臺中榮民總醫院
Taichung Veterans General Hospital

中榮官網　中榮FB

實證醫學基本課程
文獻評讀與數據擷取

實證決策管理委員會 實證醫學中心
何鴻鋆

進行方式: 課前線上學習、現場討論

- 先找好科部內兩位指導老師，撰寫CAT過程中若有疑問，先與指導老師討論。特別是專科知識討論與未來進一步研究方向。
- 請按進度先自行完成線上影音學習，於上課前完成提交初稿，以利指導者課前審視。上課時將直接針對相關進度繳交之CAT內容討論。
- 請按照預約時段準時到場，逾時不候，亦無法補課，未完成之進度遞延至下一梯次。兩梯次內未完成則需重新報名等候安排。
- 為讓您接收訊息更快速直接，學員間也可以互相討論取暖，請加入Line群組！
- http://line.me/R/ti/g/7OEJpEycyf

呈現介面使用表格

201707 R4 EBM CAT模板.doc

資深住院醫師升等實證醫學查證能力認證

指導者：

製作者：

主題		
大項目	次項目	內容
1.問題(Ask) PICO	治療指引	第一步:選有興趣的疾病，找出相關 clinical practice guideline 第二步:選定有興趣的處置/檢查，比較不同年代的相對處置變化演變 第三部:擬定問題，選擇問題型態: 處置 = therapy & harm；檢查=診斷或預後
	核心聚焦問題 (focus question for therapy)	須考慮的治療型(Therapy)問題
		P：主要診斷： 並存風險/疾病： 危險因子：
		I：
		C：
		O：
	核心聚焦問題 (focus question for harm)	須考慮的傷害型(Harm)問題
		P：主要診斷： 並存風險/疾病： 危險因子：
		I：
		C：
		O：
	核心聚焦問題 (focus question for diagnosis)	須考慮的診斷型(Diagnosis)問題
		P：主要診斷： 並存風險/疾病：
		I：(evaluated test)
		C：(reference test)
		O：
	核心聚焦問題 (focus question for Prognosis)	須考慮的預後型(Prognosis)問題
		P：主要診斷： 並存風險/疾病： 危險因子：
		I：Test (+) or higher than cut-off value
		C：Test (-) or lower than cut-off value
		O：

2. 搜尋 Acquired：Search strategy			
	搜尋資料庫 (Database)	The Cochrane library PubMed：	
	所使用關鍵字 (Key word)	P：	
		I：	
		O：	
	Filters/limits		

3. 檢索 Acquired：Key literature 20%				
	檢索結果	原治療指引引用文獻: 檢索後比原治療指引更新或更值得參考的文獻: Paper 1 Paper 2 Paper 3		
	最後列入參考文獻			
	初步評讀	Paper 1 (第一作者姓)(出版年)	Paper 2 (第一作者姓)(出版年)	Paper 3 (第一作者姓)(出版年)
	本文獻(直接且正確)解答的問題 [clearly-focused question?]	P: I: C: O: T:	P: I: C: O: T:	P: I: C: O: T:
	本文獻研究設計(符合我的問題要求) [include the right type of study?]	I. Systematic review II. Randomized control trial III. Cohort study IV. Case-control series V. Case series/Expert opinion	I. Systematic review II. Randomized control trial III. Cohort study IV. Case-control series V. Case series/Expert opinion	I. Systematic review II. Randomized control trial III. Cohort study IV. Case-control series V. Case series/Expert opinion

Original paper (RCT, cohort or lower)

4.評讀 Appraisal 評讀工具：Critical appraisal skills programme for RCT	效度 Validity/偏誤 Bias			
		Paper 1	Paper 2	Paper 3
	受試者隨機分配至治療介入各組 Randomization	偏差危險性： 高/不確定/低	偏差危險性： 高/不確定/低	偏差危險性： 高/不確定/低
	分派過程是否保密 Allocation concealment	偏差危險性： 高/不確定/低	偏差危險性： 高/不確定/低	偏差危險性： 高/不確定/低
	一開始各組條件是否相同	偏差危險性： 高/不確定/低	偏差危險性： 高/不確定/低	偏差危險性： 高/不確定/低
	照護人員是否不知道誰是實驗組 Blind to staff (PI)	偏差危險性： 高/不確定/低	偏差危險性： 高/不確定/低	偏差危險性： 高/不確定/低
	受試者是否不知道誰是實驗組 Blind to participants	偏差危險性： 高/不確定/低	偏差危險性： 高/不確定/低	偏差危險性： 高/不確定/低
	結果評估者是否不知道誰是實驗組 Blind to assessor	偏差危險性： 高/不確定/低	偏差危險性： 高/不確定/低	偏差危險性： 高/不確定/低
	隨機分配後的參與者是否都納入最後分析 Withdraw; incomplete or loss to follow up	偏差危險性： 高/不確定/低	偏差危險性： 高/不確定/低	偏差危險性： 高/不確定/低
	是否採用意向性治療分析 Intention-to-treat analysis	偏差危險性： 高/不確定/低	偏差危險性： 高/不確定/低	偏差危險性： 高/不確定/低
	參與人數是否足夠 Enough participants (power calculation)	偏差危險性： 高/不確定/低	偏差危險性： 高/不確定/低	偏差危險性： 高/不確定/低
	報告或其他偏誤 Reporting bias or Others:	偏差危險性： 高/不確定/低	偏差危險性： 高/不確定/低	偏差危險性： 高/不確定/低
	是否為優質 RCT，若不是，繼續下列 Bias 評讀：			
	各組干擾因素控制是否得當 Control for confounders	偏差危險性： 高/不確定/低	偏差危險性： 高/不確定/低	偏差危險性： 高/不確定/低
	各組除了控制處置不同外其他治療是否相當 Measurement of exposure	偏差危險性： 高/不確定/低	偏差危險性： 高/不確定/低	偏差危險性： 高/不確定/低
	證據等級 Level of evidence			
	效益 Impact			
	Main result (size of effect)與 Precise of results	Effect size [precision: 95% confidence interval /p valve/] Outcome 1: Paper 1: Absolute Risk reduction: Mean/ median differences: Odds ratio: Hazard ratio Paper 2: Paper 3:		
	評讀後初步結論			

進度

1. 題目設定與形成及精準搜尋與證據選定
2. 證據研究方法評讀
3. 證據數據擷取
4. 證據應用評估
5. FINAL CAT (Critical Appraisal Topic) 產出

2. 證據研究方法評讀

2.1 選定證據文獻

2.2 評讀表選定

2.3 bias評讀 (Validity)

2.1 選定證據文獻

3. 檢索 Acquired：Key literature 20%。	檢索結果。	原治療指引引用文獻: 檢索後比原治療指引更新或更值得參考的文獻: Paper 1 Paper 2 Paper 3
	最後列入參考文獻。	

初步評讀	Paper 1 (第一作者姓)(出版年)	Paper 2 (第一作者姓)(出版年)
本文獻(直接且正確)解答的問題 [clearly-focused question?]	P: I: C: O: T:	P: I: C: O: T:
本文獻研究設計(符合我的問	I. Systematic review II. Randomized control trial	I. Systematic review II. Randomized control trial

檢索結果(可考慮列入評讀文獻)

- 原CPG或UpToDate在相關章節的參考文獻
- 在DataBase搜尋到的文獻

最後列入(評讀)參考文獻: 出略篩選文獻符合我們臨床問題的PICO

初步評讀: (需寫出文獻PICOT與研究設計)

選定文獻「必要條件」:

- 文獻PICO符合我們臨床問題的PICO
- 較能解決該類型問題的研究設計

- 通過的文獻才進入真正評讀

2.1 選定證據文獻

3. 檢索 Acquired：Key literature，20%。	檢索結果。	原治療指引引用文獻: 檢索後比原治療指引更新或更值得參考的文獻: Paper 1 Paper 2 Paper 3		
	最後列入參考文獻。			
	初步評讀。	Paper 1 (第一作者姓)(出版年)。	Paper 2 (第一作者姓)(出版年)。	Paper 3 (第一作者姓)(出版年)。
	本文獻(直接且正確)解答的問題 [clearly-focused question?]。	P: I: C: O: T:	P: I: C: O: T:	P: I: C: O: T:
	本文獻研究設計(符合我的問題要求)。 [include the right type of study?]。	I. Systematic review。 II. Randomized control trial。 III. Cohort study。 IV. Case-control series。 V. Case series/Expert opinion。	I. Systematic review。 II. Randomized control trial。 III. Cohort study。 IV. Case-control series。 V. Case series/Expert opinion。	I. Systematic review。 II. Randomized control trial。 III. Cohort study。 IV. Case-control series。 V. Case series/Expert opinion。

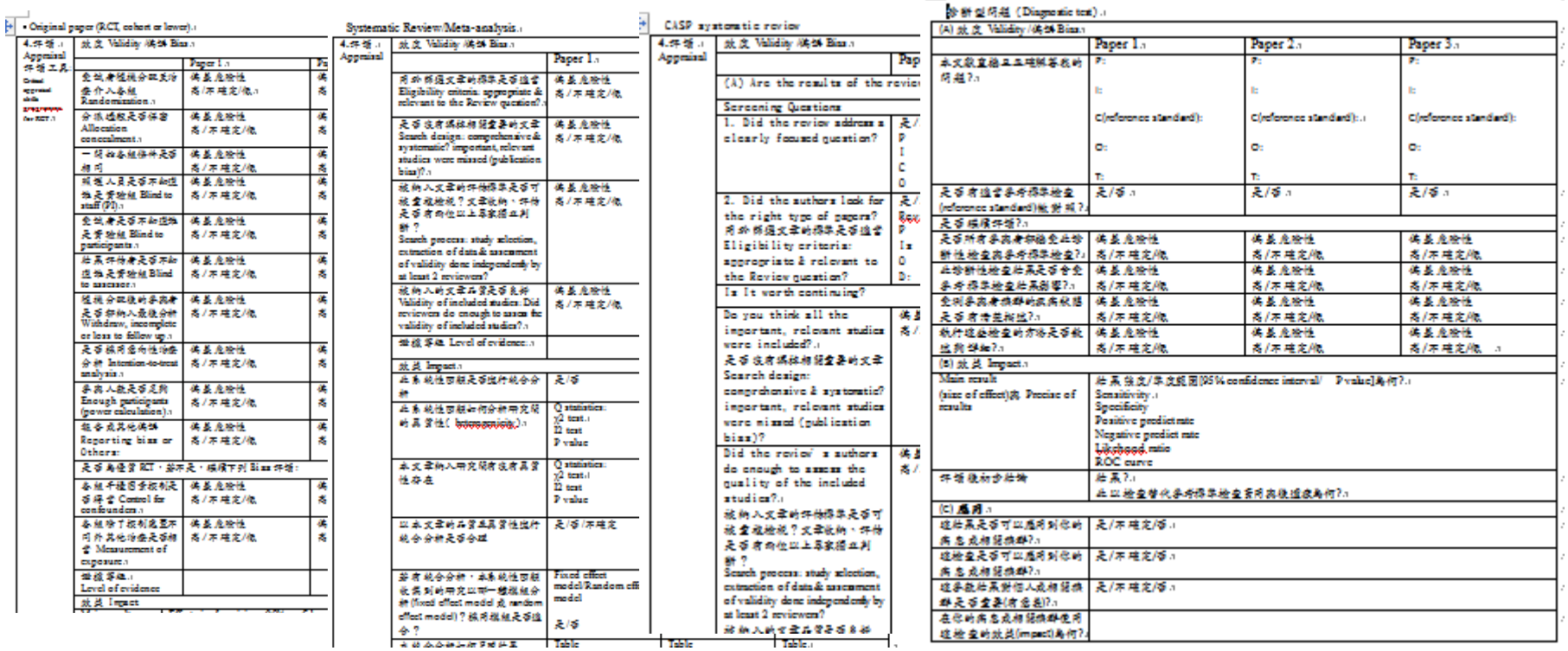
建議文獻選擇考量:

- 列出參考guideline/UpTodate中相關參考文獻
- 列出在PubMed/EmBase找到的文獻
- 依據與緣設定PICO最符合、證據等級較高、發表年較近緣則選擇
- 將選定評讀文獻中研究方法: 收案對像(P)，探討的處置(I)、對照組處置(C)與outcomes列出。另外處置使用時間/觀察時間(T)列出。假如無法找到對應項目列出，前在這篇文獻不是適當文獻。
- 研究設計方法為何?除非罕見疾病，否則無對照組研究不會列入評讀。

範例

	Chen et al.	Morelli et al.	Wong et al.
發表年份	2017	2013	2010
本文獻直接且正確解答我的問題	Yes P : 80 Taiwan patients with endometriomas undergoing laparoscopic cystectomy followed by 6 cycles of gonadotropin-releasing hormone agonist treatment I: LNG-IUS C : without LNG-IUS T: 30 months O : endometrioma recurrence 30 months after surgery; dysmenorrhea (VAS), CA125 levels, noncyclic pelvic pain, and side effects	Yes P: patients who had chronic pelvic pain due to endometriosis after conservative laparoscopic surgery I: LNG-IUD (n=44) C: estradiol valerate + dienogest estrogen progestin (EP) therapy (n=48) T: at least 24 months for the last woman operated O: pain relapse (VAS) and disease recurrence rate at 12 and 24 months after treatment; patient satisfaction with the therapy..	Yes P : 30 Hong Kong patients after conservative surgery (within 5 years) endometriosis without lesion recurrence (If evidence of bone loss or gross osteoporosis during the study, the patient was advised to withdraw) I: LNG-IUD C: Depot MPA, three-monthly T: 3 years O: symptom control, recurrence, compliance and change in bone mineral density (BMD)
本文獻研究設計符合我的問題要求	Yes, randomized control trial (definition of recurrence: endometrioma > 2cm from USG)	Yes, retrospective case series, (definition of recurrence: elevated CA125 and/or USG evidence of endometrioma and/or palpable rectovaginal septum nodule)	Yes, randomized control trial. (definition of recurrence: endometrioma >=3cm from USG)

2.2 評讀表選定



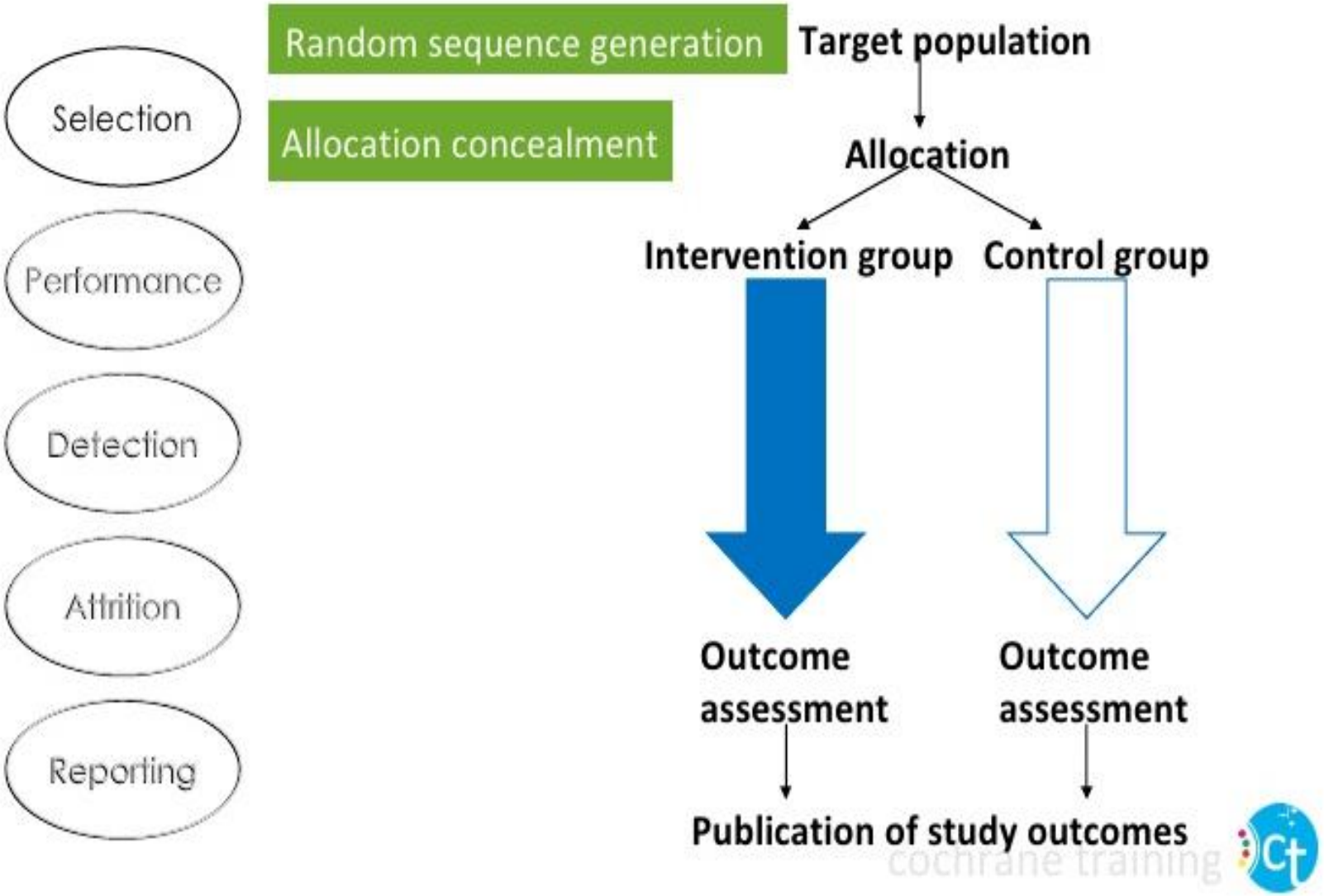
- 依照第一次上課認定所選主題為何種型態選擇模板中的表格
- origin paper用p3的，他們就不用再分RCT, cohort, case series。SR 兩者選一。診斷型的只有CASP
- 假如發現評讀文章時，無法順利竹項填入，要不是選錯文獻，要不選錯表格。

2.3 bias評讀 (Validity)

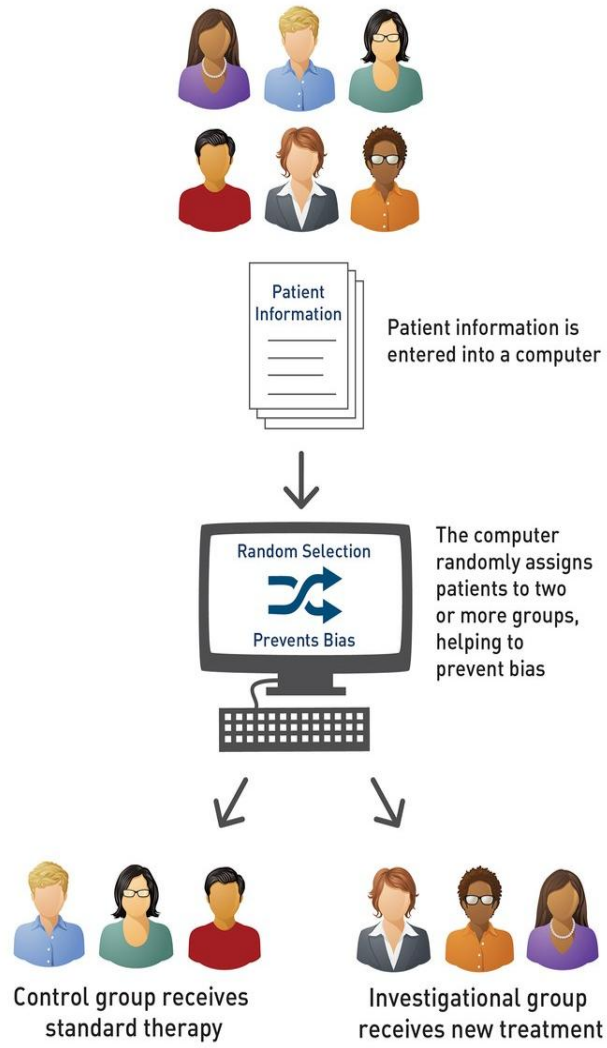
Critical Appraisal

Source	Protection
Baseline imbalance	Randomization
Performance	Blinding of caregivers, careful monitoring & analysis
Placebo-effect	Blinding of patients
Attrition	Careful follow-up & ITT analysis
Detection	Valid measurement Blinding of outcome assessors
Analytical	Careful analyses
Reporting	Report all relevant planned measurements

Sources of bias



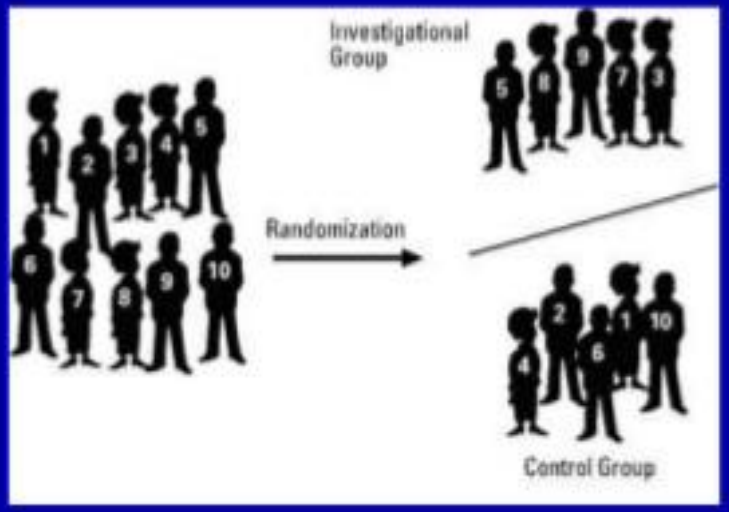
第一關: Randomization



http://www.cancer.gov/about-cancer/treatment/clinical-trials/what-are-trials/randomization/clinical-trial-randomization-infographic

常見Randomization的方法

- Simple randomization → Inacceptable
- Random table
- Block randomization
- Stratified randomization
- Minimization method
- Unequal randomization
- Allocation concealment → Preferred



Allocation Concealment

Allocation Concealment

Minimum criteria for adequate allocation concealment schemes

- Sequentially numbered, opaque, sealed envelopes (SNOSE)
- Sequentially numbered containers
- Pharmacy controlled
- Central randomisation

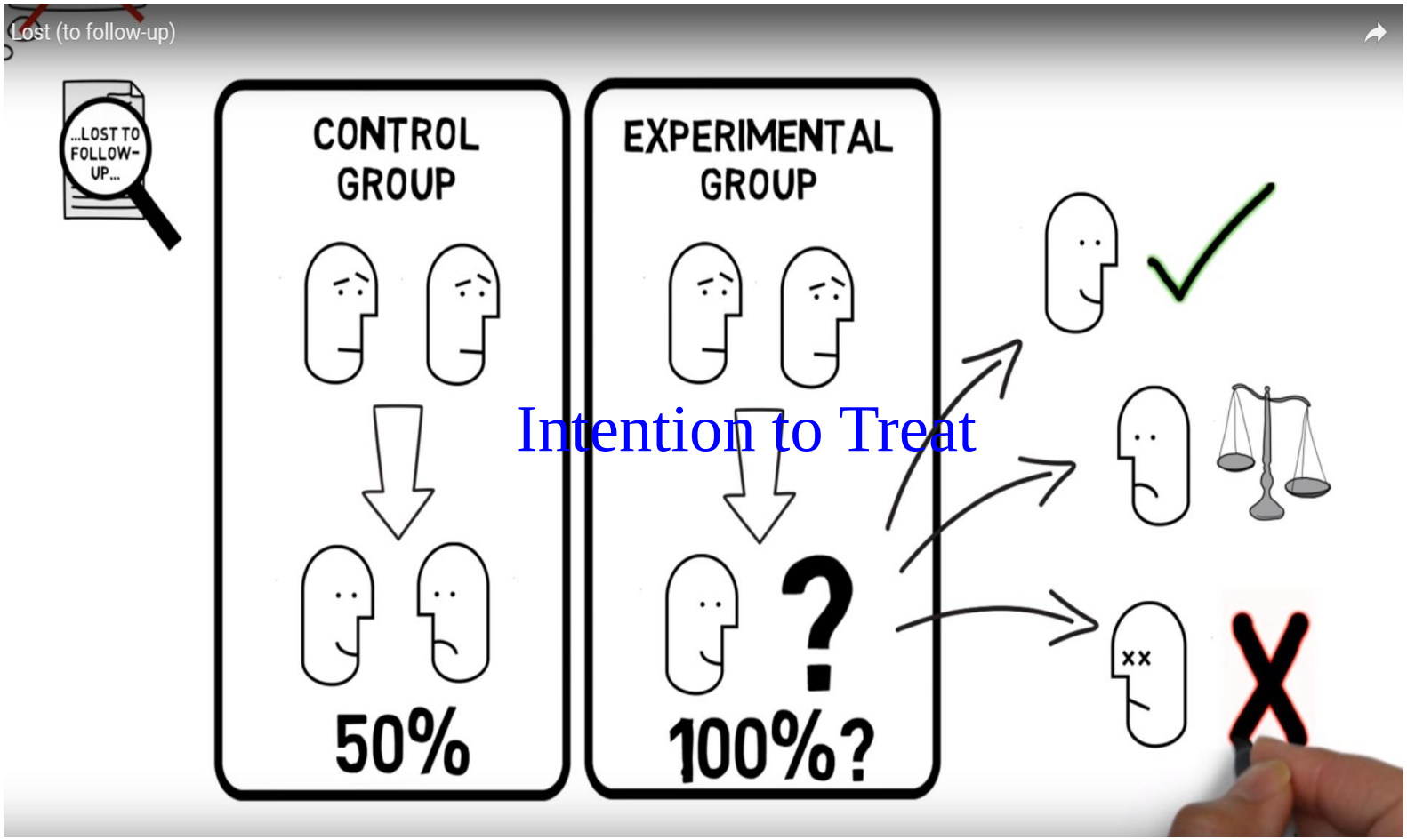
THE LANCET • Vol 359 • Feb 16, 2002 • www.thelancet.com

Allocation Concealment

Minimum description of adequate allocation concealment scheme	Additional descriptive elements that provide greater assurance of allocation concealment
Sequentially numbered, opaque, sealed envelopes (SNOSE)	Envelopes are opened sequentially only after participant details are written on the envelope. Pressure-sensitive or carbon paper inside the envelope transfers that information to the assignment card (creates an audit trail). Cardboard or aluminum foil inside the envelope renders the envelope impermeable to intense light.
Sequentially numbered containers	All of the containers were tamper-proof, equal in weight, and similar in appearance.
Pharmacy controlled	Indications that the researchers developed, or at least validated, a proper randomisation scheme for the pharmacy. Indications that the researchers instructed the pharmacy in proper allocation concealment.
Central randomisation	The mechanism for contact—eg, telephone, fax, or e-mail—the stringent procedures to ensure enrolment before randomisation, and the thorough training for those individuals staffing the central randomisation office.

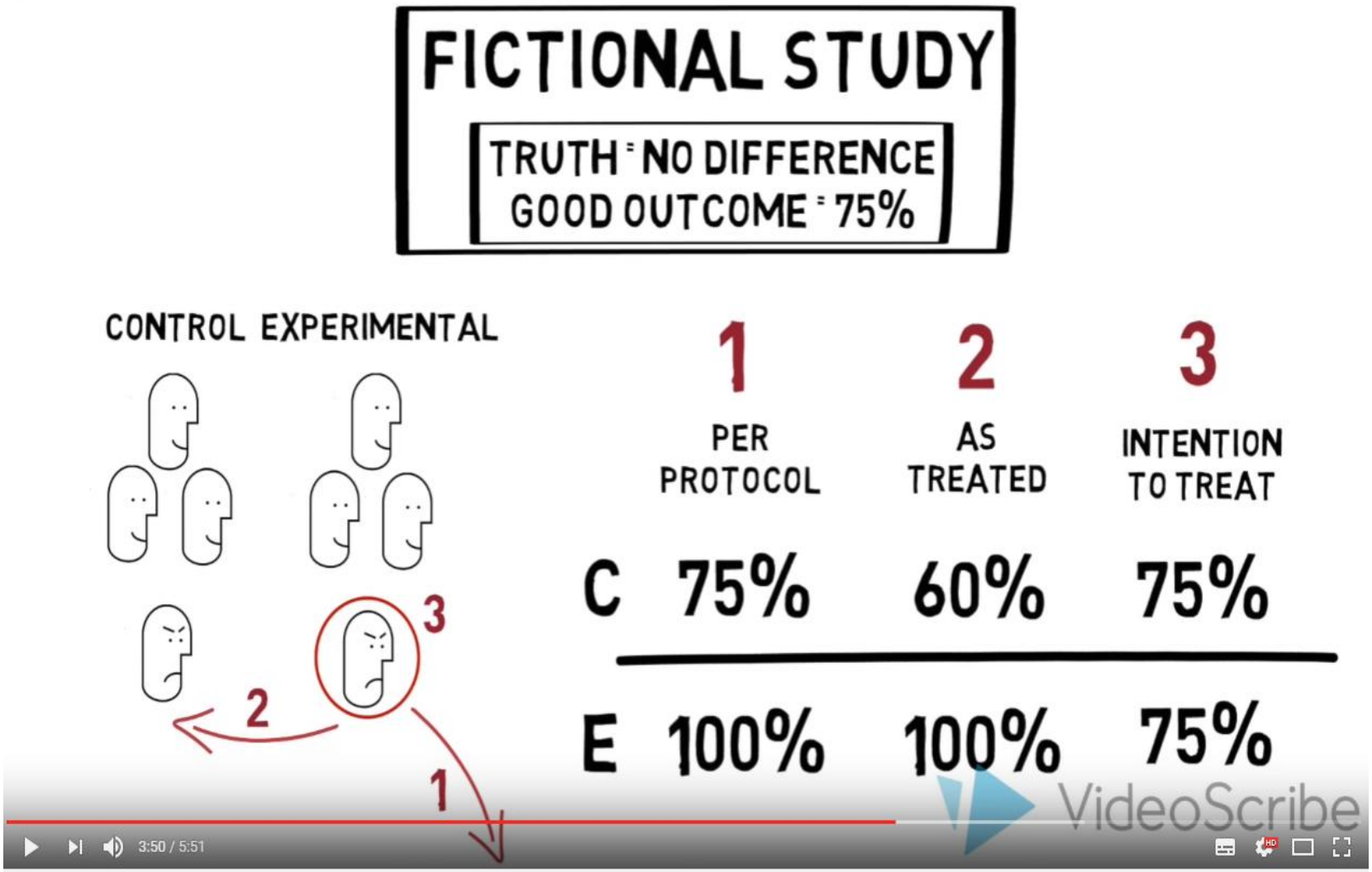
THE LANCET • Vol 359 • Feb 16, 2002 • www.thelancet.com

Lost Follow-up -- Attrition



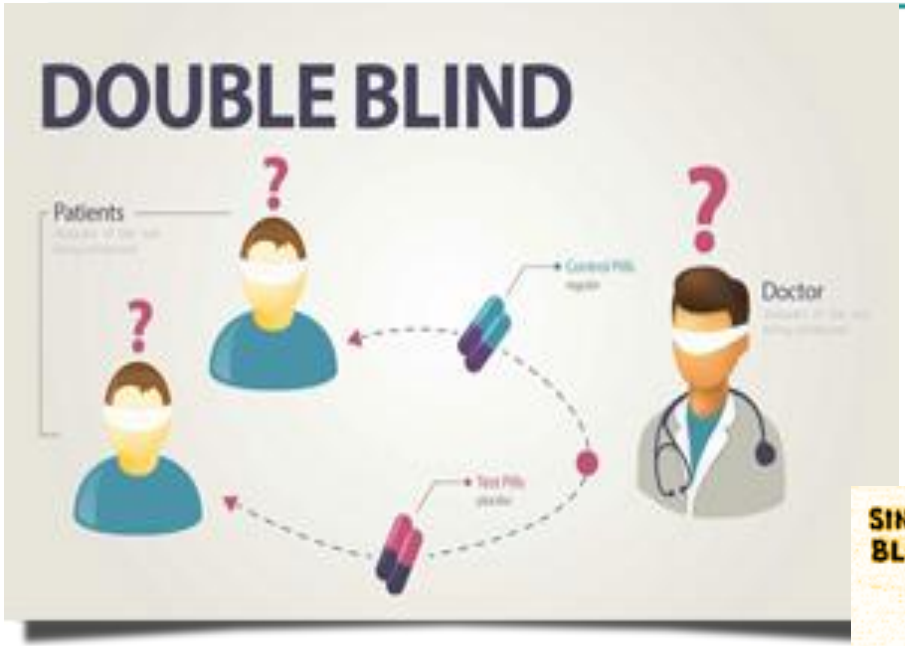
https://www.youtube.com/watch?v=dMfC-SSBZi0

Lost Follow-up -- Intention to Treat

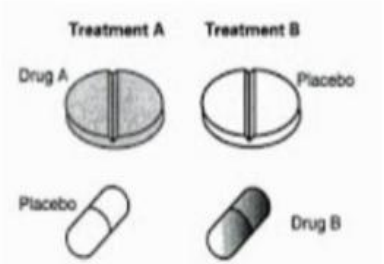


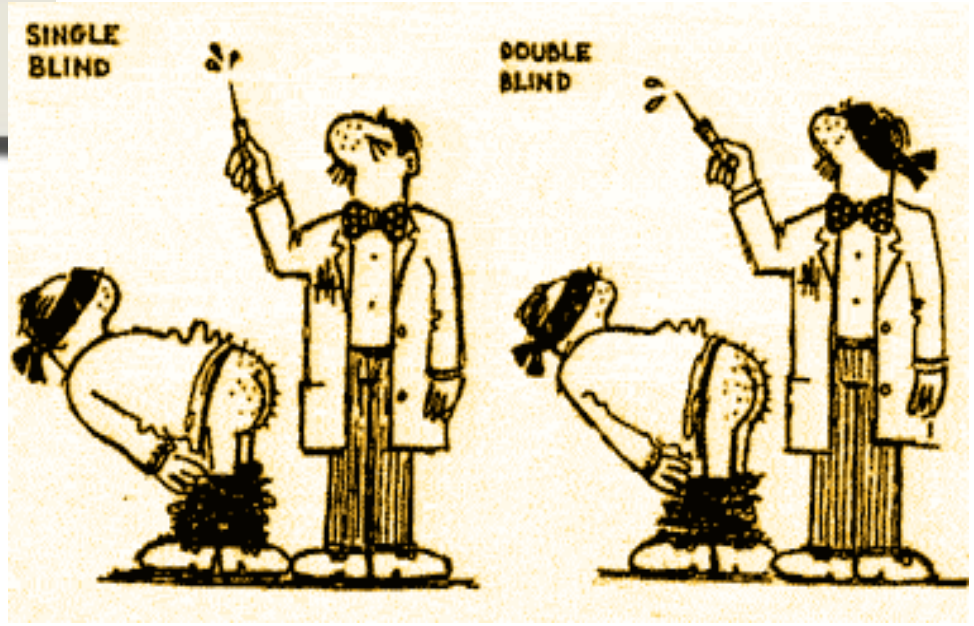
https://www.youtube.com/watch?v=Kps3VzbykFQ

Blind

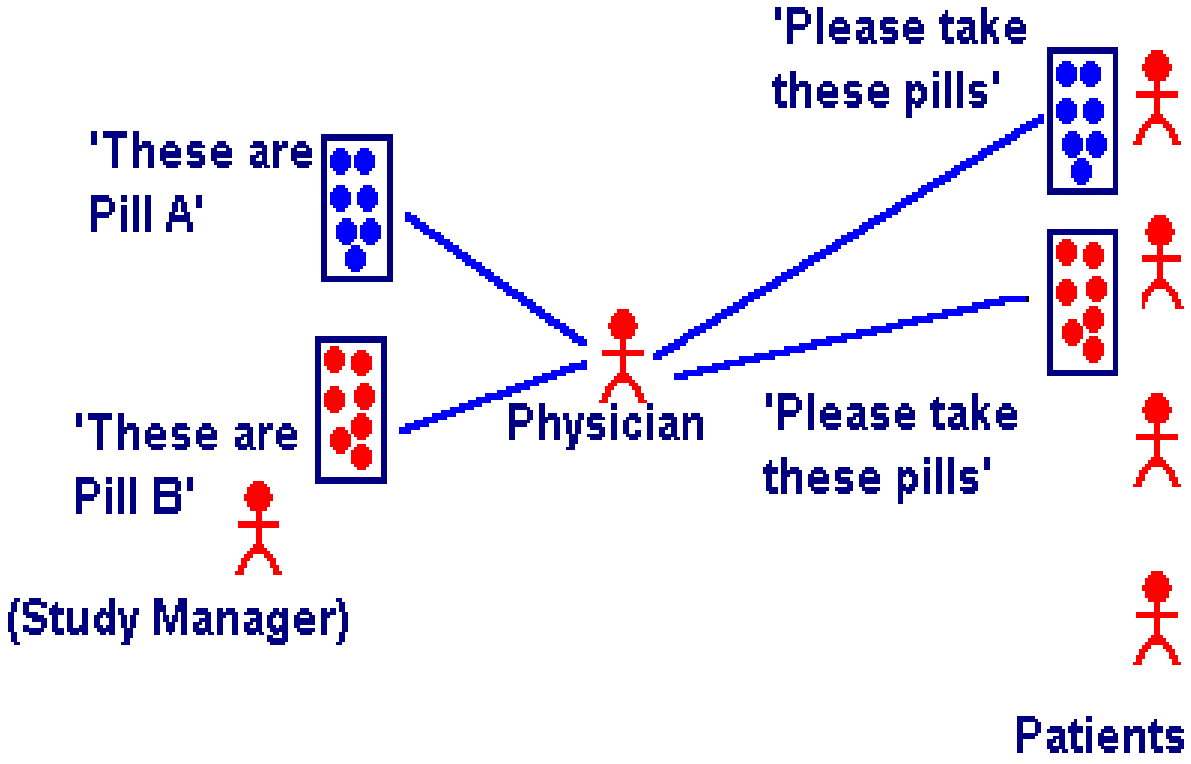


Double dummy technique





研究設計 Double-Blind



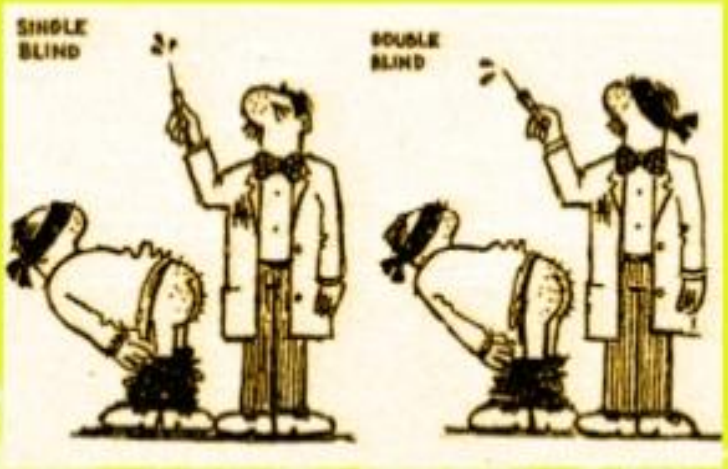
http://library.downstate.edu/EBM2/2300.htm

Blinding

A)Single blind trial : the trial is so planned that the participant is not aware whether he belongs to the study group or control group.

B)Double blind trail: The trial is so planned that neither the investigator nor the participant is aware of the group allocation and the treatment received.

c)Triple blind trial : The participant , the investigator and the person analyzing the data are all blind.



Detection bias

- Valid measurement

A good measure should be

- **Valid**
- **Reliable**
- **Sensitive**

Valid exist when

- "testing for the right thing"
- A valid measure actually measures what it is intend to measure

Criteria for Measurements

A good measure should be

- Valid
- Reliable
- Sensitive

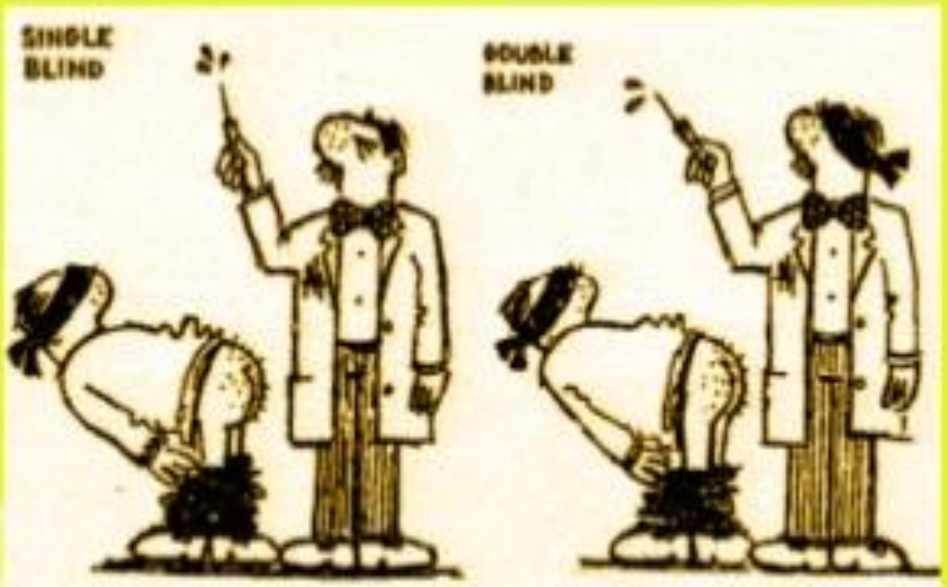
Valid exist when

- "testing for the right thing"
- A valid measure actually measures what it is intend to measure

Detection bias

- Valid measurement
- Blinding of outcome assessors

c)Triple blind trial : The participant , the investigator and the person analyzing the data are all blind.



Analytical bias

- Analyzing the data incorrectly
- Due to the way that the results are evaluated

Reporting bias/ Selective reporting

Type of reporting bias	Definition
Publication bias	The publication or non-publication of research findings, depending on the nature and direction of the results
Time lag bias	The rapid or delayed publication of research findings, depending on the nature and direction of the results
Multiple (duplicate) publication bias	The multiple or singular publication of research findings, depending on the nature and direction of the results
Location bias	The publication of research findings in journals with different ease of access or levels of indexing in standard databases, depending on the nature and direction of results.
Citation bias	The citation or non-citation of research findings, depending on the nature and direction of the results
Language bias	The publication of research findings in a particular language, depending on the nature and direction of the results
Outcome reporting bias	The selective reporting of some outcomes but not others, depending on the nature and direction of the results

https://www.youtube.com/watch?v=dMfC-SSBZi0

填寫要求範例

4.評讀 Appraisal 評讀工具:	效度 Validity /偏誤 Bias			
	評讀文章	Chen et al. 2017	Morelli et al. 2013	Wong et al. 2010
	受試者隨機分配至治療介入各組	Yes p.2. Computer-generated random numbers in sequentially sealed opaque envelopes were used to randomly allocate the patients into either the control group (n=40) or the intervention group (n=40).	No, retrospective chart review	Yes, p.247 A chart was prepared with 30 slots of randomly allocated treatment regime of either LNG-IUS or Depot MPA and each patient was assigned to each slot and the corresponding therapy in chronological order.
	分派過程是否保密	Yes p.2. Computer-generated random numbers in sequentially sealed opaque envelopes were used to randomly allocate the patients into either the control group or the intervention group	No, retrospective chart review	Yes, p.274 A chart was prepared with 30 slots of randomly allocated treatment regime of either LNG-IUS or Depot MPA and each patient was assigned to each slot and the corresponding therapy in chronological order.
	一開始各組條件是否相同	No, p.4 Table 1 Intervention group older (>3 y/o), higher weight (>2kg), higher BMI (>1), higher ASRM score, smaller diameter (<2mm), higher dysmenorhea VAS,	Unclear, Table 1 did not provide enough data p.987: Table 1. As shown, no differences were found between the two groups in terms of age, body mass index (BMI), CA125 levels, ASRM stages and VAS scores (Table 1)..	Yes, p. 275 table 1, There was no significant difference in the demographic data (including mean age, mean highest rAFS score in previous operation and BMI) (Table 1), nature of previous operation (Table 1), starting Symptom Scores (Fig. 2), baseline DEXA T-score (Fig 3), BMD of lumbar spine and hip (Table 2) between the two groups of patients
	照護人員是否不知道誰是實驗組	No, p.3 The surgeons and participants were not blinded to study allocation	No	No

進度

1. 題目設定與形成及精準搜尋與證據選定
2. 證據研究方法評讀
3. 證據數據擷取
4. 證據應用評估
5. FINAL CAT (Critical Appraisal Topic) 產出

評評讀最終目的在數據

讀結論決定相信數據的程度

數據要如何呈現

數據有那些

Raw Data type

- Binary
- Continuous
- Survival / Time to event

Group Summary

- Risk / Proportion
- Mean/Median
- Rate

Group Comparison (Rx effect)

- Difference
- Ratio
  - Risk ratio
  - Odds ratio
  - Hazard ratio

Reporting precision

- Confidence interval
- p-value
- Hypothesis test

要整理條列，不是把圖或表貼進來

範例：

效益 Impact		
結果	治療效果有多大 Paper1 Chen et al. 2017 LNG-IUD vs control 1. Endometrioma recurrence rate at 30 months 25% vs 37.5%, hazard ratio = 0.60 2. dysmenorrhea recurrence rate hazard ratio = 0.32 3. visual analog scale score 39.1±10.9 vs 30.1±14.7 Paper2 Morelli et al. 2013 EP vs LNG-IUD 1. VAS score at 24 months 19.08±0.37 vs 28.98±10.79 2. Recurrence rate at 24 months 12.5 % vs 20.5% Paper 3 Wong et al. 2010 LNG-IUS vs Depot MPA 1. Pain Score (total=6) only 36 months (0.1 vs 0.6) significant differecne, All other visits showed no significant difference 2. recurrence of endometriosis lesion>3cm none of both groups had recurrence	治療效果有多精準 Paper1 Chen et al. 2017 LNG-IUD vs expectant management 1. Endometrioma recurrence at 30 months, HR 95% CI, [0.27, 1.33], P=.209 2. dysmenorrhea recurrence rate 95% CI, [0.12, 0.83], P=.019 3. VAS, 95% CI, [1.9, 16.1], P=.014 Paper2 Morelli et al. 2013 EP vs LNG-IUD 1. VAS score at 24 months, P<0.05 2. Recurrence rate at 24 months, P = 0.30 Paper 3 Wong et al. 2010 LNG-IUS vs Depot MPA 1. Pain Score only 36 months P<0.0025

評讀最終目的在數據

評讀結論決定相信數據的程度

證據等級
(LEVEL OF EVIDENCE)

TCVGH

Oxford Centre for Evidence-Based Medicine 2011 Levels of Evidence

Question	Step 1 (Level 1*)	Step 2 (Level 2*)	Step 3 (Level 3*)	Step 4 (Level 4*)	Step 5 (Level 5)
How common is the problem?	Local and current random sample surveys (or censuses)	Systematic review of surveys that allow matching to local circumstances**	Local non-random sample**	Case-series**	n/a
Is this diagnostic or monitoring test accurate? (Diagnosis)	Systematic review of cross sectional studies with consistently applied reference standard and blinding	Individual cross sectional studies with consistently applied reference standard and blinding	Non-consecutive studies, or studies without consistently applied reference standards**	Case-control studies, or "poor or non-independent reference standard**	Mechanism-based reasoning
What will happen if we do not add a therapy? (Prognosis)	Systematic review of inception cohort studies	Inception cohort studies	Cohort study or control arm of randomized trial*	Case-series or case-control studies, or poor quality prognostic cohort study**	n/a
Does this intervention help? (Treatment Benefits)	Systematic review of randomized trials or *n*-of-1 trials	Randomized trial or observational study with dramatic effect	Non-randomized controlled cohort/follow-up study**	Case-series, case-control studies, or historically controlled studies**	Mechanism-based reasoning
What are the COMMON harms? (Treatment Harms)	Systematic review of randomized trials, systematic review of nested case-control studies, *n*-of-1 trial with the patient you are raising the question about, or observational study with dramatic effect	Individual randomized trial or (exceptionally) observational study with dramatic effect	Non-randomized controlled cohort/follow-up study (post-marketing surveillance) provided there are sufficient numbers to rule out a common harm. (For long-term harms the duration of follow-up must be sufficient.)**	Case-series, case-control, or historically controlled studies**	Mechanism-based reasoning
What are the RARE harms? (Treatment Harms)	Systematic review of randomized trials or *n*-of-1 trial	Randomized trial or (exceptionally) observational study with dramatic effect			
Is this (early detection) test worthwhile? (Screening)	Systematic review of randomized trials	Randomized trial	Non -randomized controlled cohort/follow-up study**	Case-series, case-control, or historically controlled studies**	Mechanism-based reasoning

*** Level may be graded down on the basis of study quality, imprecision, indirectness (study PICO does not match questions PICO), because of inconsistency between studies, or because the absolute effect size is very small; Level may be graded up if there is a large or very large effect size.**

**** As always, a systematic review is generally better than an individual study.**

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