流行病學方法論及實驗
(The Methods of Epidemiology and Practices)

偏好選擇流行病學故事之護理觀

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非隨機分派研究中之偏差

- 第三因子影響(interaction, confounding)
- 選擇性偏差 (selection bias)
- 錯誤分組 (miss-classification)

選擇性偏差 (selection bias)

自由時報 Liberty Times Net

奧研究：素食者比肉食者不健康

2014-04-05 10:51

〔本報訊〕國外研究發現，素食者的身體健康，竟較肉食者爲差，其罹患癌症、心肌梗塞、心理疾病的比率，均是重度肉食者的2至2.5倍。

奧地利格拉茨醫科大學（Medical University of Graz）研究指出，素食者普遍較少吸菸、喝酒，但素食者看醫生的次數比肉食者來得多，有較高的癌症、過敏、心血管疾病與憂鬱症等風險。

奧地利研究發現，素食者的身體健康，較肉食者爲差。（資料照，記者王秀亭攝）

研究者表示，這可能與素食者攝取的動物性脂肪比一般人來得少有關，人類最合宜的飲食，還需要多做研究。專家指出，素食者應避免高鹽、高油食物或吃較不新鮮的蔬菜，並適量補充維生素B群。

雌激素補充療法是否可以減少停經後女性心血管疾患(CHD)的發生?

觀察性研究結果如下：

A group: 使用荷爾蒙補充療法

B group: 不使用荷爾蒙補充療法

A組 CHD 風險 ＜＜ B組CHD風險

→荷爾蒙補充療法可預防CHD ？

- **爭議點**：

使用荷爾蒙療法之婦女其健康狀況與健康意識優於未使用荷爾蒙療法之婦女，因此具有較低之CHD風險

※ 選擇性偏差: 兩研究組之特性不同（comparability）

選擇性偏差之爭議

1) 參與研究與不參與研究之選擇偏差:　參與研究者之特性通常教育程度較高、較健康、生活型態較佳，疾病風險較低
2) 以醫院病患進行之病例-對照研究設計會造成低估心肌梗塞之相關因子(如剷雪工人之職業別)之風險 (Neyman bias).
3) 對於已知暴露因子危險之認知可造成對於相關疾病之偵測率增加：口服避孕藥與靜脈血栓之相關性研究
4) 疾病偵測率造成之偏誤: 例如雌激素使用與子宮內膜癌之相關性研究

手機使用是否會增加腦癌風險?

IARC Report to the Union for International Cancer Control (UICC) on the Interphone Study

International Agency for Research on Cancer

World Health Organization

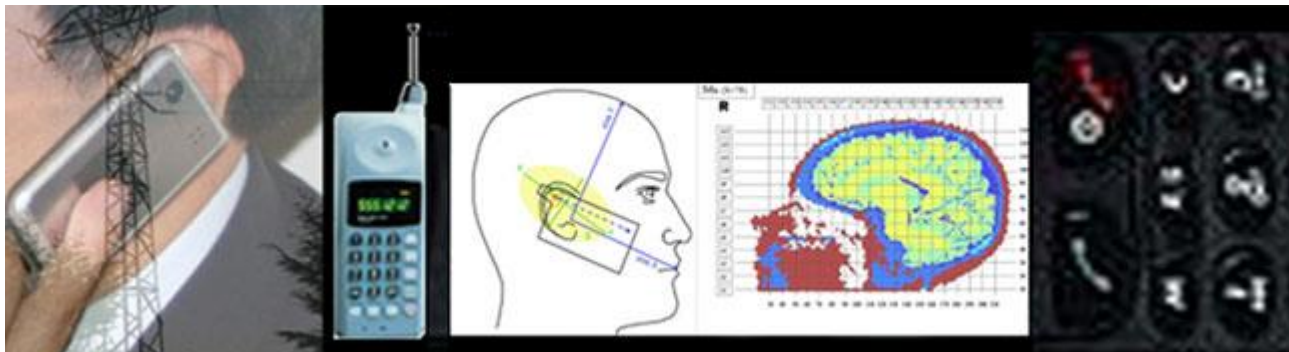
Conclusions

Glioma and meningioma

Overall, no increase in risk of glioma or meningioma was observed with use of mobile phones. There were suggestions of an increased risk of glioma at the highest exposure levels, but biases and error prevent a causal interpretation. The possible effects of long-term heavy use of mobile phones require further investigation.

Acoustic neuroma

There was no increase in risk of acoustic neuroma with ever regular use of a mobile phone or for users who began regular use 10 years or more before the reference date. Elevated odds ratios observed at the highest level of cumulative call time could be due to chance, reporting bias or a causal effect. As acoustic neuroma is usually a slowly growing tumour, the interval between introduction of mobile phones and occurrence of the tumour might have been too short to observe an effect, if there is one.



The Interphone study

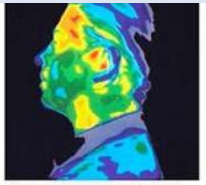
Mobile madness

The Economist

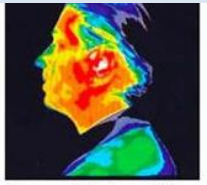
Please press "recall"

One problem was what statisticians call selection bias. Interphone began by gathering a group of people who had had the cancers of interest (glioma, meningioma, acoustic neurinoma and parotid gland tumour) and questioning them about their past use of mobile phones. The researchers then approached a number of healthy people in order to compare them with the cancer patients, and find out if there was a systematic difference in mobile-phone use between the two groups. Some of those approached agreed, and some declined. Of those who agreed to take part, 59% were regular mobile-phone users as defined by the study's protocol. Later on, those who had declined were recontacted and asked about their mobile use. Among this group, only 34% were regular users. That meant those in the control group were more likely than average to be regular users, and therefore were not representative of the population at large.

參與研究的健康(對照)民眾：有**59%**的人經常頻繁地使用手機
拒絕參與研究的民眾：　　有**34%**的人頻繁地使用手機



Thermographic Image of the head with no exposure to harmful cell phone radiation.



Thermographic Image of the head after a 15-minute phone call. Yellow and red areas indicate thermal (heating) effects that can cause negative health effects.

https://www.economist.com/node/12295222
https://www.gsmarena.com/speculations_on_the_interphone_study_outcome_cause_undue_panic-news-1215.php

臨床實例:
使用手機是否會影響人類健康？

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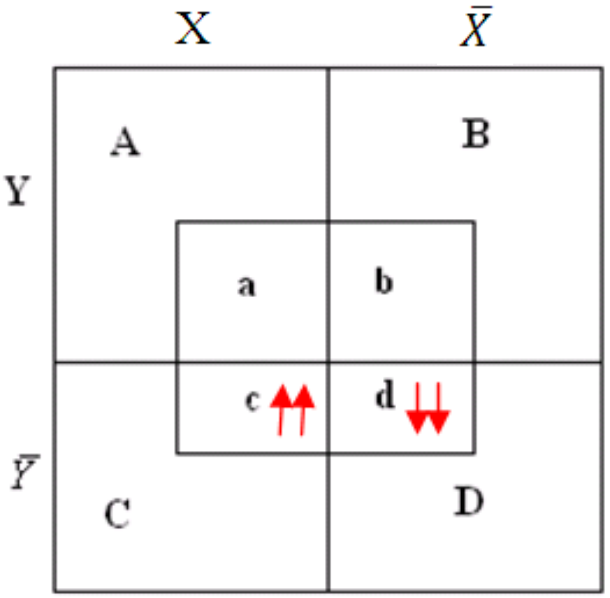
表示參與研究的對照組使用手機的頻率比一般民眾高。

X:暴露
Y:疾病狀態

$$OR = \frac{A/C}{B/D}$$

$$\hat{OR} = \frac{a/c}{b/d}$$

$$= \frac{ad}{bc}$$



低估
Underestimate

Explain the role of quantitative and qualitative methods and sciences in describing and assessing a population's health.
解釋質性與量性方法及科學在解釋及評估人口健康中所扮演的角色。
Explain the critical importance of evidence in advancing public health knowledge. 解釋實證在推展公共衛生知識中的重要性。
Explain effects of environmental factors on a population's health. 解釋環境因素對人口健康的影響。

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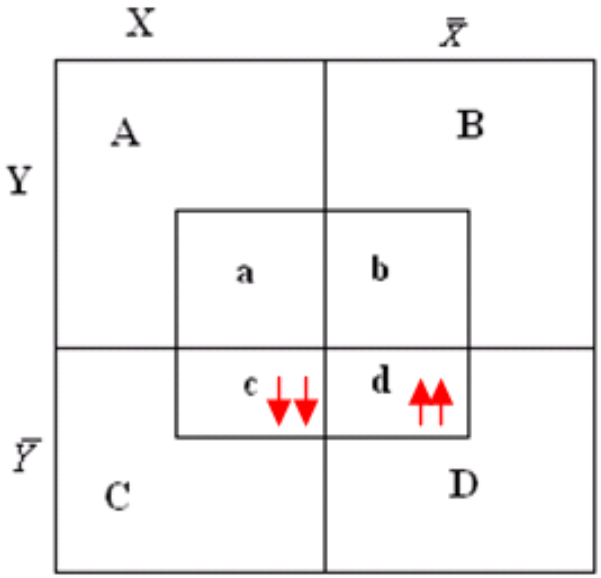

高估
overestimate

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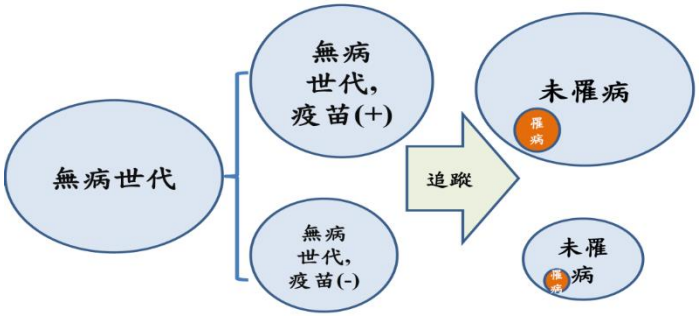
施打疫苗是否與兒童發展異常有關

疫苗引發自閉症？一場騙局

臨床實例: 疫苗使用是否與兒童發展異常有關

- **研究目的**
  - 探討麻疹、德國麻疹、腮腺炎混合疫苗施打(*X*)與行為發展異常(*Y*)的相關性



	X	$\bar{X}$	total
Y	1,000	300	1,300
$\bar{Y}$	160,000	45,000	205,000
total	161,000	45,300	206,300

1000/160000

300/45000

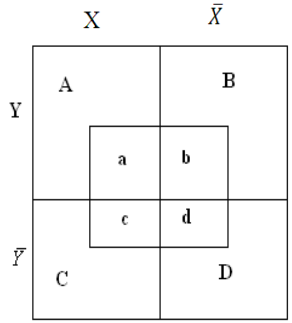
相對風險比(Relative risk, RR)

$$RR=\frac{1000/161000}{300/45300}=\frac{0.62\%}{0.66\%}=0.93$$

疾病風險勝算比(Odds ratio, OR)

$$OR=\frac{1000/160000}{300/45000}=0.94$$

•世代研究 (Cohort study): 等比例抽樣



OR= $\frac{ad}{bc}$

	X	$\bar{X}$	total
Y	1,000	300	1,300
$\bar{Y}$	160,000	45,000	205,000
total	161,000	45,300	206,300

$$RR = \frac{1000/161000}{300/45300} = \frac{0.62\%}{0.66\%} = 0.93$$

$$OR = \frac{1000/160000}{300/45000} = 0.94\ (0.9375)$$

π_X=0.2 (暴露組抽樣比例)

$\pi_{\bar{X}}$=0.5 (非暴露組抽樣比例)

	X	$\bar{X}$	total
Y	200	150	350
$\bar{Y}$	32,000	22,500	54,500
total	32,200	22,650	54,850

$$RR = \frac{200/32200}{150/22650} = \frac{0.62\%}{0.66\%} = 0.93$$

$$OR = \frac{200/32000}{150/22500} = 0.94\ (0.9375)$$

•世代研究 (Cohort study): 抽樣偏差

	X	$\bar{X}$	total
Y	1,000	300	1,300
$\bar{Y}$	160,000	45,000	205,000
total	161,000	45,300	206,300

$\pi_{XY} = 0.9$

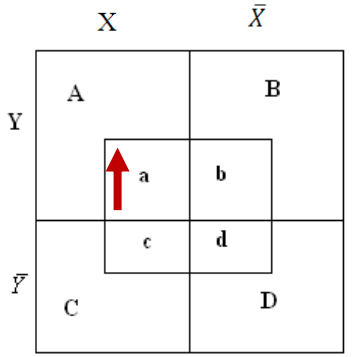
	X	$\bar{X}$	total
Y	900	60	960
$\bar{Y}$	64,000	9,000	73,000
total	64,900	9,060	73,960

$\pi_{XY} = 0.9$ (有接受疫苗且有發展異常)

$\pi_{X\bar{Y}} = 0.4$ (有接受疫苗且無發展異常)

$\pi_{\bar{X}Y} = 0.2$ (未接受疫苗且有發展異常)

$\pi_{\bar{X}\bar{Y}} = 0.2$ (未接受疫苗且無發展異常)



$$OR = \frac{ad}{bc}$$

$$RR = \frac{1000/161000}{300/45300} = \frac{0.62\%}{0.66\%} = 0.93$$

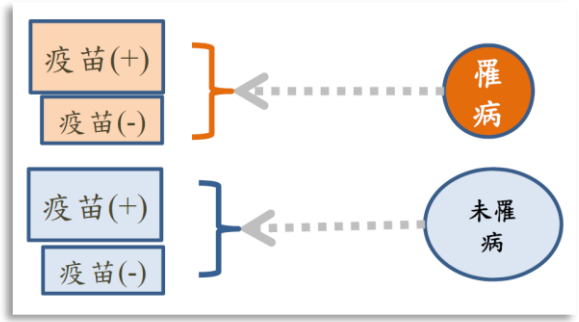
$$OR = \frac{1000/160000}{300/45000} = 0.94\ (0.9375)$$

高估 (overestimate)

$$RR = \frac{900/64900}{60/9060} = \frac{1.39\%}{0.66\%} = 2.09$$

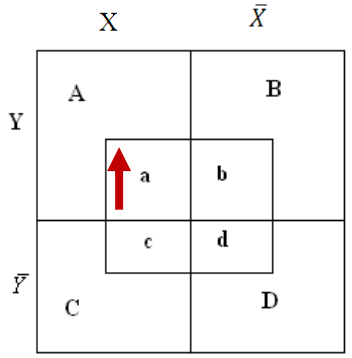
$$OR = \frac{900/64000}{60/9000} = 2.11$$

•病例對照研究設計(Case-Control study)



1000 : 300

3550 : 950



$$OR=\frac{ad}{bc}$$

	X	$\bar{X}$	total
Y	1,000	300	1,300
$\bar{Y}$	160,000	45,000	205,000
total	161,000	45,300	206,300

$$\pi_{XY}=\pi_{\bar{X}Y}=1$$

	X	$\bar{X}$	total
Y	1,000	300	1,300
$\bar{Y}$	3,550	950	4,500
total	4550	1250	5800

$$\pi_{X\bar{Y}}=\pi_{\bar{X}\bar{Y}}=0.02$$

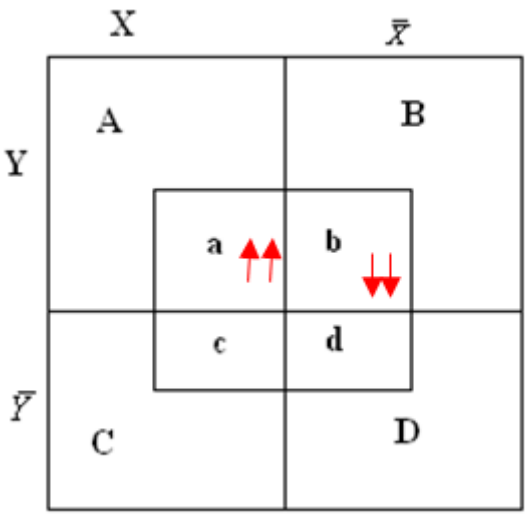
$$OR=\frac{1000/300}{3550/950}=0.89$$

Trinity Bridge

回憶性偏差(Recall bias)

- Retrospective study

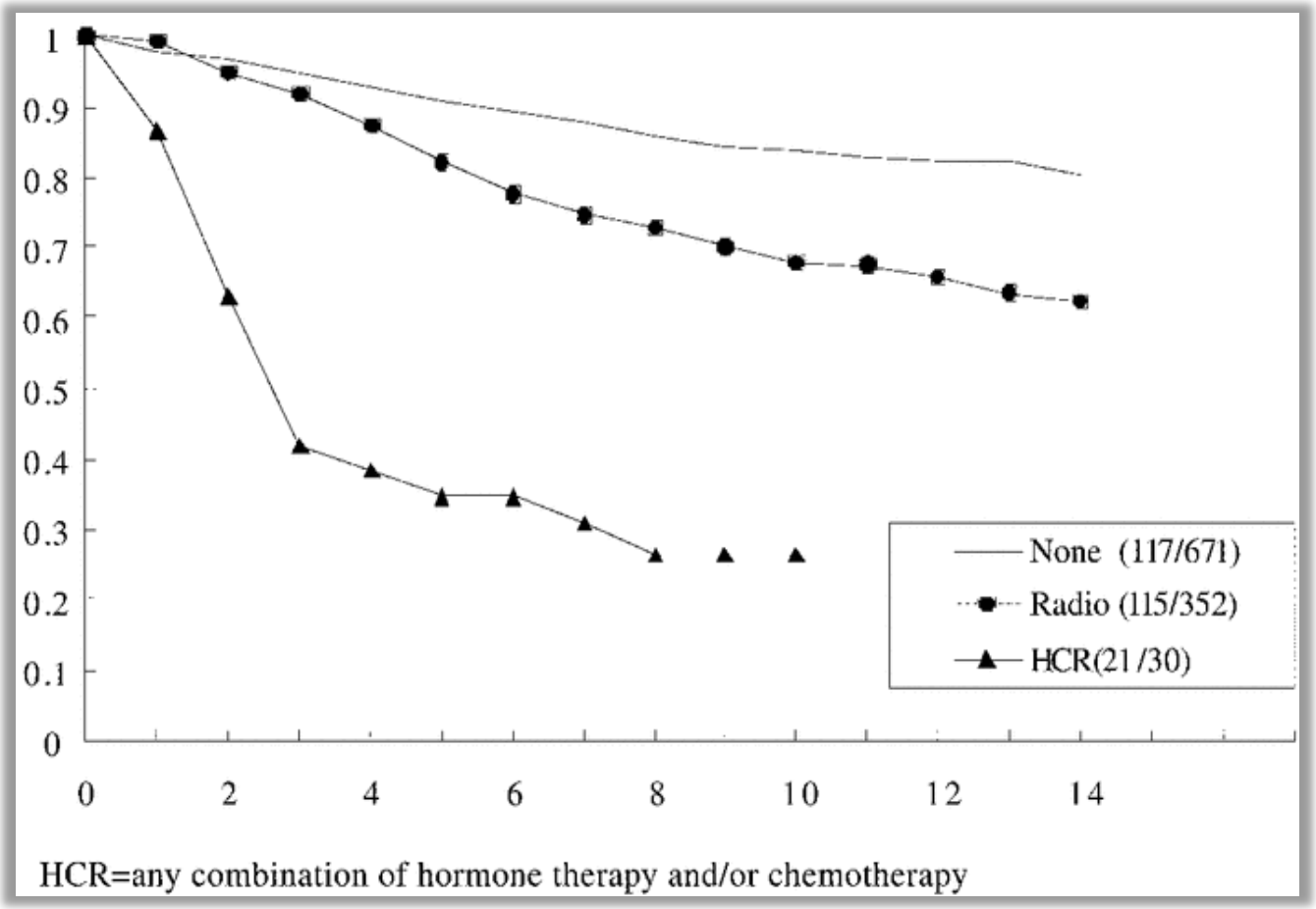
"Someone subsequently diagnosed with a brain tumour might easily be biased…
to exaggerate the former…"



- Does recall-bias lead to under-estimation or over-estimation of association between the use of mobile phone and brain tumour?

→they may lead to over-estimation

選擇性存活分析(Selected survival)

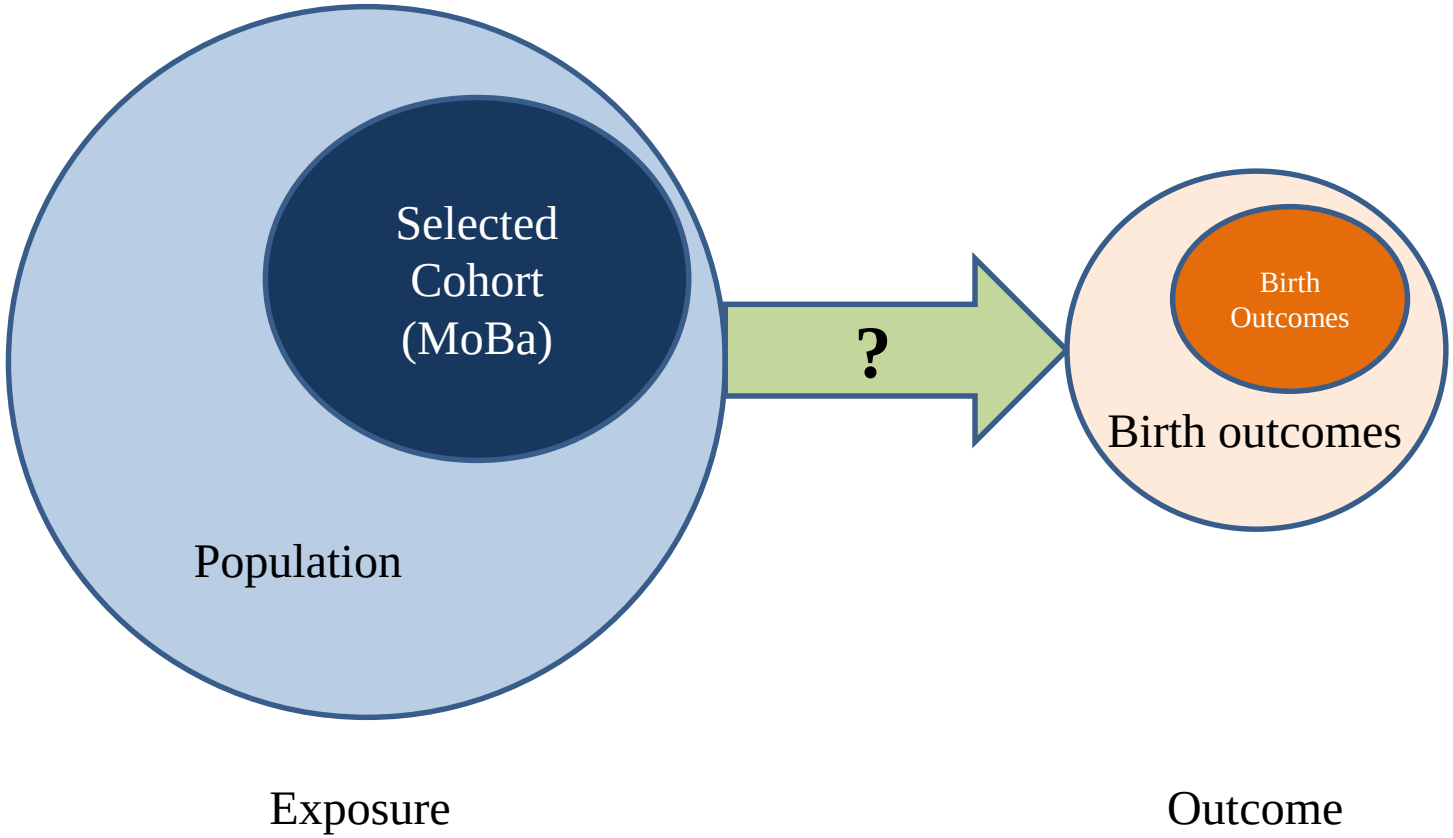


※選擇性偏差的類型

- "Comparability" problem
- Bias due to selection
  - Types of selection bias
    - Membership-bias
    - Berkson bias (admission-rate bias)
    - Neyman bias (incidence-prevalence bias)
    - detection bias (non-respondent bias)

Self-selection and bias in a large prospective pregnancy cohort in Norway

Paediatric and Perinatal Epidemiology, **23**, 597–608.



Background characteristics	Total population No. (%)	MoBa participants No. (%)	Ratio of relative frequencies [95% CI][a]
Maternal age at delivery[b]			
<25 years	67 707 (17.0)	8734 (11.9)	0.70 [0.69, 0.71]
25–34 years	266 171 (66.7)	52 638 (71.5)	1.07 [1.07, 1.08]
>34 years	64 961 (16.3)	12 207 (16.6)	1.02 [1.00, 1.03]
Marital status[c]			
Single	25 547 (6.4)	2599 (3.5)	0.55 [0.53, 0.57]
Cohabiting	172 287 (43.2)	33 930 (46.1)	1.07 [1.06, 1.07]
Married	195 944 (49.1)	36 732 (49.9)	1.02 [1.01, 1.02]
Parity			
0	162 983 (40.9)	31 763 (43.2)	1.06 [1.05, 1.06]
1	142, 211 (35.7)	26 486 (36.0)	1.01 [1.00, 1.02]
2	65 770 (16.5)	11 840 (16.1)	0.98 [0.96, 0.99]
>2	27 885 (7.0)	3490 (4.7)	0.68 [0.66, 0.70]
Previous stillbirths[d]			
0	232 408 (98.5)	41 402 (99.0)	1.00 [1.00, 1.01]
1	3220 (1.37)	387 (0.93)	0.68 [0.62, 0.74]
>1	238 (0.10)	27 (0.06)	0.64 [0.42, 0.86]
Maternal asthma			
Yes	16 468 (4.1)	3155 (4.3)	1.04 [1.01, 1.07]
Maternal epilepsy			
Yes	3066 (0.77)	554 (0.75)	0.98 [0.91, 1.06]
Pregestational diabetes			
Yes	2701 (0.68)	415 (0.56)	0.83 [0.76, 0.91]
Chronic hypertension			
Yes	2232 (0.56)	376 (0.51)	0.91 [0.83, 1.00]
All deliveries	398 849 (100)	73 579 (100)	

Exposures and pregnancy complications	Total population No. (%)	MoBa participants No. (%)	Ratio of relative frequencies [95% CI][a]
In vitro fertilization			
Yes	7353 (1.8)	1542 (2.1)	1.14 [1.09, 1.19]
Smoking[b]			
Unknown	60 254 (15.1)	9512 (12.9)	0.86 [0.84, 0.87]
No	295 618 (74.1)	59 548 (80.9)	1.09 [1.09, 1.10]
Yes	42 977 (10.8)	4519 (6.1)	0.57 [0.55, 0.58]
Multivitamin use[c]			
Unknown	66 443 (16.7)	10 310 (14.0)	0.84 [0.83, 0.85]
No	225 628 (56.6)	37 391 (50.8)	0.90 [0.89, 0.90]
Yes	106 778 (26.8)	25 878 (35.2)	1.31 [1.30, 1.33]
Folic acid use[c]			
Unknown	66 443 (16.7)	10 310 (14.0)	0.84 [0.83, 0.84]
No	185 974 (46.6)	24 551 (33.4)	0.72 [0.71, 0.72]
Yes	146 432 (36.7)	38 718 (52.6)	1.43 [1.42, 1.44]
Medication use[d]			
Yes	85 300 (21.4)	17 531 (23.8)	1.11 [1.10, 1.13]
Gestational diabetes			
Yes	3444 (0.86)	587 (0.80)	0.92 [0.86, 0.99]
Pre-eclampsia			
Yes	15 879 (4.0)	2861 (3.9)	0.98 [0.94, 1.01]
Placental abruption[e]			
Yes	1726 (0.43)	282 (0.38)	0.88 [0.79, 0.98]
All deliveries	398 849 (100)	73 579 (100)	

Exposure-outcome associations	Total population (n = 391 011)		MoBa participants (n = 72 159)		Ratio of AORs [95% CI][c]
	UOR	AOR [95% CI][b]	UOR	AOR [95% CI][b]	
Smoking and low birthweight(<2500 g)					
Smoker[d]	1.89	1.85 [1.76, 1.94]	1.88	1.77 [1.53, 2.05]	0.95 [0.83, 1.10]
Smoking and placental abruption					
Smoker[d]	1.72	1.73 [1.50, 1.98]	1.95	1.85 [1.24, 2.74]	1.07 [0.70, 1.50]
Smoking and stillbirth					
Smoker[d]	1.32	1.19 [1.06, 1.34]	1.45	1.31 [0.87, 1.97]	1.08 [0.69, 1.55]
Chronic hypertension and gestational diabetes					
Hypertension	2.55	2.31 [1.72, 3.09]	2.81	2.59 [1.28, 5.25]	1.12 [0.45, 1.95]
Birthweight and neonatal death[e]					
Birthweight <2500 g	30.2	30.2 [25.9, 35.3]	37.7	43.1 [28.7, 64.8]	1.43 [0.98, 2.07]
Vitamin use and placental abruption					
User of vitamins[f]	0.72	0.74 [0.66, 0.83]	0.72	0.75 [0.57, 0.99]	1.01 [0.79, 1.31]
Parity and pre-eclampsia					
Parity 0	1.00	1.00 Reference	1.00	1.00 Reference	1.00 Reference
Parity 1	0.46	0.47 [0.45, 0.49]	0.45	0.46 [0.42, 0.50]	0.98 [0.90, 1.07]
Parity 2	0.43	0.43 [0.40, 0.45]	0.44	0.44 [0.38, 0.50]	1.03 [0.90, 1.15]
Parity >2	0.44	0.43 [0.39, 0.46]	0.47	0.46 [0.37, 0.58]	1.07 [0.87, 1.32]
Marital status and preterm birth (<37 weeks)					
Single	1.00 Reference	1.00 Reference	1.00 Reference	1.00 Reference	1.00 Reference
Cohabiting	0.71	0.77 [0.73, 0.81]	0.64	0.70 [0.60, 0.81]	0.90 [0.79, 1.04]
Married	0.67	0.75 [0.72, 0.79]	0.58	0.67 [0.57, 0.78]	0.89 [0.78, 1.03]

Bridge of Sighs, Cambridge

2007年台灣地區18歲以上人口牙周狀況及保健行為之調查研究

Journal of Clinical Periodontology

A prediction model for periodontal disease: modelling and validation from a National Survey of 4061 Taiwanese adults

Lai H, Su C-W, Yen AM-F, Chiu SY-H, Fann JC-Y, Wu WY-Y, Chuang S-L, Liu H-C, Chen H-H, Chen L-S. A prediction model for periodontal disease: modelling and validation from a National Survey of 4061 Taiwanese adults. J Clin Periodontol 2015; 42: 413–421. doi: 10.1111/jcpe.12389.

Abstract

Aims: The aim of this study was to predict periodontal disease (PD) with demographical features, oral health behaviour, and clinical correlates based on a national survey of periodontal disease in Taiwan.

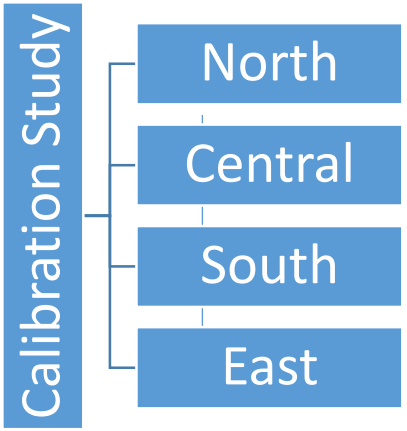
Materials and Methods: A total of 4061 subjects who were enrolled in a cross-sectional nationwide survey on periodontal conditions of residents aged 18 years or older in Taiwan between 2007 and 2008 were included. The community periodontal index (CPI) was used to measure the periodontal status at the subject and sextant levels. Information on demographical features and other relevant predictive factors for PD was collected using a questionnaire.

Results: In our study population, 56.2% of subjects had CPI grades ≥3. Periodontitis, as defined by CPI ≥3, was best predicted by a model including age, gender, education, brushing frequency, mobile teeth, gingival bleeding, smoking, and BMI. The area under the curve (AUC) for the final prediction model was 0.712 (0.690–0.734). The AUC was 0.702 (0.665–0.740) according to cross-validation.

Conclusions: A prediction model for PD using information obtained from questionnaires was developed. The feasibility of its application to risk stratification of PD should be considered with regard to community-based screening for asymptomatic PD.

Nationwide Survey

13 examiner +1 standard examiner
4601 subjects



Explain the role of quantitative and qualitative methods and sciences in describing and assessing a population’ s health. 解釋質性與量性方法及科學在解釋及評估人口健康中所扮演的角色。

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PROPERTIES OF CPI MEASUREMENTS

Community Periodontal Index (CPI)

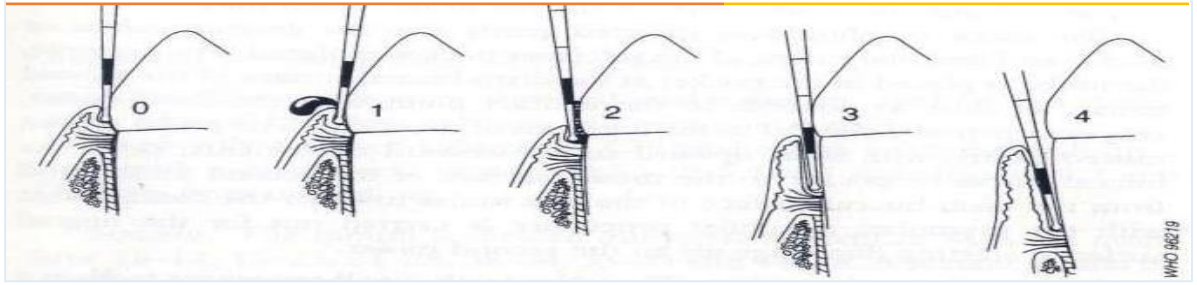
↓

Epidemiological Study

↓

Silent Periodontal Disease (PD)

Free of PD	*Mild*	*Mild*	*Moderate*	*Severe*
CPI=0	CPI=1	CPI=2	CPI=3	CPI=4



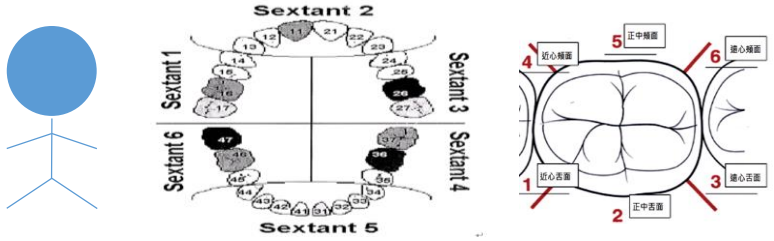
(WHO, 1997)

Examiners

Dr. A
Dr. B
Dr. C
⋮
Dr. S ← Gold standard

Examinee

district → individual → Sextant → Tooth → Site



(Hierarchical Data Structure)

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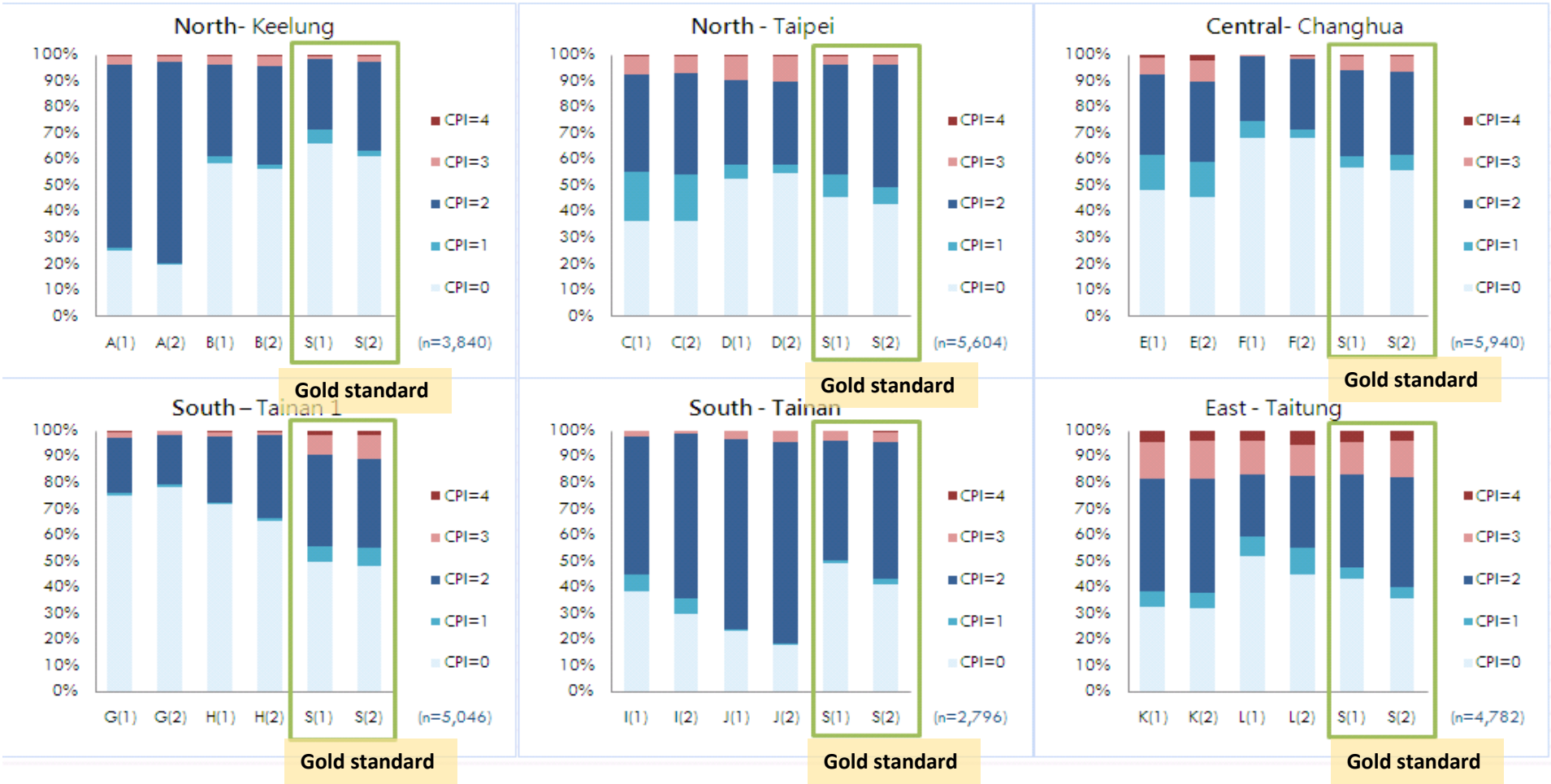
DESCRIPTIVE DATA

◆ **Percentage of CPI score** at site level by the examiners from different regions *(Site level, n=28,008)*

S: gold standard; A-K: examiner from different regions; (1) and (2): 1st exam and 2nd exam, respectively



◆**Measurement varied with regions**; there is **difference between examiner and standard examiner**

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Risk factors & PD

- Nationwide Survey -

◆The odds ratio for smoking and PD

Variable	OR	2.50%	97.50%
Smoking(Yes vs No)	2.63	2.19	3.18

◆ **Measurement error without correction**

Variable	aOR	2.50%	97.50%
Age	1.06	1.05	1.07
Education(Low vs. High)	1.36	1.11	1.66
Gender(male vs female)	1.32	1.07	1.65
Obesity(Yes vs No)	1.10	0.913	1.42
Smoking(Yes vs No)	1.96	1.53	2.50

◆ **Measurement error with correction**

Variable	aOR	2.50%	97.50%
Age	1.08	1.07	1.10
Education(Low vs. High)	1.59	1.17	2.16
Gender(male vs female)	1.57	1.15	2.14
Obesity(Yes vs No)	1.24	0.90	1.73
Smoking(Yes vs No)	2.65	1.88	3.79

錯誤分組 (MISCLASSIFICATION)

無方向性(Non-differential error)

- 敏感度(Sensitivity) =Pr(Z=1|X=1) 註記為SE
- 特異度(Specificity) =Pr(Z=0|X=0) 註記為SP

有方向性偏差(Differential error)

- 敏感度(Sensitivity) =Pr(Z=1|X=1, Y=y) 註記為SE_y
- 特異度(Specificity) =Pr(Z=0|X=0, Y=y) 註記為SP_y

Y：實際應變項
X：實際自變項
Z：觀察變項

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流行病學範例

世代追蹤研究之疾病錯誤分組

- 以無方向性偏差(Non-differential error)為例

		暴露(Exposure)(X)	
		有(1)	無(0)
疾病(Disease) (Y)	有(1)	400	200
	無(0)	600	800
		1000	1000

相對風險比值RR=(400/1000)/(200/1000)=2

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(A) 實際有暴露(X=1)

		疾病(Disease)(Y)		
		有(1)	無(0)	
觀察疾病分組 (Classified status) (Z)	有(1)	320	60	380
	無(0)	80	540	620
		400	600	1000

(B) 實際未暴露(X=0)

		疾病(Disease)(Y)		
		有(1)	無(0)	
觀察疾病分組 (Classified status) (Z)	有(1)	160	80	240
	無(0)	40	720	760
		200	800	1000

陽性預測值 (PPV)

$$= \frac{\text{盛行率} \times \text{敏感度}}{\text{盛行率} \times \text{敏感度} + (1 - \text{盛行率}) \times (1 - \text{特異度})}$$

陰性預測值 (NPV)

$$= \frac{(1\text{-盛行率}) \times \text{特異度}}{\text{盛行率} \times (1\text{-敏感度}) + (1 - \text{盛行率}) \times (\text{特異度})}$$

無方向性偏差(Non-differential error)

敏感度(SE_1)=Pr(Z=1|Y=1, X=1)=320/400=0.8

特異度(SP_1)=Pr(Z=0|Y=0, X=1)=540/600=0.9

敏感度(SE_0)=Pr(Z=1|Y=1, X=0)=160/200=0.8

特異度(SP_0)=Pr(Z=0|Y=0, X=0)=720/800=0.9

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(C)調整錯誤分組下，疾病(Disease)與暴露(Exposure)資料分佈

		暴露(Exposure)(X)	
		有(1)	無(0)
觀察疾病分組 (Classified status) (Z)	有(1)	380	240
	無(0)	620	760
		1000	1000

- 相對風險比值RR=(380/1000)/(240/1000)=1.58
- 調整錯誤分組後，相對疾病風險比值從2降低為1.58
- 若使用觀察疾病分組求相對疾病風險比值會有低估(underestimation, toward the null) 之情形

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流行病學範例

病例對照研究之暴露錯誤分組

- 以有方向性偏差(Differential error)為例

		暴露 (Exposure)(X)		
		有(1)	無(0)	
疾病 (Disease) (Y)	有(1)	600	400	1000
	無(0)	300	700	1000

得到勝算比值OR=(600x700)/(300x400)=3.5

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假設透過校正性研究，得到實際疾病(Disease)資料分布如下

(A) 實際得病(Y=1)

		真實暴露(Exposure)(X)		
		有(1)	無(0)	
觀察暴露分組 (Classified status)(Z)	有(1)	540	120	660
	無(0)	60	280	340
		600	400	1000

(B) 實際無病(Y=0)

		真實暴露(Exposure)(X)		
		有(1)	無(0)	
觀察暴露分組 (Classified status)(Z)	有(1)	180	70	250
	無(0)	120	630	750
		300	700	1000

陽性預測值 (PPV)

$$= \frac{\text{盛行率} \times \text{敏感度}}{\text{盛行率} \times \text{敏感度} + (1 - \text{盛行率}) \times (1 - \text{特異度})}$$

陰性預測值 (NPV)

$$= \frac{(1\text{-盛行率}) \times \text{特異度}}{\text{盛行率} \times (1\text{-敏感度}) + (1 - \text{盛行率}) \times (\text{特異度})}$$

有方向性偏差(Differential error)

敏感度(SE_1)=Pr(Z=1|X=1, Y=1)=540/600=0.9

特異度(SP_1)=Pr(Z=0|X=0, Y=1)=280/400=0.7

敏感度(SE_0)=Pr(Z=1|X=1, Y=0)=180/300=0.6

特異度(SP_0)=Pr(Z=0|X=0, Y=0)=630/700=0.9

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(C)調整錯誤分組下，疾病(Disease)與暴露(Exposure)資料分布

	觀察暴露分組 (Classified status)(Z)		
		有(1)	無(0)
疾病(Disease) (Y)	有(1)	660	340
	無(0)	250	750
		1000	1000

- 勝算比值OR=(660x750)/(340x250)=5.82
- 在調整錯誤分組後，勝算比值從3.5上升為5.82
- 若顯示使用觀察疾病分組求相對疾病風險比值有高估(overestimation, away from the null)

Explain the role of quantitative and qualitative methods and sciences in describing and assessing a population’ s health. 解釋質性與量性方法及科學在解釋及評估人口健康中所扮演的角色。
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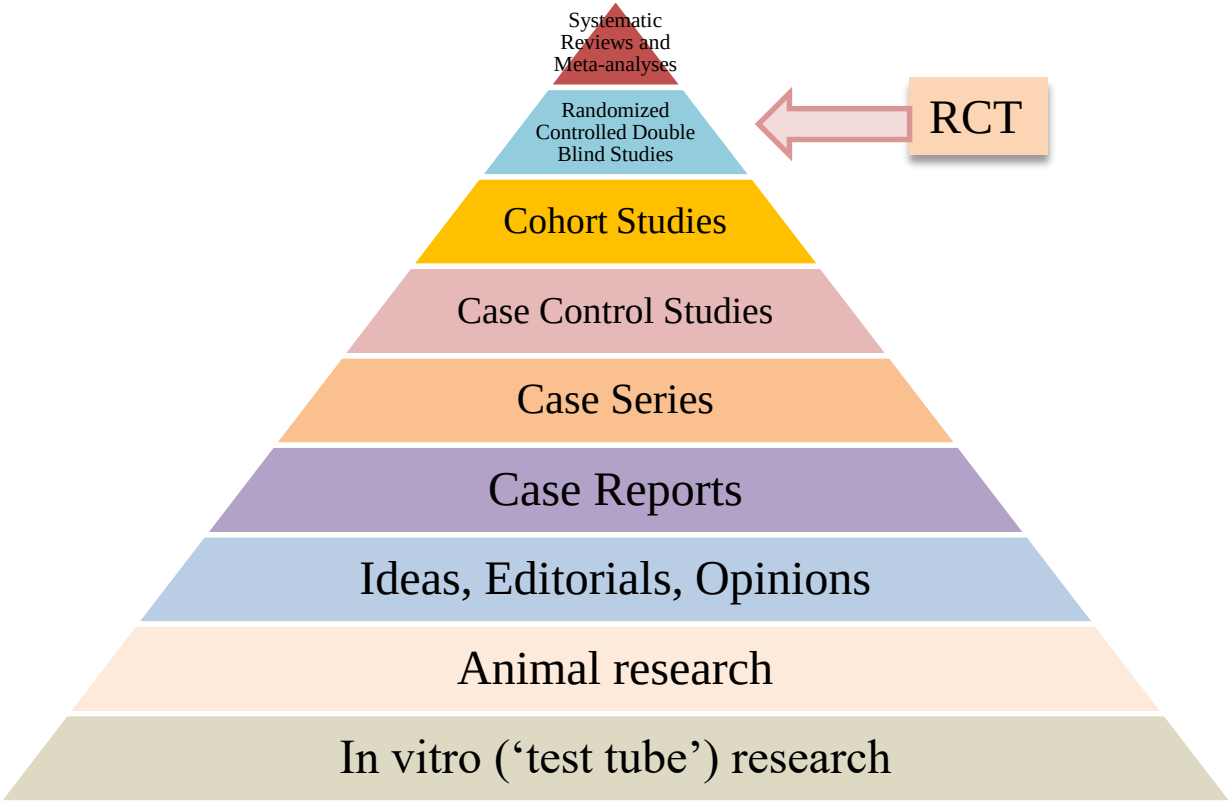
運用實證醫學方法獲得正確的推論

隨機分派研究:

Randomized Controlled Trial, RCT



實證醫學 (Evidence-Based Medicine, EBM)

- 為了使**因果關係**不受**偏差**的影響，西方醫學將解決偏差的研究設計稱為“實證醫學 (Evidence-Based Medicine, EBM) “

  - **(1) 隨機分派對照試驗(randomized trial, RCT)**
    - **移除**干擾因子及偏差(bias)
  - **(2) 前瞻性研究(prospective study)**
    - 因在果之前,無進行隨機分派
    - **控制**干擾因子及偏差

  - **(3) 病例對照研究(case-control study)**
    - 因為事件很少，需要追蹤的人數眾多故進行此研究
    - **控制**干擾因子及偏差
  - **(4) 橫斷性研究(cross-sectional study)**
    - 因果都在同一時間點做測量