目的: 了解西北五省成年人睡眠行为, 分析其与抑郁症患病风险的关联并探索相关因素在睡眠行为与抑郁症之间可能存在的中介作用。

方法: 本研究基于“西北区域自然人群队列”2017—2019 年基线数据, 探讨睡眠行为与抑郁症患病风险的关系。以睡眠行为为暴露变量, 由问卷调查得出; 以抑郁症患病情况为结局变量, 由研究对象自报告是否经区级及以上医院医生诊断为抑郁症; 协变量包括人口学特征、生活方式及健康相关因素, 通过问卷搜集获得。计量资料以均值 (标准差) 描述, 计数资料以频数 (百分比) 描述。利用 Firth 修正的 Logistic 回归模型评估睡眠行为与抑郁症患病的关联, 并通过基于因果推断的中介分析和结构方程模型探讨日间功能障碍的中介作用及睡眠行为与抑郁症的路径关系。所有分析使用 R 4.4.2 完成, 双侧检验, 显著性水平为 0.05。

结果: 本研究纳入符合条件的研究对象 130233 人, 年龄为 52.60 (13.90) 岁, 女性占 60.04%。基线报告共有 501 人患有抑郁症, 患病率为 0.38%。Logistic 回归分析显示, 校正人口学特征及行为方式后, 睡眠评分每增加 1 分, 抑郁症患病风险下降 40% ($P < 0.001$)。总睡眠时长 $< 7h$ ($OR=1.53$, 95%CI: 1.25 – 1.87)、夜间睡眠时长 $< 7h$ ($OR=1.61$, 95%CI: 1.32 – 1.95) 及存在睡眠问题 ($OR=2.01$, 95%CI: 1.41 – 2.9) 均与抑郁症患病风险升高显著相关 ($P < 0.001$)。中介分析发现, 除睡眠时长 ($< 7h$) 外, 日间功能障碍在睡眠行为和抑郁症患病的关联中起到了部分中介作用。路径分析进一步发现日间功能障碍对抑郁症患病有直接影响 ($\beta=0.220$)。

结论: 本研究发现, 短时总睡眠、夜间睡眠不足及睡眠问题均显著增加抑郁症患病风险, 且日间功能障碍起部分中介作用。结果提示, 改善睡眠质量和时长有助于抑郁症的预防与干预。

基金资助: 本项目获国家自然科学基金 (资助号: 82103944)、国家重点研发计划 (项目编号: 2017YFC0907200, 2017YFC0907201)、陕西省科技资源开放共享平台 (资助号: 2023-CX-PT-47) 资助

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基于血浆生物标志物与代谢组学的可解释机器学习方法在 脑梗死预测与风险分层中的应用研究

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【摘要】研究背景:

脑梗死 (CI) 是影响人类健康的一种随着衰老而增加的重大疾病。传统的风险模型主要基于已确定的风险因素, 通常缺乏准确预测新发脑梗死的精度。本研究旨在通过将传统风险因素、生物标志物和代谢组学相结合来改进预测和风险分层。

目的:

1. 比较脑梗死和非脑梗死患者的临床变量、生物标志物、代谢组学的差异。
2. 确定脑梗死患者的独立预测因子。开发一个基于独立危险因素的预测模型, 以识别脑梗死高危人群。

方法:

本研究使用来自英国生物样本库 (UK Biobank) 的临床生物标志物和代谢组学数据。采用 XGBoost 算法、Lasso-cox 回归和随机生存森林 (Random Survival Forests, RSF) 三种机器学习算法来筛选影响脑梗死发生的关键预测变量, 同时采用 Cox 比例风险模型来评估传统风险因素和生物标志物的组合预测性能。通过计算每个参与者的生物标志物风险评分 (BRS), 进行疾病的风险预测和分层。

结果:

与传统模型 (例如年龄 + 性别和 ASCVD) 相比, PANEL+RSF BIO+XGB NMR 的组合表明, 在所有终点的判别性能均显著改善。BRS 将个体分为低、中、高风险组, 其中高危组的发病率为 3.20%, 低危组的发病率为 0.18%。

结论:

整合传统的危险因素、生物标志物和代谢组学可以提高新发脑梗死的预测和风险分层。BRS 有望作为识别高危个体的工具, 有可能支持个性化的脑梗死预防和管理策略。

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基于医学决定水平的定量一致性评价样本量公式研制

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目的：构建并验证基于医学决定水平（MDL）处预期偏倚的样本量计算公式，以用于定量一致性评估的样本量计算

方法：应用最小二乘回归原理，本研究获得基于 MDL 处预期偏倚的样本量计算公式。同时，使用实例数据和 Bootstrap 模拟验证公式的准确性和稳健性，并与基于回归系数与截距的定量一致性样本量公式计算结果进行对比

结果：基于 MDL 进行样本量公式推导，得到公式：

$$n = \left[\frac{\left(t_{\left(n-2 \right), 1-\frac{\alpha}{2}} + t_{\left(n-2 \right), 1-\frac{\beta}{2}} \right) s_{yx}}{\left(b_0 + \left(b_1 - 1 \right) \cdot x_c + \Delta \right) \cdot s_x} \right]^2 \cdot \left[\left(s_x \right)^2 + \left(x_c - \bar{x} \right)^2 \right]$$
 通过实例数据结果可知，MDL 法样本量公式与回归法样本量公式计算得到的样本量近似一致，用这两种公式的计算结果（121/139 例样本）分别进行 MDL 分析和回归分析验证，均能得到满足定量一致性的结论且 Bootstrap 模拟验证均可得到 90% 以上的检验效能

结论：本研究首次将 MDL 与最小二乘回归融合，构建定量一致性评价的样本量公式，为该领域提供了新的样本量计算方法，增强了该领域的研究理论基础。

关键词：定量一致性评价

基于因果森林的睡眠时长与代谢综合征风险异质性研究

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【摘要】研究背景: 代谢综合征(Metabolic Syndrome, MetS)是全球范围内高发的代谢性疾病, 其发病与生活方式密切相关。根据美国国家健康和营养检查调查(NHANES)显示 2017-2018 年美国成年人 MetS 的患病率约 41.8%。睡眠时长与 MetS 风险相关, 现有研究结论存在的差异化风险特征, 尚未得到系统评估。

目的: 本研究旨在基于因果森林(Causal Forest)方法, 评估不同睡眠时长对 MetS 患病风险的关联, 并识别存在显著异质性的高风险人群。

方法: 本研究选取 2015 – 2018 年共 10,635 名年龄大于 20 岁的成年人。睡眠时长根据参与者自报工作日的平均入睡时间和起床时间计算。MetS 的定义基于美国国家胆固醇教育计划成人治疗小组 III(NCEP ATP III)。首先利用限制性立方样条分析探索睡眠时长与 MetS 发生率之间的非线性关联, 对睡眠时长进行分组; 接着采用诚实因果森林模型, 估计各组的平均处理效应(ATE)及根据个体异质效应(CATE)进行识别亚组; 最终通过 Logistic 模型评价亚组的风险差异。

结果: 睡眠时长与 MetS 呈“U 型”关系, 分为短睡眠组(<6h, n=1,026), 正常睡眠组(6 – 9h, n=8,346)与长睡眠组(>9h, n=1,263)。在诚实因果森林模型中, 短睡眠相较于正常睡眠的 ATE 为 0.021(SE=0.009), 长睡眠相较于正常睡眠的 ATE 为 0.012(SE=0.037)。最佳分裂树根据性别和年龄, 吸烟和饮酒行为特征识别出 12 个亚组, 在年龄>60 岁的男性人群中, 短睡眠相较于正常睡眠 OR(95%CI)为 0.46(0.24-0.85), 在年龄≤47 岁的女性人群中, 长睡眠相较于正常睡眠 OR(95%CI)为 0.58(0.35-0.94), 在饮酒且非吸烟人群中短睡眠相较于正常睡眠 OR(95%CI)为 1.69(1.01-2.83), 长睡眠较于正常睡眠 OR(95%CI)为 0.52(0.26-1.06)。

结论: 本研究首次应用诚实因果森林模型系统评估了睡眠时长对代谢综合征的影响及其在不同人群的异质性。短睡眠对饮酒且非吸烟人群的代谢风险影响显著, 短睡眠在老年男性人群和长睡眠在年轻女性群体中具有保护作用。提示代谢疾病防控需个性化睡眠建议。

基金资助: 无

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基于英国生物银行数据库的中老年人衰弱蛋白质风险评分 预测模型构建及验证研究

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【摘要】研究背景: 衰弱作为老年综合征核心表型, 与失能、跌倒及死亡风险密切相关。传统衰弱评估工具依赖已外显临床表征, 缺乏早期预警能力。蛋白质表达谱改变往往先于临床症状, 为衰弱早期预测提供了新的生物标志物窗口。

目的: 基于大规模前瞻性队列血浆蛋白质组学数据, 系统筛选与衰弱发生相关的血浆蛋白质标志物, 构建整合蛋白质风险评分和临床因素的中老年人衰弱预测模型, 实现衰弱风险精准预警。

方法: 基于英国生物银行 (UK Biobank, UKB) 前瞻性队列, 纳入 6,491 名基线无衰弱的中老年人 (年龄 56.0 ± 6.0 岁), 采用 Rockwood 衰弱指数 ($FI \geq 0.2$) 评估衰弱状态。利用 UKB 2,920 种血浆蛋白质数据, 结合单变量 Cox 回归和 LASSO-Cox 算法筛选关键蛋白, 构建线性加权蛋白质风险评分。采用 7:3 比例将研究对象随机划分训练集 ($n=4,544$) 和验证集 ($n=1,947$), 分别建立临床基础模型 (年龄、性别等 8 个预测因子)、蛋白质风险评分模型及联合预测模型。通过时间依赖性 ROC 曲线评估 5 年、10 年和 15 年预测效能, 并用校准曲线验证预测准确性。

结果: 中位随访 10.2 年期间, 观察到 522 例新发衰弱事件。系统筛选鉴定出 366 种与衰弱显著相关的蛋白质 (304 种风险蛋白, 62 种保护性蛋白), 最终 21 种蛋白质 (包括 ADM、BST2、CA14 等) 构建风险评分。联合模型在 10 年预测中表现最优: 训练集 AUC 达 0.723 (95%CI:0.688-0.762), 显著优于单纯临床模型 (AUC=0.661) 和蛋白质评分模型 (AUC=0.719); 验证集中联合模型 AUC 为 0.701 (95%CI:0.625-0.764), 仍优于其他模型。中期预测 (5-10 年) 为最佳预测窗口, 长期预测 (15 年) 各模型效能均下降 (AUC 范围: 0.589-0.669)。所有模型校准曲线均贴近对角线, 显示良好的预测-实际风险一致性。

结论: 本研究成功构建并验证了整合蛋白质组学特征的中老年人衰弱预测模型, 联合模型在中期 (10 年) 预测中展现最佳性能, 显著优于传统临床模型。创新性地 21 种血浆蛋白质整合为风险评分, 实现了生物标志物从相关性研究向预测应用的转化。该模型为衰弱早期识别提供了精准工具, 有助于识别高危人群并

实施靶向干预，对推进健康老龄化战略具有重要意义。

基金资助：本项目获新疆医科大学 2022 年博士科研启动基金资助。

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基于有效样本量的贝叶斯篮式试验设计研究

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目的：在篮式试验中利用贝叶斯方法跨肿瘤类型借用信息受到广泛关注。然而，目前尚无公认的在该场景下量化信息借用程度的解决方案，这给非统计学家理解此复杂设计带来了巨大挑战。本文旨在探索有效样本量（ESS）在篮式试验设计中的应用，以提升其可解释性。

方法：将 ESS 工具应用于贝叶斯篮式试验，并提出了几种基于 ESS 的信息借用策略。选择了均方误差（MSE）作为推导 ESS 的目标指标，因其明确权衡了估计偏差与方差减少的平衡。通过对 RAGNAR 研究的重新分析及模拟研究，展示了 ESS 在篮子试验分析和设计阶段的可解释性。此外，还开发了一个用户友好的桌面软件以方便 ESS 的计算。

结果：ESS 反映了信息借用对 MSE 的影响，并直观地刻画了借用程度。其与 I 类错误率和统计功效等指标可相互补充，有一定的应用价值。

结论：通过 ESS 量化信息借用程度，可极大帮助研究者设计贝叶斯篮式试验、合理评估和解释贝叶斯分析结果、进行敏感性分析，并最终在试验中借用可接受的信息量。

关键词：篮式试验设计

基于中国社区居民 MASLD 的 26 种非侵入式指标的 开发与评估

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【摘要】研究背景：代谢功能障碍相关脂肪性肝病(MASLD)逐渐成为世界范围内普遍的慢性疾病。非侵入式评价指标在 MASLD 的预测识别中扮演重要角色，但多种指标在中国社区居民中的表现仍待进一步评估，因此本研究基于 BMI、Waist、CVAI、VAI、BRI、WHR、C-index、RFM、LAP、AVI、ABSI、WHtR、BAI、DAAT 14 种肥胖相关指标，CMI、AIP、TyG、TyG-BMI、TyG-WC、TyG-WHR、TyG-WHtR 7 种心脏代谢指标，HOMA-IR、eDGR、METS-IR 3 种胰岛素抵抗指标，FLI、ZJU 2 种肝相关指数综合比较 26 种非侵入式指标对中国社区居民 MASLD 的识别能力，从而确定最佳识别因子。

目的：基于 26 种非侵入式的综合指标，确定中国社区居民 MASLD 的最佳识别因子，助力中国社区居民 MASLD 筛查。

方法：数据来源于中国居民肝脏健康促进项目海州区、盐都区项目 3617 名参与者。通过受控衰减参数诊断脂肪肝，同时脂肪肝 + 其中之一(超重/肥胖(BMI>23)、血糖异常、TG 异常、HDL 异常、高血压异常)进一步诊断 MASLD。通过构建加权 Logistic 回归探讨 26 种指标与 MASLD 的关联，采用受试者工作特征曲线下面积(AUC)评估指标的价值。并通过年龄、性别的亚组探讨指标的不同人群中的表现。

结果：研究纳入 3617 位对象，其中男性 1741 人，女性 1876 人。MASLD 的患病率为 46.45%，男性(52.61%)高于女性(40.72%)($P<0.05$)，45-65 岁(49.12%)>65 岁以上(46.42%)>18-45 岁(43.06%)($P<0.05$)。在全人群中指标曲线下面积为：ZJU(0.832)，TyG-BMI(0.829)，FLI(0.823)，METS-IR(0.817)，TyG-WC(0.808)，TyG-WHtR(0.802)，AIP，AVI，BMI，BRI，CMI，CVAI，HOMA-IR，LAP，TYG，TyG-WHR，VAI，Waist，WHtR，eDGR 该 20 个指标均 >0.70 ，除 FLI 外，其他指标在调整年龄、性别、吸烟、饮酒、睡眠等协变量后模型性能均有不同程度的提升。在性别分层中，ZJU 在男性(0.820)、女性(0.842)中的表现均为最佳，除 ABSI 外，其他指标在女性中的表现均优于男性。在年龄分层中，ZJU 在 18-45 岁(0.875)、45-65 岁(0.810)、65 岁以上(0.773)的表现均为最佳。在男性、女性、18-45 岁、45-65 岁居民中前 5 位指标均为 ZJU、TyG-BMI、FLI、METS-IR、TyG-WC，在 65 岁以上居民中排名前 5 位的指标为 ZJU、TyG-BMI、CVAI、FLI、

METS-IR。无论是全人群还是亚组中 ZJU、TyG-BMI、CVAI、FLI、METS-IR、TyG-WHtR、TyG-WC、LAP、BMI、CMI、TyG、HOMA-IR、VAI 的 AUC 均超过 0.7。

结论：针对中国社区居民 ZJU、TyG-BMI、CVAI、FLI、METS-IR、TyG-WHtR、TyG-WC、LAP、BMI、CMI、TyG、HOMA-IR、VAI 均是识别 MASLD 的重要指标。相比之下，ZJU 在全人群及亚组人群中的表现性能最佳。

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基于纵向项目反应理论-双重差分模型的农村社区老年人 失能（失智）干预效果评价

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【摘要】研究背景：全球老龄化进程加速，老年人失能（失智）问题对家庭照护与公共卫生系统构成严峻挑战。认知-运动联合干预被证实可有效延缓失能（失智）进程。我们在晋江市（全国老年人失能（失智）预防干预项目试点）选取4个农村社区，筛选60岁及以上失能（失智）高危老年人，对其进行为期12个月的“健康教育+认知训练+八段锦”联合干预。评估干预效果，对进一步优化和完善农村社区老年人失能（失智）干预方案，提升农村老年人健康水平具有重要意义。

目的：评估“健康教育+认知训练+八段锦”联合干预的效果。

方法：以60岁及以上失能（失智）高危老年人为对象，以参与干预次数 ≥ 18 次（干预总次数为24次）为干预组，未参与干预活动为对照组。分别于干预开始前及开始后3、6、9、12个月收集老年人的社会人口学特征、简易智力状态检查（Mini Mental State Examination, MMSE）、日常生活活动能力（Activities of Daily Living, ADL）、活动能力测试（Short Physical Performance Battery, SPPB）、老年抑郁量表（Geriatric Depression Scale-15, GDS-15）等数据，其中，MMSE、SPPB量表中分数越高，功能越好；ADL、GDS-15量表中分数越高，功能越差。采用纵向项目反应理论（Longitudinal Item Response Theory, LIRT）拟合受试者MMSE、ADL、SPPB及GDS-15评分（参数估计采用马尔可夫链蒙特卡洛估计），并纳入有协变量的双重差分模型（Difference-in-Differences, DID）分析干预组与对照组在第3、6、9、12个月相较于各自基线变化量的差值（净增量）。

结果：共纳入136名老年人，其中干预组62名，对照组74名。LIRT拟合较好（密度图、自相关图、运行均值图、轨迹图等详见附件）。有协变量的DID模型结果：MMSE在干预第3、6、9、12个月时净增量分别为3.11（ $P=0.087$ ）、4.95（ $P=0.008$ ）、6.79（ $P=0.001$ ）、8.63（ $P<0.001$ ），ADL在干预第3、6、9、12个月时净增量分别为-3.76（ $P=0.040$ ）、-6.48（ $P=0.002$ ）、-9.20（ $P<0.001$ ）、-11.92（ $P<0.001$ ），SPPB在干预第3、6、9、12个月时净增量分别为2.35（ $P=0.343$ ）、3.91（ $P=0.127$ ）、5.47（ $P=0.041$ ）、7.02（ $P=0.011$ ）。GDS-15在干预第3、6、9、12个月时净增量分别为2.01（ $P=0.305$ ）、1.02（ $P=0.633$ ）、0.02（ $P=0.992$ ）、-0.97（ $P=0.707$ ）。

结论: LIRT 和 DID 相结合可精准评价社区干预项目效果, “健康教育+认知训练+八段锦”联合干预可有效改善农村高危老年人认知及躯体功能。

基金资助: 本项目获中国国家重点研发计划基金资助 (项目编号: 2022YFC3603000)

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家庭支持影响育龄期女性生育意愿的路径分析—基于养育焦虑的中介效应

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【摘要】研究背景：低生育率已成为我国人口发展面临的最为紧迫的挑战，若该趋势继续严重化，我国的少子化现象将会更加普遍，人口代际更替水准下降，人口结构将朝着倒金字塔型方向发展。本研究通过结构方程模型及 Bootstrap 检验，探讨了养育焦虑、生育焦虑在家庭支持、新媒体接触与生育意愿之间的中介效应，为解析生育意愿的影响路径提供了理论依据。

目的：本研究旨在深入探讨在生育友好型社会目标框架下，山东省某市育龄女性的生育意愿、生育焦虑以及养育压力的现状。

方法：本研究调查对象的选取面向山东省某市的 20-40 岁女性，以家庭支持为自变量、生育意愿为因变量、养育焦虑为中介变量，纳入年龄、家庭所在地等控制变量采用 Process 程序来分析养育焦虑在家庭支持和女性生育意愿间的中介效应。

结果：家庭支持对生育意愿的总效应值为 0.04，直接效应值为 0.03，即家庭支持每增加 1 单位，生育意愿直接提升 0.03 单位。养育焦虑的中介效应值为 0.01，占总效应的 25% (95% CI: 0.01~0.02)，表明家庭支持可通过降低养育焦虑间接提升生育意愿，如家庭支持每增加 1 单位，养育焦虑降低 0.28 单位，进而使生育意愿提升 0.01 单位。

结论：养育焦虑在家庭支持和生育意愿间存在部分中介作用。家庭支持对生育意愿的影响部分通过缓解养育焦虑实现，家庭支持越充分，女性的养育焦虑越低，生育意愿越高。

基金项目：本项目获潍坊医学院 2023 年研究生课程思政示范课程立项—医学社会科学研究方法 (23YKCSZSF10)

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结合宏基因组学和代谢组学鉴别上消化道肿瘤及癌前病变

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【摘要】研究背景：上消化道癌（UGIC）是我国高发恶性肿瘤之一，其发生遵循“正常黏膜→低级别上皮内瘤变（LGIN）→高级别上皮内瘤变（HGIN）→癌症”演变路径，早期识别癌前病变至关重要。然而，当前筛查依赖侵入性内镜活检，亟需无创生物标志物。口腔菌群及代谢物与上消化道微生态密切相关，微生物失调和代谢异常参与肿瘤发生，但其在 UGIC 癌前病变阶段的跨组学关联及诊断价值尚未明确。

目的：本研究通过整合唾液宏基因组学和唾液/血浆代谢组学，筛选 UGIC 及癌前病变（LGIN/HGIN）的关键生物标志物，构建多组学诊断模型并验证其鉴别效能。

方法：本研究纳入山东省多中心消化道肿瘤队列 2024 年上消化道筛查人群，经内镜和病理诊断后，通过倾向得分匹配筛选健康对照（HC）、LGIN、HGIN、UGIC 各 105 例进行非靶向代谢组和宏基因组检测。运用置换多元方差分析进行各组学变异分解，代谢组数据通过广义线性回归校正混杂因素筛选差异代谢物；宏基因组学分析包括群落多样性评估、MaAsLin2 差异菌种鉴定以及 KO 基因通路富集分析。最后，应用稀疏典型相关分析（sparseCCA）和相关性分析整合多组学数据以构建多组学诊断模型。

结果：代谢组分析共鉴定出 82 个血浆差异代谢物和 156 个唾液差异代谢物，主要涉及脂肪酰基、羧酸及类固醇代谢，并随病变进展呈现“先富集后耗竭”的动态模式。宏基因组分析显示病例组微生物 Alpha 多样性显著低于 HC 组（Shannon 指数, $P < 0.001$ ）。病例组富集了具核梭杆菌、牙龈卟啉单胞菌等牙周致病菌；KO 基因通路分析提示氨基酸和脂质代谢通路异常。基于唾液代谢物和微生物标志物构建的多组学模型在区分 HC 与 UGIC 时表现出色（AUC = 0.89, 95% CI: 0.83-0.94），其诊断效能优于单一组学模型。该模型对 HGIN/UGIC 的鉴别效能亦达 AUC = 0.85。

结论：口腔菌群失调与代谢异常在上消化道癌前病变至癌阶段协同变化，多组学模型可有效区分不同病变阶段，为无创筛查提供新策略。

基金资助：本研究获国家自然科学基金资助（82222064，82473730）

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结核病患者治疗相关心理负担的影响因素及其因果路径 分析—基于混合效应模型与结构方程模型

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【摘要】研究背景: 结核病是全球致死率最高的单一传染病, 易引发较重的心理负担, 从而降低治疗依从性、恶化病情。患者心理负担受多重因素影响, 包括家庭功能、社会支持、疾病认知及治疗依从性等。新疆南疆四地州结核病高发, 心理负担问题尤为突出。

目的: 分析结核病患者治疗相关心理负担的影响因素及其因果路径, 以探讨模型拟合效果及方法学可行性, 为制定精准化心理负担干预策略提供方法学依据和证据支持。

方法: 研究采用分层整群随机抽样方法, 抽取南疆四地州 8 个县区的结核病患者进行问卷调查; 构建混合效应模型探索心理负担的影响因素; 采用结构方程模型, 探索家庭功能、家庭支持、满意度与患者治疗相关心理负担之间的因果路径, 同时检验患者服药依从性的中介效应。

结果: 本研究共收集有效数据 1483 例, 其中女性 770 人, 占 51.9 %。两水平 logistic 回归模型拟合优度最好, 作为最终模型。文化程度、疾病认知、家庭支持、依从性及满意度是心理负担的显著影响因素, 支持研究假设 1。结构方程模型结果显示, 加入中介变量后, 模型的拟合度提升。家庭功能和满意度对心理负担具有正向的直接效应, 满意度影响心理负担的直接效应为 0.350, 间接效应为 0.017, 中介效应占总效应的比例为 4.62%。家庭支持和家庭功能影响心理负担的直接效应分别为-0.096、0.117, 间接效应分别为-0.001、0.003, 完全通过服药依从性影响结核病患者心理负担, 支持假设 2。

结论: 治疗相关心理负担受多因素影响, 应针对性进行干预; 混合效应模型和结构方程模型协同应用证实了核心变量的稳健影响, 均证实了研究假设, 具有应用价值。

基金资助: 本项目获国家自然科学基金资助 (82460669)

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结核病治疗方案对预防复发的疗效和安全性:

一项系统综述和网状 Meta 分析

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【摘要】研究背景: 尽管世界卫生组织推荐了结核病治疗的标准方案, 但是临床实践及研究中仍在探索更有效的改进治疗方案, 但其长期疗效与安全性的质量比较证据仍较为有限。

目的: 本研究拟评估多种结核病改进治疗方案与 WHO 推荐的标准治疗方案的有效性与安全性。

方法: 我们注册了一项系统综述和网状 meta 分析 (PROSPERO CRD42024605512), 并检索了 PubMed/MEDLINE, Embase, OVID, EBSCOhost, and Cochrane CENTRAL 等医学数据库从开始到 2024 年 2 月发表的关于结核病治疗方案对有效性和安全性的评估文献。结局指标包括复发率、治疗成功率、治疗中断、副反应和死亡。我们使用 Bayesian 和频率法随机效应模型进行分析。证据的确定性采用 CINeMA 评估。

结果: 我们从数据库检索了 31,706 条记录并从参考文献获得 214 条记录, 经筛选纳入 63 个随机对照试验 (n=48,916), 包括了共 30 种治疗方案。研究发现含二线治疗药物与强化一线药物的长疗程治疗方案 (D_r/S/I) 相较于 WHO 标准方案, 显著降低复发风险 (风险比 RR=0.14, 95% CI 0.07-0.30; 累积排序曲线下面积 SUCRA=0.965), 但治疗中断的风险增高 (RR=8.52, 95% CI 4.14-17.64)。所有的短疗程治疗方案有效性都低于 WHO 标准治疗方案, 复发风险在 1.8 (1.03-3.14) 至 4.54 (2.30-8.74) 之间。固定剂量复方 (FDCs) 方案复发风险最高, RR 范围 2.39 (1.42-4.01) 至 12.63 (6.25-23.91)。WHO 标准治疗方案在综合疗效与安全性评估中仍居前列 (SUCRA=0.576)。

结论: 本研究表明, D_r/S/I 方案可显著降低结核病复发风险, 但需关注患者依从性与安全性挑战。缩短疗程方案与 FDC 方案疗效欠佳, 而 WHO 标准治疗方案在疗效与安全性间保持较优的平衡。

基金资助：本项目获国家自然科学基金 NO.81703319, 71804029, 广州市基础与应用基础研究一般项目 NO.2023A04J0539 基金资助, 广东省医学科研项目基金 NO. B2025312

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咖啡摄入与肝纤维化替代指标 (LSM) 的负向关联： 一项基于中国多地域人群的横断面研究

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【摘要】研究背景：咖啡现已成为全球广泛消费的饮品，近年来中国人群的咖啡消费规模亦呈扩大趋势。国外研究提示咖啡摄入对肝病的发生与发展可能具有保护作用。然而，针对中国人群咖啡摄入与肝脏相关疾病（尤其是肝纤维化）关联的研究相对有限，相关的流行病学证据仍显不足。

目的：探讨咖啡摄入与肝脏硬度测定值 (Liver Stiffness Measurement, LSM) 之间的关联性，并评估腰围在此关联中的潜在中介效应。

方法：采用横断面研究设计，纳入中国连云港海州区、盐城盐都区、十堰市茅箭区及临汾蒲县四个地区 7016 名 18 岁及以上社区居民。通过调查问卷收集咖啡摄入状况、疾病史等信息，进行体格测量（包括腰围），并使用瞬时弹性成像 (Transient Elastography, TE) 技术测定 LSM。主要结局指标为经对数转换的 LSM 值 (log-LSM)。调整的协变量包括年龄、性别、腰围、体质指数 (BMI)、II 型糖尿病史等。分别构建以腰围和 log-LSM 为因变量的多变量线性回归模型，调整相关协变量。在此基础上，应用 Bootstrap 法 (1000 次重复抽样) 建立中介效应分析框架，探究腰围在咖啡摄入与结局变量 log-LSM 间可能的中介作用。

结果：在 7016 名参与者中，咖啡摄入者与非摄入者的 LSM 均值 ($\pm$ 标准差) 分别为 4.95 ± 1.41 和 5.01 ± 1.55 ($p=0.25$)。以 log-LSM 为因变量的回归模型显示，年龄分组与咖啡摄入状况存在显著的交互作用 ($\beta = -0.055$, $p<0.01$)。针对 ≥ 40 岁人群的分层分析结果显示：在以腰围为因变量的模型中，咖啡摄入 (参照组：非摄入者) 的回归系数 $\beta = -0.799$ ($p<0.05$)，提示咖啡摄入与较小腰围相关；在以 log-LSM 为因变量的模型中，腰围的回归系数 $\beta = 0.0042$ ($p<0.001$)，提示腰围增加与 log-LSM 升高相关。Bootstrap 中介效应分析显示：平均因果中介效应 (Average Causal Mediation Effect, ACME) 为 -0.0034 ($p<0.01$)，总效应 (Total Effect) 为 -0.0207 ($p=0.12$)。该结果与总人群分析中观察到的“年龄-咖啡摄入交互作用”高度一致。

结论：本研究发现在 ≥ 40 岁人群中，咖啡摄入与较小的腰围显著负相关，而腰围与较高的 log-LSM 显著正相关。中介效应检验提示，咖啡摄入可能通过降低腰围而降低 log-LSM (即降低肝脏硬度值)，从而为减少该人群肝纤维化风险提供了潜在作用路径。

可解释性机器学习在挥发性有机化合物和抑郁症关系的应用研究

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【摘要】研究背景: 挥发性有机化合物(volatile organic compounds, VOCs)广泛存在于环境中, 是造成大气污染的重要物质, 其长期暴露还可能与心理健康问题, 包括抑郁症等精神疾病紧密相关。

目的: 探讨挥发性有机化合物代谢物(metabolites of volatile organic compounds, mVOCs)与抑郁症的潜在关联机制。并基于可解释性机器学习方法分析 mVOCs 在抑郁症发病机制中的作用, 评估其作为潜在生物标志物的应用价值。

方法: 本研究从 2015—2016 年的 NHANES 数据库中提取了关于成年人基本信息、抑郁症状状态及多种 mVOCs 等变量, 采用加权分位数和(Weighted Quantile Sum, WQS)回归模型计算 mVOCs 权重, 将数据中 60% 作为训练集验证指数稳定性, 生成变量权重图。同步应用贝叶斯核机器回归 (Bayesian Kernel Machine Regression, BKMR) 模型来估计 mVOCs 与抑郁症间的关系。并结合变量效应图和交互作用图可视化剂量-反应关系及代谢物间相互作用。

结果: 研究共纳入 1108 名研究对象, 其中 96 名抑郁症患者, 女性占比 57.3%。通过 Lasso 回归筛选出 7 种与抑郁症相关的 mVOCs 指标。WQS 回归结果显示, mVOCs 的加权指数 wqs 与抑郁症发生风险呈正相关 (OR=1.837, 95%CI:1.129-2.990, P<0.001)。由变量权重图可知, 在 7 种 mVOCs 中, 2-羟乙基-L-半胱氨酸和 1-和 2-苯基-2-羟乙基-L-半胱氨酸对 WQS 指数的贡献度最高, 表明它们在抑郁症发生中具有重要作用。BKMR 模型结果显示, 2-氰乙基-L-半胱氨酸 (PIPs=0.5416) 和 2-羟乙基-L-半胱氨酸 (PIPs=0.6048) 对抑郁症风险的预测贡献较高。由总体效应图可知, 随着 mVOCs 暴露水平的增加, 抑郁症患病风险呈现上升趋势。此外, BKMR 模型还揭示了不同 mVOCs 之间复杂的暴露-反应关系, 由双变量暴露-效应函数图可知, 2-氰乙基-L-半胱氨酸与正丙基-L-半胱氨酸呈负向交互作用, 说明两者在高浓度暴露下可能发生拮抗作用, 从而调节抑郁症的发生风险。

结论: mVOCs 混合暴露可能增加患抑郁症的风险, 其中 2-羟乙基-L-半胱氨酸和 1-和 2-苯基-2-羟乙基-L-半胱氨酸在抑郁症发病机制中可能发挥重要作用。随着 mVOCs 暴露水平的增加, 抑郁症发生风险上升, 并且不同 mVOCs 之间存在复

杂的交互作用，这些发现为抑郁症的早期筛查和干预提供了潜在的生物标志物。

*基金资助：本项目获国家自然科学基金(82003560)、山东省自然科学基金(ZR2020MH340, ZR2023MH313)资助

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空气污染对焦虑障碍就诊的短期效应： 一项时间序列分析

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【摘要】研究背景：全球焦虑障碍的疾病负担日益加重，但关于空气污染对焦虑障碍就诊的短期影响的研究结论尚不一致。

目的：本研究旨在评估短期暴露于环境空气污染物，包括细颗粒物（PM_{2.5}）、可吸入颗粒物（PM₁₀）、二氧化氮、一氧化碳、二氧化硫和臭氧，与焦虑障碍每日就诊风险的关联。

方法：空气污染物数据来自中国空气质量在线检测分析平台。焦虑障碍患者就医数据来自广东省某市医保结算数据。气象因素数据来自国家气象科学数据中心。本研究采用广义加性模型进行时间序列分析，来探索空气污染物短期暴露对焦虑障碍就医的影响，其中短期暴露根据就诊当天及前7天内的污染物水平进行评估。通过单日滞后模型和移动平均滞后模型探究污染物的滞后效应。将每日患者人数与空气污染物、气象因素按时间序列进行整理，建立数据库。利用自然平滑样条函数拟合非线性连续变量。利用广义交叉验证准则评估模型的拟合优度。

结果：六种空气污染物均与焦虑障碍日就诊量显著相关。污染物浓度每增加一个四分位距，其最大比值比（ORs）分别为：PM_{2.5}在lag1时为1.08（95% CI: 1.01, 1.16），NO₂在lag07时为1.19（95% CI: 1.05, 1.34），CO在lag02时为1.14（95% CI: 1.05, 1.23），PM₁₀在lag07时为1.12（95% CI: 1.01, 1.25），SO₂在lag7时为1.06（95% CI: 1.01, 1.12），O₃在lag7时为1.08（95% CI: 1.01, 1.15）。女性和中年人群的关联性强于其他亚组。

结论：短期暴露于环境空气污染物会显著增加焦虑障碍就诊风险。公共卫生需要关注空气污染对心理健康影响。

基金资助：本项目获广东省自然科学基金资助（2022B1515020094）

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空气污染和气象因素对新发结核病风险的综合影响：

一项时间序列研究

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【摘要】研究背景：结核病（Tuberculosis, TB）作为一种全球性重大公共卫生问题，尤其在资源有限和自然环境恶劣的地区更为严重。西藏自治区地处高原，海拔高、气压低、气候寒冷、日照强烈，且部分地区医疗资源匮乏，成为我国乃至全球结核病防控的重点地区之一。近年来，随着工业化和城市化进程推进，空气污染问题在高原地区逐渐显现，其与气象因素（如降水、温度、风速）共同构成了复杂的环境暴露体系。已有研究多聚焦于单一污染物或气象因素对结核病的影响，尚缺乏对多种环境因素联合效应的系统评估，尤其是在海拔极高、生态脆弱的特殊区域。

目的：本研究旨在基于西藏自治区 2019 至 2023 年每日结核病报告数据，结合多种空气污染物与气象因素，采用先进统计建模方法系统评估环境因素对结核病发病的综合影响，并进一步探索性别、职业等人群特征的异质性效应，以期揭示高原地区环境暴露对结核病流行的作用机制，为精准公共卫生干预提供科学依据。

方法：本研究收集了 2019 年至 2023 年期间西藏自治区每日结核病新发病例数据，以及同期的主要空气污染物浓度指标（PM₁₀、PM_{2.5}、SO₂、NO₂、O₃、CO）和气象因素（气温、降水量、风速）等环境暴露数据。为全面评估多种环境因素的综合及个体健康效应，研究采用了两类先进统计建模方法：（1）加权分位数回归（Weighted Quantile Sum Regression, WQS）模型，用于识别多重环境污染物的联合暴露效应及其主要贡献因子；（2）贝叶斯核主成分回归（Bayesian Kernel Machine Regression, BKMR）模型，用于捕捉潜在的非线性关系和高阶交互作用，并评估单一和联合暴露对结核病发病风险的动态影响。此外，通过性别、职业和时间等子组的分层分析，深入探讨不同人群在环境暴露敏感性方面的异质性。

结果：研究期间共报告结核病新发病例 18,347 例，结果显示环境因素与结核病发病呈正相关。WQS 模型显示环境因素整体对结核病日发病数具有显著正向影响（OR=1.58，95%CI: 1.46 – 1.71），其中降水和 PM₁₀ 权重较高（分别为 0.55 和 0.59）。BKMR 模型进一步证实环境因素整体与结核病发病的正相关性，降水被识别为最重要的独立风险因素，且不同环境变量间存在潜在交互作用。分层分析显示，PM₁₀ 与降水在各亚组中均为主要影响因素，其中女性群体中降水影响

更为显著，农民与学生群体中则以 PM10 影响为主。

结论：空气污染与气象因素的综合暴露对西藏地区结核病发病具有显著影响。PM10 和降水是主要的环境风险因素，不同人群中表现出一定的异质性。研究结果可为高海拔地区结核病防控策略优化、公共卫生资源分配及临床干预提供科学依据。

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老年人抑郁症患者的 IADL 和认知功能的网络结构分析

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【摘要】

研究背景: 三分之一以上的老年人患有抑郁症, 关注老年抑郁群体的健康已成为重要的公共卫生问题, 患有抑郁的老年人更容易出现认知功能障碍和工具性日常生活活动能力 (Instrumental Activities of Daily Living, IADL) 受限。

目的: 本研究旨在探讨老年抑郁患者认知功能和 IADL 的网络结构及其与饮食多样性的关系。

方法: 从中国健康长寿纵向调查 (Chinese Longitudinal Healthy Longevity Survey, CLHLS) 中选择了 4396 名 60 岁及以上的抑郁症患者。分别采用简易精神状态评价 (Mini-Mental State Examination, MMSE) 量表和中国改良版 Lawton 量表评估认知功能和 IADL。分别通过强度和桥梁强度识别中心和桥梁症状。使用流网络识别与饮食多样性直接相关的症状。采用案例丢弃自助法对网络稳定性进行了检验。

结果: IADL2(购物)是认知功能和 IADL 网络中最有影响力的中心症状。MMSE5 (语言理解和协调能力)、MMSE3 (注意力和计算能力) 和 IADL8 (乘坐公交) 是认知功能和 IADL 之间的关键桥梁症状。MMSE3(注意力和计算能力)与饮食多样性的直接相关最强。

结论: 本研究探讨了患抑郁老年人的认知功能和 IADL 之间的相互关系。IADL2 (购物) 受限可作为认知下降的敏感标志。针对 MMSE5 (语言理解和协调能力)、MMSE3 (注意力和计算能力) 和 IADL8 (乘坐公交) 桥梁症状的干预措施有可能缓解该人群的 IADL 受限和认知障碍。此外, 注重饮食多样性可能会减轻认知下降对患抑郁老年人的负面影响。

基金资助: 无

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连续型终点临床试验的两阶段贝叶斯样本量估计方法研究

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【摘要】研究背景: 在固定设计的临床试验中, 研究者常通过预试验获取关键参数, 并以此估计正式试验的样本量。然而, 直接应用参数的预试验估计值可能导致正式试验的样本量低估, 造成检验效能不足的风险。相较而言, 适应性设计的动态调整机制与贝叶斯方法将参数视为随机变量的特性提供了更稳健的解决方案。

目的: 样本量重估能够依据期中分析计划, 利用累积数据对参数进行动态调整, 保证最终的检验效能达到预先设定的目标。贝叶斯方法允许在已有先验知识的基础上, 依据累积数据更新后验概率, 为样本量调整提供概率化决策依据。本研究旨在构建两阶段贝叶斯样本量估计框架, 融合样本量重估的动态调整特性与贝叶斯概率决策优势, 实现基于期中分析数据的样本量优化。

方法: 针对连续型终点的双臂临床试验, 本研究建立了包含初始估计与期中重估的两阶段框架。第一阶段基于正态-伽马共轭先验建立后验分布, 通过预设的贝叶斯后验概率阈值计算满足“结论性”条件的最小初始样本量; 第二阶段引入贝叶斯预测概率决策机制, 基于期中数据推导新增样本量的后验预测分布, 动态求解使预测概率超过决策阈值的最小新增样本。并通过蒙特卡洛模拟系统评估方法性能, 包括样本量需求较频率学方法的减少幅度以及贝叶斯决策阈值对 I 类错误率的调控作用。

结果: 模拟研究表明: 设置无信息先验时, 本方法与频率学方法估计结果具有良好一致性; 设置有效先验可显著降低样本量需求 (较频率学方法减少 10%-20%); 当本方法运用于多个亚组时, 通过调整贝叶斯决策阈值 (0.95-0.99) 可有效控制

FWER 于 5% 以下, 同时维持检验效能达 80% 目标水平。

结论: 本研究提出的完全贝叶斯两阶段框架兼具方法学优势: 通过整合先验信息降低初始样本量需求, 依托动态重估机制保障检验效能, 为临床试验提供了一种基于概率决策的灵活样本量估计方法。

基金资助: 本研究获国家重点研发计划 (2023YFC3503000) 资助

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流产与卵巢癌发病风险的 Meta 分析

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【摘要】研究背景: 卵巢癌是全球第二大常见妇科恶性肿瘤, 在世界范围内其发病率呈升高趋势, 且患病群体逐渐趋于年轻化。与其他妇科癌症相比, 卵巢癌的死亡率较高, 占女性癌症死亡率的 4.2%。根据 2021 年统计数据显示, 我国女性卵巢癌发病率为 4.54/10 万人, 已成为我国女性致死率最高的妇科恶性肿瘤。卵巢癌患者的死亡率之所以高, 主要因为卵巢癌的早期诊断困难, 患者确诊时往往已经处于卵巢癌的中、晚期, 不利于患者的治疗和预后。

因此, 需要通过降低或消除卵巢癌的危险因素来降低卵巢癌的发病风险, 预防卵巢癌的发生。对于大多数女性来说, 流产是一个可以改变卵巢癌发病风险的最重要的影响因素, 但是关于流产与卵巢癌的发病风险之间关系的研究结果存在争议。多项研究发现, 流产可以提高卵巢癌的发病风险, 然而, 在一些研究中未检测到卵巢癌发病风险和妊娠次数的正相关关系。本研究通过 *Meta* 分析来进一步确定流产与卵巢癌的发病风险间的相关关系, 为保护易感人群、预防卵巢癌的发生提供科学依据。

目的: 流产 (人工流产和自然流产) 次数与卵巢癌发病风险关系的结论与既往研究不一致。采用 *Meta* 分析的方法评价流产与卵巢癌发病风险的关系。

方法: 计算机检索关于流产与卵巢癌的病例对照研究和队列研究, 检索时间截至 2025 年 4 月。采用 Q 检验和 I^2 统计量进行异质性检验, 根据各研究间的异质性大小, 选择随机效应模型或固定效应模型合并效应值。采用 *Meta* 回归分析和敏感性分析探讨研究间的异质性。Egger 检验评估研究的发表偏倚。

结果: 共纳入 4 篇队列研究和 44 篇病例对照研究。*Meta* 分析结果显示, 流产与卵巢癌的发病风险呈负相关 ($OR=0.82, 95\% CI: 0.72-0.93$)。分别对自然流产和人工流产合并效应值, 自然流产和人工流产与均卵巢癌的发病风险呈正相关, 合并的 OR 分别为 2.29 ($95\% CI: 1.94-2.70$), 3.14 ($95\% CI: 2.43-4.04$), 剂量-反应关系分析显示, 流产与卵巢癌发病风险呈非线性关系 ($P<0.01$)。在排除导致异质性的关键因素前后, 均未观察到显著影响和发表偏倚。

结论: 本研究结果提示流产可能与卵巢癌风险升高有关, 仍需要进一步研究证实。

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笼诱法两种诱饵诱蝇效果对比分析

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摘要：目的 了解糖醋诱饵和鱼内脏诱饵诱蝇效果的差异。方法 采用笼诱法，以糖醋和鱼内脏为诱饵，分析比较两种诱饵诱蝇情况差异。使用 Excel2007、JASP 0.19.3 对数据进行整理分析，统计分析采用贝叶斯配对样本 t 检验、贝叶斯相关性分析、贝叶斯线性回归分析。结果 鱼内脏法和糖醋法均诱蝇 3 科 5 属 7 种。鱼内脏法对家蝇科 ($BF_{10}=11.860$) 和丽蝇科 ($BF_{10}=12.267$) 诱捕数量均优于糖醋法。鱼内脏法在不同生境、不同月份中诱蝇密度均优于糖醋法 (BF_{10} 分别为 20.058 和 13.747)。鱼内脏法和糖醋法诱蝇的蝇密度呈现中等程度相关 (Kendall's $\tau=0.563$, $BF_{10}=22.712$)；以不同生境不同月份鱼内脏法诱蝇的蝇密度为因变量 y，糖醋法为自变量 x，经贝叶斯线性回归分析，得到贝叶斯线性回归方程 $y=62.875+12.849x+\epsilon$ ，该方程 $BF_m=3.148$, $R^2=0.327$ 。结论 糖醋诱饵可以作为日常蝇类监测笼诱法的通用诱饵。

关键词：鱼内脏诱饵；糖醋诱饵；诱蝇情况；贝叶斯分析

Comparative analysis of the effectiveness of two bait types in cage traps for fly attraction

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Abstract Objective To understand the differences in the fly-attracting effects between sugar vinegar bait and fish scarps bait. Methods Using the cage trapping method with sugar vinegar and fish offal as baits, the differences in fly attraction between the two types of bait were analyzed and compared. Data were organized and analyzed using Excel 2007 and JASP 0.19.3. Statistical analyses were conducted using Bayesian paired-sample t-tests, Bayesian correlation analysis, and Bayesian linear regression analysis. Results Both the fish scarps bait and the sugar-vinegar bait attracted flies from 3 families, 5 genera, and 7 species. The fish scarps bait outperformed the the sugar vinegar bait in trapping numbers for both Muscidae flies($BF_{10} = 11.860$) and Calliphoridae flies ($BF_{10} = 12.267$).. The fish scarps bait demonstrated higher fly density across different habitats and months compared to the sugar vinegar bait ($BF_{10} = 20.058$ and 13.747, respectively). The fly densities

attracted by the fish scarps bait and the sugar vinegar bait showed a moderate correlation (Kendall's tau = 0.563, BF10 = 22.712). Using the fly density from the fish scarps bait in different habitats and months as the dependent variable y , and the sugar-vinegar bait as the independent variable x , Bayesian linear regression analysis yielded the equation $y = 62.875 + 12.849x + \varepsilon$, with BFm = 3.148 and $R^2 = 0.327$. Conclusion The sugar vinegar bait can continue to be used as a general approach for daily fly monitoring using cage traps.

Key Words: Fish scarps bait; sugar vinegar bait; fly attraction situation; Bayesian analysis

内脏脂肪、生活方式与代谢相关脂肪性肝病风险的关系

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【摘要】研究背景: 在非肥胖人群中, 代谢相关脂肪性肝病的发病率有所上升。非肥胖的定义通常为体型正常, 但未考虑内脏脂肪的异常累积。体型正常但内脏脂肪异常的个体可能忽视坚持严格的健康生活方式, 从而增加发生代谢相关脂肪性肝病的潜在风险。

目的: 阐明在非肥胖人群中, 不健康的生活方式在内脏脂肪异常和代谢相关脂肪性肝病风险之间的中介作用。

方法: 纳入 2010-2023 年深圳市基本公共卫生服务中 26289 名合并高血压和糖尿病的非肥胖老年人, 观察组定义为内脏脂肪异常, 对照组定义为内脏脂肪正常。使用中国内脏脂肪指数识别内脏脂肪异常, 使用加权评分量化身体活动、吸烟饮酒、盐摄入量等生活方式。构建因果中介模型, 分析不健康的生活方式在内脏脂肪异常和代谢相关脂肪性肝病风险之间的中介作用。

结果: 26289 名参与者中, 平均随访 5.5 年 (145342 人年), 其中 11791 名参与者发生代谢相关脂肪性肝病, 观察组的发病比例高于对照组 (22.1% vs 19.1%)。与对照组相比, 观察组采取不健康生活方式的比例增加 2.347 倍 (95% CI: 2.254~2.443); 采取不健康的生活方式使代谢相关脂肪性肝病的风险增加 11.2% (95% CI: 8.7~13.8)。内脏脂肪异常通过不健康生活方式的中介作用, 使代谢相关脂肪性肝病的风险增加 41.2% (95% CI: 3.5~92.7), 中介比例为 19.8% (95% CI: 12.1~33.6)。

结论: 在合并高血压和糖尿病的非肥胖老年人中, 不健康的生活方式是内脏脂肪异常增加代谢相关脂肪性肝病风险的主要中介因素。整合多种干预措施, 如促进健康生活方式和利用有效的药物治疗代谢综合征, 将是减轻该人群的代谢相关脂肪性肝病负担的关键。

基金资助: 本项目获国家自然科学基金 (82373684, 82204154)、国家重点研发计划 (2022YFC3600804)、深圳市“医疗卫生三名工程” (SZSM202311001) 资助。

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妊娠早期早产风险预测模型的构建和验证： 基于 85 个大型队列研究的系统评价和荟萃分析

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【摘要】研究背景：早产是全球新生儿死亡的首要原因，每年约 1500 万例早产，经济负担达 250 亿美元。早期筛查和干预可显著降低早产及其并发症风险。而现有筛查方法存在滞后，亟需开发孕早期预测工具已提升早产风险的早期识别和干预能力。

目的：该研究旨在系统探究妊娠早期可识别的早产风险因素，构建并验证孕早期的早产风险预测模型。

方法：本研究通过对现有早产风险因素的大型队列研究进行系统评价和荟萃分析，以形成派生队列。然后，利用有统计学意义的风险因素的合并风险比和 95% 置信区间，在预测模型内进行风险评分赋值，并在雅芳父母与儿童纵向研究队列 (Avon Longitudinal Study of Parents and Children, ALSPAC) 中对模型的预测效能进行外部验证，全面评估其预测性能。最后，基于孕早期模型的风险评分进行分层 (低、中、高和极高风险)，纳入孕中期可识别的风险因素，进一步评估模型预测性能。

结果：派生队列纳入了 85 项研究，共有 8555379 例妊娠。最终纳入孕早期早产风险预测模型的风险因素是年龄 < 20 岁，年龄 ≥ 35 岁，年龄 ≥ 40 岁，体重指数 (body mass index, BMI) $< 18.5 \text{ kg/m}^2$ ，BMI $\geq 30.0 \text{ kg/m}^2$ ，生殖间隔 < 6 个月， $6 \leq$ 生殖间隔 < 11 个月，辅助生殖，吸烟，早产史，孕前糖尿病，慢性高血压，慢性肾病，甲状腺功能减退，甲状腺功能亢进，孕前抑郁，孕前贫血，经产妇， $120 \leq$ 收缩压 < 140 ，收缩压 ≥ 140 ，舒张压 ≥ 90 ，和流产史。使用外部队列进行模型验证，曲线下面积 (AUC) 为 0.663 (95%CI 0.619 - 0.707)。最佳截断值为 15.0 分，对应的灵敏度为 0.400，特异度为 0.892。孕中期纳入可识别的风险因素后，AUC 值增加到 0.746 (95%CI 0.707 - 0.786)，不同风险分层下 AUC 为 0.640 - 0.813 不等。

结论：本研究构建的孕早期早产风险预测模型是一种简便直观的工具，可在妊娠早期识别早产高风险人群。结合孕中期可识别的风险因素，该模型在预测早产方面表现出良好的潜力。可为早产的早期个性化风险评估提供有力支持。

基金资助：本研究获浙江省自然科学基金 (ZCLY24H2601)、宁波大学 "One-Health" 交叉学科研究项目、国家自然科学基金 (81602940)、宁波市医学重点学科建设项目 (2022-F28)。

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Predictive value of systemic immunoinflammatory index for in-hospital mortality and ICU mortality in critically ill hypertensive nephropathy patients: analysis of the MIMIC-IV database

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【 Abstract 】 Objective: To investigate the relationship between systemic immunoinflammatory index (SII) and in-hospital mortality and ICU mortality in critically ill hypertensive nephropathy (HN) patients. **Methods:** A retrospective cohort study was conducted based on MIMIC-IV database. Critically ill hypertensive nephropathy patients treated in the ICU between 2011 and 2020 were included. The relationship between SII and in-hospital mortality and ICU mortality was analyzed using multivariate Cox proportional hazard models, and the non-linear relationship between SII and in-hospital mortality and ICU mortality was evaluated using restrictive cubic splines (RCS) and Kaplan-Meier curves. Subgroup analysis was also used to assess the robustness of the relationship between SII and in-hospital mortality and ICU mortality in hypertensive nephropathy patients. **Results:** A total of 1591 patients with hypertensive nephropathy were included, of which 686 died in hospital. Fully adjusted Cox proportional hazard model showed that SII was associated with in-hospital mortality and ICU mortality in hypertensive nephropathy patients ($P < 0.05$), and RSF showed that there was a nonlinear correlation between SII and in-hospital mortality in hypertensive nephropathy patients (P nonlinearity = 0.0448, P overall trend = 0.0485). Kaplan-Meier survival curve results showed that there were significant differences in in-hospital mortality and ICU mortality in hypertensive nephropathy patients with different levels of SII ($P < 0.05$), and the results of subgroup analysis confirmed the robustness of the association between SII and in-hospital mortality and ICU mortality. **Conclusion:** SII is an important predictor of prognosis in critical hypertensive nephropathy patients, and higher levels of SII are significantly correlated with in-hospital mortality and ICU mortality. This finding provides clinicians with a potential prognostic assessment tool to help identify high-risk patients early and intervene accordingly.

生成对抗网络增强的多重填补方法构建及应用

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【摘要】研究背景：数据缺失是真实世界研究中的常见问题。作为常用的数据填补方法，多重填补（MI）充分考虑缺失数据的变异性，并能根据专业知识预设填补值范围。但其假定有时难以成立，可能会造成估计偏差。近年来，生成对抗填补网络（GAIN）应用于缺失数据填补领域。GAIN 无需监督和预训练，属单值填补方法，未考虑缺失数据的变异性。且其初始填补值是 0，无信息先验。MI 和 GAIN 主要优缺点能够互补，若能结合，或可提升真实世界研究中多个协变量缺失数据的填补效果并提供更丰富的方法学选择。

目的：构建生成对抗网络增强的多重填补方法（GAIN enhanced MI, GEM），通过模拟研究和实例应用，与 GAIN 和 MCMC 方法（马尔科夫链蒙特卡罗法）进行比较，评价其在不同情境下的填补效果。

方法：通过模拟研究，设置结局为连续型，二分类分组变量和 7 个协变量，3 种缺失机制（完全随机缺失 MCAR、随机缺失 MAR、非随机缺失 MNAR）、4 种样本量（500、1000、2000、5000）、10 种缺失比例（1%~10%），共 120 种模拟情境。每种情境模拟 1000 次，设置 3 个不同类型协变量含缺失数据。分别从对观测真值的估计（标准化均方误差、错误分类比例）和对参数值的估计（偏倚、绝对误差均值、95% 置信区间覆盖率）两个方面对评价填补效果，并在真实世界数据中进行实例应用。

结果：研究结果表明，在三种缺失机制下，对于连续型协变量和二分类协变量，GEM 的观测值缺失填补效果均优于 MCMC，GEM 和 GAIN 间无明显差异；对于有序多分类变量，GEM、GAIN 和 MCMC 间的观测值缺失填补效果无明显差异。对于连续型协变量和有序多分类协变量，GEM、GAIN 和 MCMC 在三种缺失机制下均有较好的参数值估计效果。对于二分类协变量，当缺失机制为 MCAR 时，三种方法得到的参数点估计值均较准确，而 MCMC 的绝对误差均值相对更小；当缺失机制为 MAR 时，MCMC 得到的参数点估计值较准确且绝对误差均值较小；当缺失机制为 MNAR 时，GEM 得到的参数点估计值较准确且绝对误差均值较小。GEM 在实例应用中表现稳健。

结论：GEM 方法在不同缺失机制下填补效果稳健，尤其在复杂缺失机制（MNAR）下有一定优势，为真实世界研究中的多个协变量数据填补提供了更丰富的方法学选择。

基金资助：本项目获国家自然科学基金资助（82373687）

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生存监督函数型主成分分析及其在非小细胞肺癌预后动态预测中的应用

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目的: 纵向数据反映疾病随时间进展的情况, 为生存事件的风险预测提供了重要信息。函数型主成分分析 (FPCA) 能够对纵向数据进行降维, 提取其轨迹变化特征, 已经被广泛应用于动态预测研究中。然而, 经典 FPCA 的特征提取过程是独立于生存结局进行的, 所得到的主要函数型主成分不一定具有对结局的最大预测能力。为了进一步改善基于 FPCA 的动态预测模型的预测效果, 本研究旨在提出一种生存监督功能主成分分析 (SSFPCA) 方法。

方法: 开发 SSFPCA 方法, 在 FPCA 的目标函数中整合限制性平均生存时间 (RMST) 伪值和主成分得分的协方差, 从而提取按与生存结局的关联程度排序的纵向特征。通过模拟研究, 评估 SSFPCA 在四种时变系数情景下的预测性能, 并与 sFPCA, FPCA 和 JM 比较。为了公平比较, 对 FPCA、sFPCA 和 SSFPCA, 仅选择第一个主成分得分来构建预测模型。最终, 将 SSFPCA 应用于切除的非小细胞肺癌队列, 以提取与预后相关的癌胚抗原 (CEA) 轨迹特征, 并开发一个动态的非小细胞肺癌预后预测模型, 以实现更准确的预后预测。

结果: 在模拟研究中, SSFPCA 和 sFPCA 模型相比 JM 和 FPCA 表现出更高的 AUC 和更低的 BS, 表明有监督方法在改善预测准确性上的优势。本研究提出的 SSFPCA 的性能整体上略优于 sFPCA。在 NSCLC 预后预测研究中, 基于 CEA 重复测量值, SSFPCA 所提取的第一个生存监督主成分重要性超过了病理分期。与 FPCA 模型相比, SSFPCA 模型在预测术后 3 年和 5 年生存的 AUC 分别升高 0.053 和 0.032, BS 分别降低 0.010 和 0.007。基于构建的 SSFPCA 模型可实现 NSCLC 患者个性化预后动态预测。

结论: 在基于纵向数据和生存数据的动态预测场景下, 本研究开发的 SSFPCA 模型能够提取与生存结局相关的主成分, 进一步改善动态预测模型的预测性能。模拟研究证实了本研究提出的 SSFPCA 相比传统动态预测方法在预测性能上的优势, 并在 NSCLC 队列中实现了更准确的 NSCLC 预后动态预测。

关键词: 函数型主成分分析

生存结局序贯多重分配随机试验的期中分析方法研究

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【摘要】研究背景: 适应性治疗策略(Adaptive treatment strategies, ATS)是由治疗过程中一系列单独定制的疗法组成, 在特定时间点重复评估患者的中间结果, 并相应地调整治疗顺序或剂量。序贯多重分配随机试验 (Sequential Multiple Assignment Randomized Trials, SMART) 由于其高效性被认为是用于评估 ATS 治疗效应的金标准试验设计。生存资料在临床试验中非常常见, 在 SMART 设计下满足等比例风险假设的可能性较小, 因此在 SMART 设计下构建适用于生存结局指标且不要求等比例风险假设的统计推断方法十分必要。

目的: 本研究拟在生存结局的 SMART 设计中构建以限制性平均生存时间 (Restricted Mean Survival Time, RMST) 为效应指标的统计推断方法, 并在设计中引入期中分析以期达到减少试验样本量和缩短试验时间的目标。

方法: 本研究围绕生存结局的 SMART 设计, 以 RMST 为效应指标, 构建基于 RMST 的 ATS 成对比较和全局比较的假设检验方法。其次我们将期中分析引入 SMART 设计, 在每次分析时检验全局原假设, 若拒绝原假设则试验中止并确定最优 ATS 集合, 否则进入下一阶段直至试验结束。在方法上我们针对 RMST 指标可能导致检验统计量不满足独立增量性质的情况, 构建适用于独立增量性质不满足时的一类错误控制方法。

结果: 模拟研究显示固定权重和动态权重的 RMST 估计量具有良好的统计性能。生存结局 SMART 期中分析设计在不同的原假设模拟场景下一类错误均良好控制; 在备择假设场景下, 期中分析若在受试者招募期进行时, 与固定设计相比相同检验效能下期分析设计能减少样本量, 缩短 5.7671%~22.2200%的试验时间; 若期中分析在受试者招募期后进行时, 与固定设计相比相同的样本量下期分析设计能缩短 7.8120%~59.0640%试验时间。所提方法使用模拟的 CALGB 8923 临床试验数据进行了实例展示, 引入期中分析可能减少 136 例样本量或缩短三年试验周期。

结论: 本研究提出的加权 RMST 估计量提供了一种评估 ATS 治疗效应的新方法, 并基于 RMST 构建了 SMART 设计下 ATS 成对比较和全局比较的假设检验方法, 进一步基于 RMST 将期中分析方法引入 SMART 设计, 提出有效的一类错误控制方法, 与固定设计相比能减少样本量或缩短试验时间, 提高了试验效率。

基金资助: 本项目获国家自然科学基金资助 (82273727)

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使用 Monte-Carlo 模拟和实例数据验证基于回归的定量一致性评价样本量计算公式

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【摘要】

目的 验证基于回归的定量指标一致性评价样本量计算公式在不同数据分布、不同变异程度、以及不同一致性总体条件下的适用性。**方法** 事先设定检验效能的预期水平。使用 Monte-Carlo 模拟法, 通过设定不同的总体参数, 产生相应的虚拟数据总体。随后分别从虚拟总体中抽取小样本预试验以计算样本量, 并在相应样本量条件下从虚拟总体中重复 1000 次抽样以获得模拟把握度。为了获得模拟把握度的分布情况, 重复进行 100 次模拟验证过程, 并将模拟把握度的分布情况与预期水平进行比较。同时, 本研究还将使用一个临床试验实例数据以验证在实际临床应用中回归公式的适用性。**结果** 单参数 Monte-Carlo 模拟的结果显示, 无论预期把握度设定为 80% 还是 90%, 均有近 80% 的模拟验证试验的把握度达到预期水平。在不同总体参数设定条件下, 模拟验证试验把握度的第 25 百分位数水平平均稳定在预设把握度附近。实例数据验证进一步验证了回归公式在实际应用中的适用性。总体而言, 基于回归的定量一致性评价样本量计算公式在不同数据条件下均展示了良好的稳健性, 在该公式计算结果下, 均有预期数量的模拟验证试验可达到设定的把握度。**结论** 本研究进一步完善了基于回归的定量一致性评价的方法学体系, 为该方法的正确应用及推广提供了理论支持。

【关键词】 定量指标, 回归, 一致性评价, 样本量, Monte-Carlo 模拟

基金资助: 首都卫生发展科研专项 (首发 2024-2G-4211)、国家自然科学基金青年项目 (No.12301369)、国家自然科学基金面上项目 (No.12271286)

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使用大规模人群测序数据进行基因型填补可提升罕见变异 关联研究的效能

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目的： 以英国生物样本库 (UKB) 中 150,119 名个体的 WGS 数据作为“金标准”，评估使用两个填补参考面板 (HRC+UK10K 和 TOPMed) 进行罕见变异填补的覆盖度与准确性及二者对罕见变异关联性分析效能的提升程度。

方法： 本研究以 UKB 中 150,119 名参与者的 WGS 数据作为金标准，通过四个分析阶段系统评估基于两种参考面板 (TOPMed 和 HRC+UK10K) 所填补的罕见变异数据情况：(1) 对比两种填补数据在罕见变异填补表现上的差异；(2) 对三大种族 (白人、黑人、亚洲人) 进行跨种族基因型一致性分析；(3) 对 45 种复杂性状进行全面的关联测试，包括单变异测试与基因集测试；(4) 针对肺癌与卵巢癌，整合 SNP 芯片 GWAS 与 WGS GWAS 进行疾病特异性分析，再分别进行 meta 分析识别额外的罕见变异/基因。

结果： 对极罕见变异 ($MAC \leq 5$)，TOPMed 填补数据的平均 RSQ 可达 0.6，在三大族中与 WGS 变异的一致性较高 (Cramer's $V > 0.75$)。在相同样本量下，两份填补数据的效能均低于 WGS，但将 TOPMed 填补数据的样本量扩展至 488,377 人后，定量性状的显著罕见变异检出率提升 27.71%，二元性状提升约 10 倍。填补数据与 WGS 的 GWAS 结果联合分析还能发现 WGS 单独分析时未检出的新变异和基因，显示出大规模填补数据在罕见变异研究中的实用价值，尤其在 WGS 资源有限时具有重要意义。

结论： 在大规模罕见变异关联研究中，当目标人群的 WGS 数据有限或不可获得时，基于 TOPMed 参考面板的填补是一种相对可靠的选择。此外，大样本量的填补数据在某些情境下可在分析效能上超过小样本量的 WGS 数据。总体而言，SNP 芯片采用大规模人群测序数据作为参考面板获得的填补数据与 WGS 数据的 GWAS 结果进行整合分析，有助于更深入理解罕见变异在复杂性状与疾病中的作用。

关键词： 罕见变异

使用模拟研究估计参考区间的新算法 refineR

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【摘要】

研究背景: 参考区间是实验室检验结果临床解读的关键, 通常基于健康人群样本建立。传统直接法需招募大量健康个体, 耗时费力且伦理挑战多, 尤其在特定人群如发展中国家的亚组中难以实施。间接方法利用真实世界数据 (RWD), 包含非病理和病理检验结果, 具有快速、低成本和伦理问题少的优势, 但数据分析难度较大。RWD 的复杂性要求更高级的统计方法来准确估计参考区间。

目的: 鉴于现有方法的局限性, 本研究提出一种新的间接方法——refineR 算法, 旨在从 RWD 中估计参考区间。refineR 算法创新性地采用逆建模技术, 通过将检验结果分离为病理和非病理分布, 识别最能解释非病理数据分布的模型。我们通过模拟研究对其性能进行评估, 并与传统直接方法进行比较, 以验证 refineR 算法在不同条件下的有效性、精确度和可靠性。

方法: refineR 算法基于逆建模, 假设 RWD 中非病理数据占大多数且可用 Box-Cox 变换正态分布建模, 包含数据预处理、模型优化和参考区间推导。为验证算法性能, 我们模拟生成三种生物标志物 (GGT、ALT、ALP) 的数据, 涵盖不同病理结果位置和比例, 并与直接法 (样本量 $N=120$ 和 $N=400$) 比较, 使用平均百分比误差 (MPE) 和总误差 (TE) 规范评估结果。

结果: refineR 法在所有方法中 MPE 最低 (2.36%), 与真实值总误差偏差在 $\pm 1TE$ 内的参考区间比例 (87.73%) 优于 $N=400$ 直接法 (80.44%) 和 $N=120$ 直接法 (60.61%)。对于低病理分数 ($\leq 15\%$) 和轻微重叠分布的测试用例, refineR 法表现出色, 但对于高病理分数 ($\geq 20\%$) 和高度重叠分布的用例偏差较大。

结论: refineR 算法能精确估计参考区间, 是直接法的可行补充。作为开源 R 包, refineR 可轻松集成到临床工作流程中, 通过稳健的参考区间估计增强个性化医疗。未来工作将增强算法以纳入协变量并探索其他数据转换方法以提高性能。

基金资助: 无

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数智化背景下 LLM 在医学统计软件课程中的应用研究

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【摘要】研究背景: 随着信息技术飞速发展, 数智化时代到来, 大语言模型 (large language models, LLM) 的技术经历几十年的演变, 如今已在日常生活中被广泛使用, 活跃在公众视野。在数智化浪潮的推动下, 我们的课堂教学形态经历着从传统向数智化的深刻转型, 课堂教学形态正逐步走向人本化、智能化与个性化。而 LLM 的易获取性、实时性和个性化反馈, 为医学和健康科学的教育工作者提供了新思路。

目的: 本研究以普适性 LLM 为基础, 构建医学统计专用的大语言模型应用于统计软件教学中, 并在课程中实施指导和干预, 评估基于 LLM 的医学统计软件教学改革效果。

方法: 开课前采用问卷调查学生学习背景和对 LLM 使用的愿景, 并在课中进行 LLM 的介绍与使用教育。结课后利用问卷调查, 结合学生的课程成绩, 采用卡方检验和秩和检验进行差异性比较, 从多个角度评估改革效果。

结果: LLM 的引入虽未改变学生对学习难度 (引入前 85.25% v.s. 引入后 77.97%,

$P=0.510$) 和兴趣 (引入前 59.02% v.s. 引入后 50.85%, $P=0.714$) 的态度, 但提升了一半同学的学习主动性 (50.85%), 更多同学将 LLM 列为答疑解惑的最优选

(引入前 1.64% v.s. 引入后 23.73%, $P<0.001$); 67.79% 的学生愿意将 LLM 融入未来学习并推荐给身边同学。

结论: 改革后的教学融合有效促进了学生的课后学习和实践积极性, 增强了思辨能力的培养; 但 LLM 在教学中的实际作用可能被我们高估。本研究为 LLM 作为支持学习的交互式医学教育工具的潜在应用提供了参考, 为后续的课程教学改革提供依据。

基金资助: 本项目获中山大学本科教学质量与教学改革工程类项目资助 (51000-12253008)

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双胎妊娠孕晚期贫血与新生儿并发症的关联：

一项回顾性队列研究

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【摘要】研究背景：双胎妊娠因独特的生理特征可能面临更复杂的贫血相关风险。然而，既往研究多为单胎妊娠期贫血与新生儿结局之间的相关性，很少有研究探讨双胎妊娠期贫血的影响。

目的：本研究旨在探讨双胎妊娠中母亲孕晚期贫血与新生儿并发症之间的关联。

方法：采用单中心回顾性队列设计，纳入 2018 年 1 月至 2022 年 12 月西北妇女儿童医院分娩的妊娠 ≥ 24 周双胎活产孕妇及新生儿。根据世界卫生组织 (WHO) 标准定义孕晚期贫血 (血红蛋白 <110 g/L)，分级为轻度 (100 – 109 g/L) 和中重度 (中度+重度, <100 g/L)。通过广义估计方程 (GEE) 调整混杂因素，分析孕晚期贫血与双胎新生儿并发症的关联。

结果：本研究共纳入 3097 例双胎孕妇，贫血组有 1003 例，其中轻度贫血组 499 例，中重度贫血组 504 例。校正混杂因素后，分析结果表明：与无贫血组相比，贫血组新生儿脑室周围-脑室内出血 (aOR: 1.47; 95%CI: 1.24, 1.75)、呼吸窘迫综合征 (aOR: 1.41; 95%CI: 1.12, 1.77)、支气管肺发育不良 (aOR: 1.81; 95%CI: 1.04, 3.13)、败血症 (aOR: 1.99; 95%CI: 1.11, 3.57) 及新生儿贫血 (aOR: 1.28; 95%CI: 1.01, 1.61) 风险显著升高，新生儿肺炎风险降低 (aOR: 0.19; 95%CI: 0.07, 0.56)。分层分析结果表明：轻度贫血仅与脑室周围-脑室内出血风险增加及肺炎风险降低相关；中重度贫血与新生儿脑室周围-脑室内出血、呼吸窘迫综合征、支气管肺发育不良、坏死性小肠结肠炎 (aOR: 1.62; 95%CI: 1.02, 2.59)、败血症及新生儿贫血风险较高相关，与新生儿肺炎风险较低相关。

结论：双胎妊娠孕晚期贫血显著增加多种新生儿并发症风险，且中重度贫血的影响更为广泛。建议加强孕期贫血筛查及分层管理，以改善新生儿预后。

关键词：双胎妊娠；孕晚期贫血；新生儿并发症；广义估计方程；回顾性队列

基金资助：本项目获国家自然科学基金资助 (82103924)

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糖尿病患者心理痛苦现状及影响因素研究

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【摘要】研究背景: 糖尿病作为典型的慢性非传染性疾病, 其管理依赖药物治疗、饮食控制、体重管理及自我监测的多维协同干预体系。治疗环节的任意偏差都会导致血糖出现波动甚至出现并发症, 对患者生理健康构成威胁。与此同时, 长期治疗负担衍生的心理应激已成为糖尿病管理的重要挑战, 心理痛苦在患者群体中呈现高发性特征。

目的: 本研究旨在通过流行病学调查, 揭示糖尿病患者心理痛苦的现状, 分析其潜在的影响因素, 为构建精准化心理干预策略及临床综合治疗方案提供循证依据, 最终实现患者身心健康水平的提升。

方法: 采用便利抽样法从山东省济南市 5 个社区招募符合纳入标准的糖尿病患者作为研究对象。研究工具包含: ①人口学特征调查表 (涵盖年龄、文化程度、家庭经济状况等 10 项变量); ②糖尿病痛苦量表 (Diabetes Distress Scale, DDS), 该量表具有良好的信效度 (Cronbach's $\alpha > 0.8$)。研究共发放问卷 220 份, 回收有效问卷 205 份, 有效回收率为 93.18%。数据处理采用 SPSS 26.0 统计软件, 依次进行描述性统计、单因素 χ^2 检验及多元 Logistic 回归分析, 检验水准设定为 $\alpha = 0.05$ 。

结果: 本研究的 205 例患者中, 患者存在心理痛苦的有 142 例, 占 69.3%, 提示糖尿病患者心理痛苦呈高发态势。单因素 χ^2 检验显示, 年龄、文化程度、家庭人均月收入、医疗付费方式、病程、糖尿病并发症、患糖尿病的同时是否患有其他疾病以及是否同时接受其他疾病的治疗等因素有统计学意义 (P 均 < 0.05)。Logistic 回归分析模型显示, 以上单因素分析中除年龄、医疗付费方式和有无并发症外, 其余因素均有统计学意义 (P 均 < 0.05)。

结论: 糖尿病患者发生心理痛苦的现象处于较高水平; 年龄高、文化程度低、家庭人均月收入低、病程长、有糖尿病并发症、患有其他疾病和糖尿病治疗的同时接受其他疾病的治疗是糖尿病患者发生心理痛苦的危险因素。

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武汉市中小学生不同营养状况与筛查性近视共患现况研究

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【摘要】研究背景: 近年来, 儿童青少年群体中出现了“小眼镜”、“小胖墩”和“小豆芽”等形象, 这些昵称背后隐含着近视、营养不良和超重肥胖等健康问题, 不仅严重危害儿童青少年的个体健康, 还可能对国家未来的人口素质、社会经济发展乃至国防安全产生深远影响。2024 年, 国家卫生健康委发布了《近视防治指南 (2024 年版)》, 并联合教育部、体育总局等 16 个部门启动了“体重管理年”活动, 充分表明了国家对儿童青少年健康问题的高度重视, 并致力于通过多部门合作, 采取全面的公共卫生干预措施, 以改善儿童青少年的健康状态。

目的: 分析武汉市中小学生不同营养状况与筛查性近视共患情况, 探究其主要影响因素, 为制定有效干预措施和多病防控策略提供参考依据。

方法: 2023 年采用分层整群随机抽样法, 对武汉市 13 个区 22929 名中小学生进行体格检查和问卷调查。通过卡方检验比较不同组间的差异, 采用多因素 logistic 回归方法分析不同营养状况与筛查性近视共患的主要影响因素。

结果: 2023 年武汉市中小学生营养不良率、超重肥胖率、筛查性近视率、营养不良与筛查性近视共患率和超重肥胖与筛查性近视共患率分别为 36.2%、5.98%、65.52%、3.90%、23.5%。不同营养状况与筛查性近视共患率男生均高于女生 ($P < 0.05$), 远城区超重肥胖与筛查性近视共患率最高, 营养不良与筛查性近视共患率最低; 随着年龄的增加, 共患率均呈现上升趋势 ($P_{\text{趋势}} < 0.05$), 血压越高, 超重肥胖率、筛查性近视率和共患率越高, 营养不良率和共患率越低 ($P < 0.05$)。logistics 回归分析结果显示, 调整年龄、城乡, 血压偏高、父母亲同时近视、饮酒、每日饮奶、课后运动场所、电子产品使用时长是营养不良和筛查性近视共患的主要因素; 血压偏高、父母亲近视、主动吸烟、被动吸烟、饮酒、每日食用新鲜蔬菜、中高强度运动达标是超重肥胖和筛查性近视共患的主要因素。

结论: 武汉市中小学生营养状况、筛查性近视及共患现况不容乐观。干预措施要强调个人、家庭和学校多方参与, 重点关注学生养成健康生活方式。

基金资助: 本项目获 2023 年武汉市知识创新专项曙光计划项目基金资助

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西藏鼠疫风险的时空分析：

多源数据驱动的综合模型构建与验证

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摘要

研究背景: 鼠疫是由鼠疫耶尔森菌引起的高致死率传染病, 西藏作为青藏高原核心区域, 独特的高寒地貌和气候条件使其生态系统高度敏感。现有研究多聚焦于整个青藏高原, 缺乏对西藏地区鼠疫流行及其气候变化响应的深入探讨。

目的: 本研究旨在通过多模型集成与时空动态建模, 揭示西藏鼠疫疫源地的环境驱动机制及分布演变规律, 评估气候变化下的潜在风险。

方法: 基于西藏 2000-2021 年鼠疫疫点监测数据, 整合最高温度、降水、归一化植被指数 (NDVI) 土地利用与土地覆盖、土壤湿度、坡度、坡向、人口空间分布 8 种环境变量, 采用 BIOMOD2 平台集成 10 种算法, 分四时段 (2000-2004、2005-2009、2010-2015、2016-2021) 构建鼠疫风险预测模型, 并以 2022 和 2023 年独立数据验证模型外推能力, 结合 R 和 QGIS 等软件对四个时期鼠疫疫源地风险分布进行模拟并计算其面积和质心变化, 揭示西藏鼠疫疫源地时空演变特征。

结果: 集成模型 (EM) 在外部验证中表现优异 (2022 年 AUC=0.98, TSS=0.92, KAPPA=0.88; 2023 年 AUC=0.99, TSS=0.99, KAPPA=0.99) 显著优于单一模型。

研究发现人口空间分布、降水量、最高温度及 NDVI 为关键驱动因子。集成模型得到的鼠疫风险分布图显示, 疫源地质心呈现阶段性迁移。2000-2004 年高风险区 (风险概率>750) 集中于拉萨、日喀则东部及那曲东部, 2005-2009 年范围有所收缩, 质心向东北偏移, 2010 年后质心先向东南移动, 随后转向西北, 与人类活动及气候变化密切相关。

结论: 集成建模显著提升了预测精度, 本研究通过多模型集成与时空动态模拟, 揭示了西藏鼠疫疫源地分布特征及质心的时空演变规律, 并有效捕捉了人类活动、气候变化对疫源地分布的复杂影响, 为西藏鼠疫高风险区精准防控提供了科学依据与空间决策支持。

基金资助: 本项目获国家自然科学基金面上项目资助(72374153)

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吸烟与中国全因死亡和过早死亡的关联： 一项队列研究

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【摘要】研究背景：吸烟与多种疾病相关，并被认定为全球第二大死亡危险因素。目前，中国 2010 年以后的队列研究尚未发现烟草烟雾与死亡率或过早死亡之间的关系。

目的：本研究旨在使用 2011 年以来具有全国代表性的队列调查中国吸烟行为特征及其与死亡率和过早死亡之间的关系。

方法：本研究采用具有全国代表性的数据集（China Health and Retirement Longitudinal Study, CHARLS, 2011–2012），并与 2013 年的随访数据进行关联。CHARLS 是一项持续进行的具有全国代表性的调查，对 45 岁以上的人群进行了纵向随访。吸烟状况（非吸烟者、已戒烟者、吸烟者、吸烟包年数、开始吸烟年龄和戒烟年龄）作为自变量，全因死亡率和过早死亡（定义为男性 72.7 岁前和女性 76.9 岁前死亡）作为因变量。采用 Cox 比例风险回归模型估计吸烟量和吸烟量对全因死亡率和过早死亡的影响。

结果：本研究共纳入 16,701 名受试者。吸烟者 (hazard ratio [HR]=1.37, 95%CI=1.02, 1.83) 和戒烟者 (HR=1.75, 95%CI=1.24, 2.46) 与全因死亡率之间存在显著关联。吸烟者 (HR=1.58, 95%CI=1.04, 2.39) 和戒烟者 (HR=2.25, 95%CI=1.38, 3.66) 均与过早死亡风险增加相关。与不吸烟者相比，吸烟包年数 ≥ 30 与总体人群 (HR=1.59, 95%CI=1.03, 2.43) 和女性 (HR=3.38, 95%CI=1.22, 9.38) 的过早死亡风险增加相关。此外，我们的研究结果还显示，吸烟包年数与总体人群 (P=0.002) 和女性 (P=0.010) 过早死亡风险呈线性趋势。

结论：本研究利用中国具有全国代表性的数据，发现吸烟状况对全因死亡率和过早死亡存在负面影响。研究还发现了吸烟包年数与过早死亡之间的线性趋势。

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线性回归中设置容错阈值的最小二乘法优化算法研究

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【摘要】研究背景: 传统最小二乘法 (Ordinary Least Squares, OLS) 在生物医学数据建模过程中, 当数据中存在临床可接受的微小误差时, 模型会因过度拟合这类微小误差而降低预测精度。以预测为目的的回归应用中, 部分测量误差若在既定阈值内, 将其视为“零误差”是更合理的, 但 OLS 无法自适应识别此类误差, 致使模型稳健性不足。当前研究对微小残差的累积影响关注不足, 尚未形成系统化的、针对性的解决方案, 亟需引入顾及“零误差”的优化建模策略。

目的: 引入“推荐容错阈值”, 探索迭代重加权最小二乘法 (Iteratively Reweighted Least Squares, IRLS) 优化算法, 解决 OLS 对临床可忽略微小误差的过度拟合问题, 通过参数化分析求出“推荐容错阈值”区间, 提升回归模型在生物医学场景中的预测稳健性。

方法: 以 OLS 和 IRLS 的数理原理为基础, 在迭代中引入以残差绝对值百分位数为判定标准的动态阈值机制, 对小于阈值的临床可忽略微小误差赋予零权重, 构建优化算法。采用平均绝对误差 (Mean Absolute Error, MAE) 和配对 t 检验, 在 1000 次蒙特卡洛模拟实验中对比优化 IRLS 算法与 OLS 在拟合和预测情况下的性能差异, 并利用 National Health and Nutrition Examination Survey (NHANES) 数据验证算法的适用性。同时将动态阈值参数化 (百分位数 P0 ~ P60) 进行敏感性分析, 确定兼顾噪声过滤与数据信息保留的“推荐容错阈值”。

结果: 与 OLS 相比, 优化 IRLS 模型的拟合阶段 MAE 降低 0.5‰-8‰, 预测阶段 MAE 降低 0.8‰-6‰, 改善幅度具有统计显著性 ($P < 0.05$)。动态阈值设定在残差绝对值的百分位数 P27 ~ P40 时, 模型拟合精度和预测稳定性最佳, 该区间内算法能有效过滤临床阈值内的微小误差并保留关键数据信息。NHANES 数据验证显示, 优化 IRLS 模型在“推荐容错阈值”内的拟合与预测误差均低于 OLS 模型。

结论: 本研究提出的动态阈值容错机制 IRLS 优化算法, 通过自适应地将临床视角可忽略微小误差设置为零值, 提升了线性回归模型对真实临床效用的体现能力。“推荐容错阈值”为实际应用提供了具备可操作性的参考, 该算法为疾病预后预测和公共卫生决策提供了方法论支持。

基金资助: 暂无

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心血管疾病动态风险预测模型构建与验证：

一项基于 ARIC 队列的研究

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【摘要】研究背景：心血管疾病（CVD）是全球死亡的首要原因，约占总死亡数的三分之一。现有的 CVD 风险预测模型如 Framingham 风险评分、SCORE 2 和 PREVENT 等均基于单次基线数据构建，属于静态预测模型，无法捕获风险因素的时间动态变化。已有研究表明，血压、血脂等关键生理指标在个体生命历程中存在显著波动，这些纵向变化模式蕴含重要的预测价值。

目的：构建整合纵向生理指标信息的 CVD 动态预测模型，并与传统静态模型进行性别特异性比较，评估其在预测区分度、校准度和净重新分类方面的改善效果。

方法：纳入 ARIC 队列 13,026 名参与者，在前两次随访均有所需指标的测量，按 7:3 比例随机分为训练集和验证集。分性别构建包含基线变量（年龄、性别、吸烟状况、降压药使用、糖尿病）的基础模型，使用联合模型分别加入单个纵向变量，包括血压指标（SBP、DBP）、血脂指标（HDL-C、LDL-C、TC、TGS、non_HDL、TC/HDL 比值、动脉粥样硬化指数 AIP）及体重指数 BMI。进一步构建 SBP 与其他指标组合的多变量联合模型，在观察时间分别为 0、4、7、10 年时分别动态预测第 20 年的 CVD 风险。

结果：加入单变量纵向信息后，预测性能均显著提升，其中 SBP 的纵向信息提供了最大改善。加入 10 年随访的 SBP 纵向信息后，男性的受试者工作特征曲线下面积 AUC 从 0.681 升至 0.712，Brier 评分从 0.0450 降至 0.0356；女性 AUC 从 0.711 升至 0.728，Brier 评分从 0.0282 降至 0.0222。在多变量联合模型中，三变量组合优化判别能力更显著：男性最优组合为加入 SBP、TGS、TC/HDL（AUC=0.730，BS=0.0337，净重分类改善率 NRI=36.5%），女性最优组合为加入 SBP、HDL、non_HDL（AUC=0.747，BS=0.0193，NRI=41.7%）。此外，随着纵向信息的增加，模型预测性能逐步提升，观察期为 7 年和 10 年时改善尤为显著。

结论：整合血压和血脂纵向测量信息的动态预测模型显著提高 CVD 风险预测准确性，且纳入纵向信息越多，改善更明显。这提示在 CVD 风险评估实践中，定期监测关键生理指标变化趋势可实现更精准的个体化动态风险预测。

基金资助：本项目获国家自然科学基金资助（项目批准号：82473730、82222064）

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新会区华支睾吸虫感染及食用鱼生行为的家庭聚集性分析

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【摘要】研究背景: 华支睾吸虫病是我国重要的食源性寄生虫病, 食用未熟淡水鱼生是其主要传播途径。既往研究多集中于个体层面的危险因素, 缺乏对家庭聚集性及其影响机制的系统分析。明确家庭聚集特征有助于优化干预策略、提升防控精准性。

目的: 了解新会区华支睾吸虫感染与食用鱼生行为现状, 基于二级多水平 logistic 回归模型, 分析感染与行为的家庭聚集性特征及其影响因素。

方法: 数据来自 2022 年 8 月-2023 年 3 月对江门市新会区居民进行的关于华支睾吸虫感染的环境-认知-行为调查。采用二级多水平 logistic 回归模型分析华支睾吸虫感染以及食用鱼生行为的家庭聚集性及其潜在影响因素。首先构建不含固定效应的零模型并计算类内相关系数 (ICC) 判断家庭聚集性; 若 $ICC > 0$, 则表明感染或行为在家庭层面存在聚集。随后纳入个体层面的性别、年龄、认知、行为、环境因素等变量作为固定效应, 采用后退法逐步筛选显著变量, 并分析其对 ICC 的影响。

结果: 共纳入新会区 274 户家庭的 878 名居民。华支睾吸虫感染率为 13.1%, 食用鱼生率为 36.3%。多水平 logistic 回归分析结果显示, 感染存在明显的家庭聚集性 ($ICC=0.97$, 95%CI: 0.95-0.98)。男性、成年人、食用鱼生者和未使用无害化厕所者均为高风险人群。模型在纳入食用鱼生行为后, ICC 值明显下降, 提示该变量解释了部分家庭聚集性。食用鱼生行为本身也具有家庭聚集性 ($ICC=0.56$, 95%CI: 0.45-0.66)。认知得分越高, 行为发生率越高; 20-59 岁、有家庭成员吃鱼生、有朋友吃鱼生以及易受社会环境影响人群更易食用鱼生。将家人鱼生行为纳入模型后 ICC 明显下降。

结论: 新会区华支睾吸虫感染及食用鱼生行为在家庭中均表现出明显聚集性, 其聚集性可部分由行为习惯或家庭环境因素所解释。防控策略应注重家庭为单位的健康教育和行为干预, 充分发挥家庭成员间的相互影响, 强化其正向引导, 提升防治效果。

基金资助: 本项目获广东省自然科学基金资助 (2022A1515010042)

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中国中老年人群 C 反应蛋白-甘油三酯葡萄糖指数与心血管疾病因果效应评估及预测研究

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【摘要】 目的: C 反应蛋白-甘油三酯葡萄糖指数 (C-reactive Protein-triglyceride Glucose Index, CTI) 是用于评价炎症和胰岛素抵抗的综合指标, 本研究旨在评估 CTI 对心血管疾病 (Cardiovascular Disease, CVD) 因果效应及预测价值。**方法:** 数据来源于 2011 年至 2020 年的中国健康与养老追踪调查 (China Health And Retirement Longitudinal Study, CHARLS)。根据四分位数将 CTI 划分为四组: Q1 (<8.10)、Q2 (8.10-8.60)、Q3 (8.60-9.18)、Q4 (>9.18), 使用加速失效时间模型 (Accelerated Failure Time Model, AFT) 构建 CTI 与 CVD 发病风险模型进行生存分析; 构建广义相加模型 (Generalized Additive Model, GAM) 拟合 CTI 和 CVD 风险的非线性关联; 使用贝叶斯加性回归树模型 (Bayesian Additive Regression Tree Model, BART) 计算 CTI 与 CVD 风险的平均处理效应 (Average Treatment Effect, ATE), 评估因果效应。**结果:** 本研究纳入 2011 年符合纳排标准的研究对象共 6990 例, 9 年的随访时间中, 1937 例发生 CVD。在校正所有的影响因素后, AFT 模型结果显示, 与 Q1 组相比, Q2 组[$TR=0.932$ (95% CI : 0.878, 0.990)]、Q3 组[$TR=0.903$ (95% CI : 0.849, 0.961)]、Q4 组[$TR=0.870$ (95% CI : 0.810, 0.935)]均会缩短中老年人群的 CVD 发病时间; GAM 模型显示 CTI 和中老年人群 CVD 风险呈非线性关联, 当 CTI 值为 7.68 时, CVD 风险最低为 14.6%。BART 模型因果效应估计显示, 与 Q1 组相比, Q2 组[$ATE=0.044$ (95% CI : 0.037~0.051)]、Q3 组[$ATE=0.084$ (95% CI : 0.077~0.091)]、Q4 组[$ATE=0.119$ (95% CI : 0.112~0.127)]均会增加 CVD 发病风险。**结论:** CTI 是中国中老年人群 CVD 发病风险的独立预测标志物, 因果效应分析表明 CTI 升高会增加 CVD 发病风险。

医学领域贝叶斯统计学知识图谱的构建研究

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研究背景: 贝叶斯统计学通过融合先验信息与数据更新后验分布的特性, 在医学研究中逐渐成为重要统计学方法。随着知识图谱技术为知识结构化提供新路径, 本研究立足医学领域需求, 通过构建贝叶斯统计教材的知识框架与内容体系, 推动其教学效率与实践应用的协同提升。

研究目的: 通过构建知识图谱, 系统归纳贝叶斯统计方法的基础知识以及其在医学领域的应用, 为医学领域贝叶斯统计学教材的编撰及总结提供材料的同时, 也为今后需要学习此学科的学生提供坚实的基础。

研究方法: 应用 Python 软件编写爬虫程序, 从 PubMed 网站抓取与医学贝叶斯统计相关的文献标题和摘要。根据《A First Course in Bayesian Statistical Methods》、《Doing Bayesian Data Analysis》、《Bayesian data analysis》等多本教材与专著构建本体模式层, 并通过数据清洗与 BIO 实体标注方式完成数据库的构建。利用 BERT 模型对所收集的数据进行命名实体识别及关系提取, 以形成知识点三元组 (实体-关系-实体)。基于获得的名词型实体, 加入从数据库中筛选出的短语型知识点。最终, 将获得的三元组导入 Neo4j 图数据库平台, 实现知识图谱的存储与可视化。

研究结果: 本研究基于 BERT 模型对医学文献与教材语料进行实体识别与关系抽取, 模型加权平均 F1 分数分别达 0.74 和 0.79, 成功构建医学贝叶斯统计学知识图谱。通过提取 1485 个知识点三元组并导入 Neo4j 数据库, 实现了知识框架的可视化展示与查询功能。图谱围绕“贝叶斯统计基础”“推断与计算”“模型及其应用”“决策与模型评估”四大模块, 系统整合核心理论与医学实践关联。研究成果不仅为智能问答系统提供结构化知识支持, 还可服务于教材体系优化与教学效率提升, 推动医学贝叶斯统计学的应用发展。

研究结论: 研究所构建的知识图谱能够有效组织和呈现复杂的统计知识, 为医学贝叶斯统计的教学、科研和实践提供支持。此外, 该知识图谱也可作为智能问答系统、个性化推荐系统以及智能学习平台的知识基础, 进一步推动医学贝叶斯统计学的智能化应用。

基金资助: 本研究获国家重点研发计划 (2023YFC3503000) 资助

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诱导期剂量与美沙酮维持治疗早期脱失的非线性关联： 一项回顾性队列研究

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【摘要】研究背景：美沙酮维持治疗（MMT）指南中保守的诱导期给药策略可能延迟参与者获得充足剂量，导致早期脱失，阻碍其维持治疗与获益。现有证据多关注线性关联，但二者间潜在的非线性关系及关键拐点尚不明确。

目的：首次深入探究 MMT 诱导期剂量与早期脱失风险之间的非线性剂量反应关联，量化其剂量拐点，为制定基于真实世界证据的诱导期剂量优化指南提供关键科学依据。

方法：回顾性收集广东省 11 家 MMT 门诊 2006-2021 年中首次接受治疗的参与者数据。以入组治疗后第一周的美沙酮服用剂量平均值作为诱导期剂量，治疗后 30 天的脱失情况作为研究结局。使用 Logistic 回归模型评估诱导期剂量与早期脱失之间的关联，并使用倾向性评分逆概率加权以控制混杂。利用限制性立方样条（RCS）回归模型和阈值效应分析探索潜在的非线性关联与拐点。基于所有协变量进行亚组分析探索交互作用。

结果：研究纳入 3723 名参与者，早期脱失率为 14.96%（557 人），诱导期剂量的中位数 42.14mg/天（IQR: 21.19mg/天）。调整混杂因素后，诱导期剂量与早期脱失呈现显著负相关（OR: 0.98, 95%CI: 0.97-0.98），逆概率加权回归结果一致。RCS 分析揭示了显著的非线性关联（ $P_{\text{非线性}} < 0.001$ ）。阈值效应分析确定关键拐点为 65.00mg/天。剂量 < 65.00mg/天时每增加 1mg/天，脱失风险降低 3%（OR=0.97, 95% CI: 0.96-0.98），≥ 65.00mg/天时无显著关联。敏感性分析在排除 33 名（0.89%）剂量极高（超出均数 ± 3 SD）者后，拐点降至 38.33mg/天。剂量 < 38.33mg/天时风险降低 4%/mg（OR=0.96, 95% CI: 0.94-0.97），≥ 38.33mg/天时风险仅降低 2%/mg（OR=0.98, 95% CI: 0.97-0.99）。亚组分析显示每日吸毒次数与诱导期剂量交互作用显著（ $P = 0.043$ ），在吸毒次数 < 5 次的亚组中效应显著（OR=0.97, 95% CI: 0.95-0.98），≥ 5 次的亚组中关联不显著。

结论：研究首次量化揭示了美沙酮诱导期剂量与早期脱失存在非线性关系及关键拐点（65mg/天和 38mg/天）。结果支持在诱导期剂量快速增量至不低于 38mg/天，且不超过 65mg/天，以显著降低早期脱失风险。这为修订现行保守的 MMT 诱导期剂量指南提供了重要的循证依据，推荐设定 38-65mg/天作为关键的早期

剂量优化区间。

基金资助：本项目获国家自然科学基金资助（82073664）

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基于因果机器学习的出血性中风个体化治疗效应异质性研究

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【摘要】研究背景: 传统临床研究方法通常假设治疗方案对所有患者作用一致, 该假设忽视了患者之间可能存在的个体差异。如何准确识别与量化这种个体的异质性已成为现代精准医学的重要研究方向。近年来, 新兴的因果机器学习方法, 如 Rboost 方法, 因能够有效捕捉治疗效应的个体差异, 逐渐展现出良好的应用前景。

目的: 本研究旨在探索基于 Rboost 方法识别和量化治疗效应异质性的可行性及效果表现, 并以出血性中风患者的个体化治疗效应评估为实例, 具体验证该方法的实际应用价值。

方法: 基于 361 例出血性中风患者随机对照试验数据, 应用 Rboost 方法估计每位患者的基线效应、治疗倾向评分和治疗效应, 并对影响治疗效应的重要特征进行排序。利用

5 折交叉验证对模型性能进行评估, 并与 Rlasso、Rridge、Relastic、随机森林及贝叶斯加性回归树方法的预测效果进行对比。

结果: 收缩压、中性粒细胞百分比、血清钠浓度、舒张压以及基底节出血等特征是影响患者个体治疗效应的关键变量。Rboost 方法的准确度 (0.87)、F1 值 (0.92)、马修斯相关系数 (0.59) 和 Brier 评分 (0.10) 均优于其他方法, 表现出较好的个体化治疗效应预测能力。

结论: Rboost 方法能够有效识别和量化出血性中风患者个体间的治疗效应异质性, 既能进行群体层面的治疗效应评估, 也能精准预测个体的预期治疗效果, 为临床决策提供重要的个体化依据, 具有较高应用价值。

基金资助: 本项目获国家自然科学基金资助 (项目编号: 82405194 和 81903589)

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原发性肝癌 (PLC) 现状及相关危险因素的 Meta 分析

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【摘要】

研究背景: 肝癌是中国常见的恶性肿瘤之一, 严重威胁居民生命健康。肝癌的病因尚不完全清楚, 目前认为其发病是多因素、多步骤共同作用的结果, 常见的危险因素包括 HBV 或 HCV 感染、饮酒、黄曲霉毒素等但也可发生于没有任何已知危险因素人群。目前对肝癌影响因素的研究很多, 但研究中仍存在结论不明确或不一致, 且研究样本量不够大与研究质量没有得到有效评价等问题。因此, 本研究对肝癌危险因素的相关研究进行 meta 分析, 综合定量评价各危险因素与肝癌之间的关系, 为我国人群的肝癌防控提供理论依据。

目的: 对肝癌发病危险因素的相关研究进行综合定量和 meta 分析, 为肝癌的防控和卫生决策提供理论依据。

方法: 系统地检索 Pubmed、中国知网、万方数据库等发表的肝癌影响因素的研究, 检索自数据库建立到 2024 年的所有中英文文献。用纽卡斯尔-渥太华量表评价文献质量, 用 R 4.0.2 软件进行 meta 分析。

结果: 共检索文献 1555 篇, 根据纳入与排除标准筛选, 最终有 63 篇研究纳入系统评价。meta 分析结果显示, 肝癌的危险因素按照其关联性由强到弱依次为: HBV 感染、个人肝病史、HCV 感染、心理因素、癌症家族史、饮用不良水源、饮酒、糖尿病、食用发霉腌制食品、精神因素、吸烟、工作生活条件差、性格忧郁、经济状况差, 合并 OR 值最高为 14.22 (10.99, 18.39), 最低为 1.97 (1.56, 2.49)。喝茶、果蔬、文化程度高是保护因素, 合并 OR 值最高为 0.49 (0.34, 0.72), 最低为 0.26 (0.15, 0.47)。敏感性分析、发表偏倚检验与剪补法分析结果显示, 本研究纳入的文献整体上敏感性低, 发表偏倚控制较好。

结论: 病毒感染、肝病史、饮酒等不健康生活方式为我国人群肝癌发病的危险因素, 饮茶、果蔬等为保护因素。建议积极接种乙肝疫苗, 改变不良饮食习惯和生活方式, 加强肝癌的早预防、早发现、早诊断、早治疗。

*基金项目: 国家自然科学基金项目 (81803337; 81872719; 82003560); 山东省自然科学基金项目 (ZR2023MH313); 山东省高等学校青创人才引育计划 (No.2019-10-156, Lu-Jiao)

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云南省肥胖相关结直肠癌死亡趋势及年龄-时期-队列效应分析

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【摘要】研究背景: 肥胖是结直肠癌、肝癌等癌症的危险因素, 并有超越吸烟成为癌症主要影响因素的趋势。从 1990 年到 2022 年, 全球肥胖症发病率增加了 1 倍多。

目的: 分析 1992-2021 年云南省结直肠癌及肥胖相关结直肠癌的死亡趋势, 并评估年龄、时期、队列的影响。

方法: 利用 2021 全球疾病负担研究(Global burden of disease study 2021, GBD2021) 云南省 1992-2021 年结直肠癌及肥胖相关结直肠癌死亡率和年龄标化死亡率, 使用 Joinpoint 回归模型分析年龄标化死亡率(age-standardized death rate, ASDR)变化; 利用年龄-时期-队列模型(APC 模型)分析年龄、时期及队列因素对肥胖相关结直肠癌死亡的影响。

结果: 1992-2021 年云南省结直肠癌年龄标化死亡率从 14.65/10 万下降到 12.97/10 万, 平均年度变化百分比为 -0.44% (-0.80~-0.08)。肥胖相关结直肠癌年龄标化死亡率从 1992 年的 0.02/10 万上升到了 2021 年的 0.04/10 万, 平均年度变化百分比为 3.08% (3.02~3.15)。随着年龄增加, 男性和女性肥胖相关结直肠癌死亡率上升, 年龄效应均在 ≥ 85 岁年龄组达最高值。随着年份的推移, 时期效应均在 2017-2021 年时期组达到最高值, 男性和女性时期效应的 RR 分别为 2.46 (95% CI 2.23~2.72) 和 1.73 (95% CI 1.52~1.96)。随着出生年份的推移, 以 1952 年出生的人群为参考, 1962 年以后出生人群死亡风险快速的上升, 并在 1977 年出生的人群达最高值, RR=2.31 (95% CI 1.87~2.85)。女性在 1967 年出生人群死亡风险达最高, RR=1.55 (95% CI 1.38~1.74), 男性在 1987 年出生人群达到最高点, RR=3.67 (95% CI 2.12~6.35)。

结论: 1992-2021 年云南省结直肠癌年龄标化死亡率降低, 但肥胖相关的结直肠癌年龄标化死亡率升高。随着年龄的增加和年份的推移, 肥胖相关结直肠癌死亡率上升, 男女性别均可看到相同的趋势。

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孕期微量营养素干预与青少年多维健康结局的关联分析

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- 2.

摘要 目的 已有研究表明, 孕期补充多种微量营养素有益于胎儿出生结局, 并可能促进儿童发育。然而, 孕期微量营养素补充是否会对子代远期的多维健康状况产生影响, 目前尚不清楚。本研究基于一项西北农村地区孕期微量营养素干预随机对照试验的随访数据, 旨在探讨孕期补充叶酸 (FA)、铁叶酸 (IFA) 及多种微量营养素 (MMN) 三种方案对子代在青少年期多维度健康状况的远期影响。

方法 数据来源于 2016 年完成的青少年随访评估, 纳入健康结局指标完整的青少年 1767 人。青少年多维健康结局评估采用两种方法: 一是基于体格指标 (身高、体重、BMI 等)、血压、智力、睡眠和行为问题构建的健康综合得分; 二是利用 K 均值聚类法, 根据上述指标划分出的三种健康模式 (代谢问题高风险组、行为问题高风险组、健康问题低风险组)。采用广义估计方程模型 (GEE) 分析孕期不同营养素干预对子代健康综合得分的影响, 多元 Logistic 回归模型探讨不同营养素干预与健康模式之间的关联。进一步分析孕期营养素干预的起始时间与持续时间对干预效果的潜在修饰作用。**结果** 纳入研究对象 1767 人, 平均年龄 12 岁 (标准差为 0.78), 其中男性 1050 名 (59%); 性发育已经启动 1416 名 (83%)。控制相关协变量后, GEE 模型结果显示孕期 MMN 干预对子代健康综合得分无显著影响 ($\beta=0.04$, 95% CI: -0.61~0.68); 多元 Logistic 回归结果表明, 相较于 FA 组, MMN 干预显著降低青少年代谢问题高风险的可能性 (OR=0.70, 95% CI: 0.54~0.92)。而 IFA 组在健康综合得分或健康模式上与 FA 组均无显著差异。进一步分析发现, 当微量营养素干预起始时间 < 12 孕周时, IFA 组和 MMN 组在代谢问题风险方面均显示有一定的保护作用 (IFA 组: OR=0.65, 95% CI: 0.43~0.98; MMN 组: OR=0.63, 95% CI: 0.42~0.97; FA 为参比组), 但营养素补充的持续时间及起始时间均未表现出明显的效应修饰作用。**结论** 孕期补充多维营养素可降低子代在青少年期代谢问题的发生率, 且孕早期开始营养干预可能更有利于改善子代远期健康结局。

【关键词】青少年; 孕期营养素补充; 远期健康结局

运用 Anderson-Gill 计数过程模型评价纤维蛋白原与非小细胞肺癌总体生存的关联

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【摘要】研究背景: 肺癌是我国最常见的癌症类型和导致人群死亡的主要原因之一。非小细胞肺癌 (Non-small-cell lung cancer, NSCLC) 占肺癌类型的 80%-85%, 其预后通常好于小细胞肺癌。研究表明, 性别、吸烟史、临床分期、治疗方式以及肺部合并症等因素显著影响 NSCLC 患者的预后。此外, 大部分 NSCLC 患者存在凝血功能异常, 许多凝血指标可用于评估患者的预后和生存率。纤维蛋白原 (Fibrinogen, FBG) 作为评估凝血功能的重要指标, 近年来越来越多的研究关注其与癌症患者总体生存 (Overall Survival, OS) 的关联。然而, 关于 FBG 与 NSCLC 患者 OS 关联的研究结果尚不一致。值得注意的是, 相关研究大多采用 Cox 比例风险模型来探讨研究变量在某一时刻与患者 OS 的静态关联, 未能充分考虑血液指标动态变化的特点。然而在临床实践中, 许多指标是典型的时依性变量, 其在患者生存期内呈现动态变化。因此, 相较于某一时刻的静态关联, 分析患者生存期内动态变化的指标与 OS 的关联更能准确反映实际情况, 从而更好地指导临床实践。

目的: 通过构建 Anderson-Gill 计数过程模型 (AG 模型), 探索动态变化的纤维蛋白原对非小细胞肺癌患者预后的潜在意义, 为非小细胞肺癌患者的临床治疗提供重要的参考依据。

方法: 本研究回顾性收集 2013 年 1 月至 2018 年 12 月在昆明医科大学第三附属医院经病理检查确诊为非小细胞肺癌的 748 例患者信息。采用 Kaplan-Meier 法绘制生存曲线, 构建 AG 模型估计生存期内纤维蛋白原与非小细胞肺癌患者总体生存的关联, 利用限制性立方样条函数拟合两者的剂量-反应关系。

结果: 生存期内共有 530 例患者发生死亡, 多因素 AG 模型结果提示纤维蛋白原是非小细胞肺癌患者总体生存的独立预后因素, 其中较高的纤维蛋白原水平提示较差的总体生存 ($HR=1.35$, $P<0.05$)。同时纤维蛋白原水平与非小细胞肺癌患者总体生存呈现出显著的非线性关系 ($p\text{-Nonlinear}=0.68>0.05$)。

结论: 较高的纤维蛋白原水平是非小细胞肺癌患者总体生存的危险因素, AG 模型是估计时依性变量与生存结局关联的理想选择。

【关键词】 纤维蛋白原; 非小细胞肺癌; 总体生存; Anderson-Gill 计数过程模型

基金资助: 本项目获云南省基础研究计划面上项目基金资助 (202201AT070200); 获云南省教育厅科技创新团队、昆明医科大学一流学科团队基金资助 (2024XKTDTS16)

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职业性噪声暴露对听力损失和血压的影响： 一项基于职业健康核心指标常规监测的横断面研究

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【目的】

职业性噪声暴露是制造业、建筑业等行业重点职业病危害因素，既往研究多关注其对听力的直接影响，而对血压异常等全身性健康风险的探讨尚不充分，尤其是噪声与听力损失的协同效应仍存在显著空白。本研究旨在探讨职业性噪声暴露对四类听力损失（WHO 定义的听力损失、双耳高频平均听阈提高、较好耳平均听阈加权值提高、高频合并语频听力损失）及血压异常（高血压、正常高值、单独收缩期高血压、单独舒张期高血压）的影响，以及评估听力损失在噪声致血压异常中的中介作用及两者联合效应。

【方法】

研究采用横断面研究设计，依托“广东省重点职业病监测项目——职业健康核心指标常规监测”，以参加职业健康检查的劳动者为研究对象，通过标准化职业健康检查获取听力检测（纯音听阈测试）、血压测量（诊室血压）、工作场所职业病危害因素及人口学信息。统计分析：使用 R 4.3.2 软件，采用多因素 logistic 回归分析噪声暴露与结局的关联，校正年龄、性别、BMI、吸烟、工龄等混杂因素；按人口学特征分层评估异质性；采用人群归因分数（PAF）量化疾病负担。

【结果】研究共纳入 1360915 名劳动者，其中职业性噪声暴露组 885237 人（65.05%），未暴露组 475678 人（34.95%）。职业性噪声暴露显著增加听力损失和血压异常患病风险，在听力损失方面，与高频合并语频听力损失风险增加最为显著（OR=2.43，95%CI: 2.33-2.54）；在血压异常方面，则以对单独收缩期高血压的影响尤为明显（OR=1.42，95%CI: 1.39-1.46）。听力损失与血压异常之间也存在显著关联，其中高频合并语频听力损失对单纯收缩期高血压风险影响最强（OR=1.41，95%CI: 1.32-1.51），较好耳平均听阈加权值提高组可增加高血压患病风险 27%（OR=1.27，95%CI: 1.24-1.30）。此外，职业性噪声暴露与听力损失的联合效应显著增加血压异常患病风险，尤其是噪声暴露合并高频语频听力损失时单纯收缩期高血压患病风险增加 93%（OR=1.93，95%CI: 1.79-2.08）。亚组分析结果显示，噪声暴露与听力损失和血压异常的关联在年龄分组中呈现“U”型规律，其中 18-29 岁青年群体表现出最强的关联性，尤其在高频合并语频听力损失方面最为显著。BMI 分层分析发现，噪声暴露与听力损失的关联在体重过低

(BMI<18.5) 人群中最强, 尤其在高频合并语频听力损失方面最为显著 (OR=3.37, 95%CI: 2.76-4.15), 且随着 BMI 增加, 关联强度呈现逐渐降低的趋势。人群归因分析显示, 消除职业性噪声暴露可减少 14.44%-48.23% 的听力损失病例和 8.13%-21.64% 的高血压病例。

【结论】

本研究研究发现职业性噪声暴露显著增加听力损失和血压异常的患病风险, 且在青年群体、体重过低人群中的关联更强, 因此, 在制定职业防护相关政策时需优先纳入健康监测与干预范围。噪声暴露与听力损失的联合效应在血压异常结局中, 均高于单一暴露效应, 提示工作场所需同步实施噪声控制与听力保护措施。

中高强度运动和超重肥胖的联合作用与儿童青少年血压偏高的关联

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【摘要】研究背景: 近年来, 我国儿童青少年血压偏高检出率呈逐年上升趋势, 而既往研究多集中于单一因素对血压偏高的影响, 较少探讨超重肥胖与运动的联合作用或交互作用, 也不清楚运动是否能抵消超重肥胖对高血压的危害。

目的: 探讨儿童青少年中高强度运动和超重肥胖的联合作用与血压偏高的关联, 为血压偏高的科学防控提供依据。

方法: 使用分层随机整群抽样方法, 抽取武汉市 13 个行政区 91 所学校的 7-18 岁儿童青少年进行体格检查和问卷调查, 采用单因素和多因素 Logistic 回归模型分析中高强度运动和超重肥胖与血压偏高的关联及二者的联合作用, 运用相乘模型和相加模型计算中高强度运动和超重肥胖与血压偏高的交互作用。

结果: 共纳入 21 864 名儿童青少年, 年龄为 (14.38 ± 2.59) 岁, 男生 11 485 (52.53%) 名, 血压偏高 4 572 (20.91%) 名。调整相关协变量后, 非每天中高强度运动者、超重肥胖者血压偏高检出率分别较每天中高强度运动者、非超重肥胖者更高, OR 值 (95%CI) 分别为 1.334 (1.185~1.503)、2.129 (1.990, 2.278), 均 $P < 0.05$ 。联合作用分析显示, 非每天中高强度运动且非超重肥胖者、每天中高强度运动且超重肥胖者、非每天中高强度运动且超重肥胖者血压偏高检出率较每天中高强度运动且非超重肥胖者依次增高, OR 值 (95%CI) 分别为 1.268 (1.071, 1.501)、2.001 (1.596, 2.510)、2.710 (2.290, 3.207), 均 $P < 0.05$, 且在亚组 (女性、小学、非吸烟者及汉族) 中仍然有意义。交互分析提示, 非每天中高强度运动和超重肥胖对血压偏高既无相乘交互作用 ($OR=1.068$, $95\%CI=0.843\sim1.353$), 也不能说明存在相加交互作用, 相对超额危险度 (RERI)、归因百分比 (AP) 和协同指数 (SI) 分别为 0.441 (0.013, 0.770)、0.162 (0.013, 0.296) 和 1.347 (0.985, 1.841)。

结论: 中高强度运动和超重肥胖对血压偏高的检出风险不存在交互作用, 但存在联合作用, 每天中高强度运动可部分抵消超重肥胖对血压偏高的危险。建议控制儿童青少年 BMI 的同时, 鼓励其每天进行中高强度运动以降低血压偏高的风险。

基金资助: 本项目获武汉市科技局基础研究项目基金资助 (2023020201010205)

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中国老年人群艾滋病报告发病与死亡的趋势分析、年龄-时期-队列效应及预测研究

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【摘要】研究背景: 近年来, 中国老年人群艾滋病 (HIV/AIDS) 流行趋势显著上升, 已成为新的公共卫生挑战。随着老龄化加剧及医疗技术进步, 老年 HIV/AIDS 病例增加, 评估老年群体 HIV/AIDS 的报告发病和死亡趋势, 对优化防控策略、实现“健康中国 2030”目标具有重要意义。

目的: 本研究旨在探讨中国老年人群 HIV/AIDS 报告发病和死亡的历史趋势 (2004-2018 年), 分析年龄-时期-队列效应, 并预测未来 (2019-2030 年) 报告发病和死亡率的变化趋势。

方法: 本研究利用中国公共卫生科学数据中心提供的 2004-2018 年 HIV/AIDS 发病与死亡数据, 研究对象为 50-79 岁老年人群, 数据按年龄组 (5 年一组) 和性别分类。采用贝叶斯年龄-时期-队列 (APC) 模型进行统计分析, 模型使用一阶高斯随机游走 (RW1) 先验估计效应值, 采用二阶高斯随机游走 (RW2) 先验预测未来发病与死亡趋势。

结果: 2004-2018 年间, 中国老年人群 HIV/AIDS 报告发病率显著增加, 男性从 0.56/10 万增至 20.78/10 万, 女性从 0.28/10 万增至 7.84/10 万; 死亡率男性从 0.05/10 万增至 6.65/10 万, 女性从 0.02/10 万增至 1.63/10 万。年龄效应方面, 男性发病效应值持续波动 (从 0.09 降至 -0.05), 女性显著下降 (从 0.46 降至 -0.94); 死亡效应性别差异明显, 男性 75-79 岁最大 (0.31, 95%CI: -0.01~0.60), 女性 50-54 岁最大 (0.09, 95%CI: -0.27~0.44)。然而, 在时期效应和队列效应方面, 没有发现显著性别差异。时期效应方面, 发病和死亡效应值均持续上升 (男性发病: -2.23~1.49; 女性发病: -1.95~1.46; 男性死亡: -3.21~1.73; 女性死亡: 女性: -2.65~1.51)。队列效应波动明显, 总体趋势先升后降, 男性发病效应值在 1938 年最高 (0.20), 1963 年最低 (-0.25); 女性则在 1945 年最高 (0.15), 1924 年最低 (-0.23); 男性死亡效应值在 1940 年最高 (0.35), 1924 年最低 (-0.50); 女性则在 1943 年最高 (0.36), 1924 年最低 (-0.66)。预测显示, 到 2030 年男性报告发病率将升至 96.25/10 万, 女性 44.90/10 万; 男性死亡率升至 48.27/10 万, 女性 13.67/10 万。

结论: 中国老年人群 HIV/AIDS 报告发病与死亡率持续上升, 未来仍将显著增加, 老年男性人群受影响更为严重。面向老年群体实施干预、加强性教育、早期筛查及抗病毒治疗推广, 重点关注老年男性, 是降低老年人群 HIV/AIDS 负担的关键。

基金资助: 本项目获国家自然科学基金 (82103947)、广州市科技计划项目 (202206080003, 2024A04J4623) 基金资助。

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中国高血压患者 24 小时尿钠、尿钾排泄及钠钾比与血压的 关联

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【摘要】

研究背景: 高血压患者中尿钠、尿钾及其比值与血压的剂量反应关系尚不清楚。

目的: 探究我国高血压患者 24 小时尿钠、尿钾和钠钾比与血压的关联强度。方法: 数据源于 2005-2009 年中国前瞻性城乡流行病学研究基线横断面调查。使用多元线性回归模型分析 24 小时尿钠、尿钾和钠钾比与收缩压、舒张压的关联, 并使用限制性立方样条绘制关联曲线。

结果: 共纳入 17 920 名高血压患者, 平均年龄 54.7 ± 8.8 岁, 女性 10 143 人 (56.6%)。平均尿钠排泄 5.7 ± 1.7 g/d, 尿钾排泄 2.1 ± 0.5 g/d, 钠钾比 2.8 ± 0.8 。校正混杂因素后, 尿钠排泄每增加 1 g/d 与收缩压 (1.49 mm Hg [95%CI, 1.32~1.66]) 和舒张压 (0.19 mm Hg [95%CI, 0.09~0.29]) 升高有关。尿钾排泄每增加 1 g/d 与收缩压无关, 与舒张压 (-0.69 mm Hg [95%CI, -1.06~-0.32]) 呈负相关。钠钾比每增加一个单位, 与收缩压 (3.44 mm Hg [95%CI, 3.08~3.79]) 和舒张压 (0.74 mm Hg [95%CI, 0.53~0.95]) 升高有关。

结论: 尿钠和钠钾比与收缩压和舒张压呈正相关, 尿钾只与舒张压呈负相关。建议减少钠摄入、增加钾摄入来加强我国高血压患者血压管理。

基金资助: PURE 中国区研究部分经费来自加拿大 McMaster 大学人群健康研究所, 部分经费来自新探健康发展研究中心, 部分经费来自国家心血管病中心/国家心血管疾病临床医学研究中心 (NCRC2020002; NCRC2023-GSP-GG-36; NCRC2023-012; 2022-PUMCH-C-026; 2022-GSP-PT-10; 2020YFC1107900)

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中国偏头痛和紧张型头痛的发病趋势分析及预测研究

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【摘要】研究背景：头痛疾病是一类常见的神经系统疾病，具有较高的患病率和致残率。中国是头痛疾病的高发地区，且发病率呈逐年上升趋势，对中国国民健康和社会经济造成了巨大压力。了解头痛疾病的流行趋势并进行提前干预，能节省大量公共财政的资金，提高国家年轻劳动力的生活质量。

目的：分析 1990-2021 年我国偏头痛和紧张型头痛的人群分布特征与整体发病趋势规律，探究年龄-时期-队列效应对发病风险的影响，识别高风险人群并预测未来发病情况，为相关政策制定提供支撑，助力实现“健康中国 2030”规划目标。

方法：本研究基于 GBD 2021 数据库中分性别和年龄的偏头痛和紧张型头痛的发病数据，采用描述性研究分析整体发病趋势；利用 Joinpoint 模型分析平均年度百分比变化；运用 APC 模型评估年龄、时期和出生队列效应对发病风险的影响；利用 BAPC 模型预测未来发病情况。

结果：描述性研究结果显示，中国偏头痛和紧张型头痛发病均呈先上升后下降的趋势，女性发病高于男性，紧张型头痛高于偏头痛。Joinpoint 分析结果显示，我国偏头痛和紧张型头痛 ASIR 均呈上升趋势，男性高于女性。APC 模型结果显示，偏头痛的发生风险在 10-14 岁组最大，此后呈波动性下降趋势，随时期推移下降，随出生队列的推移上升；而紧张型头痛发生风险随年龄增加呈波动性变化，在 65-69 岁组达到最高值，随时期推移先上升后平稳，随着出生队列的推移先下降后上升。BAPC 模型预测结果显示：预计到 2030 年，中国全人群和男性人群偏头痛的 ASIR 将增加，女性的 ASIR 将下降；紧张型头痛的 ASIR 在男性和女性群体中均呈增长趋势。

结论：中国偏头痛和紧张型头痛发病整体呈上升趋势，女性高于男性，年轻群体易患偏头痛，老年群体易患紧张型头痛。未来我国两类头痛疾病负担将加重，尤其是 60 岁以上老年群体。提示应制定针对性的公共卫生政策，以青春期为防控重点，早期识别并实施预防策略，加强女性和老年群体头痛管理。

基金资助：本项目获四川省科技厅重点研发项目 (No. 2024YFFK0348) 和教育部人文社会科学研究规划基金项目 (24YJAZH217) 基金资助

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中国人群癫痫遗传易感位点的全基因组关联分析研究

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【摘要】

研究背景: 癫痫是一种常见的神经系统疾病, 遗传因素在其发病机制中扮演重要角色。全基因组关联分析 (GWAS) 为揭示癫痫的遗传基础提供了有力工具。然而, 针对中国人群的癫痫 GWAS 研究仍较为有限。

目的: 本研究旨在通过 GWAS 鉴定中国人群中与癫痫显著相关的单核苷酸多态性位点 (SNP), 为阐明癫痫的遗传机制提供新证据。

方法: 本研究纳入了 2024 年 1 月至 7 月于中山大学第七附属医院首诊的癫痫患者作为病例组 (共 110 人) 和非癫痫患者作为对照组 (共 1503 人)。参与者的血液样本采用 Infinium Asian Screening Array (ASA) BeadChip 24+ v1.0 进行基因分型, 使用 Michigan Imputation Server 2 对常染色体基因型进行插补。经软件质量控制后, 保留 1571 名个体和 613.2 万个 SNP。采用逻辑回归模型进行关联分析。

研究结果: 通过 GWAS 分析, 本研究发现 107 个与癫痫显著相关的 SNP ($P < 5 \times 10^{-5}$), 经多重检验校正后保留 94 个显著位点。其中, CADM2 基因内含子区域的 rs77016639 显示出最强关联 ($P < 0.0001$, 优势比[OR]=5.854), 其次为 CADM2 基因内含子区域的 rs11127879 ($P < 0.0001$, OR=5.408) 和 WDR20 基因同义变体 rs6575900 ($P < 0.0001$, OR=4.112)。这些 SNP 主要集中于 3 号、10 号和 14 号染色体, 涉及 CADM2 (3 号染色体)、HTR7 (10 号染色体)、HSP90AA1、WDR20 及 MOK (14 号染色体) 等基因。

结论: 本研究成功鉴定出多个与中国人群癫痫发病相关的遗传位点, 为后续功能验证和精准诊疗提供了重要线索和依据。

基金资助: 广东省珠江人才计划项目

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中国西北地区 40 岁以上女性初潮年龄的长期趋势

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【摘要】研究背景：初潮年龄（AAM）是女性生殖生命周期的起点，过早启动不仅影响青春期发育，更与围绝经期及绝经后女性的长期健康风险显著相关。AAM 受遗传、营养、环境及社会经济等多因素综合影响。流行病学研究表明，全球及中国女性初潮年龄呈提前趋势。既往中国研究多聚焦东部发达地区，而针对具有多民族特色、经济发展相对滞后的西北地区研究尤为匮乏。深入分析西北地区该人群 AAM 的长期变迁规律及其群体差异，对于揭示其生殖健康特征、评估特定健康风险、并制定精准化预防保健策略至关重要。

目的：描述中国西北地区 40 岁以上女性初潮年龄的长期趋势。

方法：选取 2017-2019 年建立的西北区域自然人群队列基线调查中 62948 名女性作为研究对象，采用 Joinpoint 回归模型和一般线性模型分析初潮年龄的长期趋势，评估初潮年龄随时间变化的速率差异。同时，从民族、城乡和教育程度等维度进行分层分析，探讨不同人群特征对初潮年龄变化的影响。

结果：62948 名女性年龄分布范围为 40~79 岁，出生年份跨度 40 年（1945~1984）。40 年间，初潮年龄呈现显著下降趋势（ $P < 0.001$ ），1945-1949 年和 1980-1984 年出生女性平均初潮年龄分别为 (16.00 ± 2.19) 岁和 (14.20 ± 1.92) 岁。1945-1954 年、1955-1962 年、1963-1978 年出生女性初潮年龄分别年均提前 0.07 岁（ $P < 0.001$ ）、0.02 岁（ $P < 0.001$ ）、0.05 岁（ $P < 0.001$ ），1979-1984 年出生女性初潮年龄维持平稳。分层分析显示，城镇女性的初潮年龄呈现出追赶并超过了农村的下降趋势；女性教育水平越高下降速率越快；汉族和回族相较其他民族下降速率更快。

结论：西北地区女性平均初潮年龄逐步提前，至 1979 年后出生女性趋于平稳，40 年间提前了 1.8 岁，不同民族、受教育程度及城乡之间的变化趋势呈现不同特点，卫生部门应根据不同地区采取灵活调整的卫生保健策略。

基金资助：本研究获国家重点研发-精准医学重点专项资助（项目批准号 2017YFC0907200）

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中国中医药资源配置与服务利用协同关系的时空演变及驱动因素研究

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【摘要】研究背景: 中医药作为中国传统文化瑰宝, 在国家政策支持下快速发展, 但其资源配置与服务利用存在区域不均衡问题。研究其协同关系及驱动因素, 有助于优化资源配置, 推动中医药事业可持续发展。

目的: 本研究旨在分析 2012-2021 年中国省际中医药资源配置与服务利用的协同关系及其时空演变, 探讨影响其空间差异的驱动因素与交互作用, 提出区域差异化发展策略, 以推动中医药事业的可持续发展。

方法: 本研究基于 2012-2021 年《中国统计年鉴》等官方数据, 构建中医药资源配置与服务利用两个子系统指标体系, 采用改进熵值法确定权重。运用地理探测器模型, 从因子探测与交互探测角度, 分析区域人口、经济、财政及可及性等因素对协同效应的驱动作用, 同时借助耦合协调度模型等评估两系统协同效应及发展水平, 结合时序演变、空间分布及空间自相关分析, 揭示其时空特征、空间聚集性及交互机制, 为制定差异化中医药协调发展策略提供科学依据。

结果: 中国省际中医药资源配置与服务利用系统总体趋于协调发展, 但存在区域差异, 东部优于中西部。空间自相关分析显示, 协同效应的空间聚集性先增后减, 局部形成热点区和冷点区。地理探测器模型分析表明, 协同效应的空间演变受人口密度、老龄化率和非农产业占比等多重因素共同作用, 表现为非线性增强或双因子交互效应, 且不同时期关键驱动因素有所不同, 前期为人口密度与非农产业占比, 后期为老龄化率与人均 GDP。

结论: 中国省际中医药资源配置与服务利用协同关系总体趋于协调, 但存在空间不均衡性和聚集性。协同效应受人口密度、老龄化率、非农产业占比等多个驱动因素的共同作用。因此, 在制定中医药协调发展策略时, 应建立分层次资源配置支持体系, 强化区域合作与交流, 深入研究驱动因素, 制定差异化发展策略, 促进中医药资源与服务利用均衡发展。

基金资助: 本项目获四川省科技厅重点研发项目 (No. 2024YFFK0348) 和教育部人文社会科学规划基金项目 (24YJAZH217) 基金资助。

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中老年内在能力变动轨迹与中风发生率之间的关联性研究

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目的：探讨老年人群内在能力（IC）动态演变轨迹与中风发病风险的关系，通过异质性亚群识别实现中风高危人群的精准分层。

方法：研究纳入 2011-2016 年中国健康与退休纵向研究（CHARLS）中具有 IC 重复测量数据的 8321 名老年参与者，采用 GBTM 拟合 IC 的纵向变化轨迹，以 2017-2020 年新发中风事件为主要结局，使用 Cox 比例风险回归模型检验 IC 轨迹与中风风险之间的关联。

结果：参与者被分为 3 个 IC 轨迹，分别命名为低稳定 IC 轨迹、中稳定 IC 轨迹和高稳定 IC 轨迹，占研究人群的 41.70%、41.63%和 16.67%。与低稳定 IC 轨迹组的参与者相比，中稳定和高稳定 IC 轨迹组的参与者中风风险降低，多变量调整后的风险比分别为 0.82 (95% CI,0.69 – 0.98)和 0.63 (95% CI,0.47 – 0.85)。

结论：老年人内在能力（IC）纵向轨迹与中风风险相关，高稳定 IC 水平可降低风险。本研究证实 IC 的多维健康价值，基于 GBTM 的轨迹分层精准识别高危人群，为个体化动态干预提供依据。未来需验证 IC 干预对中风一级预防的作用，推动个性化健康管理。

关键词：组轨迹模型

中美印梅毒发病时间趋势比较及预测研究

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【摘要】研究背景: 梅毒是全球性公共卫生问题, 中国、美国和印度作为人口大国, 均为梅毒高负担国家。对比分析三国发病趋势和防控成效, 可为不同发展阶段国家优化防控策略、加强全球联防联控提供科学依据, 助力实现可持续发展健康目标。

目的: 本研究旨在分析 1990-2021 年中国、美国和印度梅毒分性别和年龄的发病趋势及年龄-时期-队列效应对三国梅毒发病风险的影响, 并预测 2022-2030 年中美印三国梅毒的发病趋势, 为优化防控策略提供科学依据。

方法: 本研究基于全球疾病交换数据库 (GHDx) 提供的 1990-2021 年中美印三国分性别、年龄的梅毒发病数据, 采用 Joinpoint 回归模型分析 1990-2021 年中美印三国不同性别、不同年龄组的梅毒发病趋势; 运用年龄-时期-队列模型分析年龄效应、时期效应与出生队列效应对中美印三国梅毒发病风险的影响; 运用贝叶斯年龄-时期-队列模型 (BAPC 模型) 构建中美印三国梅毒发病预测模型, 预测 2022-2030 年三国梅毒的发病趋势。

结果: 1990-2021 年, 中国、美国和印度梅毒标化发病率 (ASIR) 总体呈下降趋势, 女性下降趋势快于男性。然而, 2019-2021 年中国女性 ($APC=12.18\%$; $95\%CI [2.19, 23.15]$) 和印度女性 ($APC=37.16\%$; $95\%CI [30.63, 44.03]$) APC 增长明显。年龄-时期-队列模型结果显示, 年龄效应方面, 中美印男性和女性梅毒发病风险随年龄的增加先增大后减小, 25-29 岁男性和 20-24 岁女性发病风险最高; 时期效应方面, 中美印男性的梅毒发病风险随年份的推移而增加, 2017-2021 年达到顶峰, 女性呈现先上升后下降的趋势, 2002-2006 年达到顶峰; 出生队列效应方面, 中美印男性和女性的梅毒发病风险均随出生队列的推移而下降。BAPC 模型预测结果显示, 到 2030 年, 中国、美国男女和印度男性梅毒 ASIR 呈下降趋势, 印度女性呈上升趋势。

结论: 中美印三国防控成效显著但存在性别和年龄差异, 建议重点加强孕产妇、20-29 岁青年人群及男男性行为者等高风险人群梅毒的预防和筛检, 强化性健康教育, 提高公众对梅毒的认识和防范意识并促进高效筛检技术创新。中国应进一步完善防控体系建设, 推动全球公共卫生事业的协同发展。

基金资助: 本项目获四川省科技厅重点研发项目 (No. 2024YFFK0348) 和教育部人文社会科学研究规划基金项目 (24YJAZH217) 基金资助

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肿瘤药物响应预测模型的泛化能力提升研究： 基于图卷积网络的多模态数据融合与验证策略优化

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【摘要】研究背景: 恶性肿瘤的高度异质性导致患者对抗肿瘤药物响应差异显著, 基于基因组学的精准治疗是重要方向。高通量测序促进了药物响应预测模型发展, 但现有算法普遍存在泛化性能差、临床适用性不足的问题。图卷积神经网络 (GCN) 在处理图结构数据方面有潜力, 但其依赖直推式学习限制了泛化能力, 融入归纳式学习并优化验证策略是关键。

目的: 本研究提出关系异构图卷积网络 (R-HGCN), 将细胞与药物间响应关系预测定义为二部异构图 (BHG) 的链路预测任务, 旨在融合多模态数据与异构图神经网络解决该问题。

方法: 构建以细胞系和药物为节点的二部异构图网络, 依据敏感性阈值定义细胞-药物连边关系。基于细胞系基因表达谱获取细胞节点特征, 通过异构图神经网络聚合邻域信息获取药物节点特征, 最终利用 R-HGCN 进行链路预测。

结果: 在 GDSC 数据集中, R-HGCN 预测准确度达 0.87 ($AUC=0.85$, $AP=0.87$, $F1=0.80$); 在 CCLE 数据集中, 准确度提升至 0.9。与多个基准模型相比, R-HGCN 在准确度和精确度上均有提升。模型稳健性验证显示其泛化能力优于现有方法: 在 PDX 数据中预测 AUC 为 0.62, 在 TCGA 数据中 AUC 为 0.71。此外, 利用模型解释器对参与基因打分, 结果显示靶向药物的靶点基因排名靠前, 表明模型具有生物可解释性。

结论: 基于二部异构图神经网络构建的药物响应预测模型 R-HGCN, 在预测准确性和泛化性上均显著优于基线方法, 并具备生物可解释性, 展现出潜在的临床应用价值。

基金资助: 本项目获国家自然科学基金 (资助编号: 82373680) 和陕西省重点研发计划社会发展领域一般项目 (资助编号: 2025SF-YBXM-204) 资助

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纵向数据下影响正常人群及轻度认知障碍患者发生

阿尔兹海默症的脂蛋白及代谢物分析

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【摘要】 目的: 本研究通过高维惩罚广义估计模型 (PGEE) 和纵向随机森林进行变量筛选, 结合纵向多状态模型分析正常人群及轻度认知障碍患者 (MCI) 发生阿尔茨海默症 (AD) 的脂蛋白及代谢物影响。

方法: 选取 2004 年至 2012 年间, 诊断为正常、轻度认知障碍和阿尔茨海默症的 246 名 ADNI 数据库研究对象, 收集其脂蛋白和代谢物数据。采用 PGEE 和纵向随机森林对 250 个脂蛋白和代谢物数据进行降维, 筛选出主要变量, 并将其纳入纵向多状态模型分析阿尔茨海默症的发生风险。

结果: 筛选出 8 个主要变量, 分析显示低密度脂蛋白胆固醇 (LDL-C)、血糖和总甘油三酯 (TG) 是正常人群和轻度认知障碍人群向阿尔茨海默症发展的危险因素; 而高密度脂蛋白胆固醇 (HDL-C) 在认知轻度障碍转阿尔茨海默症中起保护作用 (HR: 0.867)。中间密度脂蛋白胆固醇 (IDL-C) 在正常人群向认知障碍转归时有保护作用 (HR: 0.567), 但在其他路径中为危险因素。载脂蛋白 A1 (ApoA1)、高密度脂蛋白胆固醇和 ω -3 脂肪酸均能降低正常人群发生阿尔茨海默症的风险, 而高密度脂蛋白胆固醇和 ω -3 脂肪酸则是轻度认知障碍患者向阿尔茨海默症转归的危险因素。

结论: 低密度脂蛋白胆固醇、中间密度脂蛋白胆固醇、血糖和总甘油三酯是正常人群和轻度认知障碍向阿尔茨海默症发展的危险因素, 而高密度脂蛋白胆固醇和 ω -3 脂肪酸具有保护作用。载脂蛋白 A1 和高密度脂蛋白胆固醇是轻度认知障碍向阿尔茨海默症发展的保护因素。

关键词: 阿尔茨海默症; 纵向随机森林; 纵向多状态模型; 危险因素

基金资助: 本项目获 81803337、81872719、82003560 基金资助

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射血分数降低型心力衰竭患者再入院风险预测模型的构建 及验证

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基金项目：山西省基础研究计划资助项目 (202403021221210)；长治市基础研究计划项目 (JC202415)；山西省研究生实践创新项目 (2024SJ411)

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【摘要】背景 心力衰竭在老年人群中具有较高的死亡率和再入院率，而射血分数降低型心力衰竭患者由于其独特的病理生理特征，在诊断和管理方面面临着较大的挑战。**目的** 应用不同机器学习算法构建射血分数降低型心力衰竭患者再入院的风险预测模型，并筛选出最优模型。**方法** 本研究选取了2020年1月至2024年6月期间在长治医学院附属医院住院的537例患者，收集老年患者电子健康档案和随访记录。采用随机抽样法将患者数据按7:3划分为训练集和验证集。基于8种机器学习算法构建预测模型，并通过受试者工作特征曲线 (ROC) 对模型的预测性能进行评估。**结果** 在537例患者中，204例 (37.9%) 发生再入院。经过比较，随机森林算法表现最佳，其性能指标如下：曲线下面积 (AUC) =0.85，准确率=0.77，召回率=0.75。SHAP分析显示，NT-ProBNP、hsTnI、ALB、UA和UREA是最关键的预测因子。**结论** 在评估的8种机器学习算法中，RF模型的预测准确率最高。

关键词：射血分数降低的心衰；再入院；机器学习；预测模型；SHAP

复合膳食抗氧化指数与女性恶性肿瘤的关联

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摘要：背景 恶性肿瘤（乳腺癌、宫颈癌、卵巢癌及子宫癌）是导致全球女性死亡的主要病因。研究表明，膳食抗氧化成分可通过调控氧化应激信号通路影响癌症病理进程，但针对女性特异性恶性肿瘤与复合膳食抗氧化指数 (composite dietary antioxidant index, CDAI) 的关联研究尚不清楚。目的 基于美国国家健康与营养调查 (NHANES) 大样本队列数据，探究 CDAI 与女性特异性恶性肿瘤的流行病学关联，为女性癌症防控的膳食策略优化提供循证依据。方法 纳入 2013-2023 年 NHANES 中 12624 例 ≥ 20 岁女性 (平均年龄 51.15 岁)，基于两次 24 小时膳食回顾数据计算 CDAI (整合维生素 A/C/E、锌、硒及类胡萝卜素摄入量)；应用 Spearman 相关分析评估 CDAI 与妇科肿瘤的线性关联，按 CDAI 四分位分组 (Q1-Q4) 构建多变量 Logistic 回归模型 (分阶段校正人口学、社会经济及生活方式混杂因素)，计算调整后优势比 (OR) 及 95% 置信区间 (95%CI)，并行亚组异质性检验。结果 CDAI 与子宫癌 ($r=-0.023$, $P=0.01$)、宫颈癌 ($r=-0.25$, $P=0.005$) 呈显著负相关，与乳腺癌及卵巢癌无统计学关联 (P 均 >0.05)。多因素模型显示，CDAI 最高四分位组 (Q4) 子宫癌风险较 Q1 组降低 51.2% ($OR=0.488$, 95%CI: 28.5%-83.4%)，且趋势检验显著 ($P=0.011$)。亚组分析提示 CDAI 的保护效应在年龄 <60 岁及肥胖人群中更显著，且未发现年龄、种族等因素的交互作用 (P 均 >0.05)。结论 膳食抗氧化成分的协同补充可显著降低子宫癌发病风险，其中维生素 C/E 及锌的协同摄入模式具有潜在预防意义，为女性肿瘤精准营养干预提供新视角。

Manuscript Title: Based on the Oral Health Network: Explore Links between Oral Health, Biological indicator, Chronic Liver Disease , and All-Cause Mortality

Abstract

Background Periodontitis is a global risk factor for non-alcoholic fatty liver disease (NAFLD) and chronic hepatitis (CH), with unclear Biological indicator roles in its link to their mortality.

Methods Using data from the National Health and Nutrition Examination Survey (NHANES) (2009 – 2014), we analyzed the associations between periodontitis and the prevalence of NAFLD and CH. Multivariate logistic regression, random forest, Boruta, and XGBoost models were employed to identify feature variables. The Kaplan-Meier method assessed the impact of periodontitis, NAFLD, CH, and related variables on all-cause mortality. Dose-response relationships were explored using stratified analysis, interaction studies, and multivariate Cox and restricted cubic spline (RCS) models. Structural equation modeling elucidated the underlying mechanisms of the impact of periodontitis, biomarkers, NAFLD, and CH on mortality.

Results Among 11,414 periodontitis patients, 1,265 (11.1%) died. In periodontitis and coronary CH patients with a TyG index between 9.0 and 9.3, all-cause mortality slightly increased, but decreased when the index exceeded 9.3. In NAFLD patients, mortality slightly decreased when the TyG index ranged from 9.5 to 9.8, but rose sharply when it exceeded 9.8. WBC count significantly impacted mortality in patients with periodontitis combined with CH or NAFLD, with sharp increases when WBC exceeded $6.1 \times 10^9/L$ in CH patients and $7.6 \times 10^9/L$ in periodontitis and coronary NAFLD patients. Hypertension was identified as a key factor influencing chronic liver disease and all-cause mortality. Periodontitis may exacerbate liver burden by elevating WBC count and hypertension, increasing prevalence and mortality in CH patients, and modulate WBC levels to affect metabolic markers, increasing NAFLD risk.

Conclusions Biological indicator like TyG index, WBC count, and hypertension are crucial in reducing chronic liver disease and all - cause mortality risks in periodontitis patients. Monitoring these indicators is helpful for the early identification and intervention of NAFLD and CH.

Coordinated Evaluation of the Efficiency and Equity of the Community-Based Integrated Medical and Elderly Care Service Resources in China

Abstract

Background The community-based integrated medical and elderly care model integrates healthcare and elderly care resources to ensure high-quality services for the aging population. However, due to its late inception and incomplete policies, pilot projects in some areas have led to low efficiency and inequitable resource distribution. This study analyzed resource dynamics from 2017 to 2022, aiming to provide meaningful insights and practical references for other developing countries facing similar challenges.

Methods Data were sourced from the China Statistical Yearbook and China Civil Affairs Statistical Yearbook. Allocation efficiency was evaluated using the Data Envelopment Analysis (DEA) model, while equity was measured through the Gini coefficient, Theil index, and Resource Density Index (RDI). Spatial statistical techniques were employed to identify clustering patterns and delineate cold and hotspot areas. To ensure comparability, the Resource Density Index was standardized using the entropy weight method and paired with efficiency values to analyze the coordination between resource allocation efficiency and equity.

Results Resource totals increased during the study period, but significant regional disparities persisted. Efficiency improved rapidly in the eastern regions, with Tibet and Inner Mongolia performing well, while inequity in the western regions remained pronounced. Zhejiang was the only high-high cluster for efficiency, with hotspot areas shifting from the northeast to Xinjiang and Tibet. Conversely, Xinjiang and Tibet were low-low clusters for equity, while Jiangsu and other eastern provinces demonstrated better coordination. Central, western, and northeastern regions faced dual challenges of low efficiency and equity, highlighting the urgent need for targeted improvement and strategic interventions.

Conclusion China's integrated medical and elderly care services have achieved notable progress; however, significant regional disparities persist, particularly in the western regions, where both efficiency and equity require urgent attention. To address these challenges, the government should prioritize increased investments in the central and western regions, strengthen infrastructure in low-clustered areas, and enhance talent development programs and policy support. Promoting regional collaboration and providing targeted assistance are critical to fostering balanced and integrated development across the country.

潜在剖面与聚类分析法评价青少年多维度健康结局的应用 对比及实例分析

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项目基金: 国家自然科学基金 (82103867); 陕西省重点研发计划 (2024SF-YBXM-310)

【摘要】目的 比较潜在剖面分析、K 均值聚类与高斯混合聚类在评价青少年多维度健康结局指标中的应用表现, 为评价多维度健康结局分析策略的选择提供参考依据。**方法** 数据来源于在陕西农村地区开展的一项关于青少年健康评价的横断面研究, 纳入的健康结局指标包括行为问题得分、认知得分、肺活量、心率、体质指数、收缩压和舒张压, 分别对其进行潜在剖面分析与聚类分析, 将人群分成不同健康模式的亚组; 通过 Davies-Bouldin 指数和 Calinski-Harabasz 指数评价各方法的聚类效果。最后采用 logistic 回归探究青少年不同健康模式的共享病因影响因素。**结果** 纳入研究对象共 1767 人, 中位年龄 12 (11, 12) 岁, 其中男性 1050 名 (59%); 性发育已经启动 1416 名 (83%)。潜在剖面分析、K 均值聚类与高斯混合聚类均将青少年分为 3 类, 且各亚组的健康模式表征类似。以潜在剖面分析分类结果为例, 3 类健康模式可命名为“体格发育预警组”(占总样本量 29.2%)、“基本健康组”(60.2%)和“高行为问题组”(10.6%)。内部评价指标显示, 潜在剖面分析与 K 均值聚类效果优于高斯混合聚类。Logistic 回归影响因素分析结果显示, 较大年龄、性发育已经启动的青少年体格发育预警危险性更高; 年龄越大、男性的青少年也更容易发生情绪行为问题。**结论** 潜在剖面分析可以较好地识别群体中多维度健康结局的健康模式。青少年不同维度的健康结局可能相互影响, 并表现出聚集性趋势, 形成一定的健康模式。针对健康模式的病因学研究, 可以识别不同健康结局的共享危险因素, 为不同干预措施的“打包”式精准定制提供科学依据, 最大化干预措施对多维度健康结局的协同效应。

基于机器学习构建 6-19 岁青少年重金属暴露 与肥胖关联的可解释模型

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摘要

背景: 近几年随着工业产品的日益发展且青少年肥胖患病率的增加, 在日常生活中人们很容易暴露于环境中的重金属混合物, 然而重金属混合物在人体内易蓄积、半衰期长但大多数研究侧重单一重金属与肥胖的关系。此外, 既往的研究大多基于传统统计学方法。引入一种新的分析方法可能有助于更准确地确定重金属暴露与青少年肥胖之间的关系。**目的:** 本研究基于 5 种机器学习方法使用血液和尿液中重金属浓度构建青少年肥胖的机器学习(ML)模型, 找出最优模型, 并对模型的可解释性进行分析。**方法:** 对 NHANES 数据库共 2136 例样本, 使用 AdaBoost、XGBoost、SVM (支持向量机)、KNN (K-近邻) 和 BP (反向传播) 五种算法进行青少年肥胖的机器学习(ML)模型的构建, 并使用 AUC 和精准率-召回率曲线评估模型预测性能, 最后选出最佳预测模型。并结合基于 SHapley 加法解释(SHAP)对模型的可解释性进行分析。**结果:** XGB 模型识别重金属对青少年肥胖的关联最佳, 测试集 AUC 为 0.90, 血液中锰、铅、硒和尿液中钴、铅、锡、钡对青少年肥胖有影响, 其中血硒影响最大。并且血液中的铅和尿液中的钴、铅、锡对模型的贡献值为负值。血硒、血硒和尿液中钡对模型的贡献值为正值。**结论:** XGB 为最佳预测模型, 血液中的铅和尿液中的钴、铅、锡对模型的贡献值为负值。血硒、血硒和尿液中钡对模型的贡献值为正值。还需要进一步的研究来证实这些纵向研究结果。

中国中老年人抑郁症的发病特征和风险预测模型的构建

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摘要

目的: 本研究旨在分析中老年人群抑郁症特征及风险因素, 通过机器学习构建预测模型, 并开发在线工具供用户评估个人抑郁症风险, 以支持抑郁症的早期预防和干预。

方法: 本研究的研究对象来自于中国健康与退休前瞻性队列研究(China Health and Retirement Longitudinal Study, CHARLS)数据库中 2011-2020 年的数据, 抑郁症发病率研究中纳入了 11388 名研究对象, 抑郁症风险预测研究中纳入了 5668 名研究对象。本研究通过单因素差异性分析中的 χ^2 检验和 Z 检验进行基线特征描述, 使用 Lasso 回归(The Least Absolute Shrinkage and Selection Operator)进行变量的筛选。将数据集按照 6:2:2 的比例随机划分为训练集、验证集和测试集。使用逻辑回归 (Logistic Regression, LR)、岭回归 (Ridge Regression, RR)、支持向量机 (Support Vector Machine, SVM)、随机森林 (Random Forest, RF) 以及 XGBoost (Extreme Gradient Boosting, XGBoost) 共 5 种机器学习方法构建抑郁症风险预测模型, 将训练集输入模型进行训练, 将测试集输入模型进行十折交叉验证, 对模型进行内部验证。并结合受试者工作特征 (ROC) 曲线及曲线下面积 (AUC) 评估模型预测性能。最后, 使用 SHAP (SHapley Additive exPlanations) 工具分析预测模型的可解释性, 判断模型在决策过程中各个特征的重要性。本研究采用 python3.9.1 软件进行数据处理与分析。

结果: 抑郁症累积发病率随时间增长, 从 2 年的 17.81% 上升至 9 年的 26.93%, 女性、农村居民和西部地区人群发病率更高。Lasso 回归识别出性别、肌肉质量和自评健康状况为主要影响因素。女性较男性有更高的抑郁风险; 肌肉质量越好, 抑郁风险越低; 良好的自评健康与积极生活态度相关, 有助于减少抑郁症状。模型性能评估上, XGBoost 在预测中老年人群抑郁症发病率方面表现最佳 (AUC 值由 0.824 提升至 0.915), SVM 次之但在特异度方面表现优异。随机森林训练效果好但泛化能力有限, Logistic 和 Ridge 回归结果稳定但性能稍逊。因此, XGBoost 为最优选择, SVM 适用于高特异度的情景。基于 XGBoost 模型的 SHAP 分析进一步确认了性别、肌肉质量和自评健康状况的重要性及其多维度影响机制。

结论: XGBoost 在预测中老年人群抑郁症发病率方面为最优模型。性别、肌肉质量和自评健康状况对于抑郁症预防和干预至关重要, 并建议未来研究与临床实践

应重点关注这些因素以提高抑郁症高风险人群的识别和针对性预防措施的有效性。

创新点：首先，本研究首次系统运用 CHARLS 数据库中的多维度纵向数据进行中国中老年人群抑郁症风险评估。其次，通过对比多种机器学习模型确定最优模型，为后续研究提供方法学依据。最后，基于最优模型开发的在线平台，实现了个性化抑郁风险评估与预防建议功能，有效提升了公众对抑郁症的认知及自我管理能力。

Competing Weibull Survival Models with Regularizations for Multiple Cause

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August 2024

Abstract

System failures often arise from the simultaneous effects of multiple causes, making it challenging or even impossible to attribute a failure to a single cause. This situation frequently occurs in fields such as epidemiology, where multiple contributing causes of death are common, and in biomarker research for neurodegenerative diseases. We propose a competing Weibull model with regularisations for multiple causes, incorporating a data-driven, individualised, and time-varying winning probability (relative importance) matrix. By preserving linear structures in competing groups, it allows for clear interpretation while also accommodating non-Weibull distributed time. The model parameters are estimated using maximum likelihood estimation within an expectation-maximisation (EM) algorithm framework, ensuring consistency and asymptotic normality. We demonstrate the model's effectiveness through numerical simulations and applications to biomarker combinations predicting progression from mild cognitive impairment (MCI) to Alzheimer's disease, as well as survival times of hospitalised patients. Our approach consistently outperforms traditional Weibull and Cox proportional hazards models in addressing cause-mixture challenges and identifying informative biomarker combinations.

基于集成嵌套拉普拉斯近似的计量与两分类资料纵向与生存数据联合模型构建及应用研究

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【摘要】目的: 针对当前联合模型中多变量纵向子模型常关注于计量资料且参数估计效率低的问题, 构建基于计量与两分类资料纵向与生存数据联合模型, 提升运算效率, 拓展当前应用范围。 **方法:** 共分为模拟研究和实例研究两部分。通过构建计量与两分类资料纵向子模型与生存子模型, 将构建的联合模型按照不同关联结构在不同随访次数、样本量及关联系数场景下, 使用集成嵌套拉普拉斯近似参数估计方法进行模拟研究, 并选择最优的关联结构。实例研究选取中国健康与养老追踪调查受访者进行纵向研究, 通过联合模型研究认知功能得分和抑郁情况对发生心血管事件的影响。 **结果:** 模拟研究发现联合模型在当前值关联结构中具有较好的稳定性, 表现出较低的绝对偏倚 (0.0009~0.1421)、参数标准误 (0.0077~0.0351) 及较准确的 95% 置信区间覆盖率 (0.825~0.965)。实例研究发现认知功能得分和抑郁情况因素对心血管发生的影响在男女性别上存在差异, 认知能力得分仅在男性中被认为具有关联 ($HR=1.035$, 95% CI : 1.008~1.062), 抑郁情况对男女性的危险程度分别为 ($HR_{男}=1.207$, 95% CI : 1.101~1.324; $HR_{女}=1.515$, 95% CI : 1.203~1.907)。 **结论:** 构建的计量与两分类资料纵向与生存数据联合模型在集成嵌套拉普拉斯近似参数估计方法下有较好的模拟效果和稳定性, 为当前的纵向与生存数据分析提供新的统计学方法参考。

A Clinically Interpretable Deep Learning Model for Dynamic Prediction Using Restricted Mean Survival Time

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【Abstract】

Background: In the field of healthcare, survival prediction models have exhibited immense value in clinical practice. Most existing models utilize survival probability as the prediction outcome; however, in the context of chronic progressive diseases such as Alzheimer's disease, the restricted mean survival time (RMST) reflects the patient's life expectancy and is more intuitive to interpret. In dynamic prediction, RMST can be extended to conditional RMST (cRMST) to adjust the life expectancy on the basis of the time a patient has already survived.

Objective and method: In this paper, we developed a novel interpretable deep learning-based RMST dynamic prediction model called *Dynamic-DeepRMST*. To enhance both accuracy and interpretability, we modified the Transformer model to effectively capture longitudinal data representations for prediction and to transparently quantify the input–output relationship.

Results: Compared with existing RMST static and dynamic regressions, the proposed model demonstrated superior performance under different simulation scenarios. Furthermore, we applied Dynamic-DeepRMST to Alzheimer's Disease Neuroimaging Initiative (ADNI) data to explain the impact of covariates on survival time from both individual-level and population-level analyses, thereby providing insights for clinical prognosis. Our model not only reveals how longitudinal changes in covariates differentially affect survival time but also identifies the relevance among covariates and their importance in survival prediction evolving over time. To our knowledge, this paper is the first in which an interpretable deep learning dynamic prediction model was investigated.

TransVSurv: 基于 Transformer 的动态生存分析框架

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【摘要】

目的: 在生存分析任务中, 时序依赖性、个体异质性一直是影响模型准确建模的关键因素, 尤其是当这些因素存在复杂的交互作用时, 传统模型往往难以有效应对, 导致预测准确性和临床决策支持能力受限。

方法: 为应对上述挑战, 本研究提出了一种基于 Transformer 的动态生存分析模型 TransVSurv (Transformer-based Survival Analysis Model, TransVSurv)。该模型利用 Transformer 的多头自注意力机制捕捉时间序列中的时序依赖关系, 并通过引入变量选择层增强对静态和动态变量的建模能力, 从而提升风险预测的准确性和模型的可解释性。

结果: 对比实验结果表明, TransVSurv 在模拟数据集和真实临床数据集上均表现出色, 稳定优于现有主流方法。此外, 变量选择结果与领域先验知识高度一致, 验证了模型的可靠性和实用性。

结论: TransVSurv 能有效融合时间依赖信息与变量选择机制, 提升生存分析中的预测准确性与解释能力, 为复杂健康数据的风险建模提供了一种通用、可扩展的新框架。

Model-free feature screening based on data aggregation for ultra-high dimensional longitudinal data

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Abstract

Ultra-high longitudinal data feature screening procedures have been widely studied, but most require model assumptions. The screening performance of these methods may not be excellent in the presence of model misspecification. To address this, we propose a novel model-free method where feature screening is performed by data aggregation, a technique widely used in massive data. Distance correlation is used to measure the dependence between predictors and response at each time point separately, while longitudinal correlation is modeled by a specific cumulative distribution function to achieve efficiency. In addition, we extend this new method to reduce the correlation between highly correlated predictors. Asymptotic properties of our proposed methods are strictly proven, including sure screening and rank consistency properties. Numerical examples show that our methods outperform several longitudinal data and model-free feature screening procedures in different longitudinal supervised problems. Finally, we apply the new method to analyze a gut microbiome dataset to demonstrate its superior empirical performance.

基于单细胞转录组测序和机器学习的多发性硬化症诊断模型构建

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【摘要】 目的: 多发性硬化 (Multiple Sclerosis, MS) 是一种以中枢神经系统慢性炎症和神经退行为主要特征的自身免疫性疾病。虽然发病率较低, 但因其预后不良且致残率高, 早期诊断对延缓神经损伤及改善患者结局至关重要。然而, 现有临床检测手段 (如脑脊液分析和影像学评估等) 存在费用高、操作复杂且特异性不足等局限性。因此, 筛选高特异性且采样便捷的血液生物标志物构建诊断模型, 对构建“筛查-诊断-干预”三位一体的疾病早期防治路径具有重要临床价值; 方法: 本研究整合单细胞转录组测序 (Single-cell RNA sequencing, scRNA-seq) 与批量转录组测序 (Bulk RNA sequencing, Bulk RNA-Seq) 数据, 从“细胞水平”到“个体水平”跨层次地解析 MS 血液组织免疫微环境特征。首先, 对 scRNA-seq 数据中髓系细胞进行主成分分析和聚类分析, 可视化呈现 MS 患者和健康人群的细胞异质性。聚焦中性粒细胞 (Neutrophils, Neu) 亚群, 利用 Wilcoxon 秩和检验鉴定 Neu 差异表达基因 (Neutrophils Differentially Expressed Genes, Neu-DEGs), 并进行基因本体论 (Gene Ontology, GO) 富集分析和细胞通讯分析。其次, 将 Neu-DEGs 映射到 Bulk RNA-Seq 数据中, 先采用单因素 Logistic 回归初步筛选与 MS 诊断相关的 Neu-DEGs, 再结合最小绝对收缩和选择算法 (Least Absolute Shrinkage and Selection Operator, LASSO) 算法和支持向量机递归特征消除算法 (Support Vector Machine Recursive Feature Elimination, SVM-RFE) 算法进行变量降维, 得到核心 Neu-DEGs。最后, 基于多因素 Logistic 回归、支持向量机 (Support Vector Machine, SVM)、随机森林 (Random Forest, RF) 和极致梯度提升 (eXtreme Gradient Boosting, XGBoost) 四种方法构建诊断模型, 并使用准确率、召回率、特异性、精确率、F1 分数和受试者工作特征曲线下面积 (Area Under Receiver Operating Characteristic Curve, AUC) 对模型进行评价。结果:

(1) 与健康对照组相比, MS 患者血液中性粒细胞比例呈现显著上调, 并鉴定 398 个 Neu-DEGs。GO 富集分析显示, Neu-DEGs 显著富集于吞噬杀菌及细胞迁移等免疫功能。细胞通讯结果表明, MS 组 Neu 中 IL1 和 CCL 信号通路

特异性 激活，提示其介导血脑屏障渗透的潜在机制；(2) 398 个 Neu-DEGs 映射到 Bulk

RNA-Seq 数据中得到 246 个 Neu-DEGs，初步筛选 67 个与 MS 诊断相关的 Neu- DEGs，降维后得到 11 个核心 Neu-DEGs: B2M、ISG20、LYN、IFIT2、ATP2B1 、SEC14L1 、GNA13 、SULT1A1 、CTSB 、GSTK1 和 TMEM160 。

(3) 在基于四种 算法构建的 MS 诊断模型中, Logistic 、SVM 、RF 、XGBoost 验证集 AUC 值依 次为 0.771 、0.802 、0.835 、0.994 。XGBoost 模型展现出卓越鉴别效能 (准确率 =0.945, 召回率=0.974, F1 分数=0.955), 显著优于传统 Logistic 回归及随机森林 等模型。XGBoost 模型的特征重要性排序前三位的变量依次为: IFIT2 、ISG20、 GAN13 。结论: (1) MS 患者中性粒细胞通过 IL1 和 CCL 信号通路异常激活驱 动免疫炎症级联反应，其吞噬杀菌与迁移功能可能参与血脑屏障破坏及神经退行 进程。(2) 基于 11 个核心 Neu-DEGs 构建的 MS 诊断模型中，与 Logistic 回归、 支持向量机和随机森林相比，XGBoost 模型展现出最优的诊断性能。

Identifying determinants of spatio-temporal heterogeneity of Other Infectious Diarrhea in Ningxia Hui Autonomous Region, China: Insights from Bayesian Models

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Abstracts

Background Other infectious diarrhoea (OID) exerts a considerable impact in China, characterized by regional variations in incidence that present significant public health challenges. Although Ningxia is among the regions with high OID incidence, the spatial and temporal distribution patterns of morbidity risk, along with the influencing factors, have not been thoroughly investigated. This study aims to analyse the spatial and temporal distribution characteristics of OID in the Ningxia region from 2010 to 2022 and to explore the influence of meteorological conditions, socio-economic status, and natural resources division on OID incidence.

Methods Data were meticulously collected at the county level from January 2010 to December 2022 to delineate the overall incidence profile of OID and its spatial and temporal distribution in Ningxia. A Bayesian spatio-temporal model was developed to assess the relationships between meteorological, socio-economic, and natural resource factors and the heterogeneity of the spatial and temporal distribution of OID incidence risk.

Results The results indicate that the incidence of OID in Ningxia region has generally

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followed a downward trend, reaching its peak in 2018 and its lowest in 2022. Spatially, the incidence and risk of OID exhibited notable heterogeneity across regions. Temporally, OID incidence exhibited significant seasonal fluctuations, following a bimodal pattern. Bayesian spatiotemporal interaction model suggests that average monthly temperature, average family size, natural growth rate, proportion of the urban populations, number of medical institutions, number of primary schools, and land designated for agricultural use are positively correlated with OID incidence risk. Conversely, monthly precipitation, monthly sunshine hours, and land for construction are negatively correlated.

Conclusion These findings provide a scientific basis for OID prevention and control, offer references for managing OID in Ningxia, and inform the development of evidence-based public health policies and interventions.

基于人口流动的流感样病例预测与医疗资源挤兑动态模型研究

摘要

目的：本研究旨在评估急性传染病暴发期间，区域间人口流动对疫情发展及医疗资源挤兑的影响，为疫情期间的人口管控和医疗资源配置提供科学依据。

方法：以流感样感染疫情为例，选取“太原-晋中”与“临汾-运城”两组城市作为研究对象并基于流感样感染病毒传播的实际数据和百度人口迁徙指数，构建结合人口流动因素的医疗资源动力学模型。以累积感染人数、医疗资源挤兑的开始时间及持续时长作为量化指标，分析不同城市间疫情传播动态及医疗资源挤兑情况，以探讨人口迁徙率对感染规模及医疗资源挤兑的影响。

结果：模型拟合曲线与实际数据高度吻合，大部分实际数据点落在 95%置信区间内。研究表明，人口流动会对累积感染人数和医疗资源挤兑产生影响，同时这种影响会因地区而异。单向人口流动管控，对流出地可减少累积感染人数，延迟医疗资源挤兑的发生时间并缩短其持续时长，但对流入地同时会增加累积感染人数，提前医疗资源挤兑的发生时间并延长其持续时长。双向人口流动管控，在感染人数较多的地区，累积感染人数增加，医疗资源挤兑的开始时间保持不变，持续时长不变或有所延长；而在感染人数较少的地区，累积感染人数减少，医疗资源挤兑的开始时间不变，持续时长不变或缩短。

结论：医疗资源动力学模型可有效模拟人口流动、疫情传播与医疗资源挤兑之间的关系。当出现传染病疫情爆发时，可将该模型嵌入区域统一的医疗资源调度平台，并结合各地疫情态势与医疗资源能力，遵循“分区、分类、分时”的原则，实施精准干预，从而控制感染规模、缓解医疗资源挤兑、减少社会经济干扰。

从总体到亚型：医生诊断的睡眠障碍及其呼吸暂停亚型对糖尿病风险的纵向效应分析

摘要

目的：本研究旨在探讨医生诊断的睡眠障碍与糖尿病患病风险之间的关联，分析该关联在性别和种族亚组中的异质性，并检验睡眠性呼吸暂停亚型与总体效应的一致性 & 特异性。

方法：首先基于 2016 年至 2020 年美国健康与退休研究 (HRS) 的纵向数据，主分析中纳入 19,943 名 45 岁以上中老年人，亚型分析纳入 19,125 名。睡眠障碍由医生诊断确认，糖尿病通过标准化问卷评估。然后，采用倾向性得分匹配 (PSM) 方法进行 1:1 匹配，应用广义估计方程 (GEE) 模型估计睡眠障碍与糖尿病风险的关联，并通过性别 (男性/女性)、种族 (白人/黑人/其他) 分层进行亚组分析。敏感性分析剔除随访中新发睡眠障碍数据以验证结果稳健性。最后，筛选出睡眠性呼吸暂停亚型重复上述方法，并与主分析结果进行比较分析。

结果：主分析显示，医生诊断的睡眠障碍显著增加糖尿病风险 ($OR = 1.477$, 95% $CI: 1.167 - 1.870$, $P = 0.001$)。女性亚组中关联更强 ($OR = 2.084$, 95% $CI: 1.406 - 3.088$, $P < 0.001$)，而男性未达显著性 ($OR = 1.231$, $P = 0.232$)。白人亚组效应显著 ($OR = 1.720$, $P = 0.001$)，黑人 ($OR = 1.508$, $P = 0.118$) 和“其他”种族 ($OR = 0.758$, $P = 0.369$) 不显著。睡眠性呼吸暂停亚型分析对于糖尿病患病显示出更高风险 ($OR = 1.689$, 95% $CI: 1.324 - 2.155$, $P < 0.001$)，敏感性分析一致 ($OR = 1.562$, $P < 0.001$)。而在高血压 ($OR = 2.004$, $P < 0.001$)、精神疾病 ($OR = 1.346$, $P = 0.027$)，BMI ($OR = 1.038$, $P = 0.083$) 等其他因素上与主分析结果不同。

结论：医生诊断的睡眠障碍是糖尿病的重要危险因素，女性和白人中效应更显著，睡眠性呼吸暂停亚型在影响糖尿病患病风险上与总体效应一致，而在其他因素水平上存在特异性。公共卫生干预应关注睡眠健康，尤其针对女性和白人，以降低糖尿病风险。

DynaMicNet - 代谢组伪质谱成像深度生成模型开发及应用研究

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【摘要】目的: 优化代谢组学数据预处理策略, 开发基于生成式变分自编码器 (VAE) 模型的动态伪质谱成像 (pMSI) 算法框架, 构建 HIV 感染者 ART 免疫反应预测模型, 提高预测模型的准确性; **方法:** 基于 ART 动态代谢组学 LC-MS 原始检测数据, 使用 XCMS 算法对原始质谱图像进行峰检测、保留时间校正, 并评估不同峰检测参数设置下, 检测质谱峰总数及显著峰比例, 筛选最优峰检测参数集。通过 VAE 对 pMSI 进行数据增强处理, 在完成算法训练后, 提取 VAE 的 128 个潜变量作为 pMSI 的无监督深度特征。链接长短期记忆网络开发 DynaMicNet 算法, 构建 HIV 感染者 ART 免疫反应预测模型, 在训练集中采用五折交叉验证来评估 DynaMicNet 的训练效果, 并通过独立测试集进一步评估 ART 免疫反应预测模型的性能表现。模型性能评价指标包括 F1 值、AUC、准确度、灵敏度和特异度; **结果:** 噪声阈值及信噪比参数对于峰检测结果影响较大, 峰强度噪声阈值及信噪比设置越高, 峰检测算法提取的质谱峰数越少。根据遍历结果, 设置最终峰检测参数为 ppm = 15, midiff = 0.01, peakwidth = c(5, 30), noise = 500, snthresh = 5, prefilter = c(3, 1000)。ML-PLS-DA 得分图显示, 经 VAE 提取 pMSI 特征中, 免疫完全缓解和免疫不完全缓解组间的血浆样本呈现出更强的相对聚集趋势。基于 DynaMicNet 算法构建的预测模型综合性能最佳, 其 AUC, 准确度, F1 值分别为 0.722 (95%CI = 0.519, 0.905), 0.714 (95%CI = 0.524, 0.905), 0.700 (95%CI = 0.429, 0.900)。该算法相较于常规代谢组学策略, AUC 提升 24.1%, 准确度提升 18.9%, F1 值提升 29.9%; 相较于横断面 pMSI 策略, AUC 提升 16.3%, 准确度提升 9.9%, F1 值提升 45.0%; **结论:** DynaMicNet 有效提升了 pMSI 特征提取的效率和准确性, 同时也在预测模型综合性能上取得了较大提升, 为 HIV 感染者免疫反应预测提供了有力工具。

基于加速时间失效模型的生命早期烟草暴露对癫痫长期风险的影响研究

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【摘要】目的: 探讨生命早期烟草暴露, 包括围产期母亲吸烟和个体自身开始吸烟年龄, 与癫痫发病风险之间的关联, 并评估胰岛素样生长因子 1 (IGF-1) 的潜在中介作用; 方法: 基于英国生物银行 (UKB) 数据, 采用加速失效时间 (AFT) 模型及包含时间依存变量的 Cox 比例风险模型, 评估围产期母亲吸烟和个体自身开始吸烟年龄与癫痫发病风险之间的关联, 并应用中介分析探讨 IGF-1 的作用; 结果: 围产期母亲吸烟者的癫痫无病生存时间缩短 8% (TR=0.92, 95% CI: 0.87 ~ 0.98, P<0.01), 癫痫发病风险显著升高 (HR=9.25, 95% CI: 1.91 ~ 44.83, P<0.01)。与从不吸烟者相比, 儿童期、青少年期和成年期开始吸烟者的无病生存时间分别缩短 27%、18%和 13% (P<0.001), 对应癫痫风险分别升高 62%、33%和 22% (P<0.001)。IGF-1 在围产期母亲吸烟与癫痫风险关联之间的中介效应占比为 11% (95% CI: 4% ~ 68%), 在自身开始吸烟年龄的中介效应占比为 6% (95% CI: 3% ~ 14%); 结论: 生命早期烟草暴露显著增加癫痫发病风险, IGF-1 在此关联中发挥部分中介作用。应从围产期开始加强控烟策略与健康干预, 并进一步阐明 IGF-1 的生物学机制, 为癫痫的早期干预与防控提供理论依据。

基于多维项目反应理论的等级反应模型评价 PHQ-4 量表

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【摘要】

目的: 本研究以患者健康问卷-4 (Patient Health Questionnaire-4, PHQ-4) 为例, 基于多维项目反应理论 (Multidimensional Item Response Theory, MIRT) 验证量表的多维结构假设, 探索 MIRT 在心理量表效度检验中的适用性。

方法: 通过探索性 MIRT 比较一维与二维模型的拟合优度, 确定量表的潜在维度数量及各条目的维度归属; 并进一步通过验证性 MIRT 验证 4 条目量表的 7 种二维组合模型的适配度, 寻找最优的条目组合方案, 为 PHQ-4 的效度验证提供经验数据。

结果: 探索性 MIRT: 一维模型与二维模型的拟合结果存在统计学差异 ($\chi^2=70.452$, $P<0.01$), 二维模型中条目的区分度参数较一维模型更佳。根据因子载荷系数与项目信息函数曲线的结果, 条目 1 与条目 2 倾向于归属同一维度, 条目 3 与条目 4 倾向于归属同一维度。验证性 MIRT: 对 4 个条目进行两维度划分, 共存在 7 种可能的组合方式, 其中有三种组合成功收敛。其中“条目 4+条目 1、2、3”组合的多维区分度参数 (MDISC=6.41) 过高。综合考虑变量的总平方和与方差解释比例, PHQ-4 原量表在所有组合中最为均衡。

结论: PHQ-4 量表在二维结构下表现出最佳的拟合效果, 符合理论预期的参数分布, 条目维度归属与原始量表结构一致。MIRT 方法适用于 PHQ-4 的效度验证, 研究结果可为医学、心理学等领域的多维量表开发与验证提供方法学参考。

江苏省老年人焦虑、抑郁及失眠的网络分析

摘要：背景：心理健康是评估健康老龄化的重要维度。老年人群由于日常活动能力受限、社会参与减少以及自理能力下降，更容易出现焦虑、抑郁和失眠症状。本研究旨在探讨老年人群中焦虑、抑郁和失眠症状之间网络关系，识别核心症状和桥梁症状，为干预提供理论基础。方法：使用广泛性焦虑障碍量表(GAD-7)和患者健康问卷(PHQ-9)和失眠严重指数量表(ISI-7)对其焦虑、抑郁和失眠症状进行评估。通过网络分析，研究这些心理障碍的网络结构、核心症状、桥梁症状以及网络的稳定性。结果：2086 名符合要求的老年人被纳入了研究。焦虑、抑郁和失眠 3 种症状检出率分别为 26.85%、16.11%、47.75%。网络分析显示：节点 ISI02 “睡眠维持困难”、ISI06 “他人眼中，睡眠对生活质量影响”、ISI05 “睡眠对日间功能干扰”是中心节点。连接焦虑、抑郁和失眠症状的桥梁节点是 PHQ03 “睡眠问题”、PHQ09 “自杀意愿”、PHQ08 “不安”。结论：网络的中心节点都是与睡眠相关的症状，其在整个网络结构中有着重要的作用，“睡眠问题”作为最重要的桥梁节点，对于焦虑-抑郁的共病网络有着重要的作用。对这些关键症状进行干预和防治，能使老年人群的心理状态有所改善。

基于精细化 SEI_1 I_2 A 模型的某市 HIV/AIDS 传播动力学仿真与精准防控策略研究

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【摘要】目的：本研究旨在构建并应用基于某市本地数据的精细化 SEI_1 I_2 A 动态传播模型，通过引入诊断延迟分层、治疗响应机制及高危人群异质性传播特征，系统评估不同防控策略对 HIV/AIDS 疫情的长期影响，为某市制定精准、高效的艾滋病防控政策提供数据驱动的定量依据，助力实现区域艾滋病疫情的有效遏制与可持续防控。

方法：本研究构建了一个精细化的 SEI_1 I_2 A （易感-潜伏-早诊断感染-晚诊断感染-艾滋病期）动态传播模型，创新性地引入诊断延迟分层（ I_1 / I_2 ）和分阶段治疗响应机制，以更准确地反映 HIV 感染进程与干预效果的异质性。模型参数基于某市 2000-2024 年的监测数据、临床队列数据（如 CD4+T 细胞计数变化轨迹）、人口统计数据及相关文献进行多源数据融合与精细化校准。采用广义可加混合模型（GAMM）等统计方法分析关键参数。通过数值仿真，评估了基线情景下 HIV 传播趋势，并模拟了提高检测率、扩大 ART 覆盖、高危人群行为干预、母婴阻断、强化患者随访等多种干预策略的长期效果。

结果：模型成功拟合了某市历史疫情数据（ $R^2 > 0.96$ ）。基线仿真显示，若无额外干预，疫情将趋于稳定但维持在较高水平。策略仿真表明：提高检测率能显著降低潜伏感染者（ E ）峰值（约 23%）并提升早诊断比例（从 76% 到 82%）；针对高危人群的干预措施对降低易感人群（ S ）新发感染效果显著（感染率降低 18%）；提高检测率与高危人群干预具有显著的协同效应。扩大 ART 覆盖率因已接近饱和，边际效益递减。母婴阻断和患者随访强化亦有积极效果，但整体影响相对较小。

结论：本研究提出的精细化 SEI_1 I_2 A 模型能够有效捕捉某市 HIV 传播的关键动态特征。研究结果强调，未来某市 HIV 防控应实施“检测-治疗-行为干预”三位一体的精准策略，优先弥补诊断延迟短板，并强化对高危人群的综合干预。本研究为制定数据驱动的、符合地方实际的 HIV 精准防控政策提供了定量依据和决策支持。

A robust transfer learning approach for high-dimensional linear regression to support integration of multi-source gene expression data

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Abstract

Transfer learning aims to integrate useful information from multi-source datasets to improve the learning performance of target data. This can be effectively applied in genomics when we learn the gene associations in a target tissue, and data from other tissues can be integrated. However, heavy-tail distribution and outliers are common in genomics data, which poses challenges to the effectiveness of current transfer learning approaches. In this paper, we study the transfer learning problem under high-dimensional linear models with t-distributed error (Trans-PtLR), which aims to improve the estimation and prediction of target data by borrowing information from useful source data and offering robustness to accommodate complex data with heavy tails and outliers. In the oracle case with known transferable source datasets, a transfer learning algorithm based on penalized maximum likelihood and expectation-maximization algorithm is established. To avoid including non-informative sources, we propose to select the transferable sources based on cross-validation. Extensive simulation experiments as well as an application demonstrate that Trans-PtLR demonstrates robustness and better performance of estimation and prediction when heavy-tail and outliers exist compared to transfer learning for linear regression model with normal error distribution.

Review and prediction of the transmission dynamics of COVID-19 and simulation and optimization of its preventive and control measures based on compartmental models

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Abstract

Although COVID-19 has transitioned to the “post-epidemic era”, prevention and control remain challenging. Extended SEIR models (SSqEBI1I2I3HRD, SSqEEqAI1I2I3HVRD, and SEI1I2I3QHVRD) were established to analyze COVID-19 transmission dynamics during the phases of “closed city containment”, “normalized prevention and control”, and “Class B infectious disease Class B management”. The SEI1I2I3HVRD model forecasted trends for 2024. Outbreaks in Shanghai City and Beihai City during 2022 were used to compare predictions from the SSqEEqAI1I2I3HVRD model alone and with the multi-source dynamic ensemble prediction (MDEP) method. A scale-free network-based SEIAHR multi-agent model explored the effectiveness of various control strategies. The compartmental models tailored to China’s context provided accurate epidemic assessments and forecasts. R_0 values for the phases were 4.443, 1.787, and 2.129, with R_t dropping below 1.0 on days 23, 46, and 16, respectively. Predictions indicated two peaks in China in March and August 2024, showing a “ladder infection” pattern. The MDEP+SSqEEqAI1I2I3HVRD model outperformed the standalone

SSqEEqAI1I2I3HVRD model across all prediction stages, offering valuable insights into managing “multi-source, multi-wavelength, and complex” epidemic situation. Effective control measures included reducing human contact density, lowering transmission rates, isolating hub nodes and nodes with moderately high degrees, early control, extending control periods, and vaccination.

胆固醇、高密度脂蛋白和葡萄糖指数与颈动脉粥样硬化的相关性研究

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【摘要】目的: 探讨胆固醇、高密度脂蛋白和葡萄糖指数 (Cholesterol, High-Density Lipoprotein, and Glucose index, CHG) 与颈动脉粥样硬化 (Carotid Atherosclerosis, CAS) 的相关性, 为体检人群 CAS 的防控提供依据。**方法:** 本研究为横断面研究, 选取 2020 年 1 月—2024 年 12 月期间在四川省人民医院健康管理中心参加过体检且数据资料完整者为研究对象, 通过问卷调查、体格检查和生化检查收集研究对象的数据资料。采用多因素 logistic 回归模型评估 CHG 指数与 CAS 的相关性。采用限制性立方样条图 (Restricted cubic spline, RCS) 探讨 CHG 指数与 CAS 患病风险之间的剂量反应关系, 采用亚组分析评估 CHG 指数在不同人群中的适用性。**结果:** 研究共纳入 99855 名研究对象, 其中 CAS 组 57297 例, 平均年龄 (58.59 ± 11.52) 岁, 正常对照 42558 例, 平均年龄 (44.31 ± 9.47) 岁。多因素 logistic 回归分析显示, 当 CHG 指数用作连续变量时, CHG 指数与 CAS ($OR=1.58$; 95% CI : 1.52-1.65)、CIMT ($OR=1.54$; 95% CI : 1.47-1.62) 和颈动脉斑块 ($OR=1.57$; 95% CI : 1.48-1.65) 的患病率显著相关; 在所有的三个模型中, CHG 指数四分位水平升高与 CAS、CIMT 和颈动脉斑块的患病风险呈正相关。RCS 分析显示 CHG 指数与 CAS 和 CIMI 患病风险呈非线性相关 (P for nonlinear < 0.05), CHG 指数与颈动脉斑块风险呈正线性关系 (P for nonlinear=0.813); 当 $CHG \geq 12.98$ 时, CAS、CIMT 和颈动脉斑块的患病风险随 CHG 指数的增加而增加。亚组分析发现在不同性别、年龄、BMI 分层和吸烟等人群中与 CHG 指数 Q1 组相比, Q2-Q4 组 CKD 患病风险均显著上升, 且风险随四分位升高呈递增趋势。**结论:** CHG 指数水平与 CAS、CIMT 和颈动脉斑块的患病风险增加显著相关。

血清尿酸/高密度脂蛋白胆固醇比值联合空腹血糖的纵向轨迹与慢性肾脏病发病风险：一项回顾性队列研究

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【摘要】目的: 本研究旨在探讨血清尿酸与高密度脂蛋白胆固醇比值 (Serum uric acid/HDL cholesterol ratio, UHR) 联合空腹血糖 (Fasting plasma glucose, FPG) 的纵向轨迹对慢性肾脏病 (Chronic kidney disease, CKD) 发病风险的影响。**方法:** 本研究为回顾性队列研究, 选取 2015 年 1 月—2024 年 12 月期间在四川省人民医院健康管理中心参加过三次及以上年度体检且数据资料完整者为研究对象, 采用 Cox 回归模型分析 UHR 和 FPG 四分位分组与 CKD 发病风险的关联, 并通过限制性立方样条 (Restricted cubic spline, RCS) 探讨剂量反应关系。进一步运用群组多轨迹模型 (Group-based Mult-Trajectory Models, GBMTM) 识别 UHR 与 FPG 的联合轨迹, 并分析不同轨迹组的 CKD 发病风险。**结果:** UHR 和 FPG 均与 CKD 发病风险独立相关, 其四分位分组的 Cox 回归分析显示, UHR 和 FPG 的最高四分位组的 CKD 发病风险显著升高。RCS 结果显示, UHR 和 FPG 与 CKD 发病风险呈非线性增长趋势。不同 UHR-FPG 轨迹组的 CKD 发病密度存在明显差异。低 UHR-低 FPG 组 (组 1)、中等 UHR-中等 FPG 组 (组 2)、中高 UHR-中等 FPG 波动组 (组 3) 和高 UHR-中等 FPG 波动组 (组 4) 的 CKD 发病密度分别为 1.25/100 人年、1.52/100 人年、1.94/100 人年和 3.04/100 人年。组 4 人群的发病风险显著高于其他组, 是组 1 的 3.77 倍 ($HR=3.77$, 95% CI : 2.63-5.40)。**结论:** UHR 和 FPG 与 CKD 发病风险密切相关, 联合轨迹分析揭示了二者动态变化对 CKD 风险的显著影响, 为早期风险评估和防控提供了重要依据。

Covariate-Adjusted Restricted Mean Time Lost for Evaluating Causal Treatment Effects in Competing Risks Data

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【Abstract】 Objective: According to long-term follow-up data of malignant tumor patients, assessing treatment effects requires careful consideration of competing risks. The commonly used cause-specific hazard ratio (CHR) and sub-distribution hazard ratio (SHR) are relative indicators and may present challenges in terms of proportional hazards assumption and clinical interpretation. Recently, the restricted mean time lost (RMTL) has been recommended as a supplementary measure for better clinical interpretation. Moreover, for observational study data in epidemiological and clinical settings, due to the influence of confounding factors, covariate adjustment is crucial for determining the causal effect of treatment.

Methods: We construct an RMTL estimator after adjusting for covariates based on the inverse probability weighting method, and derive the variance to construct interval estimates based on the large sample properties. We use simulation studies to study the statistical performance of this estimator in various scenarios. In addition, we further consider the changes in treatment effects over time, constructing a dynamic RMTL difference curve and corresponding confidence bands for the curve.

Results: The simulation results demonstrate that the adjusted RMTL estimator exhibits smaller biases compared with unadjusted RMTL and provides robust interval estimates in all scenarios. This method was applied to real-world cervical cancer patients data, revealing improvements in the prognosis of patients with small cell carcinoma of the cervix. The results showed that the protective effect of surgery was significant only in the first 20 months, but the long-term effect was not obvious. Radiotherapy significantly improved patient outcomes during the follow-up period from 17 to 57 months, while radiotherapy combined with chemotherapy significantly improved patient outcomes throughout the entire period.

Conclusions: The covariate-adjusted RMTL estimator provides an intuitive interpretation of treatment effects on the time scale, while the dynamic RMTL difference curve further characterizes the temporal trend of treatment efficacy. This method can be used to evaluate causal treatment effects in observational competing risks data, providing strong support for clinical practice and public health policy making

Novel dynamic prediction methods based on RMST by incorporating longitudinal covariates for analyzing short- and long-term progression of Alzheimer's disease

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Abstract Background: Tracking and monitoring mild cognitive impairment (MCI) patients to intervene promptly at the imminent onset of Alzheimer's disease (AD) are crucial. However, existing dynamic survival prediction models for the conversion from MCI to AD are mostly based on hazard rates, which are less intuitive to interpret and require adherence to the proportional hazards assumption. **Objective:** To develop more interpretable dynamic prediction models using restricted mean survival time (RMST) for MCI-to-AD progression. **Method:** We propose a Bayesian joint model (JM) based on the time scale indicator of the RMST, which can capture the trajectories of multiple longitudinal covariates and dynamically predict the patient time to event. Then the Monte Carlo simulation was used to evaluate the predictive performance of JM method. Finally, to predict the dynamic progression of AD in MCI patients at different stages, based on the landmark (LM) and the JM methods for RMST, we developed an LM-based model for short-term dynamic prediction (LM-ST model) and a JM-based model for long-term dynamic prediction (JM-LT model) utilizing the ADNI database. **Results:** The simulation demonstrated that the JM method has a better prediction performance compared with the static model. The internal and external validation results indicate that the predictive performance of the LM-ST and JM-LT models surpasses that of the static RMST model. Additionally, an online web tool for the two dynamic prediction models demonstrated clinical utility. **Conclusion:** We propose a novel method and combined it with the existing LM method for AD progression, which improves the predictive power and provides a scientific basis for medical decision-making.

糖脂代谢标志物与高血压患者代谢综合症的关联及风险预测模型构建：一项基于广州市高血压患者健康管理的队列研究

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摘要

背景：代谢综合征（MetS）是心血管疾病和 2 型糖尿病的重要风险因素，其患病率因城市化、久坐生活方式和饮食变化而上升。高血压患者患 MetS 的比例显著高于血压正常者，被认为是 MetS 的高危人群。

方法：2018-2019 年，基于中国基本公共卫生服务项目纳入 228708 名研究对象，建立“广州高血压社区前瞻性队列”（GHPCC）。采用多变量 logistic 回归分析肥胖与脂质相关指标，胰岛素抵抗替代指标和生物衰老相关指标与高血压人群未来发生 MetS 的关联。采用分层分析检验在不同人群中 OR 值的异质性，并用加权线性回归评价 OR 值的趋势变化。采用多变量逐步回归和最大相关最小冗余（mRMR）筛选特征子集。采用五类机器学习方法（Logistic regression, Classification and Regression Trees, RandomForest, XGBoost, Support vector machine）构建高血压人群 MetS 风险预测模型。使用 Brier 评分、平衡准确率、ROC-AUC 和 PR-AUC 评估模型性能。

结果：所有新型综合指标均与 MetS 显著相关。体脂率(BFP, OR=2.98, 95%CI 2.91-3.06)关联性最强，其次为甘油三酯葡萄糖指数与 BMI 的乘积(TyG_BMI, OR=2.19, 95%CI 2.15-2.22)和中国人内脏脂肪指数（CVAI, OR=2.18, 95%CI 2.14-2.22）。糖脂代谢指标与高血压人群 MetS 的风险关联强度在不同性别、年龄、文化程度、吸烟状态、饮酒情况和体育锻炼频率的亚组中存在显著异质性。基线状态（男性 WC $\geq$ 90cm，女性 WC $\geq$ 85cm；空腹血糖 $\geq$ 6.1 mmol/L 或服

用降糖药; $TG \geq 1.7\text{mmol/L}$; $HDL-C < 1.04\text{mmol/L}$) 的差异也影响关联强度。在 MetS 风险预测方面, XGBoost 模型性能最优 ($ROC\_AUC = 0.759$; 平衡准确率 = 0.691; Brier 评分 = 0.164; $PR-AUC = 0.508$)。CHARLS 外部验证后, 模型性能仍保持较高水平。TyG_BMI 对模型贡献最大, Phenoage_advance、KDM 和 KDM_advance 在模型中的预测能力优于实际年龄, 当 Phenoage_advance > 0.739 岁时, MetS 发生风险超过 50%。

结论: 本研究评估了多种新型综合指标与高血压人群未来发生 MetS 的关联, 并使用 XGBoost 机器学习方法构建了最优的 MetS 风险预测模型。这为心脑血管疾病的早期预防和降低高血压人群的终末事件发生风险提供了科学依据。

精神分裂症患者预后模型的构建

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【摘要】目的: 目前针对精神分裂症患者的预后预测模型较为匮乏, 本研究旨在构建精神分裂症患者死亡风险预测模型, 探讨精神分裂症患者预后的影响因素, 并对构建的模型进行评价。

方法: 本研究为双向队列研究, 研究对象为 2017 年 1 月 1 日—2021 年 7 月 1 日的经医院确诊且纳入系统管理的保山市精神分裂症患者, 采用 Cox 比例风险模型的扩展—Anderson-Gill 模型构建患者生存预测模型, 使用一致性指数和时间依赖性受试者工作曲线对模型进行评价, 采用 5 折交叉验证进行内部验证, 并对模型进行可视化。

结果: 共有 1009 名患者纳入分析, 其中有 86 名患者死亡。构建的预测模型提示女性 ($HR=0.599$ 95%CI:0.387-0.928)、住院是患者死亡的保护因素 ($HR=0.499$ 95%CI 0.251-0.992); 睡眠情况较差 ($HR=3.824$ 95%CI: 1.482-9.867)、心电图异常 ($HR=2.185$ 95%CI:1.236-3.862) 是患者死亡的危险因素; 初次诊断时年龄越高患者死亡的风险越大 ($HR=1.044$ 95%CI 1.027-1.060); 社会功能评分越高, 死亡的风险越低 ($HR=0.889$ 95%CI:0.793-0.995)。模型的一致性指数为 0.820; 1 年、3 年、5 年的时间依赖性受试者工作曲线下面积分别为 0.814、0.866、0.848, 5 折交叉验证平均 C 指数为 0.799。

结论: 精神分裂症患者在生存期间内性别、住院情况、社会功能评分、初次诊断时年龄、睡眠情况、心电图情况与死亡风险有关, 建立的模型有较好的预测能力, 绘制的列线图及 Excel 评分计算器有助于临床评估。

1 Dynamics of Obesity Measurement Indicators and the High-Risk Periods for

2 Obesity Subtypes Across the Lifespan.

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19 Conflict of interest: The authors declared no conflict of interest. 20

21 Acknowledgments: We thank the National Institute for Nutrition and Health, China

22 Center for Disease Control and Prevention, Carolina Population Center (P2CHD-

23 050924, T32-HD-007168); the University of North Carolina, Chapel Hill; the
National

24 Institutes of Health (R01-HD-30880, DK-056350, R24-HD-050924,
R01-HD-38700);

25 and the National Institutes of Health Fogarty International Center
(D43-TW-009077, 26 D43-TW-007709) for financial support for the
China Health and Nutrition Survey

27 (CHNS) data collection and analysis files from 1989 to 2015. We also thank all
the

28 children and adults who participated in this study.

29

30 Abstract

31 Background

32 The prevalence of obesity has accelerated across all age demographics, representing

33 major public health challenges in China. However, the dynamic changes of obesity

34 measurement indicators over the lifespan still lacks consensus. It remains unclear

35 whether the susceptibilities for the onset of obesity subtypes differ across different life

36 stages.

37 Objective

38 We aimed to explore the age-related dynamic patterns of four obesity measurements

39 indicators and to identify high-risk periods for the onset of four obesity subtypes over

40 the lifespan.

41 Methods

42 The longitudinal study included a total of 18406 participants aged 7-80 years from the

43 China Health and Nutrition Survey from 1989-2015. We examined the change of four

44 obesity measurement indicators, including body mass index, waist circumference, hip

45 circumference and triceps skin fold measurements and characterized the heterogeneity

46 in the prevalence of four obesity subtypes, including general, abdominal, hip and

47 subcutaneous fat obesity using generalized linear mixed-effects models to. We also

48 predicted the incidence of four obesity subtypes in non-obesity individuals after 1-year

49 follow-up using Markov model.

50 Results

51 Four obesity-related anthropometric indicators showed strong age- and sex-dependent

52 nonlinear trajectories, peaking at aged 50 and 60 years, and declining thereafter. The

53 prevalence of obesity in men and women was similar to the overall trend, but the pattern

54 varied by obesity subtype. General and subcutaneous fat obesity peaked in the 51 – 60

55 age group, while abdominal and hip obesity peaked at 61 – 70 age group. The prevalence

56 of general and hip obesity peaks earlier in men and then stabilizes. After the age of 50, 57 women have a higher prevalence of all types of obesity than men, particularly

58 abdominal and subcutaneous fat obesity. The multi-state Markov model demonstrated

59 males exhibited slightly higher predicted incidence of general, abdominal, and hip

60 obesity before the age of 40 years. Females surpassed males in these three subtypes 61 after midlife, particularly in abdominal and hip obesity, where the incidence increased

62 markedly. For subcutaneous fat obesity, the incidence is higher in women than in men

63 throughout the life course.

64 Conclusion

65 The dynamic prevalence and incidence patterns of four obesity subtypes exhibit marked

66 differences by age and sex across different life stages. The incidence of four obesity

67 subtypes increases significantly after midlife in women, whereas reaching the peak

68 earlier in relatively stable trends in men. The age-related changes in prevalence and

69 incidence of obesity subtypes underscore the necessity of developing age-appropriate

70 prevention and intervention strategies tailored to specific demographic groups.

贵阳市大学生自杀态度在父母教养方式与自杀意念的 中介作用研究

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【摘要】目的 探讨自杀态度在贵阳市大学生父母教养方式与自杀意念中的 中介作用。**方法** 通过多阶段分层整群随机抽样的方法, 选取 2021 年 11~12 月贵阳市在校大学生为研究对象，采用父母教养方式问卷（Parental Bonding Instrument,PBI）、自杀态度问卷(suicide attitude questionnaire,SAQ)和自杀意念问 卷(Self-rating Ideaof Suicide Scale,SIOSS)进行面对面问卷调查。数据采用 jamovi 2.4.1 和 Mplus 7.11 进行分析，构建结构方程模型分析自杀态度在父母教养方式与 自杀意念之间的中介作用。**结果** 3038 名调查对象中，有自杀意念的大学生共检 出 189 人，总体检出率为 6.2%，95%CI: 5.4%~7.1%。不同性别、年级的大学生 自杀意念得分差异均具有统计学意义($P<0.001$)。父母关爱、父母控制与对自杀行 为的态度和自杀意念之间两两相关，自杀态度在父母教养方式与自杀意念之间共 建立 4 个中介模型，且全部为部分中介作用。**结论** 贵阳市大学生自杀意念检出率 为 6.2% (95%CI: 5.4%~7.1%)，父 母教养方式对自杀意念有直接影响，且部 分是通过自杀态度的中介作用实现。

Transitions in comorbidity patterns of depression and Internet gaming disorder among adolescents: A random intercept latent transition analysis

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Abstract

Purpose

Extensive research has documented a high comorbidity prevalence between depression and Internet gaming disorder (IGD). However, the distinct comorbidity patterns in adolescents have not been thoroughly investigated. Additionally, the longitudinal dynamics of these comorbidity patterns over time and the specific factors that may drive these transitions remain poorly understood.

Methods

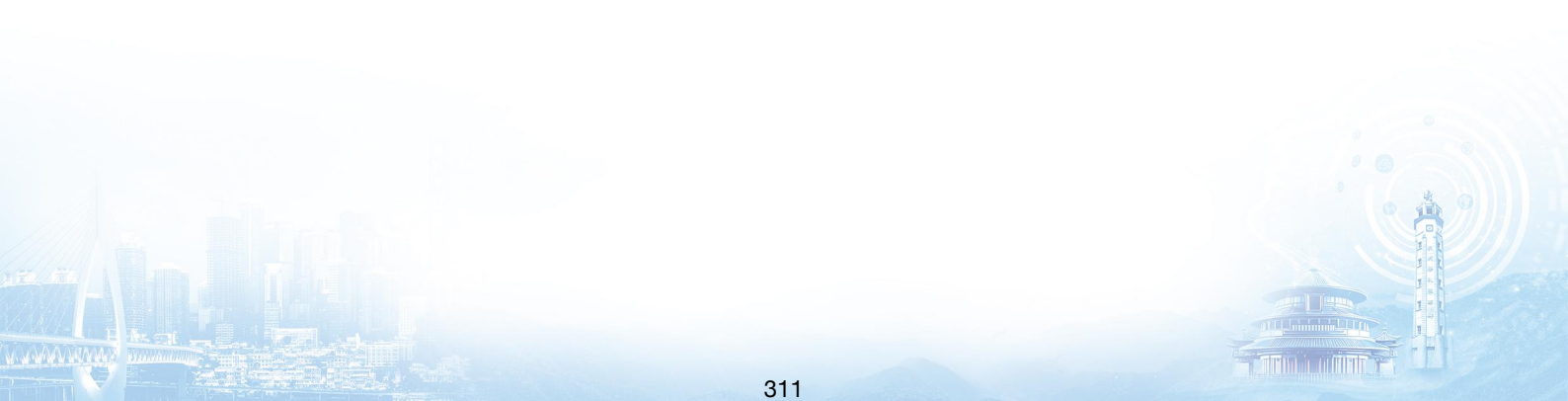
A total of 3296 adolescents (1501 boys; age baseline: 15.17 [1.44] years) were included in the current study. Latent profile analysis (LPA) was used to identify optimal comorbidity patterns of depression and IGD, while random intercept latent transition analysis (RI-LTA) was conducted to assess transitions in the comorbidity patterns over one and a half years and to identify factors influencing these transitions.

Results

Three patterns of comorbidity between depression and IGD symptoms were identified: no symptoms, low depression-high IGD symptoms, and high depression-low IGD symptoms. Results indicate that 72% of individuals exhibited a stable symptom pattern trajectory. From Time 1 to Time 2, the probabilities of remaining in the three patterns were 78.3%, 31.5%, and 51.5%, respectively. Findings also showed that sex, grade levels, boarding status, father's occupation as well as educational attainment, intra-week and weekend screen time, parent-child relationship, and perceived social support influenced the probabilities of transitions between comorbidity patterns in adolescents over time.

Conclusion

Adopting targeted interventions for different comorbidity patterns and transitions, while considering specific influencing factors, provides insights into adolescent mental health dynamics and inform more effective prevention and support strategies.



整合 GWAS 与人血浆蛋白质组数据鉴定慢性肾病相关 新型蛋白

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基金项目: 国家自然科学基金 (82173631) ; 山西省重点实验室 (201805D111006)

【摘要】 目的 探讨整合全基因组关联研究 (GWAS) 与人类血浆蛋白质组数据在鉴定 慢性肾病 (CKD) 相关潜在蛋白及治疗靶点中的应用价值。

方法 本研究基于 7213 例人群的血浆蛋白质定量性状位点 (pQTL) 数据, 结合估算肾小球滤过率 (eGFR) 的 GWAS 数据 (样本量为 567,460), 开展全蛋白质组关联研究 (PWAS), 筛选与 eGFR 密切相关的蛋白。进一步通过孟德尔随机化 (MR) 及贝叶斯共定位分析验证候选蛋白的因果关系。最后, 利用药物-基因互作数据库 (DGIdb) 评估其药物开发潜力。

结果 共识别出 88 种与 eGFR 相关的调控蛋白, MR 与共定位分析验证了其中 6 种关键蛋白 (INHBC、FLRT3、APOL3、ACP1、BTN3A3 和 NOG) 在 eGFR 变化中的潜在作用。其中, ACP1 对应的 3 种靶向药物在 DGIdb 数据库中被收录, 提示其具有作为 CKD 潜在治疗靶点的可能性。 **结论** 本研究基于多组学数据整合, 系统地识别出 6 种与肾功能相关的关键蛋白, 为 CKD 的发病机制研究及靶向治疗提供了理论依据和新思路。

Real-World Evidence Studies Better Reflect Target Population Compared to Randomized Trials: Enhanced External Validity for End-Stage Kidney Disease Care

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Abstract

Background Systematic differences between trial participants and the target patient population may limit the generalizability of research findings—a critical challenge for evidence-based medicine, known as external validity. Real-world evidence (RWE), derived from diverse real-world data sources, inherently captures the complexity of routine-clinical patient populations and treatment patterns. However, whether RWE offers better external validity compared to traditional randomized controlled trials (RCTs) remains unsubstantiated, particularly in complex multimorbidity populations, such as patients with end-stage kidney disease (ESKD).

Objective This study aimed to validate whether RWE more accurately reflects the characteristics of the target population with ESKD undergoing dialysis treatment, compared to randomized controlled trials, thereby supporting clinical decisions for complex patients.

Methods We systematically identified RCTs and RWE studies on ESKD dialysis populations through PubMed (from January 1, 2007 to December 31, 2024). Target population benchmarks were derived from the United States Renal Data System (USRDS), a national registry of ESKD patients. Representativeness deviations against this nationally representative benchmark between RCTs and RWE studies were quantified using primary outcomes (mean age, diabetes prevalence, mortality rates) and secondary outcomes (types of primary kidney disease, cardiovascular comorbidities, mean hemoglobin levels, mean albumin levels, vascular access status). Summary statistics were estimated using a random-effects model with restricted maximum likelihood estimation (REML). Deviations from USRDS reference values were assessed using one-sample t-tests, with separate analyses conducted for both study types in U.S. and non-U.S. regions. Associations between study characteristics and mortality rate were examined through multivariate regression. Subgroup analyses employed standardized mean differences as the statistical measure.

Results A total of 186 RCTs involving 71,119 participants and 173 RWE studies encompassing 50,931,214 participants were included. In nearly all key characteristics,

RWE studies were more closely aligned with USRDS benchmarks. In U.S. regions, the mean age of RWE participants was closer to the USRDS reference (RWE: 62.64 years; 95% CI, 60.59-64.64 years vs. 62.60 years) than that of RCT participants (RCT: 58.77 years; 95% CI, 57.94-59.60 years vs. 62.60 years). Similarly, RWE demonstrated closer alignment with USRDS in diabetes prevalence (RWE: 54.69%; 95% CI, 51.55%-57.82% vs. 59.90%. RCT: 51.31%; 95% CI, 47.59%-55.03% vs. 59.90%) and mortality rate (RWE: 21.62 per 100 patient-years; 95% CI, 16.11-27.13 vs. 20.30 per 100 patient-years; RCT: 7.92 per 100 patient-years; 95% CI, 6.37-9.46 vs. 20.30 per 100 patient-years). Secondary outcomes further supported RWE's greater representativeness, except for a few characteristics that reflected real-world clinical variability. In non-U.S. regions, RWE's advantages were even more pronounced, highlighting its strong transportability.

Conclusions RWE exhibits better representativeness in its alignment with the target population, and further enhances the transportability of findings to broader populations. This enhanced generalizability positions RWE as a critical tool for guiding clinical decisions in complex, comorbid, and high-risk subgroups that are often excluded from RCTs.

血清尿酸与骨质疏松或骨量减少的关系 ——涉及多种肥胖指标的中介分析

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【摘要】 目的 探讨美国人群中不同肥胖指标在血清尿酸与骨质疏松或骨量减少间关系中的中介作用;

方法 针对 NHANES 六个周期数据进行了一项横断面研究, 构建加权 logistic 回归模型分析血清尿酸、肥胖指标分别与骨质疏松或骨量减少的关联, 使用加权多变量线性回归探讨了血清尿酸与肥胖指标间的相关性, 并通过中介分析研究肥胖指标是否在血清尿酸与骨质疏松或骨质减少之间发挥中介效应;

结果 研究发现, 血清尿酸与骨质疏松或骨量减少存在显著的相关性; 血清尿酸与肥胖指标 BMI、ABSI、BRI、LAP、VAI、TyG、CI、WWI 呈正相关; BMI、ABSI、WWI 在未调整和调整的模型中均与骨质疏松或骨质减少显示出显著的关联; WWI、CI、BMI、ABSI、VAI 在血清尿酸与骨质疏松或骨质减少的关系中发挥着部分中介作用, 中介效应比例分别为 43.1%、27.9%、17.8%、11.2%以及 7.7%。性别分层中部分肥胖指标的中介效应在男性和绝经后女性中显著, BMI 在老年人中的中介效应高于其他年龄人群, WWI 与之相反;

结论 在特定范围内, 血清尿酸是骨质疏松或骨质减少的保护因素, 较高浓度的血清尿酸与较低的骨质疏松或骨量减少患病风险相关, 腹部肥胖对血清尿酸与骨质疏松或骨量减少间关系的影响相对更大。

A Bayesian phase I/II trial design to optimizing dose-schedule regimen with competing risk outcomes

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【Abstract】

Background: Identifying the optimal dose-schedule regimen in early-phase oncology trials is challenging, especially in the presence of competing risks such as disease progression (DP) and dose-limiting toxicity (DLT). Traditional dose-finding methods often ignore these competing events and fail to consider varying administration schedules.

Methods: We propose CR-EffTox, a Bayesian adaptive phase I/II trial design that jointly models time-to-event DLT and DP using cause-specific hazard functions and dynamically borrows information across dose-schedule combinations. To guide regimen selection, we introduce a novel satisfaction score based on the ratio of areas under and above cause-specific survival curves, capturing both the rate and timing of events. This score reflects the overall benefit – risk trade-off, aligning with the FDA’s definition of optimal dosage.

Results: Extensive simulation studies across nine clinical scenarios demonstrate that CR-EffTox consistently outperforms benchmark designs that either ignore competing risks (CR-EffTox_NC) or omit information borrowing (CR-EffTox_NB). CR-EffTox achieves higher correct selection probabilities, better patient allocation efficiency, and improved ethical conduct through lower unnecessary early stopping rates, all without increasing the sample size. Its advantages are particularly evident in non-monotonic or plateau-shaped dose-response scenarios.

Conclusion: CR-EffTox provides a robust and flexible framework for dose-schedule optimization in early-phase trials, offering improved accuracy and clinical relevance by incorporating competing risk modeling and benefit – risk evaluation. While computationally intensive, the design holds significant potential for more patient-centered and regulator-aligned decision-making in precision oncology.

临床研究中贝叶斯方法先验分布的选择

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【摘要】目的：贝叶斯方法因其灵活性和能够量化不确定性的优势，越来越广泛应用于临床研究中。然而，先验分布的选择对贝叶斯推断结果具有重要影响，需规范化制定先验设定流程，以提高推断的稳健性。本文旨在构建一套规范化的先验选择流程。**方法：**本文在系统回顾相关文献的基础上，总结出先验分布选择的标准化流程：(1)明确研究目标与数据特性，包括数据的类型、分布特征以及关注的参数；(2)评估是否存在可用的先验信息。若有先验信息，可依据信息强度选择合适的建模策略，若无先验数据，则可采用非信息先验或弱信息先验；然后通过模拟方法评估所选先验的表现；(3)敏感性分析检验结果对先验假设的依赖程度，验证其合理性与稳健性。(4)明确报告先验分布的选择依据及参数估计。我们设计了两个模拟场景验证该流程的实际操作性与推断表现。**结果：**通过标准化的先验选择流程，我们筛选出符合研究数据和目标的合适先验，也识别出若干不适宜的先验。例如，在场景一中，幂先验下相对风险 95%可信区间为(0.568,0.999)，排除 1，支持干预显著降低风险；绝对风险降低的 95%可信区间为(0.001,0.223)，亦不包含 0，显示干预带来明确的绝对风险降低。相比之下，未通过流程筛选的其他先验（如过宽均匀先验、偏倚强先验、弱信息均匀先验）在后验推断中表现出明显的信息不足或偏倚倾向，易低估治疗效果。**结论：**本研究提出的先验分布选择流程可规范贝叶斯分析中先验设定的步骤，减少主观性并提高推断的稳健性。模拟验证表明，规范流程下的先验选择能提升推断的科学性与临床解释性。

基于模拟目标试验的卫生政策评估：以新冠边境政策为例

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【摘要】目的：评估卫生政策的因果效应时，不仅需要考虑混杂偏倚，还需应对其他类型的偏倚，例如由于政策采用时间不一致所导致的恒定时间偏倚。本研究旨在将临床研究中的模拟目标试验（Target Trial Emulation, TTE）框架引入公共卫生政策评估领域，以识别和控制恒定时间偏倚，并以新冠边境控制政策为例，比较不同政策在延缓疫情传播方面的有效性。**方法：**本研究采用的模拟目标试验包括两个主要步骤：首先，确定一个假想目标试验；其次，基于观察性数据和克隆-删失-加权（Cloning-Censoring-Weighting, CCW）方法来模拟假想目标试验的研究设计和统计分析。在实例分析部分，我们收集了全球 174 个国家和地区的新冠疫情边境政策和传播数据，比较了不同政策（包括入境筛查、入境隔离、禁止高风险地区人员入境、全面关闭边境）在延缓各国达到首个疫情高峰方面的有效性。我们分别使用基于 TTE-CCW 方法的 Kaplan-Meier 估计量和传统未校正恒定时间偏倚的 naive Kaplan-Meier 估计量进行实例分析，并进行结果对比。**结果：**传统方法与 TTE-CCW 方法的估计结果存在显著差异。在存在恒定时间偏倚的情况下，传统方法得到结果显示全面关闭边境比入境筛查更有效的趋势（风险比 [95% 置信区间]：0.98 [0.79, 1.21]）。然而，在使用 TTE-CCW 校正偏倚后，结果显示入境筛查比全面关闭边境更有效的趋势（1.07 [0.88, 1.30]），即两种方法的估计结果在效应方向上完全相反。进一步分析揭示了上述结果的机制：采用入境筛查的国家明显早于采用其他政策的国家，并且在早期实施政策比政策类型本身更为重要。**结论：**研究结果提示，在政策评估中，除了需要考虑混杂因素外，还应关注其他类型的偏倚，如恒定时间偏倚的影响。本研究提出的适用于卫生政策评估的 TTE 框架能够有效识别并控制恒定时间偏倚。

Global Burden of Ischemic Heart Disease Attributable to High Body Mass Index/Low Physical Activity Among People Aged 55 Years and Older

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Abstract

Background: This study aimed to quantify the global ischemic heart disease (IHD) burden attributable to high body mass index (BMI) and low physical activity (PA) in adults aged ≥ 55 years using data from the Global Burden of Disease 2021 study.

Methods: We extracted data of deaths, disability-adjusted life years (DALYs), and age-standardized rates of IHD attributable to high BMI and low PA among people aged ≥ 55 years from the Global Burden of Disease 2021 study. The estimated annual percentage change (EAPC) and decomposition methodology were utilized to quantify the temporal trends and decompose deaths and DALYs by population age structure, population growth, and epidemiologic changes. We used *Nordpred* to forecast mortality trends from 2022 to 2046.

Results: From 1990 to 2021, global deaths for IHD attributable to high BMI and low PA among people aged ≥ 55 years nearly doubled, despite declines in age-standardized death rates ([EAPC = -0.89, 95% CI: -0.96, -0.81], [EAPC = -1.20, 95% CI: -1.24, -1.16]). Among people aged ≥ 55 years, the burden of IHD attributable to high BMI was predominantly observed in males, while the burden attributable to low PA was more prevalent in females. Population growth and aging drive this rising burden.

Conclusion: Countries and regions should implement proactive health management strategies targeting high BMI/low PA in older populations and develop tailored preventive and therapeutic measures to reduce the burden of IHD.

Sleep, Physical Activity, and Social Participation in Relation to Depression: A Cross-sectional Study of Middle-aged and Older Chinese Adults with Cardiovascular-Kidney-Metabolic (CKM) Syndrome

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Abstract

Objective: To examine the associations between sleep duration, physical activity, social participation and depression among middle-aged and older Chinese adults with cardiovascular-kidney-metabolic (CKM) syndrome, and to investigate how these relationships vary across different CKM syndrome stages (0-4).

Methods: Using data from the China Health and Retirement Longitudinal Study (CHARLS) 2015, we analyzed 7,636 patients with CKM syndrome. Depression was assessed using the 10-item Center for Epidemiologic Studies Depression Scale (CES-D-10). Health behavior factors were determined through self-report questionnaires. Multivariable logistic regression models, restricted cubic splines, and mediation analysis were used for the analysis.

Results: Compared to stage 0, Stage 3 (OR=1.44, $P<0.001$) and stage 4 (OR=1.50, $P<0.001$) were significantly associated with higher depression risk. Sleep duration (OR=0.83, $P<0.001$) and social participation (OR=0.88, $P<0.001$) showed significant negative associations with depression. Restricted cubic spline models revealed significant nonlinear relationships between sleep duration/physical activity and depression (both $P<0.001$). Optimal ranges for depression prevention were sleeping duration of 7-11 hours daily, physical activity below 3000 METs-min/week, and

social participation scores above 1. Among the three factors, sleep duration showed the strongest association with depression (β (Std)=-0.417, $P<0.001$).

Conclusion: Middle-aged and older adults with advanced CKM syndrome face significantly higher depression risk. For the CKM population, maintaining adequate sleep duration (7-11 hours), engaging in moderate physical activity (0-3000 METs-min/week), and participating in social activities help prevent depression. However, for advanced-stage CKM patients, vigorous physical activity may increase adverse event risks. These findings support integrating mental health interventions into comprehensive CKM syndrome management protocols.

Leveraging spike-and-slab lasso for adaptive shrinkage in polygenic score prediction

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ABSTRACT

Objective: The polygenic score (PGS) model can help us better predict complex traits

and disease and potentially facilitate clinically risk stratification. However, existing PGS methods still face limitations in balancing computational efficiency and prediction

performance. Methods: We introduce SSL, a novel polygenic score (PGS) method

leveraging genome-wide association studies (GWAS) summary statistics and a

reference panel data within a penalized regression framework. SSL utilizes a spike-and-

slab lasso penalty function to adaptively shrinkage SNP effects similar with Bayesian

methods, and an ensemble learning step to aggregate PGS generated across tuning

parameters. Results: Through diverse simulation scenarios and real dataset, SSL

demonstrated robust and accurate prediction compared to other representative PGS

methods. For quantitative trait, SSL exhibited an average improvement of 21.4% and 20.9% versus penalized methods, Lassosum and Lassosum2, and demonstrated similar

performance with the state-of-the-art Bayesian method (PRSCs). Notably, SSL

consistently outperformed all alternative methods examined in the binary traits,

yielding average accuracy gains on AUC range from 1.11% to 7.56%. Further, SSL

realized an 11-fold speed-up over PRSCs in computational performance. Conclusions:

Overall, our results show that SSL bridges the critical trade-off between computational

tractability and prediction performance for PGS applications.

基于时间分层病例交叉设计的极端温度 与脑卒中死亡关联以及二氧化氮的交互作用研究

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【摘要】目的：本研究基于时间分层病例交叉设计，探讨了极端温度 (ETEs) 与 二氧化氮 (NO_2) 短期暴露对脑卒中死亡风险的单独及交互作用。**方法：**研究选取 2013 年至 2019 年山东省 10 个县/区的 8959 例脑卒中死亡病例。采用时间分层病例交叉设计，结合气象数据、空气污染数据及患者信息进行分析。**结果：**极端温度的影响：短期暴露于热浪显著增加脑卒中死亡风险，且风险随温度阈值升高和持续时间延长而增强。例如，当温度持续 3 天超过第 90 百分位数时，死亡风险增加 22.3% ($\text{OR}=1.223$, 95% $\text{CI}:1.100-1.361$)。而寒潮与脑卒中死亡风险无显著关联，可能与居民对低温的适应性行为有关。 NO_2 的影响： NO_2 浓度与脑卒中死亡风险呈正相关，每四分位数范围(IQR)浓度升高对应的死亡风险增加 7% ($\text{OR}=1.07$, 95% $\text{CI}:1.01-1.12$)。暴露反应曲线显示，中高 NO_2 浓度会增加脑卒中死亡风险。交互作用：未发现极端温度与 NO_2 对脑卒中死亡风险存在显著的加性交互作用 ($P>0.05$)，但部分热浪指标与 NO_2 的协同效应趋势值得进一步研究。**结论：**短期暴露于热浪整体上会显著增加中风死亡风险，且风险效应随温度阈值升高和持续时间延长呈现增强趋势。 NO_2 浓度与脑卒中死亡风险呈现正相关。且中高浓度的 NO_2 暴露会显著增加脑卒中的死亡风险。

基于细胞交互与多重校正的循环肿瘤细胞自动检测方法

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【摘要】

目的: 循环肿瘤细胞 (Circulating Tumor Cells, CTCs) 是来源于原发肿瘤或转移肿瘤, 通过组织基质进入血管的肿瘤细胞。CTCs 可作为生物标志物预测肿瘤转移, 其准确检测可以有效辅助癌症的早期诊断和预后, 对于治疗方案的选择具有重要指导意义。因 CTCs 的稀有性与异质性, 其准确检测存在一定的难度, 需要结合富集细胞与细胞识别两个过程。在细胞识别过程中, 需要从细胞病理制片中定位 CTCs 并判断细胞类型, 其识别效果直接影响早期诊断结果。然而, 目前尚缺乏有效且标准化的 CTCs 识别方法, 临床实践中仍以病理医师镜下阅片为主。而该方式易受主观因素影响且严重依赖医师的经验, 存在诊断结果和结果解释不一致的情况, 且诊断的准确度和效率低下。近年来, 许多研究将各种基于深度学习的目标检测方法应用于异常细胞识别, 但尚未有研究给出高效精准的 CTCs 智能化识别方法, 而且 CTCs 的识别还存在不同类型或亚型的细胞形态特征相近导致鉴别困难等实际临床难点。因此, 亟待对相关的算法进行研究和改进, 给出识别准确度更高、泛化能力更好的 CTCs 识别方法。

方法: 本研究开发了一种基于细胞交互与多重校正的检测 (Cascade Mining Detector, CMD) 方法, 用于从苏木素-伊红 (hematoxylin-eosin, H&E) 染色的细胞病理图像中自动定位并识别循环肿瘤细胞 (CTCs), 辅助病理人员做出更准确的诊断。所提出方法的核心为两个面向任务难点而设计的模块, 通过模仿病理学家识别异常细胞的方式, 提升模型识别的准确性。首先为自注意力模块, 该模块通过聚合细胞间的信息来学习要强调或抑制的细胞特征, 使模型重点关注可疑细胞; 其次为难分样本采样器模块, 通过结合 CMD 方法级联的多阶段结构来多次优化细胞分类预测结果, 加强模型对形态特征相近细胞的鉴别能力。本研究通过多中心收集建立的数据集 (共包含 133 例患者, 1247 张图像块) 完成 CMD 检测模型的搭建与评估, 通过消融实验来验证两个模块的效果, 比较 CMD 多个阶段

的识别结果以探索模块与级联结构的作用，并与国际代表性的多种先进方法（Faster RCNN、Cascade RCNN、Sparse RCNN、SSD、FCOS、Retina Net、AttFPN 和 RRAM&GRAM）进行比较。研究使用平均精确率（Average Precision, AP）作为模型识别细胞准确性的主要评价指标。

结果：多中心数据集实验结果表明，本研究提出的自注意力模块与难分样本采样器模块分别提升了模型学习细胞特征与鉴定细胞类别的能力，CMD 方法在独立测试数据集上识别细胞的准确性与稳定性均优于多种基于深度学习的代表性细胞识别方法。

消融实验结果中，基线方法 AP 值为 65.4%，单独结合自注意力模块后 AP 值为 67.0%，单独结合难分样本采样器模块 AP 值为 69.9%，共同结合两个模块的 CMD 方法达到最优表现，AP 值为 71.2%。CMD 方法多阶段分别的识别结果比较中，AP 值表现为逐阶段提升（分别为 62.8%，70.6%与 71.2%），表明方法能够按照模块的设计学习到重点的细胞特征，并逐步优化细胞分类能力。与国际代表性方法的比较结果中，CMD 方法的 AP 值平均超出其他方法 15.7%，高于 Faster RCNN（63.9%），Retina Net（58.8%），AttFPN（66.5%）与 RRAM&GRAM（63.7%）等方法。对细胞病理图像的识别测试中，以 CMD 方法建立的模型只需要 1~2 秒的时间即可获得异常细胞的可视化定位，并且鉴别细胞类型的准确性优于其他代表性方法。

结论：本研究提出的 CMD 方法在 CTCs 识别中是有效且稳健的，相同实验条件下显著优于多种国际代表性方法，可以达到实际应用水平。基于该方法的细胞识别系统可以有效辅助病理医师完成循环肿瘤细胞（CTCs）识别，促进癌症的早期诊断和干预，为癌症治疗的临床决策提供支撑。

Divergent Risk Factor Dynamics Underlying Gastrointestinal Cancer Mortality Trends: A Comparative Analysis of China and the United States (1992–2021)

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Background: The disease burden of gastrointestinal cancers (esophageal cancer(EC), gastric cancer(GC), colorectal cancer(CRC)) remains substantial, and risk-factor-attributable mortality is shifting. Comparing China and the United States(US) (1992-2021) clarifies prevention priorities.

Methods: Based on the Global Burden of Disease (GBD) database, the Joinpoint regression model was employed to calculate the average annual percentage change (AAPC) in age-standardized mortality rates (ASMR) attributable to risk factors for the three cancers. The Age-Period-Cohort (APC) model was utilized to decompose age, period, and birth cohort effects. Additionally, the Autoregressive Integrated Moving Average (ARIMA) model was applied to predict mortality trends for these cancers associated with behavioral and metabolic risk factors from 2022 to 2031.

Results: From 1992 to 2021, China experienced an overall decline in EC and GC mortality attributable to behavioral risk factors, while smoking/alcohol-related EC mortality showed an upward trend in ≥ 80 -year-olds (local drift >0). In the US, EC and GC mortality declined across all risk factors, with alcohol use being the sole contributor to a slight EC mortality increase (AAPC = 0.43). For CRC in China, metabolic risks—high body-mass index(HBMI) (AAPC = 2.49%) and high fasting plasma glucose(HFPG) (AAPC = 2.12%)—showed marked upward trends, peaking in adults aged 30-34 (local drift: HBMI = 3.79, HFPG = 2.12). Meanwhile, the risk peak of high processed meat intake (AAPC=1.28%) similarly concentrated in 30-34-year-olds (local drift=2.63), while the risk peak of alcohol consumption (AAPC=0.30%) delayed to older adults aged 85-89 years (local drift=0.94). Despite declining mortality from diet low in milk (DLIM) and low physical activity (LPA) (AAPC <0), cohort effects indicated CRC mortality resurgence in post-1977 birth cohorts. In the US, while CRC mortality declined overall, post-1960 birth cohorts exhibited rising risks from HFPG, diet high in processed meat (DHIPM), LPA, HBMI, and alcohol use. Projections for 2022-2031 suggest persistent metabolic risk-driven

CRC mortality growth in China and potential behavioral risk-related EC mortality rebound in the US.

Conclusion: China requires address the smoking and alcohol use-related EC burden in aging populations and prioritize metabolic risk control in CRC, while the US requires vigilance against alcohol-driven EC mortality. Both nations need targeted interventions for early-onset CRC risk factors to combat dual challenges of aging populations and lifestyle shifts.

Considerations for Leveraging Real-World Data to Support Regulatory Decision-Making: Bridging the Gap between Noisy Data and Robust Evidence

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Abstract: The focus of this article is on the key considerations for the generation of real-world evidence (RWE) when leveraging real-world data (RWD) to support regulatory decision-making. Randomized controlled trials (RCTs) are the gold standard for evaluating the safety and efficacy of medical products, while RCTs' soaring costs, limited generalizability caused by strict eligibility criteria and artificial settings, and ethical or technical feasibility, particularly in rare or severe diseases and vulnerable populations, have made the implementation of RCTs challenging, causing some to look for real-world studies (RWS) as alternatives. RWD could be used in a variety of study designs, in which incorporating RWD as an external or hybrid control is widely used for regulatory submission. However, the characteristics of RWD are messy, incomplete, heterogeneous, and subject to different types of measurement errors and biases, posing unique issues regarding study integrity, transparency, and reproducibility. It is crucial to take some key issues, especially in population comparability, intervention as well as outcome definition consistency and data reliability. In terms of analysis of RWD, statistical methods are essential for making sense of RWD, obtaining causal relationships, testing/validating hypotheses, and generating regulatory-grade RWE to inform regulatory decision-making. Statistical methods like propensity score (PS), Bayesian borrowing, and the integration of the former two methods have been developed to reduce potential biases and improve precision. More innovative methods beyond the traditional statistical methods need to be developed to adjust for potential confounders and improve the capabilities of RWD for causal inference.

The Relationship between Metabolic Heterogeneity of Obesity and functional disability among Middle-aged and Elderly Adults in China

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Abstract

Aims: This study aimed to examine the impact of obesity-metabolic phenotypes and their transitions on functional disability in older adults, to inform early intervention strategies.

Methods: Data from the Chinese Longitudinal Aging Study (CHARLS) were used. Metabolic-obesity phenotypes were categorized into four groups: MHNW (metabolically healthy normal weight), MHOO (metabolically healthy overweight/obese), MUNW (metabolically unhealthy normal weight), and MUOO (metabolically unhealthy overweight/obese). Functional disability was assessed using basic (BADL) and instrumental (IADL) activities of daily living. Continuous and categorical variables were compared using Kruskal – Wallis and chi-square tests, respectively. Cox proportional hazards models were applied to estimate hazard ratios (HR) and 95% confidence intervals (CI), adjusting for age, sex, and other confounders. Subgroup and sensitivity analyses were conducted. Statistical analysis was performed using R Studio 4.3.1; $P < 0.05$ was considered significant.

Results: A total of 6,631 participants (median age: 58.2 years) were analyzed. MUOO group had the highest adiposity and metabolic disturbances. MUOO individuals showed the highest risk of BADL disability (HR: 1.64, 95% CI: 1.38 – 1.95), followed by MUNW (HR: 1.39, 95% CI: 1.12 – 1.73). Elevated risks were also observed in dressing (HR: 1.80, 95% CI: 1.30 – 2.49), toileting (HR: 1.75, 95% CI: 1.34 – 2.2), and bathing (HR: 1.71, 95% CI: 1.33 – 2.18). In IADL, MHOO showed the highest risk. MUNW showed no significant association. Transitioning from MHOO to MUOO significantly increased ADL and IADL disability risks (HR: 2.46 and 1.97, respectively), highlighting the impact of metabolic deterioration on functional decline.

Conclusion: Metabolic dysfunction, particularly in combination with obesity, is a key predictor of functional disability in older adults, surpassing the impact of obesity alone.

睡眠时长对我国老年人成功老龄化的因果效应及剂量反应 关系研究

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【摘要】研究背景：随着中国人口老龄化进程加速，提升老年人健康水平已成为重大公共卫生议题。现有证据表明，睡眠时长异常与多种健康问题相关，但其与成功老龄化的因果关系仍存在争议，且多数研究依赖单次测量，未能捕捉睡眠时长的动态变化。

目的：本研究旨在利用纵向数据，通过控制时变混杂因素，量化睡眠时长与成功老龄化的因果关联，并探索其非线性关系，为制定精准干预策略提供依据。

方法：基于中国健康与养老追踪调查 (China Health and Retirement Longitudinal Study, CHARLS) 2011—2018 年四期纵向数据，纳入 5044 名老年人 (共 10149 人年观察)。采用复合指标评估成功老龄化，通过边际结构模型 (MSM) 估计睡眠时长的因果效应，并利用二次项回归和限制性立方样条 (RCS) 检验非线性关系。模型通过逆概率加权调整时变混杂因素，并纳入教育水平、居住地等基线协变量。

结果：加权 Logistic 回归显示，前一期睡眠时长与后一期成功老龄化之间存在显著的非线性剂量-反应关系。限制性立方样条回归模型进一步验证了睡眠时长与成功老龄化之间的非线性关系，在短于 6.7 小时的区间内，睡眠时长每增加 1 小时，成功老龄化几率显著提升 34.4%；超过该阈值后，睡眠的边际效益以每增加 1 小时降低 19.8% 的速度递减。预测概率图显示最优睡眠区间为 6~8 小时。此外，教育程度 ($OR=1.506, P<0.001$) 和适度饮酒 ($OR=1.291, P=0.006$) 为保护因素，而农村居住 ($OR=0.629, P<0.001$) 与跌倒史 ($OR=0.687, P=0.002$) 为风险因素。

结论：本研究首次通过动态因果模型，系统分析了睡眠时长与成功老龄化之间的因果关系及其非线性效应。研究发现，通过逆概率加权调整时变混杂因素后，睡眠时长与成功老龄化非线性关系稳健存在，支持睡眠时长的独立效应。研究结果为制定促进成功老龄化的干预策略提供了科学依据，强调维持 6~8 小时睡眠对促进成功老龄化的重要性。未来可基于此制定个性化睡眠管理策略，尤其需关注农村及高风险人群。

疫苗长期效果评价的扩展检测阴性设计及应用研究

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【摘要】目的: 在真实世界进行疫苗有效性评价以及长期效果评价已成为当前公共卫生研究领域的核心议题。本文旨在探索适用于疫苗长期效果评价的研究设计;
方法: 对检测阴性设计 (Test-Negative Design, TND) 进行扩展即对检测阴性人群持续随访, 在固定研究时长模式下考虑疫苗效力恒定和两种时依疫苗效力以及两种滚动转组的疫苗持续接种机制, 构建基于时间限制性样条的多元 logistic 回归模型和半参数广义加性模型, 实时评价疫苗长期效果;
结果: 仅考虑疫苗效力时两模型的拟合能力并无明显差异; 当考虑不同转组模式时两模型与基于 TND 估计的疫苗有效性 (Vaccine Effectiveness, VE) 产生不同程度的偏差, 均低估了 VE。多元 logistic 回归模型相比半参数广义加性模型产生的偏差略小。VE 变化曲线受接种率及已接种人群流感样概率的影响较大, 而受流感样概率均值和未接种人群流感样概率的影响较小, 其中考虑呈线性衰减的时依疫苗效力时引入指数滚动转组设计带来的偏差最小。为减小模型与基于传统 TND 之间的偏差, 在两模型中引入异质性影响因素构建衍生的时依混合效应模型, 发现两模型均在一定程度上增加估计 VE 的准确性;
结论: 在 TND 基础上进行固定研究时长模式下的扩展 TND 设计为评价疫苗长期效果提供了一个具有可行性的新思路, 以期推广至更多种类的疫苗。通过实例数据分析, 验证了模拟实验中加入转组设计后两模型的拟合效果优于半参数广义加性混合效应模型。但未全面考虑其他异质性影响因素以及因素之间的交互作用, 需进一步探索时依混合效应模型并增强模型的稳健性。

Trends in morbidity and mortality from unspecified and undetermined injuries in the United States, 2001-2022

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Abstract

Introduction: Accurate coding quality is essential for reliable injury surveillance, rigorous evaluation of interventions, and evidence-based policymaking. The present study was designed to analyze trends in the proportions of unspecified and undetermined injuries in both injury mortality and morbidity, as well as their influence on the trends of specific injury types. **Methods:** Age-adjusted injury morbidity data, injury mortality data, and demographic information in the United States between 2001 and 2022 were extracted from the WISQARS dataset. The proportions of unspecified injury and undetermined injury were calculated to evaluate coding quality for injury morbidity and mortality. Joinpoint regression were employed to estimate the AAPCs and the respective 95% confidence intervals (CI). Line charts and bar charts were used to demonstrate the overall and subgroup trends. The proportionate method was used to redistribute injury morbidity and mortality with unspecified codes to cause-specific codes, which was used to evaluate the impact of unspecified codes on the injury trends. **Results:** The proportions of unspecified injury in injury morbidity (AAPC = -1.77%, $P < 0.05$) declined significantly between 2001 and 2022, as did the proportions of unspecified (AAPC = -3.69%, $P < 0.05$) and undetermined (AAPC = -1.87%, $P < 0.05$) injury in injury mortality. The unspecified and undetermined injury mortality differed by age group. Notably, the 60-69 age group exhibited increasing trends in both the proportion of unspecified injury among injury morbidity and undetermined injury among injury mortality. Additionally, the proportion of undetermined injury in mortality showed significant rises in both 0-4

(AAPC = 2.54%, $P < 0.05$) and 5-14 (AAPC = 2.99%, $P < 0.05$) age groups. Across U.S. states, the proportion of unspecified injury in injury mortality showed an increasing trend exclusively in North Dakota and Mississippi, while the most significant decreases were observed in Oregon and Vermont (AAPC = -7.90%, $P < 0.05$). 15 states exhibited rising proportions of undetermined injury in mortality, with New Mexico demonstrating the most substantial increase (AAPC = 10.22%, $P < 0.05$). In contrast, Massachusetts showed the most pronounced decline (AAPC = -12.35%, $P < 0.05$). The redistribution of unspecified injuries had the greatest impact on machinery morbidity trends, and struck by/against and fire/hot object mortality trends;

Conclusions: The proportions of unspecified and undetermined injuries in injury mortality and morbidity declined between 2001 and 2022, but large disparities existed across sex groups, age groups and U.S. states. The redistribution of unspecified injuries has a significant impact on injury-specific morbidity and mortality rates.

整合多组学和大规模功能注释识别因果变异 和提高跨种族复杂性状的多基因风险评分

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【摘要】目的: 精细定位与多组学的功能注释旨在识别影响复杂性状的因果变异, 提高遗传预测的准确性和可解释性。**方法:** 本研究提出多组学功能性多基因风险评分框架 (MultiFun-PRS), 这是一种计算可扩展的分析体系, 通过整合多组学数据与大规模功能注释来设定先验因果概率从而更准确地进行精细定位 (例如, SuSiE), 旨在提高因果变异识别的准确性及种族内/跨种族的多基因风险评分 (Polygenic risk scores, PRS) 的性能。**结果:** 基于模拟数据的模拟试验表明, 与传统的 C+T 相比, 上述框架可有效控制假阳性率, 增加正确识别的因果单核苷酸多态性 (Single nucleotide polymorphisms, SNP) 数量, 并提升 PRS 的预测效能。基于真实基因数据的模拟试验表明, 与基于遗传力分配 SNP 先验的 PolyFun 方法相比, MultiFun 使先验因果 SNP 概率的准确性提升 20.66%; MultiFun+SuSiE 使因果 SNP 覆盖度提高 33.31%; MultiFun-PRS 使 PRS 预测性能提升 5.30%, 且当多组学数据存在重叠时, 预测效果会进一步提高。对 UK Biobank 中脂质性状的全基因组分析表明, 相比于 PolyFun, MultiFun 将先验因果概率的准确性平均提高了 20.00%。利用潜在因果变异构建不同群体的 PRS 时, MultiFun-PRS 显著提高了大部分种族内和跨种族的预测效果, 且较 PolyFun+SuSiE 消耗更少的时间和内存资源。我们将 MultiFun/MultiFun-PRS 框架封装成 “MultiFunPRS” R 包 (<https://github.com/predictionmodel/MultiFunPRS>), 并提供完整文档以方便研究者理解和运用。**结论:** 综上, MultiFun/MultiFun-PRS 通过整合多组学数据与功能注释来精准捕获因果关系, 并提高种族内和跨种族的 PRS 效果, 极大地促进了对复杂性状的遗传结构的理解, 并优化了不同种族的风险预测。

老年人血清尿酸水平与衰弱状态之间的关系： 一项基于 NHANES(2007-2018 年)的横断面研究

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【摘要】 目的 探讨老年人血清尿酸水平对衰弱状态的影响情况。**方法** 采用 68 个生化指标、心理状态与身体状况等变量构建衰弱指数(Frailty index, FI, 被调查者根据衰弱指数分为正常组($FI \leq 0.15$)、衰弱前组($0.15 < FI \leq 0.25$)和衰弱组($FI > 0.25$)。本研究使用美国公共数据库国家健康和营养检查调查, 进行加权 logistic 回归分析、亚组分析与非线性分析, 探索血清尿酸水平对衰弱状态的影响。**结果** 校正年龄、性别、种族、教育水平、婚姻状况、吸烟状态、收入贫困比、饮酒频率等协变量后, 血清尿酸水平对衰弱前和衰弱发生的 OR 值分别为 1.221 (1.155,1.290) 和 1.378 (1.294,1.467)。血清尿酸对衰弱前和衰弱具有危险效应的最小剂量分别是 6.2mg/dL 与 5.6mg/dL; 血清尿酸对衰弱状态的影响发生改变的阈值是 7.1mg/dL, 超过阈值后, 其对衰弱风险的影响升高。**结论:** 血清尿酸是老年人衰弱的危险因素, 高尿酸血症的老年人更应注意衰弱的预防。

疾控人员集聚与城市化协调发展的时空特征及影响机制研究——基于中国 31 省面板数据的多模型实证分析

摘要：背景：在全球积极推进公共卫生体系建设以及城市化水平不断提升的大背景下，疾病预防控制工作的重要性愈发凸显。中国作为城市化发展大国，对疾病预防控制体系建设有着多重需求。城市化的快速发展在带来诸多机遇的同时，也引发了一系列问题，促使公共卫生资源分配不均问题加剧。目前，我国大部分的研究只是关注疾控资源分配的单一分析，却很少细化研究疾控人员集聚程度与城市化水平之间的关系。**目的：**本研究旨在分析 2010-2021 年我国 31 个省份疾控人员集聚程度与城市化水平的耦合协调关系及因果关系，为疾控中心在城市化进程中的发展规划提供参考依据。**方法：**用熵值法评估疾控中心人员集聚程度与城市化水平，对两者的耦合协调关系进行实证研究。以结构方程模型（SEM）为计量工具，筛选 18 项指标构建指标体系，构建结果方程模型，解析城市化各维度对疾控人员集聚程度的影响。**结果：**基于集聚度理论的两系统间集聚分布的时空演变结果显示，我国疾控人员集聚程度指数呈“U”变化趋势，空间上呈现“西部大于中部大于东部”的分布格局，而城市化水平指数则持续上升且呈现“东部大于中部大于西部”的特征，耦合协调结果表明，我国疾控人员集聚程度和城市化水平间的耦合协调关系整体处于“高耦合-低协调”状态，耦合度值在 0.9131-0.9551 之间，协调度值在 0.5101-0.5745 之间，协调度空间分布呈现“东部领先”的格局，而耦合度空间分布呈现“西部领先”的格局。结构方程模型结果表明，经济城市化水平和空间城市化水平促进疾控人员集聚，而人口城市化水平和社会城市化水平反而产生抑制作用，反映出资源配置滞后于城市化进程的结构性矛盾。**结论：**我国疾控人员集聚程度与城市化水平间的集聚分布呈现时空错配特征，疾控人员集聚程度和城市化水平间集聚分布的时间发展趋势存在显著差异，同时其空间分布格局也表现出明显的不一致性，我国绝大部分省份的疾控人员集聚程度与城市化水平的耦合度长期处于高水平阶段，表明两个系统之间联系紧密。而疾控人员集聚程度与城市化水平之间协调发展不平衡，两系统间整体协调度不高。城市化的不同维度对疾控人员集聚程度产生了差异化作用。建议建立疾控资源动态调配机制，提高经济激励，并依托空间规划建设区域性疾控中心。**创新：**本研究创新性地构建了“耦合协调分析-因果识别”的双链条研究框架，研究成果为疾控资源配置提供了新范式：一是建立了可量化的耦合协调评估体系，二是提出了差异化的区域配置策略，为“健康中国”建设提供了科学的实践路径。

Effect of Built Environment on the Causal Association between Nighttime Heat Exposure and Mortality in Stroke Patients: A Case-Crossover Study in Shandong Province, China

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Abstract

Background: Short-term extreme heat has been increasingly associated with cardiovascular mortality. However, robust causal evidence regarding the specific impact of nocturnal heat exposure on mortality among stroke patients remains scarce. Furthermore, the potential effect modification of the built environment on this association is not well understood.

Methods: Utilizing data from stroke patients in Shandong, China, we employed a time-stratified case-crossover design, integrated with inverse probability weighting (IPW) and conditional logistic regression, to estimate the lag 0-7 effects of nocturnal

Abbreviations: ALAN (artificial light at night), NDVI (normalized difference vegetation index), UHI (urban heat island), DALY (disability-adjusted life years), IPW (inverse probability weighting), PS (propensity score), CI (confidence interval), NO₂ (nitrogen dioxide), PM_{2.5} (particulate matter $\leq 2.5 \mu\text{m}$), O₃ (ozone), CO (carbon monoxide), SO₂ (sulfur dioxide), DAG (directed acyclic graph).

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heat exposure on mortality among these patients. Stratified analyses were conducted by age, sex, stroke subtype, and urban/rural residence. We further investigated potential effect modification by built environment characteristics, including greenness, artificial light at night (ALAN), residential land density, and building volume, on this association.

Results: Nocturnal heat exposure significantly increased the mortality risk among stroke patients, with the strongest effects observed at lag 1 and 2 days. Specifically, at lag 2, the odds of all-cause, cardiovascular, and stroke-specific mortality in stroke patients increased by 17.8%, 22.5%, and 26.0%, respectively. Elevated risks were identified among older adults, men, patients with hemorrhagic stroke, and rural residents. High greenness significantly attenuated the mortality risk associated with nocturnal heat exposure, whereas other built environment factors demonstrated limited modifying effects.

Conclusions: This study provides causal evidence that nocturnal heat exposure increases short-term mortality risk among stroke patients. Greenness mitigated this risk, underscoring the need for built environment interventions within climate adaptation strategies to protect vulnerable populations.



The Associations of Energy Intake with All-cause Mortality among Adults with Cardiometabolic Diseases: A National Prospective Cohort Study

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[Abstract]

Objectives To examine the associations of energy intake with all-cause mortality among American adults with cardiometabolic diseases and provide evidence for the potential optimal energy intake for specific adults. **Methods** Data from the US National Health and Nutrition Examination Survey 1999-2018 was used in the prospective cohort study. Energy intake (kcal/kg per day) was calculated by calorie intake (kcal per day) divided by ideal and actual body weight (kg). Cardiometabolic diseases in our study include obesity, hypertension, diabetes mellitus, high cholesterol level, congestive heart failure, stroke, and coronary artery diseases. Cox proportional hazard regression models were employed to evaluate the adjusted hazard ratios (HRs) and 95% confidence intervals (CIs) of energy intake with all-cause mortality. Their dose-response relationships were explored by Restricted cubic splines. **Results** 19127 American adults with cardiometabolic diseases were included in the current analysis. The mean time of follow-up was 8.88 ± 0.11 years. Results revealed a nonlinear relationship between energy intake and all-cause mortality. When adjusted for ideal body weight (IBW), participants consuming 30-<40 kcal/kg IBW/day exhibited the lowest mortality risk (HR=0.792, 95% CI: 0.629 – 0.978, P=0.028). Significant heterogeneity emerged across sex, age, and physical activity (PA) subgroups. Females showed reduced mortality at 20-<30 kcal/kg IBW/day (HR=0.702, P=0.005) and 30-<40 kcal/kg IBW/day (HR=0.738, P=0.047), whereas males demonstrated no significant associations. Younger participants (<60 years) had maximal protection at ≥ 40 kcal/kg IBW/day (HR=0.553, P=0.021), while older adults (≥ 60 years) benefited at lower intakes (20-<30 kcal/kg IBW/day: HR=0.781, P=0.030). Low-PA individuals mirrored overall risk reduction (30-<40 kcal/kg IBW/day: HR=0.804, P=0.037), but

moderate-to-high PA subgroups showed null associations. Similar patterns emerged for actual body weight-adjusted intake, with optimal intake at 30-<40 kcal/kg/day (HR=0.762, P=0.018). Subgroup findings were consistent: younger adults required higher intake (≥ 40 kcal/kg/day: HR=0.488, P=0.002), while older adults showed protection at 20-<30 kcal/kg/day (HR=0.702, P=0.005). Dose-response analyses confirmed significant nonlinear relationships for both weight-adjustment methods (P-nonlinearity<0.05) in overall, female, older, and low-PA subgroups. **Conclusion** Significantly nonlinear relationships existed between energy intake and the risk of all-cause mortality in the population with cardiometabolic diseases. The lowest risk of all-cause mortality appeared in the overall participants with daily energy intake of 30 to <40 kcal/kg ideal or actual bodyweight. Nevertheless, observed subgroup heterogeneity underscores the limitations of population-wide dietary recommendations, thereby highlighting the clinical relevance of personalized nutrition guidance.

基于真实世界数据的伏环孢素不良事件信号挖掘

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【摘要】

目的: 通过美国食品药品监督管理局 (Food and Drug Administration, FDA) 不良事件报告系统 (A adverse event reporting system, FAERS) 数据库挖掘氯苯唑酸的不良事件 (adverse events, AE) 信号。

方法: 本研究从FAERS 数据库中提取2021 年第一季度至2024 年第三季度收录的不良反应报告。采用报告比值比 (reporting odds ratio, ROR) 以及英国药品和保健产品 管理局 (Medicines and Healthcare Products Regulatory Agency , MHRA) 对伏环孢素相关 AE 信号进行挖掘, 并与药品说明书进行对比分析。MHRA 法调整了PRR 的检测标准, 并将卡方值(χ^2) 作为信号生成的条件之一。韦伯分布用来分析不良事件诱发的时间。 为了更深入的检测AE 的信号, 我们选择两个对照组进行信号挖掘, 即全部药物和其他 钙调磷酸酶抑制剂 (解剖学治疗学及化学分类系统ATC-L04AD)。

结果: 研究期间共收集到 4986 份不良反应报告, 涉及 13856 例不良事件。信号检测结果显示, 与其他所有药物相比, AE 最常涉及的系统器官类别是胃肠道系统疾病。治疗中断 (ROR=23.14, PRR=21.98) 被确定为最常见的阳性AE 信号。尿蛋白/肌酐比率 升高 (ROR=431.09, PRR=427.27) 是最强的阳性 AE 信号。此外, 与其他的钙调磷酸 酶抑制剂相比, 检测到一些独有的AE, 例如关节僵硬 (ROR=21.11, PRR=21.10) 和睡眠过度 (ROR=19.19, PRR=19.18)。共确定了 11 个未在伏环孢素说明书中标记中列出 的潜在AE, 其中最强的阳性信号是月经不调 (ROR=7.65, PRR=7.65)。我们发现了 11 个与DME 列表匹配的AE 信号。急性肾损伤的报告数量最多, 其次是肾功能衰竭。

结论: 在开具伏环孢素处方时, 临床医生应警惕涉及胃肠道系统疾病和肾脏相关的AE。此外, 应更多关注新发现的AE, 例如月经不调和尿中带血。

关键词: 伏环孢素, 狼疮肾炎, 药物警戒, 比例失衡分析, FAERS

Potential Causal Links of Long-term PM_{2.5} Components Exposure with Acute Myocardial Infarction Mortality: a Nationwide Study in the United States

Abstract:

There was limited evidence on the relationship between acute myocardial infarction (AMI) mortality and fine particulate matter (PM_{2.5}), particularly with its components.

Nationwide studies providing causal insights were even more scarce. We collected annual and county-level data of AMI mortality and the concentrations of PM_{2.5} and its five major components—including elemental carbon, organic carbon, sulfate, nitrate, and ammonium—along with temperature and socioeconomic factors across the United States, 2004-2019. By integrating a difference-in-differences causal inference approach with quantile G-computation methodology, we observed (i) a relative risk (RR) of AMI mortality of 1.019 (95% CI: 1.013, 1.025) per IQR (i.e., 2.92 $\mu\text{g}/\text{m}^3$)

increase in PM_{2.5} concentration and a relative risk (RR) of AMI mortality of 1.118 (95%CI: 1.103, 1.132) for each unit increase in PM_{2.5} component mixture concentration; (ii) among the five major components, sulfate contributed most with the largest weight(0.693); (iii) the impact of the PM_{2.5} component mixture was amplified by increases in winter mean temperature; (iv) In counties with lower poverty levels, the relative risk (RR) of the PM_{2.5} component mixture on AMI mortality was 1.029 (95% CI: 1.007, 1.051), primarily driven by sulfate (weight:

0.817). In eastern counties, the RR was 1.019 (95% CI: 1.007, 1.031), compared to western counties, similarly driven by sulfate (weight: 0.707); and (v) long-term

regular physical exercise significantly attenuated the effects of PM_{2.5} mass and component mixtures on AMI mortality, with relative risks (RR) of 1.004 (95% CI:

1.003, 1.005) and 1.057 (95% CI: 1.034, 1.080). These findings suggested that long-term exposure to PM_{2.5} was associated with increased AMI mortality, and that reducing sulfate emissions, particularly in the eastern United States, alongside promoting daily physical exercise could effectively mitigate the burden of PM_{2.5}-related AMI mortality in the United States.

ICE-Net 因果分析方法的建立及应用研究

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【摘要】目的：本研究提出一种融合神经网络、贝叶斯因果网络与信息论的 ICE-Net(Information Causal Effect Network)因果分析方法，旨在识别疾病治疗过程中关键的因果路径并精准量化因果效应，从而深入揭示治疗各阶段间复杂的因果机制；**方法：**首先，利用最大互信息神经估计器(MINE)从治疗过程的多维数据中提取潜变量，通过神经网络捕捉潜在非线性关系；其次，采用贝叶斯因果网络构建治疗过程潜变量与结局变量间的因果关系模型，通过 Hill Climbing Search 算法进行网络结构学习，识别治疗过程中的关键因果路径；最后，基于信息论提出因果效应分解方法，将已识别因果路径的影响分解为单独效应、协同效应和冗余效应，系统评估各治疗阶段潜变量对结局的贡献。为验证该框架的有效性，设计三组系统性模拟实验，全面评估所提方法在因果识别能力、鲁棒性及泛化性能方面的表现，其中第三组实验通过增量扰动法验证因果效应分解的准确性与稳定性。收集急性 ST 段抬高型心肌梗死(STEMI)临床数据；将 STEMI 患者治疗过程分为七个关键阶段：院前急救、急诊/入院检查、危险评估、溶栓治疗、PCI 治疗、住院药物治疗和出院前医嘱；利用 28 个治疗过程指标和 1 个临床结局指标的系统分析，识别治疗全程中的关键因果路径和节点；**结果：**构建融合神经网络、贝叶斯因果网络及信息论的多阶段疾病治疗因果分析方法框架，通过模拟实验验证，多阶段因果分析方法框架在潜变量提取、因果结构学习和效应量化方面均显示出显著优势：MINE 方法大样本条件下($N \geq 10,000$)及非线性场景中表现尤为突出，；贝叶斯因果网络在潜变量数量 ≥ 8 时准确率稳定在 94% 以上，能够准确识别潜变量与结局变量之间的关键因果路径；信息论因果效应分解方法在大样本条件下($N \geq 100,000$)信息增益率趋近于零，因果分解方法能够精确识别和量化变量间的直接因果关系，而不受间接路径的干扰。贝叶斯因果网络得到治疗过程与结局变量的有向无环图，通过因果分解法获得因果效应：治疗阶段通过两条因果路径影响患者院内死亡的发生(Y_1)：院前急救→急诊/入院检查→再灌注 PCI 治疗→ Y_1 ，以及院前急救→急诊/入院检查→住院药物治疗→ Y_1 ，院前急救阶段的因果贡献最高，为 0.0751；**结论：**本研究构建的多阶段疾病治疗因果分析方法框架实现了从宏观治疗策略到微观临床指标的全链条因果分析，通过识别和量化各治疗阶段的因果关系，为治疗时间窗敏感的急危重症疾病建立因果分析范式。

基于 TyG-ABSI 联合指数的脑卒中风险预测模型及跨种族验证

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摘要: **目的** 构建并验证基于 TyG-ABSI 指数的脑卒中风险预测模型, 评估其跨种族预测效能, 为临床提供精准的脑卒中风险评估工具。**方法:** 整合 CHARLS 和 NHANES 数据库, 通过 Lasso 回归筛选影响因素, 采用加权相关性分析挖掘变量关系。构建决策树、随机森林、支持向量机、XGBoost、KNN 和 Stacking 集成模型, 比较准确性(Accuracy)、精确度(Precision)、F1-Score、特异度(Specificity)、灵敏度(Sensitivity)和受试者工作特征曲线下面积 (AUC) 指标, 利用 SHAP (Shapley Additive Explanations) 方法进行可解释性分析。**结果:** 随机森林模型在训练集、内部验证集和外部验证集中均表现最优, 且具有良好的跨种族泛化能力。TyG-ABSI 联合指数在预测脑卒中风险方面优于单一指标 ABSI 和 TyG。SHAP 分析增强了模型的临床可解释性。**结论:** 基于新型生物标志物 TyG-ABSI 联合指数构建的随机森林模型预测脑卒中风险具有较高的准确性, 且适用于不同种族人群。

身体质量指数和腰围与衰弱轨迹的 J 型关联：

一项中国中老年人人群的纵向研究

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【摘要】目的：基于全国代表性队列，探究中国中老年人人群 BMI、WC 与 衰弱进展的动态关联，为早期干预延缓衰弱进展提供依据；**方法：**本研究数据 来源于中国健康与养老追踪调查（China Health and Retirement Longitudinal Study, CHARLS）2011-2018 年纵向数据，纳入 4395 名基线时未出现衰弱的个体。衰弱程度采用包含 40 项指标构建的衰弱指数（Frailty Index, FI）进行量化，

FI $\geq$ 0.25 定义为衰弱，并通过组基轨迹模型（GBTM）识别衰弱轨迹。采用多因素 Cox 回归和限制性立方样条（RCS）分析 BMI/WC 与衰弱轨迹的非线性关联，并调整社会人口学特征、行为方式及临床混杂因素。通过完整案例分析、滞后时间排除以及联合肥胖指标（BMI-WC）等敏感性测试验证结果的稳健性；**结 果：**研究识别出两条显著不同的衰弱轨迹：低风险稳定组（72.10 %）和高风险快速进展组（27.90 %）。分析显示，BMI ($P_{\text{nonlinear}} < 0.001$ ；拐点：22.27 kg/m²) 和性别特异性 WC（男性：78.87 cm；女性：79.50 cm； $P_{\text{nonlinear}} < 0.01$ ）均与衰弱进展风险呈 J 型关联。当超过这些阈值时，衰弱进展风险分别增加 72 %（肥胖：HR=1.72，95% CI: 1.48-1.99）和 42 %（腹型肥胖：HR=1.42，95% CI: 1.27-1.58）。值得注意的是，中心性肥胖对衰弱进展的预测价值高于 BMI，这一现象在女性中尤为明显。敏感性分析证实了结果的稳健性；**结论：**BMI 和 WC 与衰弱轨迹呈 J 型关联，提示全身性肥胖和腹型肥胖均可加速中国中老年人人群的衰弱进展，且风险在超过特定 BMI/WC 阈值后显著上升。针对腹型肥胖的早期干预可能有助于改善衰弱轨迹，为延长高危中老年人人群的健康寿命提供了关键路径。

Using patient-reported outcomes for the dynamic prediction of adverse aftermaths for discharged COPD patients

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[Abstract] **Background:** This study aims to enhance the precision of risk prediction by developing dynamic models based on patient-reported outcomes (PROs). **This would help** estimate **the** time-varying risks of adverse outcomes **after hospital discharge, for** patients with chronic obstructive pulmonary disease (COPD). **Methods:** A cohort of COPD inpatients discharged from five hospitals in Shanxi Province, China **between December 2020 and April 2022** was prospectively followed. The primary **endpoints were either** rehospitalization or all-cause mortality within three years **of** discharge. Three dynamic prediction models were constructed: Joint Latent Class Model (JLCM), Shared Random Effects Model (SREM), and Landmarking approach. Model performance was assessed **by** using **the** time-dependent area under the receiver operating characteristic curve (AUC), Brier scores, and calibration plots. Individual-level trajectories of PRO scores and **the** associated risk probabilities were also visualized. **Results:** **Three hundred and forty-four** patients were included, among whom 111 (32.27%) experienced adverse outcomes. The SREM model consistently outperformed the others, demonstrating the highest AUCs and lowest Brier scores across all **the** landmark time points, with calibration curves closely aligned with the ideal diagonal. In the survival submodel, the association parameter for PRO scores was statistically significant ($P < 0.001$); each one-point increase in PRO score was associated with a 4.3% reduction in mortality risk ($HR = 0.957$, 95% CI : 0.933~0.980). Educational attainment, procalcitonin, and C-reactive protein levels were also independently associated with adverse outcomes. In the longitudinal submodel, **a** higher dyspnea grade was negatively correlated with PRO scores. **Conclusions:** PRO scores serve as a dynamic and clinically informative marker for monitoring **the post-discharge** prognosis in COPD patients. The SREM model demonstrated superior dynamic prediction performance, offering robust support for personalized clinical decision-making and targeted intervention.

Clinical Trial registration and Informed consent:The study was approved by the Ethics Committee of the Second Hospital of Shanxi Medical University (No. 2022YX123) and registered with the Chinese Clinical Trial Registry (ChiCTR2200064900). Written informed consent was obtained from all participants.

Robust Undersampling for Class Imbalance under High-Dimensional Asymptotic Geometry

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【Abstract】 Objective: To investigate the impact of class imbalance on classification performance in high-dimensional settings, particularly where informative signals are diffusely distributed across features, as commonly encountered in domains such as tumor detection, remote sensing, and behavioral surveillance. **Method:** We revisit the high-dimensional geometric framework of Hall (2005), which models data as simplices in asymptotic space and provides necessary conditions for the existence of a perfect separating hyperplane. Building on this, we present the first theoretical analysis of class separability under class imbalance and noise. We derive three consistent and unbiased distance-based estimators for the classification condition, offering computational advantages over traditional covariance-based approaches. To address violations of the classification condition induced by class imbalance, we propose a Simplex-Preserving Optimized Sampling (SPOS) algorithm that iteratively selects a geometrically representative and maximally separable subset of data. **Results:** Empirical evaluations on synthetic high-dimensional datasets with Gaussian, Bernoulli, and Poisson feature types show that SPOS effectively maintains the original simplex structure and improves hyperplane separability across a range of class imbalance ratios. **Conclusion:** Our study provides novel theoretical insights and practical algorithms for learning from imbalanced high-dimensional data, demonstrating that preserving geometric structure is critical for enhancing classification performance in challenging settings.

慢性肺部疾病患者衰弱症状网络演化：基于 CHARLS 数据

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【摘要】 目的 慢性肺部疾病患者衰弱症状的演化规律目前尚未得到研究。方法 选取中国健康与养老追踪调查 (China Health and Retirement Longitudinal Study, CHARLS) 2011 年数据中 ≥ 45 岁且患有慢性肺部疾病的人群为研究对象, 分别在 2013 年、2015 年、2018 年进行追踪调查衰弱状况, 利用网络分析探索其动态演变规律。结果 衰弱动态网络分析结果显示致残性躯体症状的中心性始终维持较高水平, 显著高于疾病类症状; 各时段网络的核心症状呈现动态变化: T1 期为“做家务”, T2-T4 期转变为“走 1km”; 此外, 网络间比较结果显示, T1vsT4、T2vsT3、T3vsT4 的全局强度存在显著差异。T2vsT3 和 T1vsT4 显示结构上存在显著差异。结论 致残性躯体症状在衰弱症状网络中处于核心地位, 是驱动衰弱进程的关键影响因素。早期干预这些关键因素, 对慢性肺部疾病患者衰弱的早期识别、管理及干预具有重要的理论意义。

公式章 1 节 1癌症多组学预后的注意力机制与门控融合可 解释性预测模型构建及应用研究[△]

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摘要

研究背景和目的:

随着高通量测序技术的发展和普及, 研究人员能够获得更加丰富的多组学信息数据。然而, 组学数据具高维度、复杂性和异质性的特点, 如何从中挖掘出有价值的信息是癌症多组学研究的关键挑战。与此同时, 人工智能的飞速发展促使深度学习技术广泛应用于癌症组学数据分析, 但现有深度学习模型在癌症预测中, 仍未能充分探索不同组学间的交互关系与协同机制。在数据降维过程中, 常因未能有效保留基因关键信息, 和忽视生物通路在癌症发生发展中的调控作用, 导致模型预测准确性与生物学可解释性不足。癌症预后预测是优化临床诊疗策略、提升患者生存质量的关键环节, 但多数癌种因分子机制复杂、缺乏有效预测手段, 难以实现癌症精准化治疗。针对上述问题, 本文以低级别胶质瘤 (LGG)、卵巢癌 (OV) 等 8 种癌症数据为例, 构建了癌症多组学预后预测模型, 深度融合癌症多组学信息与通路信息, 实现对癌症预后的精准预测, 并借助可解释性模块探究影响癌症预后的关键基因; 发现与癌症相关的生物标志物, 为癌症精准医疗提供理论依据与实践支撑。

研究内容及方法:

(1) 数据下载及预处理: 从 TCGA 数据库获取 LGG、OV 和 LUAD 等 8 种癌症的 mRNA、lncRNA 和 miRNA 数据, 对数据进行预处理后, 按照生存结局划分长期 (LTS) 和短期生存 (非 LTS) 组。采用随机森林进行数据降维, 通过重要性排序筛选出重要性排名前 100 的 miRNA 和排名前 2000 的 mRNA、LncRNA。

(2) 模型构建: 构建 MoPAG 模型, 该模型集成组学注意力与通路注意力机制信息, 并通过门控模块自适应调整两种注意力信息的融合权重, 实现多组学数据与通路信息的深度整合。

(3) 数据整合与实验设计: 将 MoPAG 模型与 Logistic 回归、随机森林、支持向量机等 10 种传统机器学习分类模型以及深度学习 DeepKEGG 模型进行对比。

再对比分析不同组学数据组合在预后预测中的性能。然后开展消融实验，评估不同模块组合下模型在癌症预后预测任务中的性能表现。

(4) 模型可解释性分析与临床关联验证：引入 DeepLIFT 算法，量化基因特征对模型输出的贡献度，将 LGG 数据中贡献度排名前 50 的基因作为核心 (HUB) 基因。然后，对 HUB 基因进行 GO 功能注释分析和 KEGG 信号通路分析，并构建蛋白质互作 (PPI) 网络及 mRNA-miRNA 对应关系网络。基于 HUB 基因，采用中位数分层策略将样本划分为低危组与高危组，运用 Kaplan-Meier 生存曲线与对数秩检验，评估 MoPAG 模型筛选出的生物标志物，为模型预测结果提供临床证据支持。

研究结果：

(1) 模型性能突出：在 LGG、OV、HNSC、BLCA、LIHC、COAD、KIRC、LUAD 数据中，MoPAG 模型展现出优异的预测性能，在各数据集的测试集上 AUC 值分别达 0.904 ± 0.049 、 0.725 ± 0.035 、 0.708 ± 0.066 、 0.704 ± 0.054 、 0.693 ± 0.071 、 0.670 ± 0.044 、 0.667 ± 0.083 和 0.648 ± 0.070 ，在 LGG、OV 和 LUAD 数据中 AUC、ACC、F1 和 AUPR 指标上均呈现最优表现，综合性能优于深度学习模型 DeepKEGG 及其他 10 种机器学习模型，在其他数据集中，性能都能稳定排到前五及以上。

(2) 多组学整合优势显著：三组学整合模型在 LGG、OV 癌症中预测效能最佳，AUC 值分别达 0.904、0.725。不同组学数据组合中，LGG 中 mRNA 单组学 (AUC 0.852) 与 LncRNA+mRNA 双组学 (AUC 0.883)、OV 中 mRNA 单组学 (AUC 0.508) 与 mRNA+miRNA 双组学 (AUC 0.707) 都分别表现突出。

(3) 模块功能验证：消融实验表明，在 LGG 数据中，通路注意力模块与门控融合模块组合 (AUC 0.862) 性能最优，通路注意力模块在与不同模块协同中均表现优异。

(4) 生物标志物发现：通过 DeepLIFT 算法成功筛选 LGG 的 HUB 基因，通过文献佐证与生信分析双重验证了 HUB 基因在分子网络中的核心地位，LGG 生存分析证实 DCTN6、PEX10 等基因在高低危组生存差异显著 ($P < 0.005$)。

研究结论：

本研究基于多组学数据，构建 MoPAG 模型用于 LGG、OV 和 LUAD 等 8 种癌症数据集的预后预测。通过集成组学注意力信息与通路注意力信息，结合门控策略实现多源信息深度融合，显著提升模型预测性能与泛化能力。通过文献佐证与生信分析双重验证，本研究筛选的 HUB 基因在分子网络中的核心地位得到充分证实。为癌症精准医疗提供了理论支撑，为后续转化应用与临床实践奠定坚实基础。

基于 fMRI 与认知测试的阿尔兹海默病诊断模型研究

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【摘要】目的：本研究基于功能脑网络图论属性和神经心理学量表的多结构化数据，应用集成机器学习方法，对阿尔茨海默病 (Alzheimer's Disease, AD) 的进展阶段进行分类，包括：正常认知 (Normal Cognition, NC)、轻度认知障碍 (Mild Cognitive Impairment, MCI)、AD。通过构建AD 多分类模型，辅助 AD 早期诊断，发现脑网络影像学标记。**方法：**基于图论 (Graph Theory, GT) 方法，结合神经心理学测试量表，根据病程发展对NC、MCI、AD 进行分层多分类诊断，包括AD-MCI、AD-NC 以及 MCI-NC。采用少数类合成过采样技术 (Synthetic Minority Over-sampling Technique, SMOTE) 处理样本类别不平衡问题；采用支持向量机递归特征消除 (support vector machine-recursive feature elimination, SVM-RFE) 算法进行特征选择。利用支持向量机 (Support Vector Machine, SVM)、随机森林 (Random Forest, RF)、逻辑回归 (Logistic Regression, LR)、极限梯度提升树 (Extreme Gradient Boosting, XGBoost) 等算法构建分类模型，采用十折交叉验证进行模型性能比较，得到最优分类模型。模型评估指标包括准确率 (Accuracy, ACC)、精确率 (Precision)、召回率 (Recall)、F1 得分以及受试者操作特征 (receiver operating characteristic, ROC) 曲线下面积 (area under curve, AUC)。**结果：**基于SVM-RFE 的特征选择保留了前 10 个最优特征，三组分类中以节点效率、节点局部效率拓扑指标为主，不同分组关键指标分布区域不同，左中央前回等影像学标记占比显著。使用功能脑网络图论属性结合神经心理学量表构建AD 分类辅助诊断模型，显示XGBoost、RF 模型性能优于 SVM、LR 模型。在AD-MCI 分类中，RF、XGBoost 准确率分别为 88.96%，89.06%，AUC 分别为0.9528，0.9565。在AD-NC 分类中，RF、XGBoost 准确率分别为 84.27%，88.87%，AUC 分别为0.9155，0.9528。在MCI-NC 分类中，RF、XGBoost 准确率分别为 80.35%，80.51%，AUC 分别为0.8812，0.8842。加入神经心理学量表后AD-MCI 分类中，RF 准确率为90.84%，AUC 为0.9666，XGBoost 准确率为92.01%，AUC 为0.9691。在MCI-NC 分类中，RF 准确率为82.48%，AUC 为0.8919，模型性能均有所提升。**结论：**研究发现基于脑影像特征与神经心理学测试可对 AD 病程进行早期分类诊断，实现疾病早期预警。集成学习分类器 XGBoost 和RF 性能最好，优于SVM 和LR 分类器，有助于提升诊断的准确率。

Multi-Objective Clinical Prediction and Decision Support Using Synchronized Optimization of Large Language Models: A Case Study of Functional Dyspepsia

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[Abstract] Background: Functional dyspepsia (FD), a common functional gastrointestinal disorder, significantly impairs patients' quality of life. Traditional clinical prediction methods are limited in meeting the demands of clinical decision support. The development of artificial intelligence technologies offers new possibilities for predicting disease outcomes and quality of life, paving the way for personalized treatment. **Objective:** This study aims to enhance particle swarm optimization (PSO) driven by large language model (LLM), introduce a synchronized optimization process of feature selection and hyperparameter optimization, and build a prediction model for FD therapeutic effects using machine learning (ML). It also explores the application of this model in clinical decision support. **Methods:** This multicenter retrospective study included

data from 2,120 patients between January 2022 and December 2024, divided into a training set (1,157 cases), an internal test set (289 cases), and an external test set (674 cases). We proposed a prompt-enhanced particle swarm optimization (PEPSO) and implemented synchronized optimization of large language models (LLM-SO). Using 28 clinical features and an automated machine learning (AutoML) framework, we constructed classification and regression models to predict treatment response and quality of life index improvement. We used the SHAP method for interpretability analysis and developed a clinical decision support system. **Results:** In the classification model, the key features affecting FD were education level, subtype, gender, NDSI (epigastric pain), NDSI (epigastric bloating), and NDSI (irregular diet). In the regression model, the key features affecting quality of life were education level, subtype, gender, NDLQI (sleep disturbance), and NDLQI (dietary and beverage issues). AutoML achieved the best predictive performance on both the internal and external datasets. On the external test set, the ROC-AUC for classification was 0.9127, the PR-AUC was 0.9413, the R^2 for regression was 0.8816, and the MAE was only 2.3251. **Conclusion:** This study successfully established models for predicting therapeutic outcomes and quality of life in FD patients using the PEPSO and developed a decision support system. These models are expected to help customize and adjust treatment plans for different patients, improve clinical efficacy, and reduce medical costs.

TLMR: Transfer Learning based Two-sample Mendelian Randomization Method for Heterogeneous Population

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摘 要

目的: 针对两样本孟德尔随机化(MR)研究中人群异质性所导致的因果效应估计偏倚问题, 提出一种新的稳健 MR 方法——TLMR (Transfer Learning based Mendelian Randomization). 在控制未知混杂偏倚与潜在的水平多效性偏倚的同时, 实现在不同程度人群异质性下的无偏因果效应估计.

方法: 基于迁移学习策略, 在最小化模型假设的前提下, 通过利用遗传工具变量与可观测的效应修饰因子, 将暴露模型从源人群迁移至目标人群, 从而修正人群异质性给传统 MR 方法带来的估计偏倚. 通过模型拓展, TLMR 适用于连续型结局数据与二值型结局数据. 进一步, 通过反向迁移结局模型, 实现对两个人群中因果效应的分别估计. 在数值模拟中遍历人群异质性水平在内的所有影响估计结果的关键参数, 并与目前

1 使用最广泛的 4 类共计 8 种 MR 方法进行比较, 以系统评估 TLMR 的性能表现. 并在实例中应用 TLMR 系统分析体质指数 (BMI) 对肺功能的影响, 以评估 TLMR 的实用性能.

结果: 模拟研究结果表明, 在存在人群异质性与效应修饰的情况下, TLMR 方法能得到无偏的因果效应估计, 而相比较的 8 种 MR 方法均出现了显著的偏倚; 即使在人群同质或无效应修饰的情况下, TLMR 的表现仍然不弱于现有方法. 真实数据分析进一步验证了 TLMR 的有效性, 其估计结果与主流研究一致, 且在不同肺功能指标间以及不同人群间保持一致的结论, 而对比方法的结果则存在矛盾或偏离主流结论.

结论: TLMR 方法有效应对了两样本 MR 设计中因人群异质性引发的估计偏倚问题, 能在不同异质性水平下实现更稳健、准确的因果效应估计其对二值结局数据和结局模型反向迁移的拓展进一步增强了方法的适用性与实用价值

瘦型非酒精性脂肪肝:

可解释机器学习预测模型的开发和验证

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【摘要】目的: 本研究旨在使用基于人群的横断面数据库通过机器学习方法识别瘦型非酒精性脂肪肝病风险预测。方法: 数据来自全国健康和营养检查调查 (NHANES) 2017 年至 2020 年 3 月的数据库。瘦型 NAFLD 由肝脏瞬时超声弹性成像中的受控衰减参数 (CAP) 定义。采用最小绝对收缩和选择运算符 (LASSO) 回归分析、随机森林 (RF)、Boruta 进行特征选择。使用六种机器学习方法: 朴素贝叶斯 (Bayes)、多层感知 (MLP)、随机森林 (RF)、逻辑回归 (LR)、RF、支持向量机 (SVM) 和 XGBoost。通过受试者工作特征曲线下面积 (AUC)、灵敏度、特异度、准确率和 F1 评分对 6 个模型以及现有评价系统 FLI 进行性能评估和比较。并通过特征重要性、SHapley 加法解释 (SHAP 值)、SHAP 瀑布图、力图提供可视化解释。

评估模型, 并通过校准曲线、决策曲线分析、变量重要性图、SHapley 加法解释图、部分依赖图和局部可解释模型不可知解释图进行解释。结果: 共有 2936 名参与者被纳入开发和验证模型。XGBoost 开发的模型表现最优, 优于其他模型和 FLI, 在验证集上实现了 0.819 的 AUC、0.738 的准确率、0.753 的灵敏度和 0.735 的特异性。结论: XGBoost 模型可以更好地评估瘦型 NAFLD 的存在。基于 XGBoost 模型, 我们创建了一个名为“瘦型脂肪肝预测系统” (<https://xybseu.shinyapps.io/2025>) 的基于 R Shiny Web 的应用程序。为医疗临床专业人员提供了一种便捷性工具, 以提高 Lean NAFLD 诊断的准确性并支持个性化治疗策略。

经火锅麻辣烫底料暴露塑化剂 DBP 和 DEHP 的膳食风险评估

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【摘要】目的: PAEs (Phthalic Acid Esters) 作为内分泌干扰物, 其接触可能增加生殖障碍、II 型糖尿病、胰岛素抵抗、肥胖以及过敏和哮喘的风险。本研究旨在利用有限数据, 通过合理的参数分布拟合火锅麻辣烫底料中塑化剂 DBP 和 DEHP 的含量分布, 并结合人群消费量数据, 初步评价不同人群通过火锅麻辣烫摄入 DBP 和 DEHP 的膳食风险; 方法: 通过采某市食品药品检验检测研究院的 91 例火锅麻辣烫底料样品, 利用极值混合模型和混合分布模型, 结合 Kolmogorov-Smirnov 检验、Anderson-Darling 检验、AIC 和 BIC 等信息准则, 本研究拟合了污染物的浓度分布, 并据此进行了暴露量和风险评估; 结果: 在 91 份火锅麻辣烫底料样本中, DBP 和 DEHP 的检出率分别为 31.87% 和 54.95%。为 DEHP 选定 2-Gamma 分布, DBP 选定 Lognormal-GPD 分布, 通过参数模型评估, 结果显示所有受检人群的两种塑化剂暴露量均未超出安全范围。但需要注意的是, 7-13 岁女性组的 DEHP 暴露量已接近健康标准, 具体为 $0.0429\text{mg}/(\text{kg}\cdot\text{d})$, 同年龄段男性组的暴露量也相对较高, 为 $0.0415\text{mg}/(\text{kg}\cdot\text{d})$ 。从危害商数 (HQ) 来看, 各人群 DBP 的暴露均在安全水平内, 但 DEHP 在人群中的高位分位数超过了安全阈值 1, 特别是 7-13 岁女性组, 在最大值情况下的 HQ 值高达 2.15; 结论: 尽管当前火锅麻辣烫底料中 PAEs 的暴露量尚未超出安全范围, 但特定人群如儿童和青少年的暴露量已接近容许参考剂量, 提示需对这些人群保持密切关注和持续监测。此外, DEHP 的高百分位暴露个体面临非致癌性风险, 需进一步的风险管理措施。

基于孟德尔随机化的中介分析方法比较

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【摘要】目的: 探究不同场景下四种基于孟德尔随机化 (Mendelian randomization, MR) 的中介分析方法的直接因果效应与间接因果效应的表现, 为选择合适的方法提供建议。**方法:** 在考虑多效性的情况下, 模拟有直接效应间接效应、有直接效应无间接效应、无直接效应有间接效应、无直接效应间接效应这几种情况, 比较两步 MR、多变量 MR、通过 GWAS 汇总数据整合进行中介分析框架并进行偏差校正 (MAGIC)、特定通路效应孟德尔随机化 (PSE-MR) 这四种方法。**结果:** 无多效性时, 两步 MR 方法表现较好。存在平衡多效性时, 两步 MR 方法 I 类错误率较低, 但检验效能较低, PSE-MR 方法检验效能较好, 但 I 类错误率较高。存在定向多效性时, MAGIC 方法的表现较好。**结论:** 在无多效性情形下, 两步 M 方法有更好的统计效能。但当存在多效性时, 综合 MAGIC、PSE-MR 方法、两步 MR 这三种方法进行因果估计。

中介分析是探索暴露到结局因果机制的有效方法。传统的中介分析方法必须满足 4 个控制混杂因素的假设: (1)控制暴露与结局之间的混杂因素; (2) 控制暴露与中介之间的混杂因素; (3)控制中介与结局之间的混杂因素; (4) 中介与结局之间的混杂因素不受暴露的影响^[1]。但是这些假设在观察性研究中很难成立, 忽略重要的混杂因素很可能会导致严重的因果效应估计偏倚。孟德尔随机化(Mendelian randomization, MR)方法利用遗传变异 SNP (Single-nucleotide polymorphisms)作为工具变量 (IVs), 能控制未知混杂因素和避免反向因果的影响^[2]。MR 方法已被广泛用于中介分析中, 通过控制未知的混杂因素, 估计中介因素在暴露与结局之间的因果作用^[2]。

全基因组关联分析 (GWAS) 的开展以及多组学研究的发展, 出现了大量高维生物医学数据, 为基于观察性研究进行因果推断带来巨大机遇, 但同时也带来了挑战^[3]。目前常用的利用 GWAS 汇总数据, 基于孟德尔随机化的中介分析方法主要有两步 MR 和多变量 MR (MVMR) 方法, 此外, 特定通路效应孟德尔随机化 (PSE-MR) 和通过 GWAS 汇总数据整合进行中介分析框架并进行偏差校正 (MAGIC) 方法也被提出, 但是缺乏对这四种方法性能比较的研究。

Global burden of anemia among women of childbearing age: Temporal trends, inequalities, and projections using the Global Burden of Disease 2021

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【 Abstract (摘要) 】 Objective: To analyze temporal trends, inequalities and projections in anemia burden among women of childbearing age (WCBA, ages 15 – 49). **Methods:** According to Global burden of Disease (GBD) study, original data sources, including population-based surveys, scientific studies, and government reports, were synthesized to estimate WCBA anemia prevalence and years lived with disability (YLD). We extracted annual estimates with 95% uncertainty intervals (UIs) from 1990 to 2021 and assessed relative prevalence risks by age, period, and cohort. Inequality was evaluated via sociodemographic index (SDI). The Bayesian age-period-cohort model was to predict progress toward the 2030 prevalence halving target. **Results:** Despite population growth increasing total case numbers, the global age-standardized prevalence rate of WCBA anemia declined from 35.64% (95% UI: 34.16 to 37.37) in 1990 to 33.77% (32.10 to 35.55) in 2021. Socioeconomic disparities persisted, with a stable concentration index around -0.21 over time, indicating sustained inequality disadvantaging lower-SDI countries, especially in Western and Central Sub-Saharan Africa and South Asia. Despite reductions in period/cohort prevalence risks, projections indicated insufficient progress toward 2030 target. **Conclusion:** The persistent global burden, inequalities, and insufficient progress in addressing WCBA anemia continue to call for improving anemia management, contextually tailored, multisectoral nutritional and non - nutritional interventions to achieve the 2030 target.

TrialChat: 基于大模型的临床试验统计学智能专家系统研发

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基金资助: 本项目获国家自然科学基金面上项目基金资助 (82473728)

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【摘要】目的: 为解决通用大型语言模型在临床试验统计学领域应用中存在知识表达碎片化、对复杂问题的推理与表达能力不足等问题, 提高模型在该垂直领域的专业性和精确性, 本研究开发了面向临床试验统计学的智能专家系统——TrialChat。方法: 提出一种“自约束全自动”的高质量微调数据集构造方法, 通过整合权威临床试验统计书籍、法律法规及报告规范知识, 构建包含 65,773 条问答对的临床试验统计学数据集, 并采用低秩适应 (LoRA) 参数高效微调方法对 Qwen 系列开源大模型进行微调, 训练得到 TrialChat-8B、TrialChat-14B 和 TrialChat-32B 模型。结果: 实验表明, 基于该方法构建的数据集能够有效提升模型在临床试验统计学任务中的表现, 在内部验证集和外部验证集上均优于主流大模型, 尤其在 BLEU、ROUGE 和 BERTScore 等多维度评估指标上表现优异, 生成内容更加精准、简洁且符合专业规范。结论: 本研究提出的“自约束全自动”微调数据集构造方法为垂直领域大模型的应用提供了高效解决方案, TrialChat 系统的构建为临床试验统计学领域提供了智能化辅助工具, 也为其他专业领域大模型的优化与落地提供了可借鉴的实践路径。

Independent and combined relationships between light at night, air pollutants, PM_{2.5} components and risk of cardiovascular-kidney-metabolic syndrome: A cohort study

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【Abstract】

Background : Cardiovascular-kidney-metabolic (CKM) syndrome, characterized by interconnected cardiovascular, renal, and metabolic dysfunctions, poses a growing global health burden. While both light at night (LAN) and air pollutants have independently been linked to adverse health outcomes, their synergistic and joint effects on CKM syndrome risk remain poorly understood.

Aims : This study aimed to assess the independent, interactive, and joint associations of LAN, air pollutants, and PM_{2.5} components with CKM syndrome.

Methods : Data from 4,361 participants aged ≥ 45 years in the China Health and Retirement Longitudinal Study (CHARLS, 2011 – 2015) were analyzed. Cox proportional hazards regression models were employed to estimate hazard ratios (HRs) and 95% confidence intervals (CIs) for CKM syndrome risk. Multiplicative and additive interactions between LAN and air pollutants were assessed using likelihood ratio tests and relative excess risk due to interaction (RERI). Joint effects were evaluated by categorizing exposures into tertiles.

Results : Over a median follow-up of 4.2 years, 792 incident CKM syndrome cases were identified. Adjusted models indicated that higher LAN exposure (highest vs. lowest quartile: HR = 1.46, 95% CI: 1.18 – 1.80) and increased levels of NO₂ (HR = 1.44, 95% CI: 1.18 – 1.75), PM_{2.5} (HR = 1.49, 95% CI: 1.19 – 1.87), PM₁₀ (HR = 1.75, 95% CI: 1.40 – 2.18), NO₃⁻ (HR = 1.42, 95% CI: 1.15 – 1.75), and NH₄⁺ (HR = 1.42, 95% CI: 1.15 – 1.75) were independently associated with elevated CKM risk. Significant multiplicative interactions were observed between LAN and all pollutants except O₃, NO₃⁻, and NH₄⁺ (P for interaction <0.05). Additive interactions further revealed synergistic effects, with RERI values ranging from 0.311 to 0.792. Joint exposure analysis showed that the combination of high LAN and high

PM₁₀ increased CKM risk by 56.3% (HR = 1.563, 95% CI: 1.092 – 2.238), while moderate co-exposure to LAN and PM_{2.5} elevated risk by 33.4% (HR = 1.334, 95% CI: 0.872 – 2.041).

Conclusion : This study provided population-level evidence of positive associations between LAN, air pollutants, and PM_{2.5} components with CKM syndrome in older adults. Significant synergistic and interactive effects were identified among these factors, highlighting the need to account for their combined influence in future CKM research.

Funding: This work was supported the Natural Science Foundation in Henan Province (222300420265) and the Open Project Program of The First Hospital of Xinxiang Medical University (XZZX2022002). The funding sources contributed not to study design, hypotheses, or manuscript preparation.

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Independent and combined relationships between nighttime light exposure, air pollution, PM_{2.5} constituents, greenness and diabetes or high blood sugar: A national prospective cohort study

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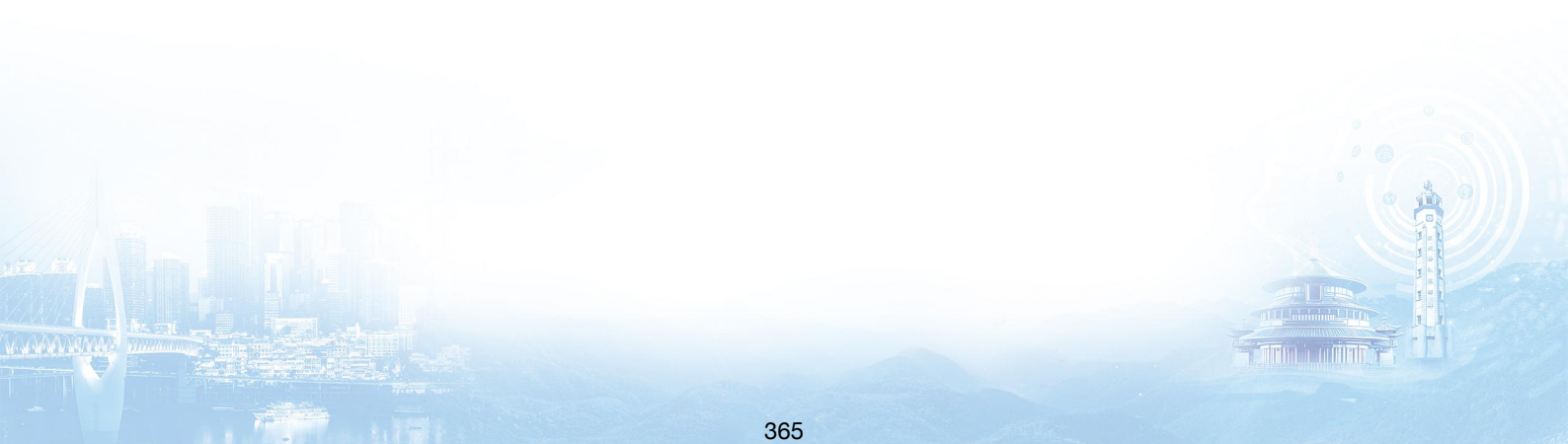
【Abstract】 Background: Diabetes or high blood sugar (D/HBS) is a major global public health challenge, with a particularly high burden among middle-aged and older adults in China. While traditional risk factors (e.g., obesity, sedentary behavior) are well-studied, the impacts of environmental factors such as nighttime light (NL), air pollution, and the normalized difference vegetation index (NDVI) on D/HBS remain underexplored. Objective: This study aimed to investigate the independent effects of NL exposure, air pollution, and NDVI on the risk of D/HBS among middle-aged and older adults. Additionally, we analyzed the interactive, joint, and mediating effects among these environmental factors to provide evidence for developing environment-based interventions to prevent diabetes. Methods: Using data from the China Health and Retirement Longitudinal Study (CHARLS, 2011 – 2015), we included 11,865 participants aged ≥ 45 years without baseline D/HBS. Cox proportional hazards models were employed to evaluate the independent effects of NL, air pollutants (PM₁, PM_{2.5}, NO₂, etc.), and NDVI on D/HBS risk, adjusting for confounders. Interaction effects, joint effects, and mediation effects were further analyzed. Results: The median follow-up duration was 4.0 years. Among the 11,865 baseline participants, 371 developed incident D/HBS. NL was significantly associated with increased D/HBS risk (per IQR increase: HR = 1.15, 95% CI: 1.06 – 1.26). High exposure to PM_{2.5} (Q4: HR = 1.46) and NO₂ (Q4: HR = 1.44) elevated risk, while higher NDVI (Q3: HR = 0.52) showed a protective effect. Synergistic effects were observed between NL and PM_{2.5} (RERI = 0.61) or NO₃⁻ (RERI = 0.59). Mediation analyses indicated that air pollutants, specifically NH₄⁺ (proportion = -68.3%) and NO₃⁻ (proportion = -64.1%), partially attenuated the protective role of NDVI. Conclusions: NL and air pollution are independent risk factors for D/HBS, with synergistic effects exacerbating disease burden. NDVI confers protection by reducing pollutant exposure. Comprehensive strategies targeting light pollution control, air quality improvement, and optimized green space planning are imperative. Future studies should integrate individualized exposure assessments and elucidate causal

environmental-metabolic pathways.

Keywords: Nighttime light exposure; Air pollution; Greenness; Diabetes/high blood sugar; Prospective cohort study

Funding: This work was supported the Natural Science Foundation in Henan Province (222300420265) and the Open Project Program of The First Hospital of Xinxiang Medical University (XZZX2022002).

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体检人群系统性炎症反应指数与颈动脉斑块的关联性研究

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【摘要】目的 通过回顾性横断面研究，探讨体检人群中系统性炎症反应指数（Systemic Inflammatory Response Index, SIRI）与颈动脉斑块（Carotid Artery Plaque, CAP）之间的关系。**方法** 研究纳入 2020 年 1 月-2024 年 12 月在四川省人民医院健康管理中心进行健康体检且至少接受过一次颈动脉超声检查的体检者。依据颈动脉粥样硬化的分类标准，将研究对象分为对照组、增厚组和斑块组。采用多因素 Logistic 回归模型分析 SIRI 与颈动脉斑块发生的关系，计算风险比（OR）和 95% 的置信区间（CI），限制性立方样条模型（RCS）分析 SIRI 与颈动脉斑块患病的剂量-反应关系。**结果** 最终纳入 115152 名调查对象。增厚组 30350 例(26.35%)，斑块组 31724 例(27.55%)，调整混杂因素后多因素 Logistic 回归显示 SIRI 每增加一个单位，颈动脉斑块患病风险增高 1.17 倍（OR=1.17, 95%CI: 1.12-1.23, $P < 0.001$ ）。RCS 结果表明，SIRI 与颈动脉斑块患病风险呈线性剂量-反应关系（ P of overall < 0.001 , P for nonliner=0.840）。**结论** SIRI 升高与颈动脉斑块的发生显著相关，提示重视全身炎症状态有助于早期筛查动脉粥样硬化；同样，通过颈动脉粥样硬化筛查也可能早期发现全身炎症的升高，均有助于早期防治心血管病。

Quantile adaptive lasso: variable selection for quantile treatment effect estimation

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Abstract

Quantile treatment effects (QTEs) can characterize different causal effect of treatment on different points of outcome distribution. Propensity score (PS) methods are commonly employed for estimating QTEs in non-randomized studies. Previous studies have shown that insufficient and unnecessary adjustment for covariates in PS models can lead to bias and efficiency loss in estimating treatment effects. Confounders may vary across different quantiles of outcome distribution. In order to allow for the selection of covariates related to the outcome at an interesting quantile corresponding to QTE, we proposed quantile adaptive lasso (QAL) method to select covariates that can provide unbiased and efficient QTE estimation. A distinctive feature of QAL is a utilization of linear quantile regression models for constructing penalty weights, enabling covariate selection in PS models separately when estimating different QTEs. Theoretical analyses showed QAL enjoys several asymptotic properties. We conducted simulations to show the superiority of QAL over the existing method in variable selection and QTEs estimation in terms of root mean square error in a range of settings. Additionally, we applied the QAL method to datasets from the China Health and Retirement Longitudinal Study (CHARLS) to explore the impact of smoking status on the severity of depression symptoms.

Global, regional, and national burden of mental disorders in adolescents and young adults aged 10-24 years from 1990 to 2021: a systematic analysis of the Global Burden of Disease Study 2021

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Abstract

Background Mental disorders pose a major public health challenge, with adolescents and young adults (AYA) aged 10-24 years bearing a substantial burden. However, comprehensive data on their temporal trends remain limited. We aimed to assess estimates and trends for burdens of mental disorders among AYA at the global, regional, and national levels from 1990 to 2021.

Methods We obtained the data of mental disorders among AYA from the Global Burden of Disease Study (GBD) 2021. To quantify the temporal trends of the age-standardised incidence rate (ASIR), age-standardised prevalence rate (ASPR), and age-standardised DALYs rate (ASDR) globally by age, sex, disease types and SDI, regionally and nationally, we employed the joinpoint regression model. We assessed the relationship between SDI and age-standardised rate using Spearman correlation.

Results Globally, the ASIR, ASPR and ASDR of overall mental disorders among

1933 ·53 in 2021, respectively (AAPC: 0 ·74; 0 ·26; 0 ·47). A larger increase occurred during the pandemic (2019-2021). Young adults had the highest burden in 2021. Despite the lowest burden, younger adolescents experienced the greatest increase in incidence among all age groups (AAPC: 0 ·81). Girls had a higher burden than boys in 2021, with a larger increase in ASPR and ASDR (AAPC: 0 ·38; 0 ·53). Major depressive disorder accounted for the highest disease burden. High SDI regions exhibited the highest burden and the three measures positively correlated with SDI in 2021 (r_s : 0 ·32 for ASIR; 0 ·52 for ASPR; 0 ·48 for ASDR, all $p < 0 ·0001$). High-income North America saw the largest increases in all three measures regionally. Nationally, The United States, Mexico and Georgia had the largest increase in ASIR, ASPR and ASDR, respectively.

Conclusions Among AYA, Mental disorders have risen globally, with a surge during the pandemic. Young adults, girls and high-SDI regions observed the highest burden, highlighting the need for targeted interventions in these groups. Early prevention strategies are crucial to mitigate the rapidly growing burden, as younger adolescents have experienced the largest increase in incidence. Policy efforts should prioritize improving mental health services for young populations to reduce both the overall burden and disparities in care.

关联规则的研究

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基金项目: 国家自然科学基金资助项目 (72264032, 72164033); 宁夏重点研发项目 (引才专项) (2022BSB03082)

【摘要】 目的 通过分析宁夏农村居民 10 年间慢性病共病的动态流行趋势, 挖掘其影响因素和共病模式, 揭示其潜在影响因素的复杂关联, 为制定慢性病防控策略与措施提供新思路。**方法** 基于课题组 2015-2024 年 10 年 4 期人群队列, 采用多阶段分层整群随机抽样法对宁夏 4 县的农村居民进行“面对面”入户调查获取数据, 内容包括健康生态学五个维度、慢性病患者情况等; 应用 Apriori 算法分析宁夏农村居民的共病模式, 利用非条件 Logistic 回归分析探讨慢性病共病与健康生态学五个维度的关联性。**结果** 2015-2024 年 10 年间慢性病共病呈增长趋势, 各慢性病共病患者率从 2015 年的 4.70% 上升至 2024 年的 9.97%, 增长了 5.27 个百分点。此外, 不同性别、年龄段、自评健康及家庭年收入分组的患病率都呈上升趋势。采用 Apriori 算法得到 20 条强关联规则, 其中 14 条关联规则与高血压有关; 10 条关联规则与脑血管疾病、椎间盘疾病、类风湿关节炎有关; 9 条关联规则与心血管疾病有关。单因素结果显示, 患两种及以上和患三种及以上共病模式下的保护及风险因素基本一致。Logistic 回归结果显示, 患两种及以上和患三种及以上共病模式下的保护及风险因素基本一致。18-44 岁、平均每天锻炼时长为 $\geq 60\text{min}$ 、自评健康状况很好是两种共病模式的共同保护因素; 一年内住院、 $\text{BMI} \geq 28.0$ 是两种共病模式的共同风险因素。两种共病模式的差异体现在以下方面, BMI 在 24.0-27.9、无抑郁状况是分别是两种及以上共病模式下的风险因素和保护因素, OR 值分别为 1.58 (95%CI: 1.20~2.07)、0.81 (95%CI: 0.68~0.97); 平均每天睡眠时长 6-8h、离家最近医疗点的距离 1-5km 是三种及以上共病模式下的保护因素, OR 值分别为 0.72 (95%CI: 0.57~0.92)、0.63 (95%CI: 0.42~0.95)。**结论** 研究发现, 高血压、糖尿病为慢性病共病模式中的核心疾病, 建议重点防控这两种疾病, 加强健康教育, 并且优化住院医疗费用等报销比例, 鼓励居民重视健康行为与生活方式, 控制慢性病共病的发生。

METEOR: A data-adaptive Mendelian randomization method for flexible and powerful detection of shared and specific exposures underlying multiple outcomes

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[Abstract] Purpose: Accurate identification of causal exposures for multimorbidity could benefit the co-prevention and co-management for multiple related outcomes, which can be conceptually incorporated into a multi-outcome Mendelian randomization (MR) framework. The current multi-outcome MR methods suffer from restriction on the format and availability of data inputs, fail to simultaneously account for the potential sample overlap between the exposure and any outcome, rely on a pre-selected set of independent or weakly correlated instrumental variables (IVs), and are unable to account for horizontal pleiotropic effects. **Methods:** To address these challenges, we propose METEOR, a novel MR method for the identification of shared and specific exposures for multiple outcomes. METEOR jointly models one exposure and multiple outcomes, accounts for the potential sample overlap between the exposure and outcomes as well as among the multiple outcomes, allows the outcomes to be from different GWAS data, self-adaptively determines IVs from a set of correlated SNPs, and explicitly models the horizontal pleiotropy. METEOR first estimates the correlations among the exposure and multiple outcomes using the genome-wide summary statistics, then infers the causal effect in a joint likelihood framework using a scalable sampling-based algorithm. **Results:** Through extensive simulations, we show that METEOR presents well-calibrated p -values for both the global test and single outcome test, and demonstrates improved power over 4 existing multi-outcome MR methods. In real data applications from UK Biobank, METEOR produces the most accurate causal effect estimates in positive control analysis evaluating the causal effects of each lipid trait on itself, reduces the false positives by 12.5% in the negative control analysis investigating

the causal effects of four lipid traits on hair color and skin color. We also perform shared exposure detection analysis to identify the metabolic risk factors for the multimorbidity across cardiovascular diseases (CVDs) and mental disorders (MDs) underlying the brain-heart axis. **Conclusion:** With extensive simulations and real applications, we have illustrated METEOR can control type I error, boost power, obtain accurate estimates, and highlight controlling BMI could benefit the co-management of the multiple CVDs and controlling blood pressure could benefit the co-management for the multimorbidity across CVDs and mental disorders (MDs).

Leveraging Transformer Models to Predict Cognitive Impairment: Accuracy, Efficiency, and Interpretability

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Keywords: Mild Cognitive Impairment (MCI), Alzheimer's Disease (AD), Transformer Model, Machine Learning, Neurodegenerative Disease Prediction

Abstract

Objective: This study aims to develop an enhanced Transformer model for predicting mild cognitive impairment (MCI) using data from the China Health and Retirement Longitudinal Study (CHARLS), focusing on handling mixed data types and improving predictive accuracy.

Methods: The Transformer integrates categorical (integer-encoded) and continuous (floating-point) data, using multi-head attention with four heads to capture complex relationships. Preprocessing involved separate embedding layers for categorical data and feed-forward networks for continuous data. The model was compared with SVM and XGBoost, trained for 150 epochs with RMSProp and a cosine annealing scheduler. Key metrics included accuracy, mean absolute error (MAE) tolerance, and training loss. An attention heatmap was generated to visualize feature importance.

Results: The Transformer outperformed SVM and XGBoost, achieving over 90% accuracy at an MAE tolerance of 3.5. The model showed rapid convergence, with loss stabilizing within 20 epochs. The attention heatmap highlighted key features, confirming the effectiveness of the multi-head attention mechanism in identifying relevant variables.

Conclusion: The enhanced Transformer model offers superior accuracy and efficiency in predicting cognitive decline compared to traditional models. Its capacity to process both continuous and categorical data and its interpretability through attention

mechanisms make it a promising tool for early detection of neurodegenerative diseases, potentially improving clinical decision-making and interventions.

人群移动模式及其在传染病建模中的应用

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【摘要】目的: 定量测量云南省昆明市全年龄组人群的移动模式, 探讨其影响因素, 并评估人群移动模式对传染病传播的影响; 方法: 采用多阶段随机抽样方法, 于2023年2月至4月在昆明市开展全年龄段人群调查, 收集调查对象人口学特征、社会经济水平、调查前一日出行轨迹及日期类型等数据。计算每人每日出行地点数、居家时间、出行总距离及活动回转半径, 并拟合多因素泊松回归、weibull回归及lognormal回归分析影响因素。以出行总距离为例, 建立耦合人群移动参数的传播动力学模型, 评估人群移动模式对传染病传播的影响; 结果: 共收集1095份合格问卷。每人每日中位出行地点数为2, 中位居家时间为18h, 中位出行总距离为3km, 中位活动回转半径为0.6km。年龄、性别、日期类型等因素与出行模式显著相关, 女性出行地点数更少 (OR=0.93, 95%CI: 0.86 ~ 1.00), 40 ~ 59岁人群出行总距离更长 (OR=38.85, 95%CI: 10.15 ~ 148.65), 7 ~ 19岁人群居家时间更短 (OR=0.72, 95%CI: 0.67 ~ 0.76)。与不考虑人群移动参数的标准模型相比, 人群出行总距离越长, 累计感染率越高, 疫情达峰时间越早, 疫情持续时间越短; 结论: 本研究揭示了人群移动模式与人口学特征及日期类型等因素的关系, 将人群移动参数运用于传染病建模中, 为传染病动力学建模提供全面、准确的人群移动行为参数, 为传染病精准预测与防控提供重要科学依据。

1A trans-omics gene-smoking interaction study of lung cancer based on consortium data

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65 study design; N.X., X.X., Y. Wang, A.W., Xuan Wang and M.Z. contributed to data analyses

66 and interpretation; Xiang Wang and Xuan Wang validated all analytical procedures and results;

67 J.Z. and Y. Wei developed the online platform; N.X., X.X. and R.Z. wrote the manuscript; Y.

68 Wei, M.E., Z.H. and H.S. critically reviewed the manuscript and results. All authors read the

69 manuscript and agreed on the final version.

70

71 Funding:

72 This study was supported by the National Natural Science Foundation of China

73 (82220108002 to F.C., 82273737toR.Z., 82373690 toY.Z., 82473728toY.W.W.),
74 Noncommunicable Chronic Diseases-National Science and Technology Major
Project
75 (2024ZD0520000and2024ZD0520003to R.Z.), the US National Institutes of
Health
76 (CA209414, CA249096, CA092824, and ES000002 to D.C.C., CA 249096 and
CA209414 to
77 Y.L.), Priority Academic Program Development of Jiangsu Higher
Education Institutions
78 (PAPD). R.Z. was partially supported by the Outstanding Young Teachers
Training Program⁷⁹ of Nanjing Medical University.
80 Running title: Trans-omics gene-smoking interaction in lung cancer
81 Descriptor number: 6.6 Gene-Environment Interaction
82 Word count (text): 3495 Words.
83
84 This article has an online data supplement, which is accessible from this issue's
table of
85 content online at www.atsjournals.org.
86
87
88
89
90
91 Abstract
92 Rationale: Genetically predicted molecular traits provide a
cost-effective approach for
93 identifying biomarkers and uncovering underlying biological mechanisms. We
extended this
94 framework to investigate gene-smoking interactions in lung cancer susceptibility.
95 Objectives: To identify trans-omics gene-smoking interactions affecting lung
cancer risk and

96 to assess how omics biomarkers modify effect of smoking.

97 Methods: We conducted a two-phase trans-omics interaction analysis of lung cancer by

98 integrating consortium-scale individual genotype data (27,737 cases vs 449,910 non-cases)

99 from the International Lung Cancer OncoArray Consortium (ILCCO-OncoArray),

100 Transdisciplinary Research Into Cancer of the Lung (TRICL), Prostate, Lung, Colorectal, and

101 Ovarian Cancer Screening Trial (PLCO), and the UK Biobank (UKB) with alliance-based

102 summary-level molecular quantitative trait loci (xQTL) data, including DNA methylation,

103 gene expression, proteomic, and metabolomic. Based on the identified biomarkers, we

104 developed a molecular modifying score (MMS) to delineate gene-smoking interaction

105 patterns and stratify high-risk smokers.

106 Measurements and Main Results: Through a rigorous two-stage analytical framework, eight

107 biomarkers showing significant interactions with smoking were identified, comprising CpG

108 sites in the nicotinic acetylcholine receptor region and gene RP11-326C3.14. The MMS,

109 constructed by integrating these biomarkers with their meta-analysis effect estimates, 110 effectively stratified lung cancer risk among smokers. Trans-omics integrative analysis

111 revealed functional relationships across molecular layers, particularly implicating the NELFE

112 gene in smoking-related carcinogenesis pathways.

113 Conclusions: The xWAS framework enables systematic discovery of trans-omics

114 gene-environment interactions across multiple molecular layers. The derived

MMS effectively

115 delineate the patterns of the interaction effects and facilitate risk stratification.
Additionally,

116 we launched a free online platform, LungCancer-xWAS-GxE

117 (<http://bigdata.njmu.edu.cn/LungCancer-xWAS-GxE/>).

118 Word count (abstract): 246

119 Key words: gene-environment interaction, smoking, genome-wide association
study, lung

120 cancer, trans-omics.

121

基于机器学习的糖尿病视网膜病变风险预测模型的构建与验证

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【摘要】目的：基于 2 型糖尿病患者的临床数据（人口统计学、生命体征、实验室指标、疾病史和生活行为方式）利用机器学习算法建立并验证糖尿病视网膜病变风险预测模型，以提高对糖尿病视网膜病变患病风险的早期识别和管理；**方法：**本研究通过单因素分析和多因素分析筛选独立危险因素，应用支持向量机、随机森林、人工神经网络、极端梯度提升和 K 近邻五种机器学习算法建立糖尿病视网膜病变风险预测模型。在内部验证集及外部验证集中，绘制 ROC 曲线并计算曲线下面积 AUC、准确度和约登指数评估模型预测效果，绘制校准曲线衡量模型的校准性能，绘制决策曲线以衡量模型的实用性，并利用 SHAP 可解释分析法对最优预测模型进行解释；**结果：**本研究从 MIMIC-IV 数据库中纳入 2 型糖尿病患者 2417 例，按照 7: 3 的比例随机分为训练集（1691 例）和内部验证集（726 例），外部验证集（1099 例）。经单因素分析和多因素分析筛选结果显示，SBP、DBP、白细胞计数等 12 个指标具有统计学意义 ($P < 0.05$)。在内部验证集中，支持向量机、随机森林、人工神经网络、极端梯度提升和 K 近邻的 AUC 值分别为 0.999、0.999、0.990、0.992 和 0.999。在外部验证集中，支持向量机、随机森林、人工神经网络、极端梯度提升和 K 近邻的 AUC 值分别为 0.629、0.831、0.685、0.657 和 0.779。随机森林模型的预测能力强于其他四种机器学习模型。SHAP 特征重要性图显示，随机森林模型中尿酸、糖化血红蛋白、LDL、TG、SBP 对模型的贡献力度较大；**结论：**尿酸、糖化血红蛋白、LDL、TG、SBP 等指标可以作为糖尿病视网膜病变早期诊断的高危风险因素。基于五种机器学习算法构建的糖尿病视网膜病变预测模型中随机森林模型的预测效能最佳，对糖尿病视网膜病变的早期诊断具有较高的价值。

Obesity aggravates the role of C-reactive protein on knee pain: A cross-sectional analysis with NHANES data

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【Abstract】 Objective: To examine the relationship between C-reactive protein (CRP) and knee pain, and further explore whether this association is mediated by obesity. **Methods:** The population was derived from 1999-2004 National Health and Nutrition Examination Survey. Logistic regression was used to analyze the relationship between CRP and knee pain in three different models, and the linear trend was analyzed. A restricted cubic spline model to assess the nonlinear dose-response relationship between CRP and knee pain. Mediation analyses were used to assess the potential mediating role of obesity. Subgroup analyses and sensitivity analyses were performed to ensure robustness. **Results:** Compared with adults with lower CRP (first quartile), those with higher CRP had higher risks of knee pain (odds ratio 1.39, 95% confidence interval 1.12 to 1.72 in third quartile; 1.56, 1.25 to 1.95 in fourth quartile) after adjusting for covariates (except BMI), and the proportion mediated by BMI was 76.10% ($P < 0.001$). BMI and CRP were linear dose-response correlated with knee pain. The odds ratio for those with obesity compared with normal to knee pain was 2.27 (1.42 to 3.65) in the first quartile of CRP, 1.99 (1.38 to 2.86) in the second, 2.15 (1.38 to 3.33) in the third, and 2.92 (1.72 to 4.97) in the fourth. **Conclusion:** Obesity mediated the systemic inflammation results in knee pain in US adults. Moreover, higher BMI was associated with higher knee pain risk in different degree CRP subgroups, supporting an important role of weight loss in reducing knee pain caused by systemic inflammation.

基于 PSO-BP 神经网络的 2 型糖尿病危险因素分析及发病风险预测研究

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【摘要】目的: 基于粒子群算法 (Particle Swarm Optimization, PSO) 优化的 BP 神经网络模型, 分析 2 型糖尿病的危险因素并预测其发病风险; **方法:** 选择 2021 年 7 月至 2022 年 8 月广东医科大学附属第一医院和广东医科大学附属第二医院内分泌科 1053 例 2 型糖尿病住院患者为病例组, 以同期体检中心 914 例健康人群为对照组。将单因素分析中 $P < 0.05$ 的变量作为输入层构建 PSO-BP 神经网络模型, 并与传统 BP 神经网络和 Logistic 回归模型比较, 综合评价模型预测性能。在此基础上, 采用平均影响值算法 (Mean Impact Value, MIV) 筛选 2 型糖尿病发病的危险因素; **结果:** 相比传统 BP 神经网络和 Logistic 回归模型, PSO-BP 神经网络模型具有更高的预测性能 ($RMSE$ 、 MAE 和 R^2 分别为 0.321、0.103 和 0.583)。MIV 算法因素筛选结果显示, 2 型糖尿病发病的危险因素为: 空腹血糖、心率、年龄、腰臂比和婚姻状况, 保护因素为: 高密度脂蛋白、蔬菜摄入、居住地、文化程度、水果摄入和肉类摄入; **结论:** 粒子群算法优化的 BP 神经网络模型对 2 型糖尿病发病风险预测效果最佳, 未来可推广至其它疾病的预测。基于 MIV 算法筛选出的 2 型糖尿病危险因素, 为 2 型糖尿病的早期预防和控制提供依据。

持续提升品牌美誉度，助力我院高质量发展建议之一 ——专家门诊退号情况分析和建议

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【摘要】

研究背景：医院好形象取决于环境、服务态度和医疗设备，我院是姓军为兵的公立医疗机构，既有提高官兵服务满意度的职责，也有让更多诊疗成果获益百姓的使命。目前医院正在高质量发展建设中，营造科学有序的就医秩序，建立良好口碑声誉尤为重要。通过把精细化管理落到实处，把医疗服务落到实处，增加病人粘性，提高满意度，提升品牌美誉度才能见成效。

目的：通过检索 2023 年 12 月某医院本部计算机后台数据库挂号信息，将 12 月退号次数大于 1 的病人，视为异常退号，通过筛选找出其中退号超过 7 次的病人，发现病人门诊号、挂号科室、专家等情况规律。

方法：利用统计分析法从退号次数及其关联的出诊专家两个维度，统计分析查找规律。

结果：1.某院专家门诊挂号情况：(1) 六个学部科室及其他学部派驻科室（心血管内科、骨科、耳鼻咽喉科、泌尿外科和肿瘤内科）专家门诊具有主要吸引力。

(2) 专家门诊优质病源在华北地区和东北地区。(3) 专家号排名靠前的专家个人和科室集中在风湿科、泌尿外科、中医科、肿瘤科和皮肤科。2.专家门诊退号情况分析：(1) 退号操作有 83%发生在移动端，窗口挂号员操作占 0.85%。专家退号中，知名专家号退号比例最高。(2) 有退号记录 7 次以上的 12 人（共退 129 次，人均 10.75 次），其门诊号之间有高度密切相关。(3) 异常退号的 12 人，提前所挂专家号排名靠前的是超声诊断科、胸外科等。(4) 异常退号次数排名靠前的专家，存在挂号量排名并不靠前的情况，而挂号量排名靠前的专家反而未发生高频次退号情况。

结论：异常退号的 12 人，应为重点监测对象，建议联合会同相关部门调取其联系方式做进一步了解；12 人提前预约专家号排名靠前的科室，退号量与挂号量排名不相符的科室和专家应重点结合实际情况予以关注，建议科室通过加强排班统筹，或提高医生工作弹性增强服务能力。从管理角度，加强信息录入，从计算机系统上也应在挂号时加以约束和提示。

主办单位

中华预防医学会生物统计分会
中国现场统计研究会医药与生物统计分会
中国数学会医学数学专业委员会

承办单位

重庆医科大学公共卫生学院
陆军军医大学军事预防医学系
北京大学重庆大数据研究院
北京大学公共卫生学院

协办单位

中国卫生信息与健康医疗大数据学会统计理论与方法专业委员会
中国卫生信息与健康医疗大数据学会卫生统计学教育专业委员会
中国统计教育学会生物医学统计分会
中国医药教育协会医药统计专业委员会
中国临床肿瘤学会生物统计学专家委员会
重庆市预防医学会