公告【彈性密集課程】

115.10.29 修訂

新開課程，2 年 1 次，機會難得。
歡迎本系大三以上、及研究所同學選修~

授課教師：石瑜 客座特聘講座

Yu Shyr

Chair, Department of Biostatistics
Harold L. Moses Chair in Cancer Research
Director, Vanderbilt Center for Quantitative Sciences (CQS)
Director, Vanderbilt Technologies for Advanced Genomics Analysis and Research Design (VANGARD)
Professor of Biostatistics, Biomedical Informatics, and Health Policy

課程名稱：「**Clinical Research in the Data Science Era: Design, Bias, Statistical Methods, and Machine Learning**」

（資料科學時代的臨床研究：設計、偏差、統計方法與機器學習）（課程大綱參見附件）

開課序號/班級/學分數：R2014/統資所/選修 1 學分

限選人數：100 名

上課教室：醫學院第四講堂

上課時間：

1. 115.12.19(六) 2:30 PM – 5:30 PM (Lab: 4:30 PM – 5:30 PM)
2. 115.12.20(日) 9:00 AM – 12:00 PM、1:00 PM – 4:00 PM (Lab: 2:30 PM – 4:00 PM)
3. 115.12.21(一) 6:00 PM – 9:00 PM (Lab: 8:00 PM – 9:00 PM)
4. 115.12.22(二) 6:00 PM – 9:00 PM (Lab: 8:00 PM – 9:00 PM)

選課方式：

1. 開放 google 表單供登記加選：https://forms.gle/gN8o7tfgK5zKjYxq8
2. 登記加選時間：~~115.10.7(三)起至 115.10.28(三)止~~。因尚有餘額，繼續接受登記加選。
3. 登記後由系辦助教至選課系統幫同學加選。

選課注意事項：本課程為彈性密集授課，學生勿與其他課程衝堂，違反者依本校學生選課辦法規定，衝堂課程均以零分計算。

(1)選課：

A. 經核准設定彈性密集開課註記後，學生可於該學期網路選課開放期間加選或承辦人員於授課截止前至系辦選課系統加(退)選。課程開始授課後不建議學生棄選，如有特殊因素煩請院(系、所)於課程結束前，酌情辦理退選。該學期學生若申請退選，成績單將留退選註記。

B. 衝堂部分：勿與其他課程衝堂(含同時段密集授課)，衝堂者以退選處理。

C. 超修部分：學士班未達原系超修標準，欲超修者須填寫超(減)修學分申請表，經教務長核准方可選修。

(2)學分費：研究生修此課程者退選須繳納學分費，學士班選修低於 9 學分者，如因加選彈性密集授課超過學分費規定學分應繳全額。

(3)成績：

A. 無休學者，彈性密集授課成績及學分將列入歷年成績單。各科成績依本校教師繳交及更正成績要點辦理，建議於密集授課截止日後兩周內或學期規定時間內，至成績上傳系統上傳核對無誤後送註冊組。

B. 如於寒暑假期間開授密集課程，該課程結束時間已超過教師學期成績繳交期限(上學期 1/31，下學期 7/10)，則該課程開課學期建議列在次學期。

Syllabus

Clinical Research in the Data Science Era: Design, Bias, Statistical Methods, and Machine Learning

資料科學時代的臨床研究：設計、偏差、統計方法與機器學習

National Cheng Kung University
December 19-22, 2026
Syllabus

Instructors Yu Shyr, Ph.D.
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This course introduces key concepts in applied artificial intelligence, machine learning, and modern biostatistics for biomedical and precision medicine research. Contemporary biomedical studies increasingly integrate molecular profiles, clinical characteristics, imaging, electronic health records, and other high-dimensional data to improve disease prevention, diagnosis, prognosis, and treatment selection. Technologies such as single-cell next-generation sequencing, spatial transcriptomics, circulating tumor DNA, microbiomics, radiomics, and other high-throughput platforms have greatly expanded the amount and complexity of biomedical data available for research.

The rapid growth of large-scale biomedical and real-world data creates substantial opportunities, but also important methodological challenges. More data and more sophisticated algorithms do not necessarily produce more reliable evidence. Poor study design, selection bias, confounding, measurement bias, missing data, inappropriate analytic methods, and overfitting can substantially compromise both traditional statistical analyses and machine-learning studies.

This course will therefore emphasize the integration of rigorous study design, bias assessment, modern statistical methodology, and machine learning. Particular attention will be given to common methodological problems encountered in published biomedical research and to practical approaches for improving reproducibility, validity, and clinical relevance. The course will also introduce emerging methods for prediction, causal inference, individualized treatment effects, and evaluation of machine-learning models.

I. Design, Bias, and Conduct of Modern Biomedical Research

This section will address fundamental principles for designing rigorous biomedical studies in the era of AI and large-scale data. Topics will include defining the primary scientific objective and endpoint, selecting appropriate study designs, determining sample size and statistical precision, and distinguishing prediction, association, and causal inference.

A major emphasis will be placed on **bias**. Students will learn to recognize selection bias, confounding, measurement bias, immortal-time bias, informative missingness, spectrum bias, data leakage, and other sources of bias that commonly arise in observational studies, real-world data analyses, and AI-based research. Strategies for preventing or reducing these biases through study design and statistical analysis will be discussed using examples from biomedical and clinical research.

Modern approaches for creating comparable treatment or exposure groups will also be introduced. These include propensity-score matching, optimal matching, full matching, inverse probability weighting, overlap weighting, coarsened exact matching, and other balancing approaches. Particular attention will be given to evaluating covariate balance rather than relying solely on traditional significance testing of baseline characteristics.

The course will also address missing data, internal and external validation, model transportability, reproducibility, and appropriate separation of training, validation, and test datasets in machine-learning studies.

II. Statistical Analysis, Machine Learning, and Causal Data Science

This section will cover statistical methods for common biomedical research designs, including randomized clinical trials, Bayesian clinical trials, cohort studies, case-control studies, cross-sectional studies, and longitudinal or repeated-measures studies. Methods for continuous, categorical, count, and time-to-event outcomes will be reviewed with an emphasis on selecting methods that appropriately address the scientific objective and study design.

Modern regression and machine-learning approaches will be introduced, including penalized regression, random forests, boosting, bagging, and stacking. The course will emphasize not only how these methods are implemented, but also how their performance should be evaluated and interpreted in biomedical applications.

Prediction-model evaluation will include discrimination, calibration, sensitivity, specificity, predictive values, ROC-based measures, and the F1 score, with discussion of when each metric is appropriate and when commonly used measures may be misleading.

The course will also introduce causal inference and individualized treatment-effect analysis. Topics will include propensity-score methods, weighting approaches, treatment-effect heterogeneity, and methods for evaluating whether predictive algorithms can identify patients who benefit differently from alternative treatments. Modern evaluation approaches such as uplift modeling and Qini statistics will be discussed in this context.

Throughout the course, published biomedical studies will be used to illustrate common statistical and methodological errors, including inappropriate subgroup analyses, failure to account for multiplicity, misuse of predictive terminology, inadequate validation, overfitting, inappropriate handling of missing data, and failure to distinguish association from prediction or causation.

The overall goal of the course is to help students develop the ability to critically evaluate modern biomedical research and to apply rigorous statistical and data-science methods in an era increasingly shaped by artificial intelligence, machine learning, real-world data, and precision medicine.

III Topics:

Date	Topic
Dec 19 (Saturday) 2:30 PM – 5:30 PM (Lab: 4:30 PM – 5:30 PM)	**Foundations of Modern Biomedical and Clinical Data Science** Overview of AI, machine learning, and modern biostatistics in biomedical research From scientific question to study design: association, prediction, and causal inference Major sources of bias in biomedical research • Selection bias • Confounding • Measurement and information bias • Immortal-time bias • Data leakage and other biases in AI and machine-learning studies Primary objectives, endpoints, and study design Sample size determination, power, and precision analysis Introduction to Bayesian methods and modern clinical trial designs **Common fatal design and statistical flaws in published biomedical research** **Lab 1:** Bayesian computation and Markov Chain Monte Carlo

Dec 20 (Sunday) 9:00 AM – 12:00 PM 1:00 PM – 4:00 PM (Lab: 2:30 PM – 4:00 PM)	**Statistical Modeling for Biomedical Research** Univariate data analysis: parametric and nonparametric methods Regression modeling for biomedical outcomes • Linear regression • Logistic regression • Poisson and negative binomial regression • Models for ordinal outcomes Model specification, variable selection, and interpretation Missing data mechanisms and principles of missing data analysis Multiple imputation and sensitivity analysis **Common statistical mistakes in biomedical data analysis** **Lab 2:** Generalized linear models, missing-data imputation, and variable selection
Dec 21 (Monday) 6:00 PM – 9:00 PM (Lab: 8:00 PM – 9:00 PM)	**Longitudinal, Survival, and Causal Inference Methods** Analysis of longitudinal and repeated-measures data • Mixed-effects models • Generalized estimating equations Time-to-event analysis and Cox proportional hazards models Causal inference using observational and real-world data Propensity-score methods and modern approaches to covariate balance • Propensity-score matching • Optimal and full matching • Coarsened exact matching • Inverse probability of treatment weighting • Overlap weighting Assessing covariate balance and diagnosing residual confounding **Bias, target populations, and interpretation of treatment effects** **Lab 3:** Mixed-effects models, GEE, and propensity-score methods
Dec 22 (Tuesday) 6:00 PM – 9:00 PM (Lab: 8:00 PM – 9:00 PM)	**Machine Learning and Modern Clinical Data Science** Machine learning for high-dimensional biomedical data Penalized regression • Ridge regression • LASSO • Elastic Net Ensemble learning • Bagging • Random forests

	• Boosting • Stacking Training, validation, testing, overfitting, and data leakage Evaluation of prediction and classification models • Sensitivity, specificity, and predictive values • ROC curves and AUC • Precision, recall, and **F1 score** • Calibration and clinical utility Treatment-effect heterogeneity and **individualized treatment effects** **Uplift modeling and Qini statistics** for evaluating treatment-selection algorithms Integration of statistical inference and machine learning in precision medicine **Lab 4:** Machine-learning applications using real biomedical data

IV. Software

1. PS Sample Size and Power Calculations (developed by William Dupont, free download).
2. R

V. Grade

Lab report (35%); Final (65%)