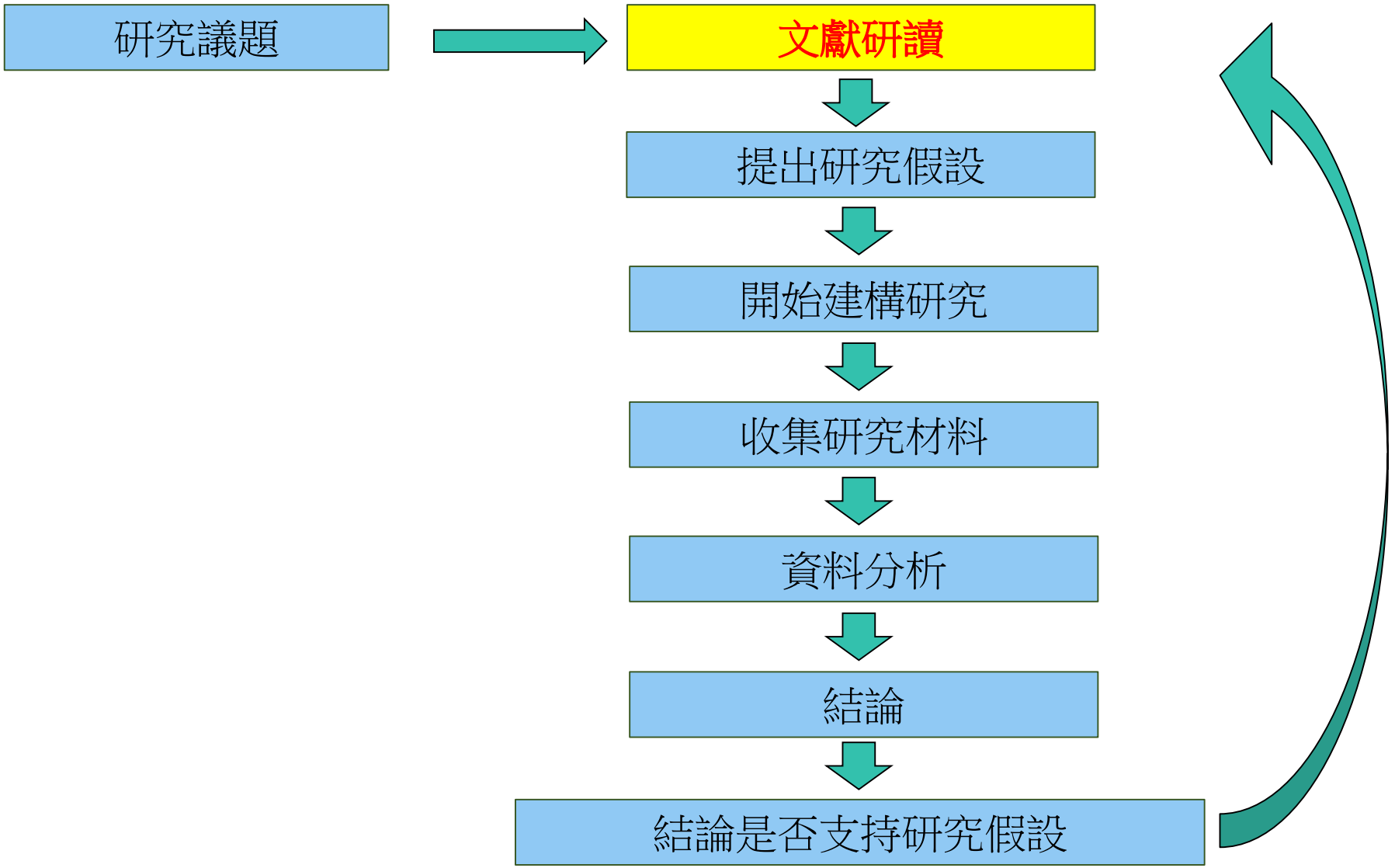
內科部研究中心第二次教學活動

解讀統計圖表與設計

內科部研究中心 研究員 許秋婷
Email: 179297@cch.org.tw
地點: 四期7樓 內科部研究中心
分機: 4738

醫學研究的流程



Identify a problem

眼睛灰灰、
腰子敗敗?

中藥四物湯
會養大子宮
肌瘤?

老年人可以
吃重鹹嗎？

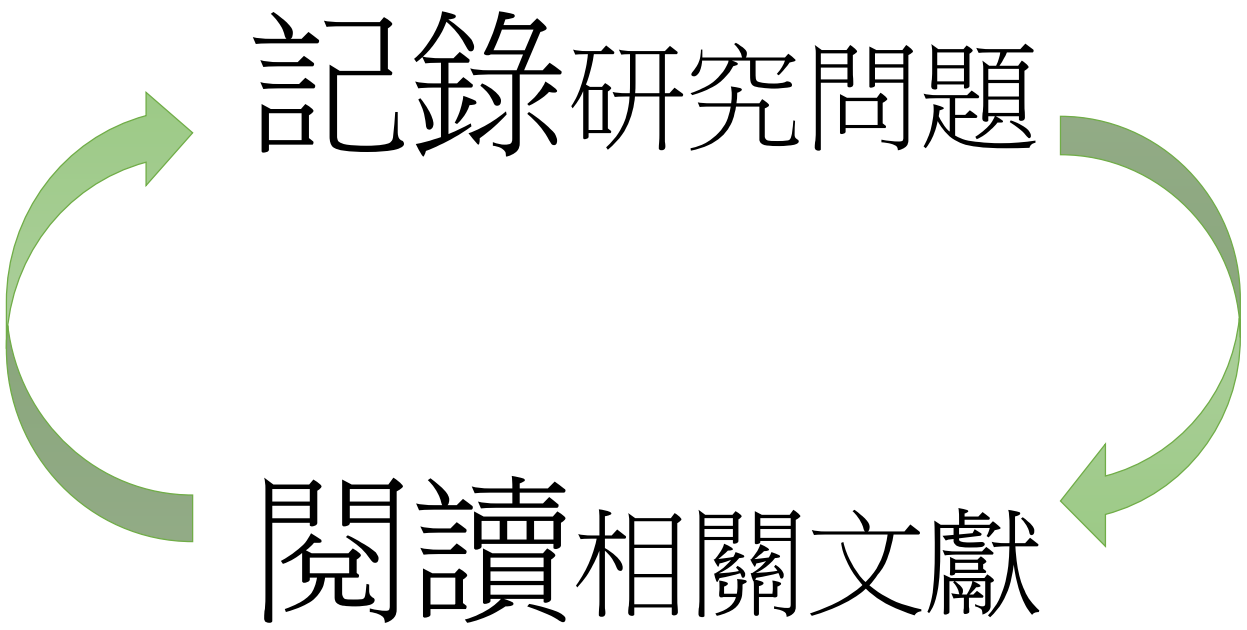
連呼吸也
會胖?

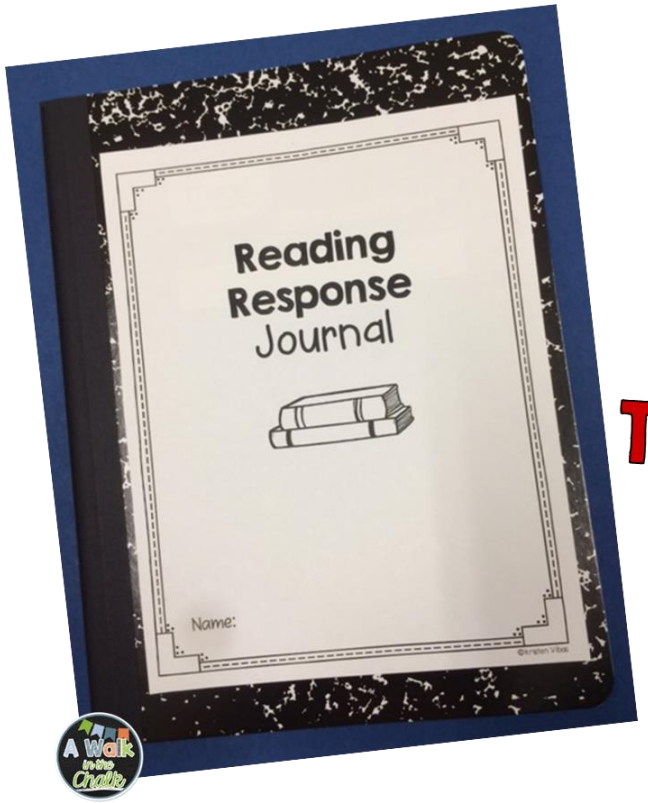
吃A藥比B
藥好嗎?

An apple a
day, keep
doctor away?

長期吃安眠
藥會不會得
癌症?

Translate to a Research Question





Turning READERS into THINKERS!

☐ 如何閱讀、了解和批判性地評量

- ◆ 這篇論文要解決什麼問題(Research Question)
- ◆ Research Question是怎麼被解決的? **Know-How**
- ◆ 研究問題的結論? 有什麼貢獻?
- ◆ 下一步，我還能做甚麼??

☐ 研究報告裡的統計資訊與研究結果

實驗設計~~~~
卡方統計， Mann-Whitney U test~~~~~~~~
KM curve…
Forest plot…是甚麼鬼東西~~~

Study Design

Hypothesis → Qualitative Data

研究對象: Study population

(1) 納入條件:

(2) 排除條件 Exclusion

(3) 主要自變項:
Exposure (E):

Non Exposure (non-E):

配對控制變數 Matched : (1:m)
(Ex: Age, gender….)

Association

統計控制變數Confounder :
次要自變項:
Example : comorbidity…

Outcome (Case control)

Primary Outcome (Y_1)

Secondary Outcome (Y_2)

Observation study

E: Exposure D: Disease(Outcome)

- Cross-sectional study橫斷式研究☺

  E ⟷ D(資料是同時收集,因果時序性不明)

  例子：IP-10和Self-Reported Sleep Quality 的關係

  ➔"association" not "predictor"

Case-control study ☺

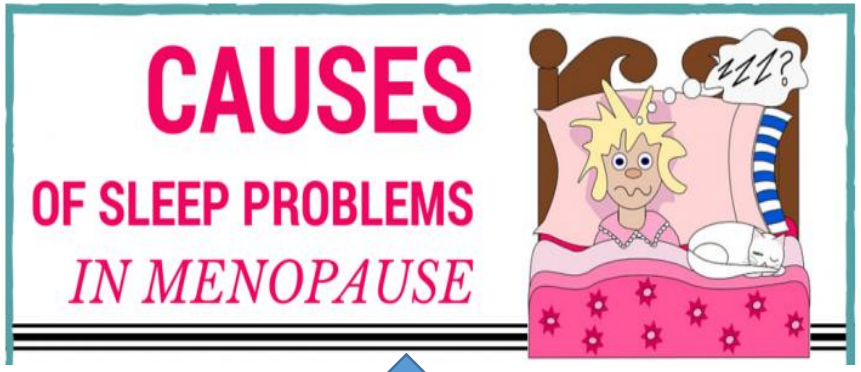
E ⟵ D(時序) (以有病的人為對象, 選取一組沒病的為對照組,比較兩組在暴露經驗上有無不同)(記憶偏差"recall bias")

- Cohort study (Fixed, Dynamic time) ☺

  E ⟶ D(時序)(依暴露經驗追蹤一段時間, 比較兩組的得病率)

Survival analysis➔ (Time, event occur indicator)

Cross-section study



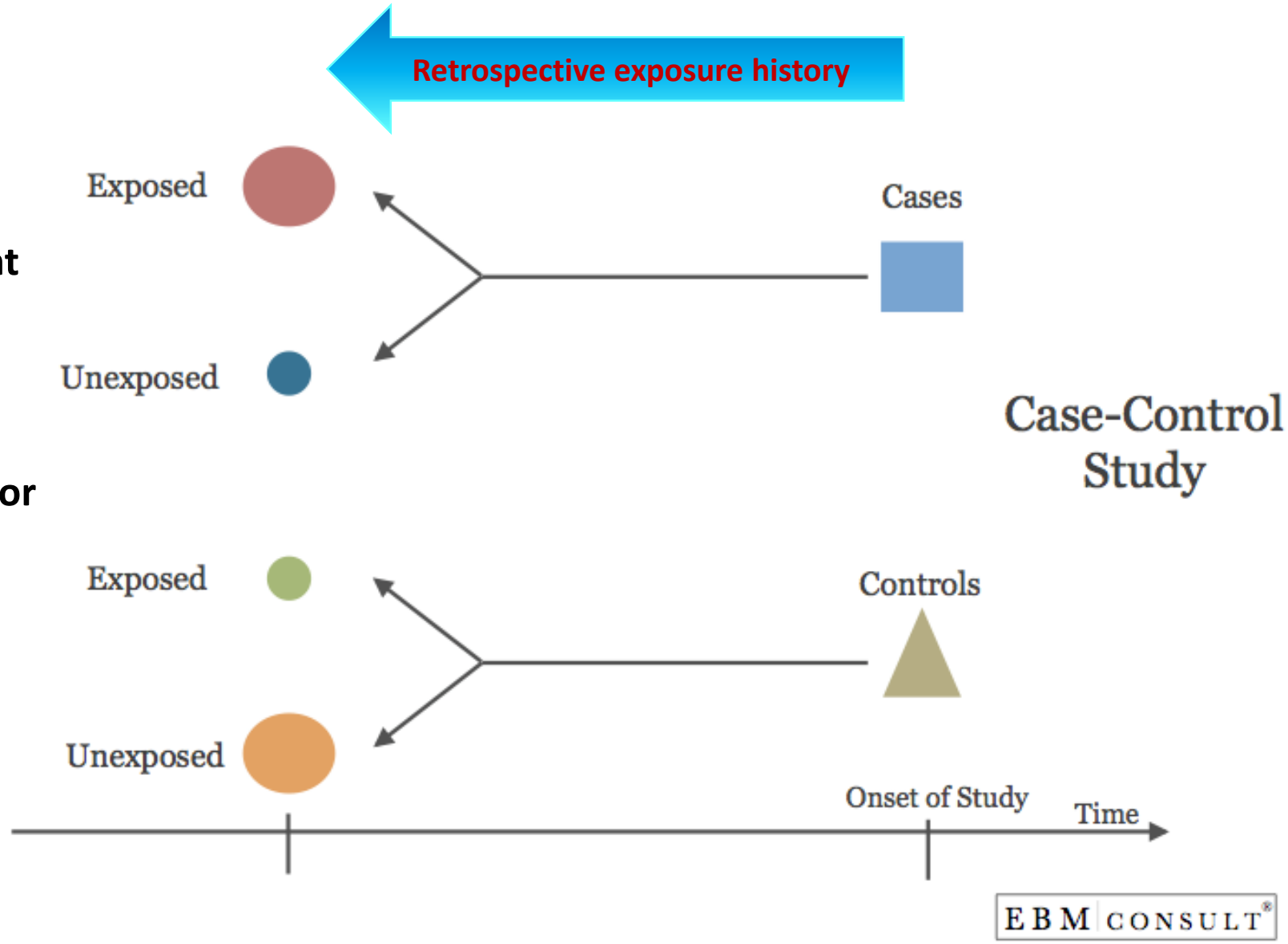
Notation:

- 同時進行，無時序性
- **Association, not predictor**

Circulating Interferon Gamma-Inducible Protein 10, Interleukin 6, and High-Sensitivity C-Reactive Protein

Case-control study

- Medication
- Specified treatment
- Procedure
- Disease-history
- Medication behavior



Case-control study 文章

Spironolactone and the risk of urinary tract cancer in patients with hypertension: a nationwide population-based retrospective case–control study

Ya-Wen Chuang[a], Mei-Ching Yu[b], Shih-Ting Huang[a], Cheng-Kuang Yang[c], Cheng-Hsu Chen[a], Ying-Chih Lo[a], Cheng-Li Lin[d,e], Kuo-Hsiung Shu[a], Tung-Min Yu[a,f], and Chia-Hung Kao[f,g,h]

See editorial comment on page 36

Hypertension

Cohort

Retrospective exposure history

Cancer (Y=1)

Non-cancer (Y=0)

➔分析上局限於 **completed data (Binary logistic regression…)**

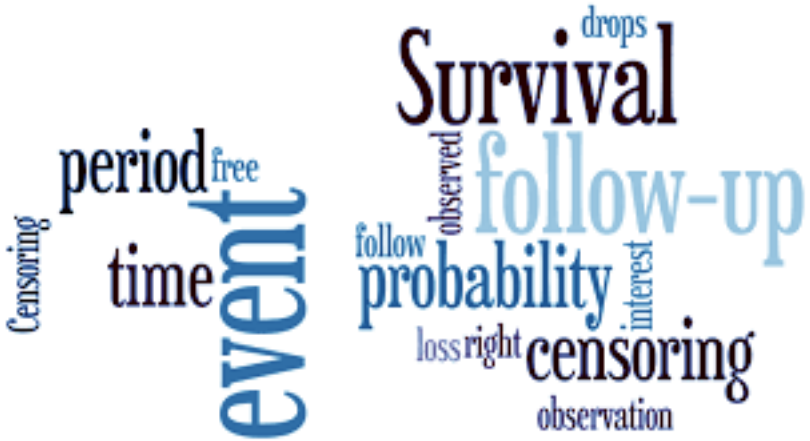
Cohort study

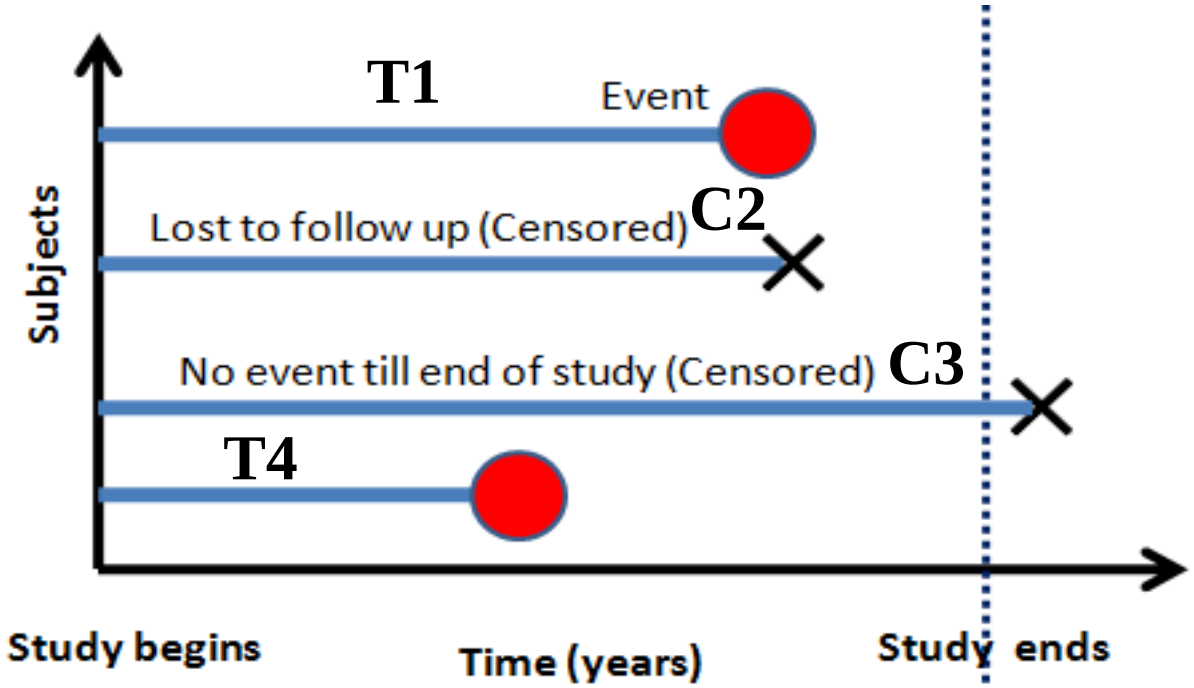
Exposure

Non-Exposure

Longitudinal follow-up

- **Recovery**
- **Recurrence**
- **Death**
- **Adverse event**
- **Disease-onset**



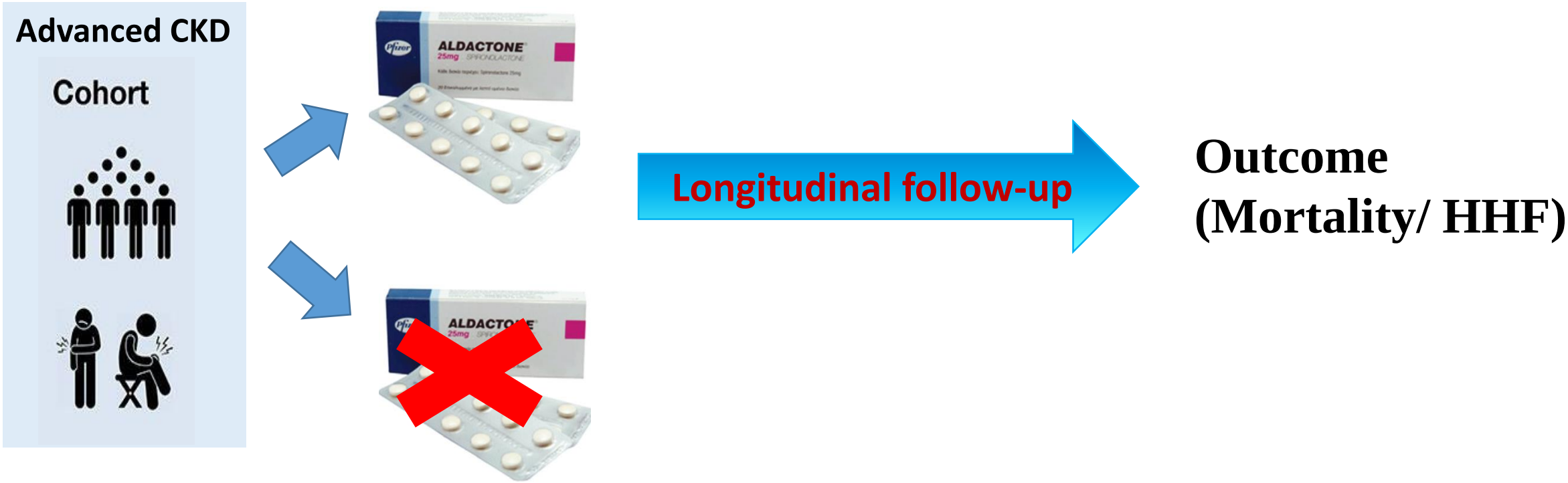


Cohort study 文章

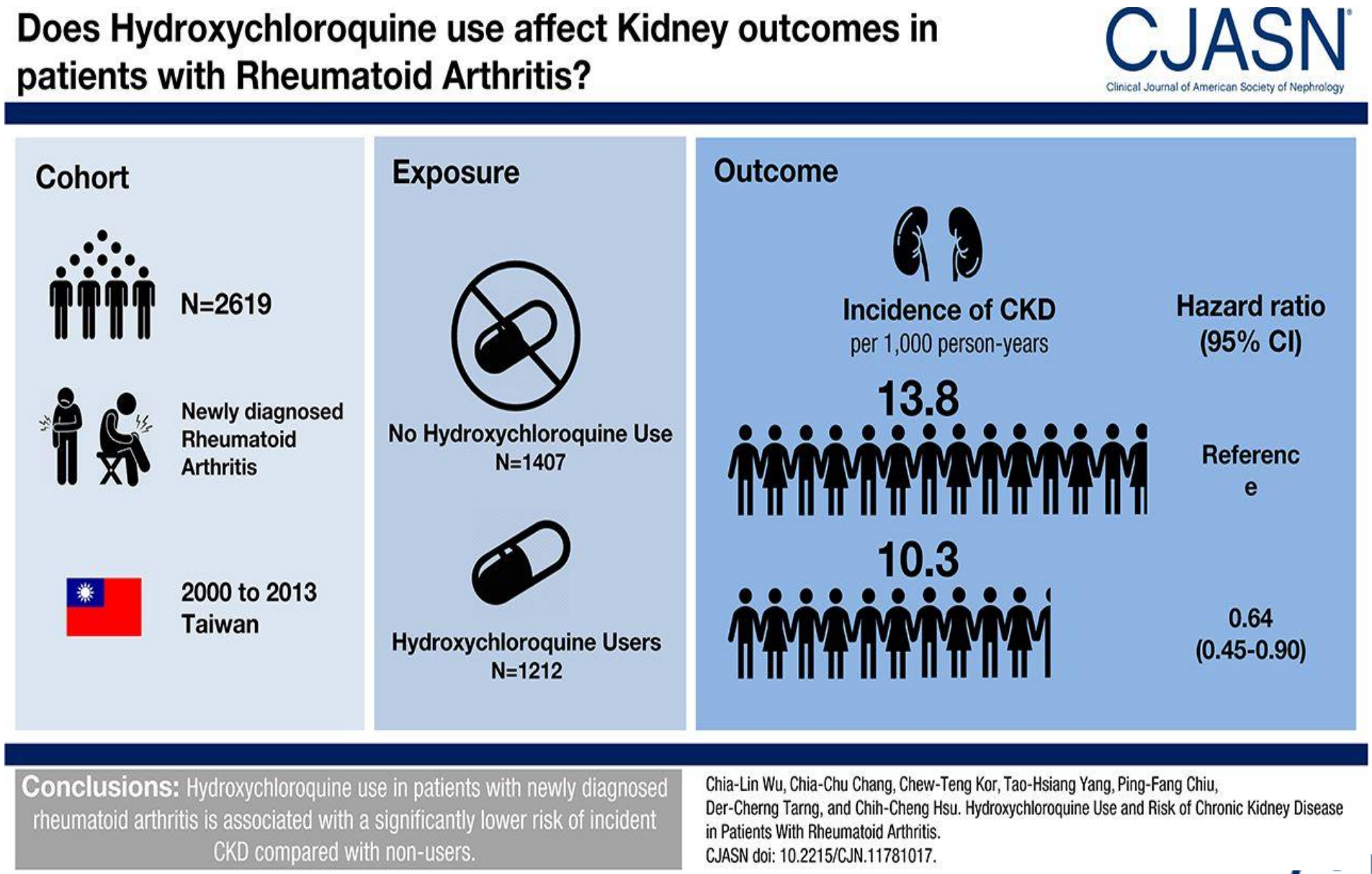
Effect of spironolactone on the risks of mortality and hospitalization for heart failure in pre-dialysis advanced chronic kidney disease: A nationwide population-based study.

Tseng WC[1], Liu JS[2], Hung SC[3], Kuo KL[3], Chen YH[4], Tarng DC[5], Hsu CC[6].

Author information



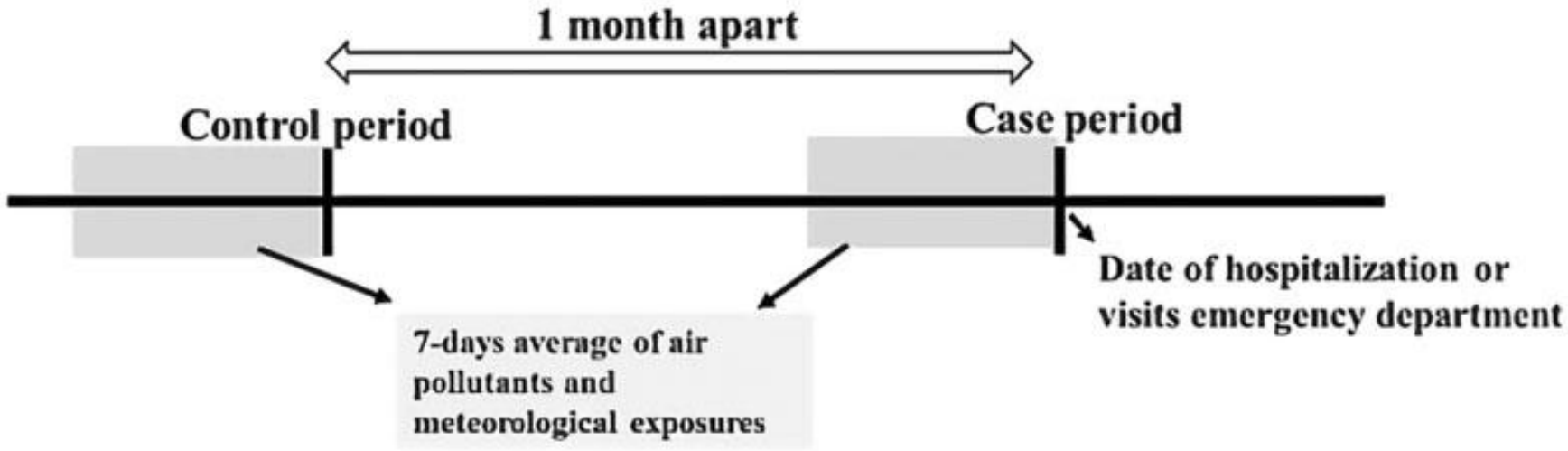
彰基 Cohort study 文章



Chia-Lin Wu et al. CJASN 2018;13:702-709

CJASN

Case-crossover study (case-self controlled study)



- **the recall bias, selection bias and undetectable potential confounding factors can be reduced in the patient-as-own-control research design**

➔ **Conditional logistic regression model**

彰基Case-crossover study 的paper

Nephrol Dial Transplant (2018) 1–7
doi: 10.1093/ndt/gfy144

ndt
Nephrology Dialysis Transplantation

ORIGIN

High particulate matter 2.5 levels and ambient temperature are associated with acute lung edema in patients with nondialysis Stage 5 chronic kidney disease

Ping-Fang Chiu[1,2,3,4,*], Chin-Hua Chang[1,*], Chia-Lin Wu[1], Teng-Hsiang Chang[1], Chun-Chieh Tsai[1], Chew-Teng Kor[5], Jhao-Rong Li[5], Cheng-Ling Kuo[3], Ching-Shan Huang[3], Cheng Chung Chu[6] and Chia-Chu Chang[1,2,3,7,8,9]

www.nature.com/scientificreports

SCIENTIFIC REPORTS

OPEN

Association of meteorological factors and air NO_2 and O_3 concentrations with acute exacerbation of elderly chronic obstructive pulmonary disease

Received: 19 December 2017
Accepted: 25 June 2018
Published online: 05 July 2018

Ming-Tai Lin[1], Chew-Teng Kor[2,3], Chun-Chi Chang[1], Woei-Horng Chai[1], Maw-Soan Soon[2], Yi-Siang Ciou[3], Ie Bin Lian[3] & Chia-Chu Chang[2,4,5,6,7]

Baseline characteristics

- Case-control study

Case

Control

TABLE 1. Baseline characteristics between urinary tract cancer group and control group

	Urinary tract cancer				
	No $N=32\,167$		Yes $N=32\,167$		
	N	%	*n*	%	*P* value[a]
Sex					0.99
Women	7675	23.9	7675	23.9	
Men	24 492	76.1	24 492	76.1	
Age group (year)					0.99
≤59	4068	14.3	4604	14.3	
60–69	8066	25.1	8070	25.1	
70–79	12 941	40.2	12 933	40.2	
≥80	6552	20.4	6560	20.4	
Mean (SD; year)[a]	70.9	10.5	71.6	10.3	<0.001
Medications					
ACEI	19 228	59.8	20 220	62.9	<0.001
ARB	13 164	40.9	15 111	47.0	<0.001

- Cohort study

Exposure

Non-Exposure

	Before propensity-score matching			After propensity-score matching		
Spironolactone	User (n = 1,363)	Nonuser (n = 25,850)	*p* value	User (n = 1,294)	Nonuser (n = 3,882)	*p* value
Age, all, yrs	68 (13.1)	65 (13.1)	<0.01	67 (13.1)	68 (12.2)	0.72
Age, subgroup, yrs			<0.01			0.10
20-44	67 (4.9)	1,739 (6.7)		65 (5)	144 (3.7)	
45-64	451 (33.1)	9,737 (37.7)		433 (33.5)	1,319 (34)	
65-74	392 (28.8)	7,577 (29.3)		366 (28.3)	1,183 (30.5)	

資料的種類

類別變數(Categorical Variable)

變數有次序(**Ordinal**)如：低中高級、輕中重度、差好優等
變數只有兩類(**Binary**)如：性別、有無發病、存活死亡等
變數有主觀給分的情形(**Score**)如疼痛指數、嚴重指數等
不同種類的特徵(**Nominal**) 如：血型、膚色、種族等

連續性變數(Continuous Variable)

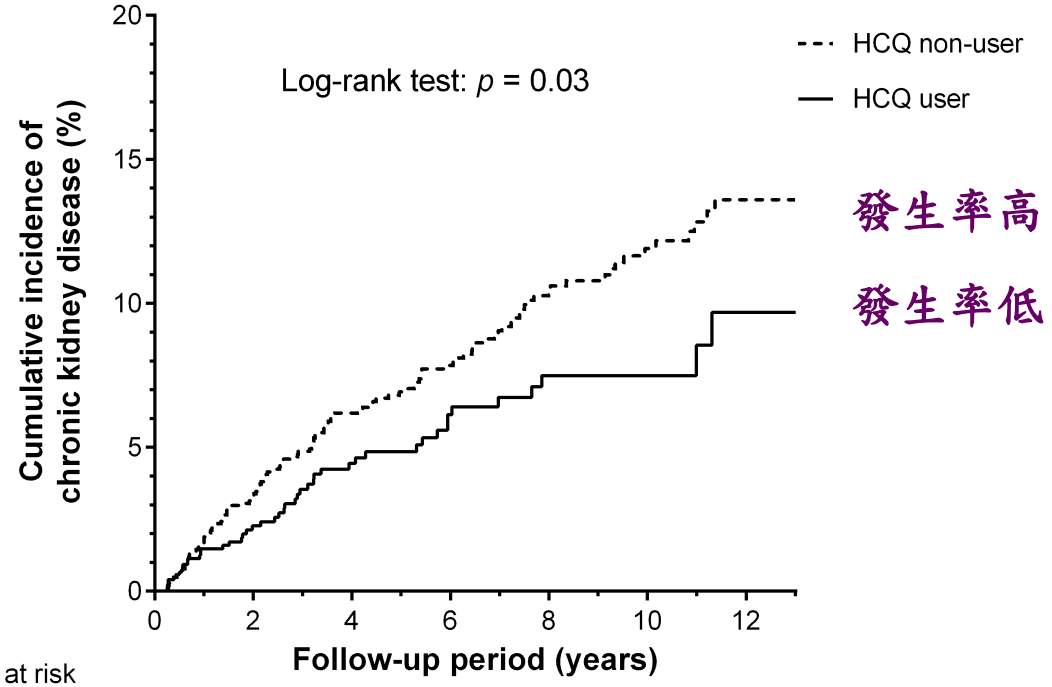
離散資料如發病次數、就醫次數、事件發生次數等
連續資料如身高、體重、年齡、**BMI** 、血壓、心跳、血糖、抽血檢查數值、排尿量、細胞激素濃度等

Baseline characteristics: 用以了解組別間資料分佈

Variables	Case/Exposure (n=1000)	Control/nonExposure (n=1000)	P-value
Category	Number (%)	性別分配沒有差異	Chi-square test
Gender, Male	**510(51%)**	**490(49%)**	**0.395(>0.005)**
Continuous			
		年齡平均數有差異	
常態分配	Mean ± SD		Student's t-test
Age	**58 ± 14**	**52 ± 14**	**0.035 (<0.005)**
		ALB中位數有差異	
非常態分配	Median (IQR)	*IQR=Q3-Q1	Mann U test
Albumin	**3.7 (3.3–4.2)**	**3.9 (3.6–4.3)**	**<0.001**

Cumulative incidence = 1-Kaplan-Meier curve (for cohort study)

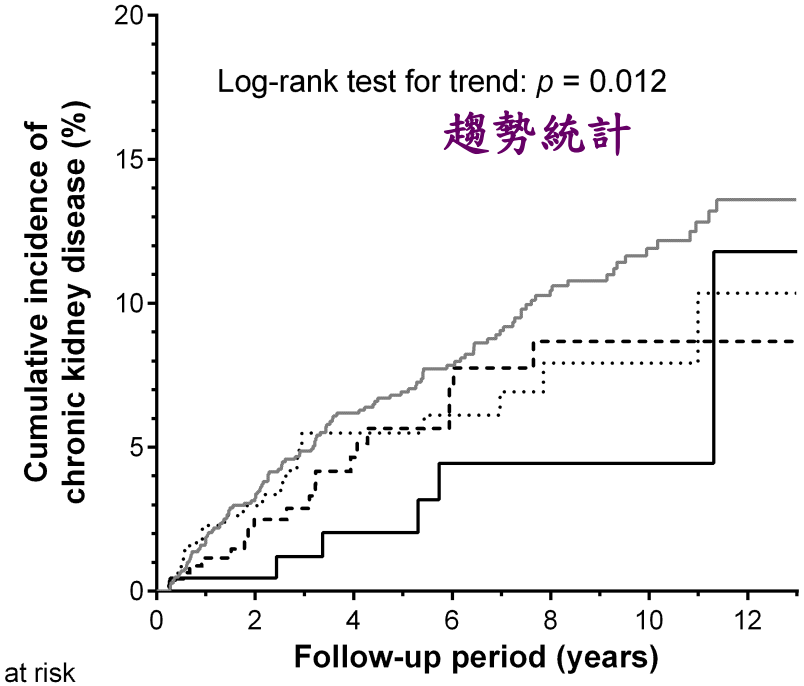
A



發生率高

發生率低

B



DDD: defined daily dose (WHO)

At risk: 每一段追蹤時間還有多少人留在樣本中

- 由KM curve初步判斷 user 的病患，CKD的累積發生率相較non-user低，同時也有reverse dose-response effect

➔需要進一步調整confounder確認藥物效果(Multivariate analysis)

Multivariate analysis (

人年發生率
event number/total follow –up time

Table 2. Risk of incident CKD in hydroxychloroquine users compared with nonusers

Exposure	Events, *n*/*N*	Incident Rate[a] (95% CI)	cHR (95% CI)	*P* Value	aHR[b,c] (95% CI)	*P* Value
Cohorts						
Hydroxychloroquine nonusers	121/1407	13.8 (11.3–16.2)	1.00	—	1.00	—
Hydroxychloroquine users	48/1212	10.3 (7.4–13.2)	0.67 (0.48 to 0.94)	0.02	0.64 (0.45 to 0.90)	0.01
Cumulative defined daily dose[d]						
Hydroxychloroquine	121/1407	13.8 (11.3–16.2)	1.00	—	1.00	—
Hydroxychloroquine users						
≤35	22/521	12.1 (7.1–17.2)	0.79 (0.50 to 1.24)	0.30	0.77 (0.48 to 1.21)	0.25
36–70	20/470	10.6 (6.0–15.3)	0.70 (0.44 to 1.12)	0.14	0.66 (0.40 to 1.07)	0.09
>70		6.1 (1.2–11.0)	0.40 (0.18 to 0.90)	0.03	0.37 (0.16 to 0.84)	0.02
P value for trend				0.01		0.004
Prescribed daily dose						
Hydroxychloroquine nonusers	121/1407	13.8 (11.3–16.2)	1.00	—	1.00	—
Hydroxychloroquine users, mg						
≤200	17/441	11.0 (5.8–16.2)	0.71 (0.43 to 1.18)	0.19	0.69 (0.42 to 1.16)	0.16
201–400	24/523	11.1 (6.7–15.5)	0.73 (0.47 to 1.13)	0.16	0.69 (0.44 to 1.08)	0.11
>400	7/248	7.3 (1.9–12.6)	0.47 (0.22 to 1.00)	0.05	0.45 (0.21 to 0.96)	0.04
P value for trend				0.02		0.01

cHR, crude hazard ratio; 95% CI, 95% confidence interval; aHR, adjusted hazard ratio; —, not applic
[a]Per 1000 person-years.
[b]Adjusted for propensity scores.
[c]All-cause death was considered a competing risk.
[d]Within 90 days after rheumatoid arthritis diagnosis.

趨勢統計

cHR= Crude Hazard ratio (Unadjusted)

aHR= Adjusted Hazard ratio (Multivariate analysis)

Dose越高，CKD發生的風險越低

Incident Rate per 1000 person year解讀:
1000位病人追蹤1年會有?人發生CKD
Nonuser: 13.8人
User: 10.3人

Subgroup analysis

Re-analysis to identify important differences in treatment effect

Subgroup

Age<50

Age: 50-65

Age>65

User VS non-user

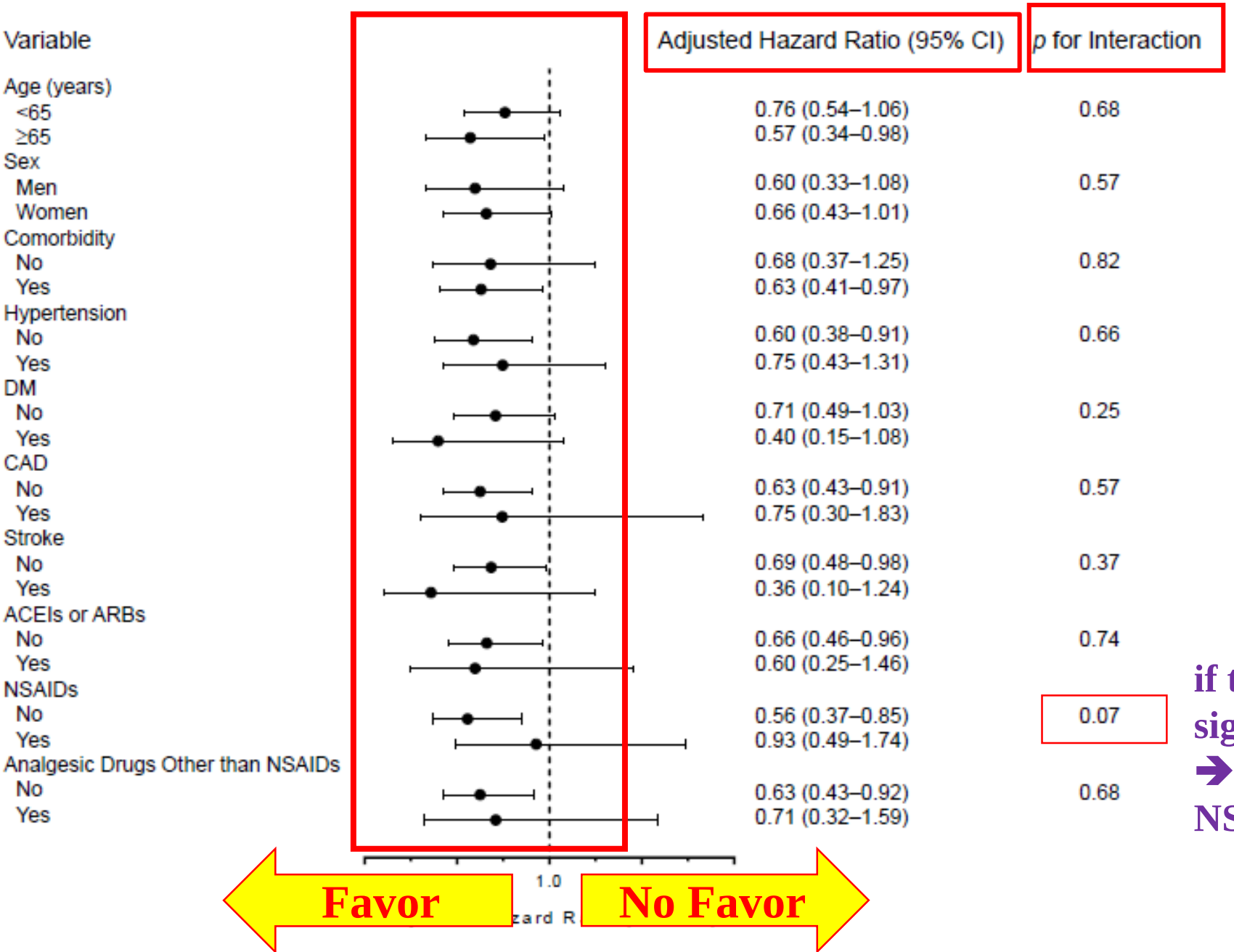
User VS non-user

User VS non-user

Forest plot

同方向，效果一樣

User vs nonuser



To compare treatment effects in subgroups

if the interaction test isn't significant, there is no observable subgroup effect

➔ you should ignore the result

if the interaction test is significant

➔ modification effect for NSAID user

Sensitivity Analysis (Robustness check)

檢查研究的結果是否會在某些操作條件之下而改變

Table 3. Sensitivity analyses for the risk of CKD

Analysis	Events, *n*/*N*	cHR (95% CI)	*P* Value	aHR[a,b] (95% CI)	*P* Value
Adjusted for all covariates in Table 1					
Hydroxychloroquine nonusers	121/1407	1.00	—	1.00	—
Hydroxychloroquine users	48/1212	0.67 (0.48 to 0.94)	0.02	0.67 (0.47 to 0.95)	0.03
Rheumatoid arthritis defined by a stringent criterion[c]					
Hydroxychloroquine nonusers	55/493	1.00	—	1.00	—
Hydroxychloroquine users	31/662	0.52 (0.33 to 0.80)	0.003	0.51 (0.33 to 0.80)	0.003
CKD defined by a stringent criterion[d]					
Hydroxychloroquine nonusers	117/1407	1.00	—	1.00	—
Hydroxychloroquine users	46/1212	0.67 (0.48 to 0.94)	0.02	0.64 (0.45 to 0.91)	0.01
Hydroxychloroquine use as a time-dependent covariate					
Hydroxychloroquine nonusers	121/1407	1.00	—	1.00	—
Hydroxychloroquine users	48/1212	0.63 (0.48 to 0.84)	0.002	0.60 (0.45 to 0.81)	0.001
Including patients with SLE and psoriasis					
Hydroxychloroquine nonusers	129/1514	1.00	—	1.00	—
Hydroxychloroquine users	52/1335	0.66 (0.48 to 0.91)	0.01	0.64 (0.46 to 0.89)	0.01
Maintaining group assignment despite discontinuation of hydroxychloroquine					
Hydroxychloroquine nonusers	136/1407	1.00	—	1.00	—
Hydroxychloroquine users	86/1212	0.63 (0.48 to 0.82)	0.001	0.59 (0.45 to 0.79)	<0.001

cHR, crude hazard ratio; 95% CI, 95% confidence interval; aHR, adjusted hazard ratio; —, not applicable.
[a]Adjusted for propensity scores.
[b]All-cause death was considered a competing risk.
[c]Defined according to the Registry for Catastrophic Illness Patients only.
[d]Defined by the most specific and clinically relevant diagnosis codes for CKD (Supplemental Table 1).