113年度衛生福利資料科學中心統計軟體推廣課程 2024.09.30 (一) 09:00-12:00 @國立成功大學 75201電腦教室

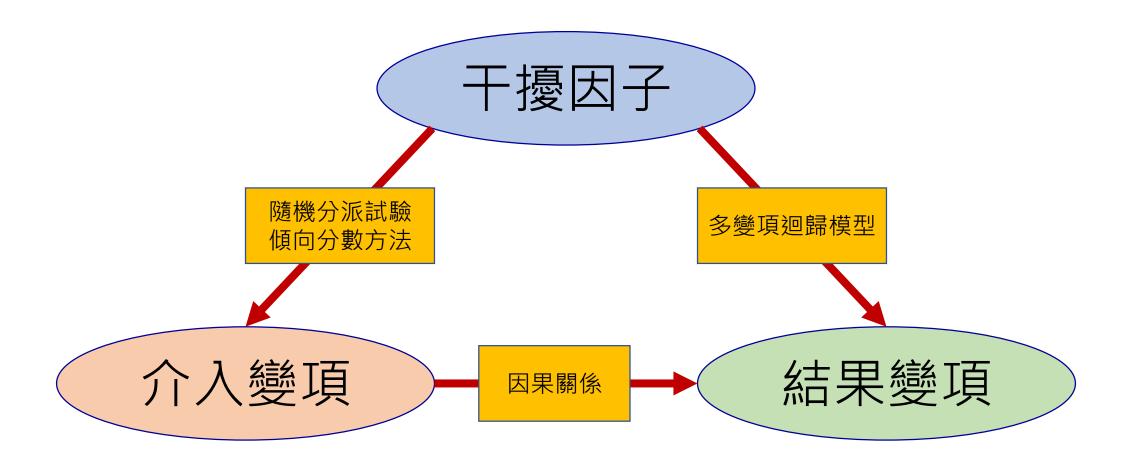
## 健康資料研究與R軟體《生物統計分析方法》

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#### 課程大綱

- 干擾因子與統計分析
- 基礎統計分析方法
  - 降血壓藥物隨機分派試驗
  - 統計分析計畫
- 模擬試驗存活分析
  - 抗凝血藥物選擇與未來糖尿病併發症風險
  - 統計分析計畫

#### 統計分析與干擾因子



#### 基礎統計分析方法

- 降血壓藥物隨機分派試驗
- 統計分析計畫

#### 降血壓藥物隨機分派試驗

• 對象 Population

• 高血壓病人

• 介入 Intervention

• 新開發藥物

• 對照 Control

• 安慰劑

• 結果 Outcome

• 血壓下降

• 設計 Study

RCT

#### 依據你最感興趣的結果變數(Y)分為

- 數值型態
  - Mean \ SD \ Person's r \ Box-plot
  - t-test \ ANOVA
  - Linear regression
- 類別型態
  - N · Percent
  - 交叉表、χ²test、Fisher exact test
  - Logistic regression

#### 模擬試驗存活分析

- AF & DM病人口服抗凝血劑選擇對 併發症影響
- 統計分析計畫

#### AF & DM病人口服抗凝血劑選擇對併發症影響

> Ann Intern Med. 2022 Apr;175(4):490-498. doi: 10.7326/M21-3498. Epub 2022 Feb 15.

# Diabetes-Related Complications and Mortality in Patients With Atrial Fibrillation Receiving Different Oral Anticoagulants: A Nationwide Analysis

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Huei-Kai Huang <sup>1</sup>, Peter Pin-Sung Liu <sup>2</sup>, Shu-Man Lin <sup>3</sup>, Jin-Yi Hsu <sup>4</sup>, Jih-I Yeh <sup>5</sup>, Edward Chia-Cheng Lai <sup>6</sup>, Carol Chiung-Hui Peng <sup>7</sup>, Kashif M Munir <sup>8</sup>, Ching-Hui Loh <sup>4</sup>, Yu-Kang Tu <sup>9</sup>
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Affiliations + expand

PMID: 35157495 DOI: 10.7326/M21-3498

#### AF & DM病人口服抗凝血劑選擇對併發症影響

• 對象 Population

Patients with AF & DM

• 介入 Intervention

NOAC

• 對照 Control

Warfarin

• 結果 Outcome

DM complications

• 設計 Study

Cohort study

#### 依據你最感興趣的結果變數(Y)分為

- 數值型態
  - Mean \ SD \ t-test \ ANOVA
- 類別型態
  - N、Percent、交叉表、χ^2test、Fisher exact test
- 處理干擾因子
  - Propensity score matching
- Time-to-event analysis
  - Kaplan-Meier plot
  - Cox proportional hazard regression

#### 原始樣本背景特質比較

Table 1. Baseline characteristics of patients (original cohort)

|  | NO             | AC    | Warfarin<br>N = 3,335 |       | SMD     |
|--|----------------|-------|-----------------------|-------|---------|
| Variable                                     | $N = \epsilon$ | 5,916 |                       |       |         |
|  | N              | (%)   | N                     | (%)   |         |
| Age*   | 73.61          | 9.73  | 68.56                 | 11.36 | 0.477   |
| Male   | 3,602          | 52.1  | 1,848                 | 55.4  | 0.067   |
| Index year group                             |                |       |                       |       | 0.846   |
| 2012-2013                                    | 849            | 12.3  | 1,504                 | 45.1  |         |
| 2014-2015                                    | 2,444          | 35.3  | 1,063                 | 31.9  |         |
| 2016-2017                                    | 3,623          | 52.4  | 768                   | 23.0  |         |
| CHA <sub>2</sub> DS <sub>2</sub> -VASc Score | 2.02           | 1.42  | 2.02                  | 1.41  | 0.001   |
| Hyperlipidemia                               | 2,435          | 35.2  | 1,164                 | 34.9  | 0.006   |
| CKD  | 815            | 11.8  | 492                   | 14.8  | 0.088   |
| Cancer                                       | 365            | 5.3   | 176                   | 5.3   | < 0.001 |

<sup>\*</sup> Expressed as mean and SD.

Abbreviations: n, number; SD, standard deviation; CKD, chronic kidney disease

### 計算與評估傾向分數 (Propensity score, PS)

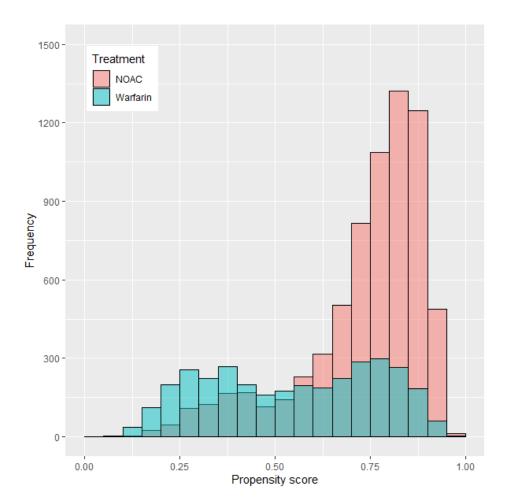
- Logistic regression model 干擾因子如何影響分組結果?
  - 使用藥物 ~ 性別 + 年齡(暫時忽略病史及指標年分)
  - $ln(\frac{P(NOAC=1)}{P(NOAC=0)}) = -3.87 + (-0.10 * male) + (0.04 * age)$
- Propensity score 這個樣本的條件被分到治療組的機率?
  - 65歲男性

• 
$$\hat{p} = \frac{1}{1 + e^{(-(-3.87 + \beta_{male} X_{male} + \beta_{age} X_{age}))}}$$

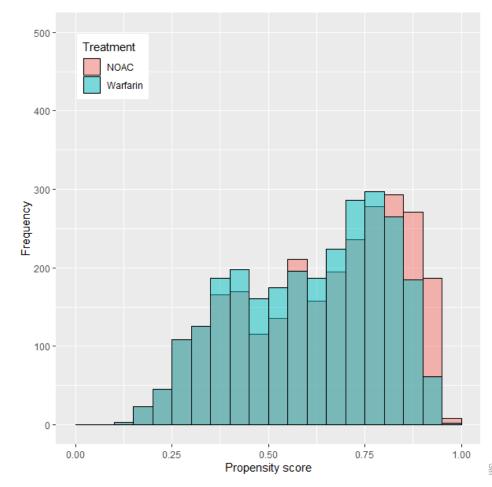
• 
$$\hat{p} = \frac{1}{1 + e^{(-(-3.87 + (-0.10 \times 1) + (0.04 \times 65)))}} = 0.2026$$

### 傾向分數分布比較

#### • 配對前



#### • 配對後



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#### 樣本背景特質比較(配對前 vs 配對後)

Table 1. Baseline characteristics of patients (original cohort)

|  | NOAC      |      | Warfarin  |       |         |
|--|-----------|------|-----------|-------|---------|
| Variable                                     | N = 6,916 |      | N = 3,335 |       | SMD     |
|  | N         | (%)  | N         | (%)   |         |
| Age*   | 73.61     | 9.73 | 68.56     | 11.36 | 0.477   |
| Male   | 3,602     | 52.1 | 1,848     | 55.4  | 0.067   |
| Index year group                             |           |      |           |       | 0.846   |
| 2012-2013                                    | 849       | 12.3 | 1,504     | 45.1  |         |
| 2014-2015                                    | 2,444     | 35.3 | 1,063     | 31.9  |         |
| 2016-2017                                    | 3,623     | 52.4 | 768       | 23.0  |         |
| CHA <sub>2</sub> DS <sub>2</sub> -VASc Score | 2.02      | 1.42 | 2.02      | 1.41  | 0.001   |
| Hyperlipidemia                               | 2,435     | 35.2 | 1,164     | 34.9  | 0.006   |
| CKD  | 815       | 11.8 | 492       | 14.8  | 0.088   |
| Cancer                                       | 365       | 5.3  | 176       | 5.3   | < 0.001 |

<sup>\*</sup> Expressed as mean and SD.

Abbreviations: n, number; SD, standard deviation; CKD, chronic kidney disease

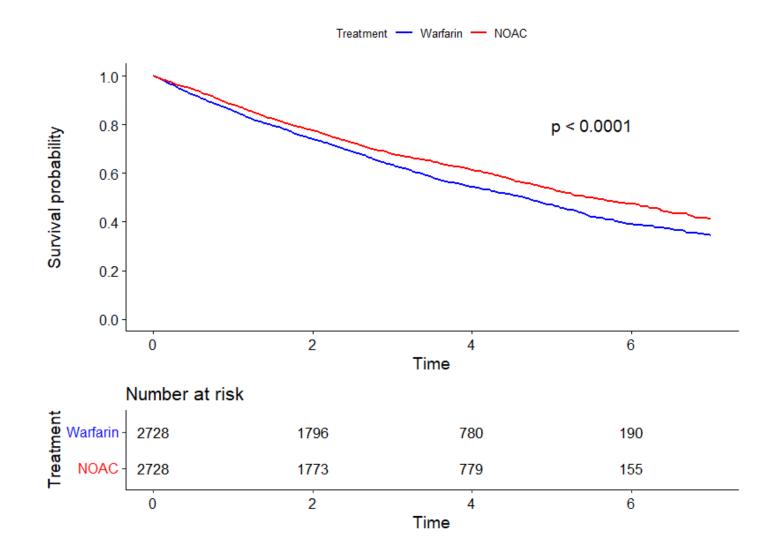
Table 1. Baseline characteristics of patients (matched cohort)

|  | NOAC $N = 2,728$ |       | Warfarin $N = 2,728$ |       | SMD   |
|--|------------------|-------|----------------------|-------|-------|
| Variable                                     |                  |       |                      |       |       |
|  | N                | (%)   | N                    | (%)   |       |
| Age*   | 72.41            | 11.65 | 70.29                | 11.17 | 0.185 |
| Male   | 1,297            | 47.5  | 1,448                | 53.1  | 0.111 |
| Index year group                             |                  |       |                      |       | 0.160 |
| 2012-2013                                    | 842              | 30.9  | 907                  | 33.2  |       |
| 2014-2015                                    | 918              | 33.7  | 1,053                | 38.6  |       |
| 2016-2017                                    | 968              | 35.5  | 768                  | 28.2  |       |
| CHA <sub>2</sub> DS <sub>2</sub> -VASc Score | 2.34             | 1.51  | 2.01                 | 1.41  | 0.222 |
| Hyperlipidemia                               | 1,162            | 42.6  | 953                  | 34.9  | 0.158 |
| CKD  | 540              | 19.8  | 356                  | 13.0  | 0.183 |
| Cancer                                       | 241              | 8.8   | 142                  | 5.2   | 0.142 |

<sup>\*</sup> Expressed as mean and SD.

Abbreviations: n, number; SD, standard deviation; CKD, chronic kidney disease

## Kaplan-Meier plot (配對後)



#### Cox proportional hazard regression

Table 2. Risk of macrovascular complication

| Original cohort          | N         | Events      | FU         | IR           | aHR (95% CI)                  | p value |
|--------------------------|-----------|-------------|------------|--------------|-------------------------------|---------|
| Warfarin                 | 3335      | 1692        | 11476      | 147.44       | 1.00 (reference)              |         |
| NOAC                     | 6916      | 2480        | 19582      | 126.65       | 0.79 (0.74-0.85)              | <.0001  |
|                          |           |             |            |              |                               |         |
| Matched cohort           | N         | Events      | FU         | IR           | HR (95% CI)                   | p value |
| Matched cohort  Warfarin | N<br>2728 | Events 1342 | FU<br>8786 | IR<br>152.75 | HR (95% CI)  1.00 (reference) | p value |

Abbreviations: n, number; FU, follow-up time (years); IR, incidence rate per 1,000 person years; aHR, adjusted hazard ratio; CI, confidence intervals.

#### Summary

- 研究目的
- 統計分析計畫
- 干擾因子
- 傾向分數配對

• 開放提問時間

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109年度R基礎課程-劉品崧老師

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