實證醫學培育基礎講習(北區)

教育主題：臨床教師培育專業課程

主辦單位：中華民國醫事放射學會、新北市醫事放射師公會、衛生福利部雙和醫院

上課時間：民國 105 年 4 月 17 日(星期日)

上課地點：衛生福利部雙和醫院

実證醫學之開課須知及教學技巧介紹

如何將EBM運用於實際臨床教學-EBM診斷型及治療型問題

衛生福利部雙和醫院
影像醫學部

蘇逸欣 組長

2016.04.17

IRS測試題

請問這部韓劇的名稱為？

(1) 太陽花
(2) 太陽的後裔
(3) 美麗人生
(4) 甘味人生

請問您有看過此部韓劇嗎？

(1) 有
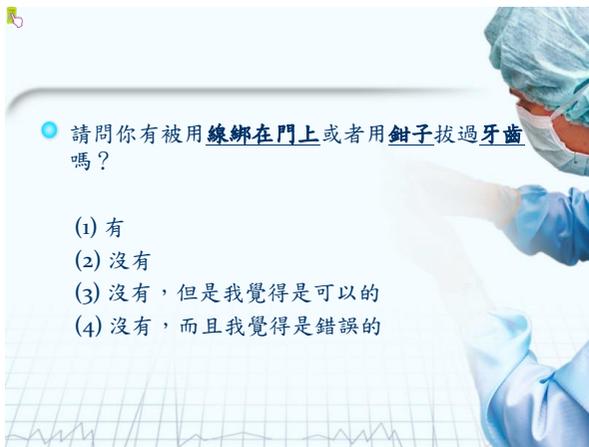(2) 沒有

請問看過此部韓劇的第15集您覺得有催淚嗎？

(1) 有
(2) 沒有

IRS練習題

請問你有用**牙膏**或**醬油**處理過**燙傷的傷口**嗎？

(1) 有
(2) 沒有
(3) 沒有，但是我覺得是可以的
(4) 沒有，而且我覺得是錯誤的

請問你**牙痛**時有用**正露丸**塞過牙齒嗎？

(1) 有
(2) 沒有
(3) 沒有，但是我覺得是可以的
(4) 沒有，而且我覺得是錯誤的

請問你有被用**線綁在門上**或者用**鉗子**拔過**牙齒**嗎？
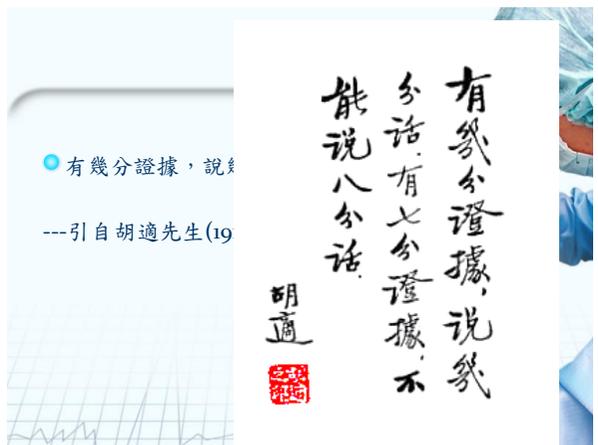
(1) 有
(2) 沒有
(3) 沒有，但是我覺得是可以的
(4) 沒有，而且我覺得是錯誤的

請問你認為**癲癇**發作時需要使患者嘴巴**咬住物品**嗎？

(1) 需要
(2) 不需要

請問你認為做完**腰椎穿刺後**，需要**平躺6小時**休息以**避免頭痛**嗎嗎？

(1) 需要
(2) 不需要

有幾分證據，說幾

---引自胡適先生(19

有幾分證據，說幾
分話，有七分證據，不
能說八分話。

胡適

Outline

- 什麼是EBM?
- 流行病學簡介
- EBM五步驟

什麼是EBM?

- 請問什麼是EBM的縮寫？

  (1) Ebay, baby boss, MM chocolate
  (2) Evidence-based medicine
  (3) Emome,bb TV,Momo cartoons
  (4) Esophagus burn medicine

什麼是EBM?

- EBM：

  實證醫學 (EBM, Evidence-based medicine)
  是以流行病學和統計學的方法，從龐大的醫
  學資料庫中嚴格評讀、綜合分析找出值得信
  賴的部分，並將所能獲得的最佳文獻證據，
  應用於臨床工作中，使病人獲得最佳的照顧。

  Fieldm & Lohrm研究報告發現醫師每天所作的決策：
  ·4%是有強而有力的臨床研究證據所支持
  ·45%是有謹慎的臨床研究證據，且醫師間有一定程度的共識
  ·51%不但缺乏有力的證據支持，在醫師間亦無共識，屬灰色地帶

什麼是EBM?

- EBM：

  西元1972年，英國臨床流行病學者Archie
  Cochrane提出「謹慎地、明確地、小心地採
  用目前最佳的證據，作為照顧病人臨床決策
  的參考」。
  〔Conscientious, explicit, and judicious use of
  current best evidence in making decisions
  about individual patients. ~ Archie Cochrane
  1972〕

什麼是EBM?

- EBM：
- 實證醫學"此一名詞自1992年加拿大McMaster
  大學Gordon Guyatt教授所領導的小組正式命名
  後，1992英國國家衛生部成立實證醫學中心，以
  Archie Cochrane之名命名，並由David L.
  Sackett擔任實證醫學中心主任，進而促成1993年
  Cochrane Collaboration的設立。

  Dave Sackett

什麼是EBM?

- EBM：
- 目前世界各地有13個國家、15個實證醫學中心
  〔Cochrane Center〕在積極推動這個工作，其
  目標是從龐大的醫學資料庫中嚴格過濾、評讀這
  些文獻，並做系統性文獻回顧及綜合分析，以方
  便應用於臨床工作中，作為照護病患的依據。

什麼是EBM?

EBM：

什麼是EBM?

EBM：

56歲男性病人突然急性腹痛及背痛至急診就醫，做了KUB攝影發現左腎隱約有結石，因為影像不清楚因此又開立了IVP檢查，病人至影像醫學科檢查時問了問題：我從報導中得知低劑量電腦斷層也可以健查出泌尿道結石，請問低劑量電腦斷層與IVP檢查有什麼差異以及他們的準確度為何？

什麼是EBM?

請問你要用什麼關鍵字來搜尋？

(1) 食尚玩家, 浩角翔起
(2) 腎結石, KUB
(3) 腎結石, IVP, 低劑量電腦斷層
(4) 蘭陵王, 陳曉東

什麼是EBM?

EBM：

Renal colic: A prospective evaluation of non-enhanced spiral CT versus intravenous pyelography.

Conclusions:
Non-enhanced spiral CT provided **greater diagnostic utility** in this randomized comparison but **no difference** in measured **outcomes.**

Mendelson, R. M. (2003) et al. Journal of Medial Image and Radiation

Outline

什麼是EBM?

流行病學簡介

EBM五步驟

流行病學簡介

流行病學（epidemiology）是研究特定人群中疾病、健康狀況的分布及其決定因素，並研究防治疾病及促進健康的策略和措施的科學。搜尋證據 (Evidence search)

流行病學的定義和特徵。描述分布的常用測量指標(發病率、罹患率、患病率、死亡率、病死率)的意義、用途與計算方法。描述疾病流行強度的常用語：爆發、流行和大流行；疾病的分布的概念及主要內容。

什麼是EBM?

- 請問霍亂病毒主要感染途徑為?

  (1) 眼神接觸以及四目交接
  (2) 主要由飲水所傳染,污染來自嘔吐物或糞便,
       食物傳染但較少見
  (3) 血液
  (4) 接吻

流行病學簡介

John Snow與霍亂的大事記

- 流行病學發展的中心人物當屬John Snow(1813－1858)這個人。他是一位臨床麻醉科醫師,但也是早期少數清楚瞭解到一個醫生的工作應該要超乎治療疾病的人之一。
- 透過一系列的觀察與研究,Snow發現1854年倫敦地區的霍亂流行是由飲用水受到人類糞便污染而引發的。

流行病學簡介

John Snow與霍亂的大事記

- 這項發現比微生物學家發現霍亂弧菌(Vibrio cholerae)的時間早32年;也比Pasteur於1865年證明微生物會造成疾病流行的觀察早了10年。

- 1854年英倫敦地區爆發霍亂流行,當時倫敦的飲水是由數家私人水公司經營。

流行病學簡介

John Snow與霍亂的大事記

- Snow分析了所有霍亂死亡個案的飲水來源後發現飲用Southwark & Vauxhall這家公司供水的人有較高的死亡率。
- 當數據顯示Southwark & Vauxhall公司所供應的家戶其霍亂死亡率是其他公司的5至10倍後,他開始懷疑霍亂流行是與Southwark & Vauxhall公司所供應的水有關。

流行病學簡介

John Snow與霍亂的大事記

- Snow正確的使用「比率」描述疾病在族群中分佈的情形是他能夠始終在正確方向上的重要因素。他接著仔細觀察Southwark & Vauxhall公司供水的來源,它發現Southwark & Vauxhall公司的水源位於河川的下游,河川上游並有人類糞便的排泄。

流行病學簡介

John Snow與霍亂的大事記

- 當Snow有了這些觀察後,他接續進行了幾個流行病學研究過程中很重要的步驟。
- 當他將霍亂病例按居住地區繪於地圖上時,他發現個案有「聚集」於Broadway Street上取水站的現象,而這也更另他相信霍亂的發生與水有關。
- 透過人時地的描述嘗試發現聚集(clustering)現象是描述性流行病學研究的核心工作。

流行病學簡介

John Snow與霍亂的大事記

- Snow的這項觀察實際上是融入了現代科學研究中**對照組（control group）**的概念，也使用了現代流行病學研究中經常使用的**假說演繹**的推論（hypothetico-deductive reasoning）。

流行病學簡介

John Snow與霍亂的大事記

- 雖然當時的生物學知識與技術並無法提供進一步的驗證支持Snow的發現，但當倫敦衛生當局於1854年9月8日將Broadway Street取水站的壓水手把**移除**後，霍亂死亡個案數隨即**急速減少**，到9月20日以後每日報告的死亡數便與9月1日暴發流行之前一樣。

流行病學簡介

John Snow與霍亂的大事記

流行病學簡介

近代流行病學
- 社區**飲水加氟**的試驗提供了能夠**預防齲齒**的氟濃度。
- **沙克疫苗**的臨床試驗證據提供了人類消滅**小兒麻痺**的利器。
- Framingham Heart Study讓人類更加瞭解**心血管疾病**的病因與預防之道。
- **吸菸**與**肺癌**及其他健康效應的研究。
- **長崎廣島原子彈爆炸存活者的追蹤研究**都讓人類更加瞭解環境與健康的互動。

Outline

- 什麼是EBM?

- 流行病學簡介

- EBM五步驟

什麼是EBM?

- EBM五步驟：

- 提出問題 (Question formulation)
- 搜尋證據 (Evidence search)
- 嚴格判讀 (Critical appraisal)
- 恰當運用 (Evidence application)
- 評估結果 (Outcome evaluation)

EBM五步驟

EBM五步驟：
- 提出問題 (Question formulation)
- 搜尋證據 (Evidence search)
- 嚴格判讀 (Critical appraisal)
- 恰當運用 (Evidence application)
- 評估結果 (Outcome evaluation)

- 提出問題 (Question formulation)

How Questions Works
Find / Focus / Search

EBM五步驟

EBM五步驟：
- 提出問題 (Question formulation)
- 搜尋證據 (Evidence search)
- 嚴格判讀 (Critical appraisal)
- 恰當運用 (Evidence application)
- 評估結果 (Outcome evaluation)

- 提出問題 (Question formulation)

Foreground
Background
Novice ⟶ Expert

EBM五步驟

EBM五步驟：
- 提出問題 (Question formulation)
- 搜尋證據 (Evidence search)
- 嚴格判讀 (Critical appraisal)
- 恰當運用 (Evidence application)
- 評估結果 (Outcome evaluation)

- 提出問題 (Question formulation)

背景問題 (**Background questions**)：5W1H

意指與疾病相關的知識性問題，問題的結構通常包括 (who、what、where、when、how、why)。

Who ：病患特性、危險因子等
What ：自然病程、症狀學等
Where ：影響的器官與系統、疾病分佈的區域等
When ：疾病好發的年齡、時間、季節等
How ：病理生理學
Why ：病因

Foreground / Background / Novice ⟶ Expert

EBM五步驟

EBM五步驟：
- 提出問題 (Question formulation)
- 搜尋證據 (Evidence search)
- 嚴格判讀 (Critical appraisal)
- 恰當運用 (Evidence application)
- 評估結果 (Outcome evaluation)

- 提出問題 (Question formulation)

背景問題 (**Background questions**)：
案例:急性心肌梗塞

Who ：老年人、男性、家族史
What ：胸痛、心電圖的變化等等
Where ：冠狀動脈阻塞的位置、程度等等
When ：氣溫低、心肌耗氧量高之活動等
How ：動脈硬化斑塊破裂、血栓形成
Why ：動脈硬化危險因子、糖尿病、高血壓、高血脂症、抽菸,肥胖,少運動

Foreground / Background / Novice ⟶ Expert

EBM五步驟

EBM五步驟：
- 提出問題 (Question formulation)
- 搜尋證據 (Evidence search)
- 嚴格判讀 (Critical appraisal)
- 恰當運用 (Evidence application)
- 評估結果 (Outcome evaluation)

- 提出問題 (Question formulation)

前景問題 (**Foreground questions**)：
指與治療病患相關的特殊性問題，通常包括有6個項目：

Therapy/Prevention：評估不同治療方式…
Harm/Etiology：評估會造成的傷害…
Diagnosis (tests)：不同診斷工具的準確度…
Prognosis：評估疾病癒後…

Foreground / Background / Novice ⟶ Expert

EBM五步驟

EBM五步驟：
- 提出問題 (Question formulation)
- 搜尋證據 (Evidence search)
- 嚴格判讀 (Critical appraisal)
- 恰當運用 (Evidence application)
- 評估結果 (Outcome evaluation)

提出問題 (Question formulation)

Therapy/Prevention：
研究治療或預防方法的有效性
例如：服用 "阿斯匹林" 是否可以預防中風？

Harm/Etiology：
研究暴露的危害或疾病的原因
例如：停經婦女使用荷爾蒙治療是否會增加乳癌的機會？

Slide 1

EBM五步驟

- 提出問題 (Question formulation)
- **Diagnosis (tests)**：
  研究檢查方法或臨床表徵對疾病診斷的有效性
  例如：Low dose CT 診斷肺癌的敏感度及特異
  度為何？

- **Prognosis**：
  建立疾病預後的預測模式，例如：利用
  Ranson's criteria 預測急性胰臟炎死亡率為何？

Slide 2

EBM五步驟

- 提出問題 (Question formulation)

Patient	**I**ntervention	**C**omparison	**O**utcome

- P：patient and/or problem(病患)
- I：intervention(處理)
- C：comparison of intervention(對照)
- O：clinical outcome(臨床結果)

Slide 3

EBM五步驟

- 提出問題 (Question formulation)

Patient or Problem	Intervention	Comparison intervention	Outcome
Description of the patient or the target disorder of interest	Could include: •Exposure •Diagnostic test •Prognostic factor •Therapy •Patient perception etc.	Relevant most often when looking at therapy questions	Clinical outcome of interest to you and your patient

Slide 4

EBM五步驟

- 提出問題 (Question formulation)

Patient or Problem	Intervention	Comparison intervention	Outcome
65 year old man with stroke and moderate carotid stenosis	Carotid endarterectomy	Medical therapy	Functional Class

- In a 65 year old man with stroke and moderate carotid stenosis, can carotid endarterectomy improve functional class after stroke compared with medical therapy?

Slide 5

EBM五步驟

- 提出問題 (Question formulation)

陳先生因為有冠狀動脈家族病史，並且最近胸口悶
悶的，因此要做相關檢查，經由自己查詢資料後得
知可以經由心臟電腦斷層或心導管檢查，希望徵詢
你的建議。

Slide 6

什麼是EBM?

- 請問你要用什麼關鍵字來搜尋？

  (1) 豬血糕, 熱狗
  (2) 冠狀動脈疾病, 心臟電腦斷層, 心導管
  (3) 胸口悶, 心臟電腦斷層
  (4) 大腸包小腸, 魯肉飯

Slide 1

EBM五步驟

○ 提出問題 (Question formulation)

Patient 病人	**I**ntervention DSCT	**C**omparison 心導管	**O**utcome 診斷準確率

○ P：patient and/or problem(病患)
○ I：intervention(處理)
○ C：comparison of intervention(對照)
○ O：clinical outcome(臨床結果)

Slide 2

EBM五步驟

○ 搜尋證據 (Evidence search)

■ 關鍵字設定
■ 資料庫選擇
■ 學習各種資料庫的搜尋方法
■ 多練習，熟能生巧

Slide 3

EBM五步驟

○ 搜尋證據 (Evidence search)

	Primary Term	Synonym 1	Synonym 2	
P (		OR	OR	) AND
I (		OR	OR	) AND
C (		OR	OR	) AND
O (		OR	OR	

■ 關鍵字設定
■ 資料庫選擇
■ 學習各種資料庫的搜尋方法
■ 多練習，熟能生巧

Slide 4

EBM五步驟

○ 搜尋證據 (Evidence search)

■ 關鍵字設定
■ 資料庫選擇
■ 學習各種資料庫的搜尋方法
■ 多練習，熟能生巧

Slide 5

■ 多練習，熟能生巧

Slide 6

5S EBM Resources (非關證據強弱!)

Model from: Haynes, R. B. (2006). Of studies, syntheses, synopses, summaries, and systems: the "5S" evolution of information services for evidence-based health care decisions. ACP Journal Club, 145(3), A8.

什麼是EBM?

- 請問你會從哪一個層級開始搜尋？

  (1) Studies
  (2) Syntheses
  (3) Synopses
  (4) Summaries

EBM五步驟

- 搜尋證據 (Evidence search)

■ 多練習，熟能生巧

EBM五步驟

- 搜尋證據 (Evidence search)

■ 多練習，熟能生巧

EBM五步驟

- 搜尋證據 (Evidence search)

各種資料庫的搜尋方法

EBM五步驟

- 搜尋證據 (Evidence search)

■ 關鍵字設定
資料庫選擇
學習各種資料庫的搜尋方法
多練習，熟能生巧

EBM五步驟

- 搜尋證據 (Evidence search)

■ 關鍵字設定
資料庫選擇
學習各種資料庫的搜尋方法
多練習，熟能生巧

EBM五步驟

● 搜尋證據 (Evidence search)

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Trip
Liberating the literature

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SEARCH PICO ADVANCED SEARCH

Population:	patient
Intervention:	TAE
Comparison:	surgery
Outcome:	outcome

- 關鍵字設定
- 資料庫選擇
- 學習各種資料庫的搜尋方法
- 多練習，熟能生巧

EBM五步驟

EBM五步驟：
- 提出問題 (Question formulation)
- 搜尋證據 (Evidence search)
- 嚴格判讀 (Critical appraisal)
- 恰當運用 (Evidence application)
- 評估結果 (Outcome evaluation)

Trip
Liberating the literature

SEARCH PICO ADVANCED SEARCH

(patient)(TAE)(surgery)(outcome)

Evidence Images Videos Explorer

284 results for "(patient)(TAE)(surgery)(outcome)", by quality

1. A Trial on SBRT After Incomplete TAE or TACE Versus Exclusive TAE or TACE For Treatment of Inoperable HCC
2. TAE and Surgery in Patients With Peptic Ulcer Bleeding Uncontrolled by Endoscopic Therapy
3. Pulmonary Protective Effects of Remote Ischaemic Preconditioning with Postconditioning in Patients undergoing Cardiac Surgery involving Cardiopulmonary Bypass

Systematic review

- 關鍵字設定
- 資料庫選擇
- 學習各種資料庫的搜尋方法
- 多練習，熟能生巧

EBM五步驟

EBM五步驟：
- 提出問題 (Question formulation)
- 搜尋證據 (Evidence search)
- 嚴格判讀 (Critical appraisal)
- 恰當運用 (Evidence application)

Trip
Liberating the literature

SEARCH PICO ADVANCED SEARCH

(patient)(TAE)(surgery)(outcome)

Evidence Images Videos Explorer

3 results for "(patient)(TAE)(surgery)(outcome)", by quality

1. Use of recombinant activated factor VII in patients without hemophilia: a meta-analysis of randomized control trials
2. Screening for Hepatocellular Cancer in Chronic Liver Disease: A Systematic Review
3. The views of young people in the UK about obesity, body size, shape and

Systematic review

- 關鍵字設定
- 資料庫選擇
- 學習各種資料庫的搜尋方法
- 多練習，熟能生巧

EBM五步驟

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- 評估結果 (Outcome evaluation)

● 搜尋證據 (Evidence search)

QUERI

Screening for Hepatocellular Cancer in Chronic Liver Disease: A Systematic Review

- 關鍵字設定
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EBM五步驟

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- 評估結果 (Outcome evaluation)

● 搜尋證據 (Evidence search)

METHODS

Data sources: Medline, PsycInfo, Cochrane Central Register of Controlled Trials, and Cochrane Database of Systematic Reviews to March 2013; clinical trial registries; reference lists; and technical advisors.

Study Selection: We examined controlled clinical trials and observational studies comparing screening to no screening, and controlled clinical trials comparing different screening intervals. We also examined controlled clinical trials and observational studies comparing one of the following active treatments to conservative treatment in patients with early-stage HCC: transarterial chemoembolization (TACE), partial hepatic resection, orthotopic liver transplant (OLT), radiofrequency ablation (RFA), and sorafenib. Because of the dearth of studies for all treatments other than TACE comparing active to conservative treatments, we evaluated noncomparative observational studies for evidence on harms and long-term survival. The population of interest was patients with chronic liver disease with or without cirrhosis.

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EBM五步驟

EBM五步驟：
- 提出問題 (Question formulation)

Effects of screening on mortality: RCTs

Two trials, both conducted in China, compared the effects of screening to no screening on mortality among participants mainly with hepatitis B. One trial used a cluster-randomized design to assign factories, business, and schools to screening or no screening groups. Screening group participants (n = 9,757) were offered serum AFP testing and ultrasonography every 6 months. The primary outcome of HCC mortality occurred less frequently in the screening group (83.2/100,000 person-years vs 131.5/100,000 person-years; rate ratio 0.63, 95% CI 0.41 – 0.98). However, this trial, carried a high-risk of bias because of several serious methodological limitations that threaten the validity of the results. The second trial used patient-level randomization stratified by township to assign hepatitis B patients to the screening intervention (n = 3,712), which consisted of serial AFP tests followed by ultrasound for high AFP values, or the usual care group (n = 1,869). HCC mortality was similar in both groups (1,138/100,000 person-years vs 1114/100,000 person-years, p = 0.86), as was all-cause mortality (1,843/100,000 person-years vs 1,788/100,000 person-years, p = NS). This trial carried an unclear risk of bias because of poor reporting of randomization and allocation concealment techniques.

Two additional trials compared different ultrasound screening intervals. One unclear risk of bias trial found no survival advantage comparing 4-month to 12-month ultrasound screening intervals in patients with serologic evidence of hepatitis B or C. A trial with low risk-of-bias compared 3-month to 6-month ultrasound screening intervals in 1,278 patients with cirrhosis from alcohol use and/or viral hepatitis and found similar all-cause mortality rates in both groups.

- 學習各種資料庫的搜尋方法
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Slide 1:

EBM五步驟：
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EBM五步驟

Oxford Centre for Evidence-Based Medicine 2011 Levels of Evidence

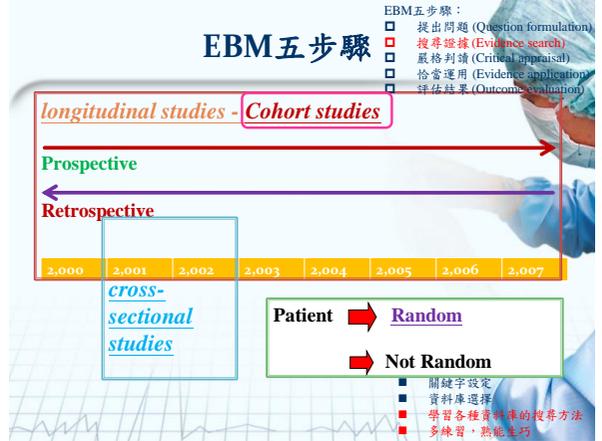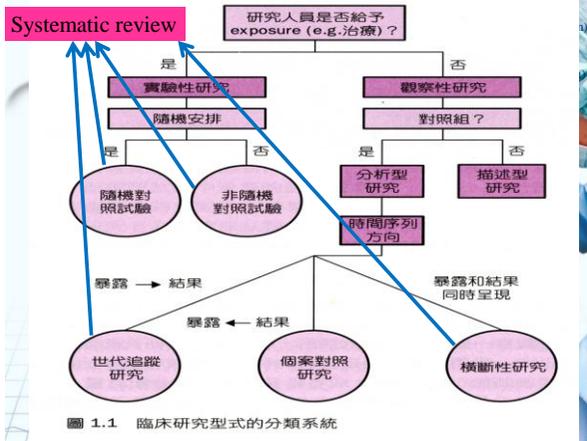| Question	Step 1 (Level 1*)	Step 2 (Level 2*)	Step 3 (Level 3*)	Step 4 (Level 4*)	Step 5 (Level 5)
How common is the problem?	Local and current random sample surveys (or censuses)	Systematic review of surveys that allow matching to local circumstances**	Local non-random sample**	Case-series**	n/a
Is 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 standards**	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

- 關鍵字設定
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Expert

Slide 2:

EBM五步驟：
- 提出問題 (Question formulation)
- 搜尋證據 (Evidence search)
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- 恰當運用 (Evidence application)
- 評估結果 (Outcome evaluation)

EBM五步驟

搜尋證據 (Evidence search)

Systematic review Cohort studies

Treatment Benefits Randomized Case-control study

- 關鍵字設定
- 資料庫選擇
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- 多練習，熟能生巧

Slide 3:

Systematic review

研究人員是否給予 exposure (e.g.治療)？

是 / 否

實驗性研究 / 觀察性研究

隨機安排 / 對照組？

是 / 否 / 是 / 否

隨機對照試驗 / 非隨機對照試驗 / 分析型研究 / 描述型研究

時間序列方向

暴露 → 結果 / 暴露 ← 結果 / 暴露和結果同時呈現

世代追蹤研究 / 個案對照研究 / 橫斷性研究

圖 1.1　臨床研究型式的分類系統

Slide 4:

EBM五步驟：
- 提出問題 (Question formulation)
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- 評估結果 (Outcome evaluation)

EBM五步驟

longitudinal studies - Cohort studies

Prospective

Retrospective

| 2,000 | 2,001 | 2,002 | 2,003 | 2,004 | 2,005 | 2,006 | 2,007 |

cross-sectional studies

Patient → Random

→ Not Random

- 關鍵字設定
- 資料庫選擇
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Slide 5:

EBM五步驟：
- 提出問題 (Question formulation)
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- 恰當運用 (Evidence application)
- 評估結果 (Outcome evaluation)

research design

PubMed.gov
U.S. National Library of Medicine
National Institutes of Health

Search: PubMed   Limits Advanced search Help   Search

Display Settings: Abstract   Send to:

Early Hum Dev. 2011 Mar 10. [Epub ahead of print]

Longitudinal study of smoking cessation before pregnancy and children's cognitive abilities at 56months of age.

Heinonen K, Räikkönen K, Pesonen AK, Andersson S, Kajantie E, Eriksson JG, Wolke D, Lano A.

Institute of Behavioral Science, P.O. Box 9, FI-00014, University of Helsinki, Finland.

Abstract
BACKGROUND: An inverse relationship exists between the rates of maternal smoking during pregnancy and children's cognitive abilities. The effect of maternal cessation of smoking before pregnancy on child's cognitive development is less clear.
AIMS: To study whether maternal cessation of smoking before pregnancy is associated with children's cognitive abilities.
STUDY DESIGN AND SUBJECTS: The original cohort included all 1535 live-born infants admitted to the neonatal wards during 1year and 658 randomly recruited non-admitted infants. The present study sample comprised 1019 (68.2%) children of the original sample born at term and free of any major impairment followed up to 56months.
OUTCOME MEASURES: Child's general reasoning, visual-motor integration, verbal competence, and language comprehension

- 學習各種資料庫的搜尋方法
- 多練習，熟能生巧

Slide 6:

EBM五步驟：
- 提出問題 (Question formulation)
- 搜尋證據 (Evidence search)
- 嚴格判讀 (Critical appraisal)
- 恰當運用 (Evidence application)
- 評估結果 (Outcome evaluation)

research design

PubMed.gov
U.S. National Library of Medicine
National Institutes of Health

Search: PubMed   Limits Advanced search Help   Search

Display Settings: Abstract   Send to:

Eur J Cardiovasc Nurs. 2011 Mar 11. [Epub ahead of print]

The impact of the metabolic syndrome on health-related quality of life: A cross-sectional study in Greece.

Tziallas D, Kastanioti C, Kostapanos MS, Skapinakis P, Elisaf MS, Mavreas V.

Department of Internal Medicine, University of Ioannina, Ioannina, Greece.

Abstract
BACKGROUND: Metabolic syndrome [MetS] is a chronic, progressive and multi-complex health problem that can trigger physical, emotional and psychosocial problems. The aim of this study is to investigate the association between MetS and health-related quality of life (HRQoL) as well as depressive and anxiety disorders.
METHODS: New consecutive patients who attended an outpatient lipid clinic for evaluation for MetS were eligible for inclusion in the study. The MetS was defined according to the new definition of International Diabetes Federation (IDF). The Medical Outcomes Study, Short Form-36 (SF-36) was used to assess HRQoL. Anxiety and depressive symptoms were assessed by a validated Greek version of the Hospital Anxiety and Depression Scale (HADS).

- 多練習，熟能生巧

research design

PubMed.gov
U.S. National Library of Medicine
National Institutes of Health

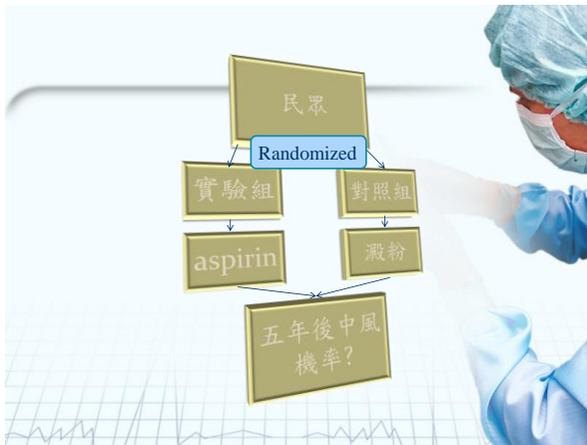Search PubMed ▾   Limits Advanced search Help

Display Settings: ☑ Abstract   Send to: ☑

Osteoarthritis Cartilage. 2011 Mar 8. [Epub ahead of print]
Systematic review of the concurrent and predictive validity of MRI biomarkers in OA.
Hunter DJ, Zhang W, Conaghan PG, Hirko K, Menashe L, Li L, Reichmann WM, Losina E.
Rheumatology Department, Royal North Shore Hospital and Northern Clinical School, University of Sydney, Sydney, NSW Australia; Division of Research, New England Baptist Hospital, Boston MA USA.
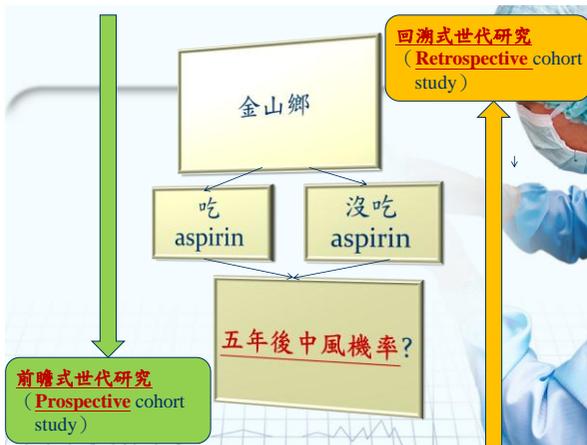
Abstract
OBJECTIVE: To summarize literature on the concurrent and predictive validity of MRI-based measures of osteoarthritis (OA) structural change.
METHODS: An online literature search was conducted of the OVID, EMBASE, CINAHL, PsychInfo and Cochrane databases of articles published up to the time of the search, April 2009. 1,338 abstracts obtained with this search were preliminarily screened for relevance by two reviewers. Of these, 243 were selected for data extraction for this analysis on validity as well as separate reviews on discriminate validity and diagnostic performance. Of these 142 manuscripts included data pertinent to concurrent validity and 61 manuscripts for the predictive validity review. For this analysis we extracted data on criterion (concurrent and predictive) validity from both longitudinal and cross-sectional studies for all synovial joint tissues as it relates to MRI

■ 多練習，熟能生巧

○ 搜尋證據 (Evidence search)
原始研究（Original Study）
■ **隨機對照實驗**（Randomized Control Trial, **RCT**）
給**實驗組**及**對照組**不同的治療，觀察其後果。
例如：實驗組吃**aspirin**，對照組吃**澱粉**，比較兩組**五年後中風的機率**。為目前臨床流行病學中公認**證據力最強**之原始介入性研究設計（primary interventional study）。在此設計中，如果能夠採行**雙盲**對照（double blinded, placebo-controlled）則干擾因素的影響可以進一步減少

民眾
Randomized
實驗組　　對照組
aspirin　　澱粉
五年後中風機率？

○ 搜尋證據 (Evidence search)
原始研究（Original Study）
■ **世代研究**（**Cohort** Study）
觀察自然暴露/治療方式的影響，長期追蹤其結果。例如：比較金山鄉有吃**aspirin**及沒有吃aspirin 的人，五年後新發中風的機率。提供**比隨機對照試驗**證據力較**次一級**之研究證據，是屬於臨床流行病學中之觀察性研究。針對幾個子群，**由接受暴露因子開始**，一直追蹤到結果。

金山鄉
吃 aspirin　　沒吃 aspirin
五年後中風機率？

回溯式世代研究（**Retrospective** cohort study）

前瞻式世代研究（**Prospective** cohort study）

○ 搜尋證據 (Evidence search)
原始研究（Original Study）
■ **病例對照研究**（**Case Control Study**）
選擇病人組及對照組，研究其暴露/治療的影響。例如：比較500 個有**中風**的個案及500 個**沒有中風**的個案，他們吃 aspirin的比例。這是**流行病學中極重要的研究方式**，雖然它的臨床**證據力**較世代研究為**低**，但可以在**短時間內以少許資金與努力**，就能得到重要的科學發現，是最有效率的研究設計，但也容易受到偏見的影響。

民眾

500個中風病人 | 500個沒有中風病人

吃aspirin比例?

● 搜尋證據 (Evidence search)

原始研究（Original Study）

■ **個案報告**（**Case Report**）

收集**同一臨床特色之病人**，回顧文獻報告加以比較。例如：收集**5位吃aspirin**預防中風結果發生**消化道出血**的病人報告及其臨床特徵，並回顧相關文獻，缺點是**缺乏對照組**，且**證據力也較低**。

5位吃 aspirin (預防中風)

文獻回顧 ← 消化道出血 → 臨床特徵

● 搜尋證據 (Evidence search)

文獻回顧（Review of Literature）

■ **系統性回顧**（**systemic review**）

系統性的文獻回顧，將個人好惡及偏差減至最低。**需引用各種文獻資料庫**，並說明查詢的關鍵字，**有引用文獻的明確標準**，不能依作者喜好選取文獻，通常會使用統計方法（**Meta-Analysis 統合分析**），以解決臨床爭議為目的。

● 搜尋證據 (Evidence search)

文獻回顧（Review of Literature）

■ **非系統性回顧**（**non-systemic review**）

傳統文獻回顧，**容易**有**個人好惡及偏差**。以作者的判斷引用文獻，通常沒有使用特殊的統計方法，以教育臨床醫師為目的。

EBM五步驟：
- 提出問題 (Question formulation)
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- 嚴格判讀 (Critical appraisal)
- 恰當運用 (Evidence application)
- 評估結果 (Outcome evaluation)

EBM五步驟

● 搜尋證據 (Evidence search)

- 關鍵字設定
- 資料庫選擇
- 學習各種資料庫的搜尋方法
- 多練習，熟能生巧

第一張投影片

EBM五步驟：
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- 恰當運用 (Evidence application)
- 評估結果 (Outcome evaluation)

EBM五步驟

○ 搜尋證據 (Evidence search)

■ 請問你個人比較喜歡的可樂是？

(1)可口可樂
(2)百事可樂
(3)他牌可樂

- 關鍵字設定
- 資料庫選擇
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第二張投影片

EBM五步驟：
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EBM五步驟

○ 搜尋證據 (Evidence search)

- 關鍵字設定
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第三張投影片

EBM五步驟：
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- 嚴格判讀 (Critical appraisal)
- 恰當運用 (Evidence application)
- 評估結果 (Outcome evaluation)

EBM五步驟

○ 搜尋證據 (Evidence search)

- 關鍵字設定
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第四張投影片

EBM五步驟：
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- 嚴格判讀 (Critical appraisal)
- 恰當運用 (Evidence application)
- 評估結果 (Outcome evaluation)

EBM五步驟

○ 搜尋證據 (Evidence search)

■ 請問研究結果中試驗者比較喜歡的可樂是？

(1)可口可樂
(2)百事可樂
(3)他牌可樂

- 關鍵字設定
- 資料庫選擇
- 學習各種資料庫的搜尋方法
- 多練習，熟能生巧

第五張投影片

EBM五步驟：
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- 搜尋證據 (Evidence search)
- 嚴格判讀 (Critical appraisal)
- 恰當運用 (Evidence application)
- 評估結果 (Outcome evaluation)

EBM五步驟

○ 搜尋證據 (Evidence search)

- 關鍵字設定
- 資料庫選擇
- 學習各種資料庫的搜尋方法
- 多練習，熟能生巧

第六張投影片

EBM五步驟：
- 提出問題 (Question formulation)
- 搜尋證據 (Evidence search)
- 嚴格判讀 (Critical appraisal)
- 恰當運用 (Evidence application)
- 評估結果 (Outcome evaluation)

EBM五步驟

○ 搜尋證據 (Evidence search)

■ 請問研究結果中試驗者比較喜歡的可樂是？

(1)可口可樂
(2)百事可樂
(3)他牌可樂

- 關鍵字設定
- 資料庫選擇
- 學習各種資料庫的搜尋方法
- 多練習，熟能生巧

Slide 1

EBM五步驟：
- 提出問題 (Question formulation)
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- 嚴格判讀 (Critical appraisal)
- 恰當運用 (Evidence application)
- 評估結果 (Outcome evaluation)

EBM五步驟

- 嚴格判讀 (Critical appraisal)-簡單判讀
- **Oxford** Evidence-Based Medicine Levels-**Level 1-5**

最主要有三個主要步驟，即為**VIP**：

- **V**（Validity/Reliability）效度/信度：文獻研究收集個案方式<u>是否嚴謹</u>，是否具<u>有效度</u>(Validity)？

- **I**（Importance/Impact）重要性、文獻統計方法是否<u>正確</u>，<u>結果是否具有重要性</u>)?

- **P**（Practice/Applicability）臨床適用性。

Slide 2

EBM五步驟：
- 提出問題 (Question formulation)
- 搜尋證據 (Evidence search)
- 嚴格判讀 (Critical appraisal)
- 恰當運用 (Evidence application)
- 評估結果 (Outcome evaluation)

EBM五步驟

V

- 嚴格判讀 (Critical appraisal)
- 文獻個案收集方式是否<u>隨機取樣</u>(Randomization)?

  Randomization、case-control study、case-series
- 個案<u>追蹤成功率</u>是否高?
- 是否進行<u>單盲</u>(Single-blind)或<u>雙盲</u>(Double-blind)測試?
- 研究進行中個案是否經由<u>嚴謹管制</u>?
- 個案是否<u>追蹤遺失</u>?

文獻研究收集個案方式是否嚴謹，是否具有效度(Validity)?
文獻統計方法是否正確，結果是否具有重要性(Importance)?
文獻是否適合應用在您病人身上?

Slide 3

I

EBM五步驟

EBM五步驟：
- 提出問題 (Question formulation)
- 搜尋證據 (Evidence search)
- 嚴格判讀 (Critical appraisal)
- 恰當運用 (Evidence application)
- 評估結果 (Outcome evaluation)

不同的問題利用不同的統計量

Therapy/Prevention	Diagnosis
RRR	Sensitivity
ARR	Specificity
NNT	PPV
Relative risk	NPV
Odds ratio(Case-control study)	LR

文獻研究收集個案方式是否嚴謹，是否具有效度(Validity)?
文獻統計方法是否正確，結果是否具有重要性(Importance)?
文獻是否適合應用在您病人身上?

Slide 4

I

EBM五步驟

EBM五步驟：
- 提出問題 (Question formulation)
- 搜尋證據 (Evidence search)
- 嚴格判讀 (Critical appraisal)
- 恰當運用 (Evidence application)

Diagnostic test	Disease			
	Present(有病)		Absent(沒病)	
Positive	731	a	270	b
Negative	78	c	1500	d
Sensitivity (敏感度)	為<u>有病者</u>診斷結果為<u>陽性</u>的比率=真陽性率=真陽性 / 生病 = a / a+c= 731/809 = 90%			
Specificity (特異性)	為<u>沒病者</u>診斷結果為<u>陰性</u>的比率 d/b+d = 真陰性率=真陰性 / 健康 = d / b+d=1500/1770 = 85%			

文獻統計方法是否正確，結果是否具有重要性(Importance)?
文獻是否適合應用在您病人身上?

Slide 5

I

EBM五步驟

EBM五步驟：
- 提出問題 (Question formulation)
- 搜尋證據 (Evidence search)
- 嚴格判讀 (Critical appraisal)
- 恰當運用 (Evidence application)

Diagnostic test	Disease			
	Present(有病)		Absent(沒病)	
Positive	731	a	270	b
Negative	78	c	1500	d
Positive Predictive Value, PPV (陽性預測值)	診斷試驗結果呈現<u>陽性且確實有病者</u>的比率=真陽性 / 陽性試驗結果 = a / a+b= 731/1001 = 73%			
Negative Predictive Value, NPV (陰性預測值)	診斷試驗結果呈陰性且確實無患病者的比率=真陰性 / 陰性試驗結果 = d / c+d = 1500/1578 = 95%			

文獻研究收集個案方式是否嚴謹，是否具有效度(Validity)?
文獻統計方法是否正確，結果是否具有重要性(Importance)?
文獻是否適合應用在您病人身上?

Slide 6

I

EBM五步驟

EBM五步驟：
- 提出問題 (Question formulation)
- 搜尋證據 (Evidence search)
- 嚴格判讀 (Critical appraisal)
- 恰當運用 (Evidence application)

Diagnostic test	Disease			
	Present(有病)		Absent(沒病)	
Positive	731	a	270	b
Negative	78	c	1500	d
prevalence	a+c/a+b+c+d= 31%			
Likelihood Ratios (相似比)	分子：疾病中診斷試驗(陽性或陰性)比率 分母：無疾病中診斷試驗(陽性或陰性)比率			
LR(+)	**真陽性率 / 假陽性率**=Sensitivity / (1-Specificity) = (a/a+c) / (b/b+d) = 90%/15% = 6			
LR(-)	**假陰性率 / 真陰性率**=(1-Sensitivity) / Specificity = (c/a+c) / (d/b+d) = 10%/85% = 0.12			

文獻是否適合應用在您病人身上?

Slide 1

I

EBM五步驟

EBM五步驟：
☐ 提出問題 (Question formulation)
☐ 搜尋證據 (Evidence search)
☐ 嚴格判讀 (Critical appraisal)

Treatment	Event	
	Positive	Negative
experimental-(RCT 或 Cohort studies)	A = 1	B = 29
control-(RCT 或 Cohort studies)	C = 9	D = 21
實驗組事件發生率 (EER, Experimental Event Rrate)	a/a+b = 0.033	
對照組事件發生率 (CER, Control Event Rate)	c/c+d = 0.30	
相對風險比率差 (RRR, Relative Risk Reduction)	|EER – CER| / CER 接受治療組比未接受治療的對照組間，不良結果機率下降之比例,伴隨95%信賴區間(CI)	

■ 文獻研究收集個案方式是否嚴謹，是否具有效度(Validity)?
■ 文獻統計方法是否正確，結果是否具有重要性(Importance)?
■ 文獻是否適合應用在您病人身上?

Slide 2

I

EBM五步驟

EBM五步驟：
☐ 提出問題 (Question formulation)
☐ 搜尋證據 (Evidence search)
☐ 嚴格判讀 (Critical appraisal)

Treatment	Event	
	Positive	Negative
experimental-(RCT 或 Cohort studies)	A = 1	B = 29
control-(RCT 或 Cohort studies)	C = 9	D = 21
絕對風險比率差 (ARR, Absolute Risk Reduction)	|EER – CER| = |0.033– 0.3|=0.267 治療組與對照組間不良結果機率差的絕對值,伴隨95%信賴區間(CI)	
需要被治療的病人數目 (NNT, Number Needed to Treat)	1/ARR = 1/0.267 =3.75 ，為減少一個不良結果所需治療4病人, 伴隨95%信賴區間(CI)	

■ 文獻研究收集個案方式是否嚴謹，是否具有效度(Validity)?
■ 文獻統計方法是否正確，結果是否具有重要性(Importance)?
■ 文獻是否適合應用在您病人身上?

Slide 3

I

EBM五步驟

EBM五步驟：
☐ 提出問題 (Question formulation)
☐ 搜尋證據 (Evidence search)
☐ 嚴格判讀 (Critical appraisal)

Treatment	Event	
	Positive	Negative
experimental-(RCT 或 Cohort studies)	A = 1	B = 29
control-(RCT 或 Cohort studies)	C = 9	D = 21
Relative risk(RR) -相對危險比	EER/CER = (a/a+b)/(c/c+d) = 0.11，用於隨機對照試驗（RCT）與世代研究（cohort study）	

■ 文獻研究收集個案方式是否嚴謹，是否具有效度(Validity)?
■ 文獻統計方法是否正確，結果是否具有重要性(Importance)?
■ 文獻是否適合應用在您病人身上?

Slide 4

I

EBM五步驟

EBM五步驟：
☐ 提出問題 (Question formulation)
☐ 搜尋證據 (Evidence search)
☐ 嚴格判讀 (Critical appraisal)

Treatment	Event	
	Positive	Negative
Exposed(Case-control study)	A = 1	B = 29
Not exposed (Case-control study)	C = 9	D = 21
Experimental event Odds	a/b = 0.034	
Control event Odds	c/d = 0.43	
Odds ratio-勝算比	(a/b)/(c/d) = ad/bc = 0.08，通常被使用於個案對照研究之中。為試驗組中發生結果的勝算（Odds）與對照組中發生結果的勝算，此兩者間的比值就稱為勝算比（OR）	

■ 文獻研究收集個案方式是否嚴謹，是否具有效度(Validity)?
■ 文獻統計方法是否正確，結果是否具有重要性(Importance)?
■ 文獻是否適合應用在您病人身上?

Slide 5

I

EBM五步驟

EBM五步驟：
☐ 提出問題 (Question formulation)
☐ 搜尋證據 (Evidence search)
☐ 嚴格判讀 (Critical appraisal)
☐ 恰當運用 (Evidence application)
☐ 評估結果 (Outcome evaluation)

- 嚴格判讀 (Critical appraisal)-有深度判讀-**CASP**
- Systematic reviews之評讀
  - Q1. Did the review ask a clearly-focused question?
  - Q2. Did the review include the right type of study?
  - Q3. Did the reviewers try to identify all relevant studies?

■ 文獻研究收集個案方式是否嚴謹，是否具有效度(Validity)?
■ 文獻統計方法是否正確，結果是否具有重要性(Importance)?
■ 文獻是否適合應用在您病人身上?

Slide 6

I

EBM五步驟

EBM五步驟：
☐ 提出問題 (Question formulation)
☐ 搜尋證據 (Evidence search)
☐ 嚴格判讀 (Critical appraisal)
☐ 恰當運用 (Evidence application)
☐ 評估結果 (Outcome evaluation)

- 嚴格判讀 (Critical appraisal)-有深度判讀
- Systematic reviews之評讀
  - Q4. Did the reviewers assess the quality of the included studies?
  - Q5. If the results of the studies have been combined, was it reasonable to do so?
  - Q6. How are the results presented and what is the main result?
  - Q7. How precise are these results?

■ 文獻研究收集個案方式是否嚴謹，是否具有效度(Validity)?
■ 文獻統計方法是否正確，結果是否具有重要性(Importance)?
■ 文獻是否適合應用在您病人身上?

I **EBM五步驟**

○ 嚴格判讀 (Critical appraisal)-有深度判讀
○ Systematic reviews之評讀
   Q8.Can the results be applied to the local population?
   Q9.Were all important outcomes considered?
   Q10.Should policy or practice change as a result of the evidence contained in this review?

■ 文獻研究收集個案方式是否嚴謹，是否具有效度(Validity)?
■ 文獻統計方法是否正確，結果是否具有重要性(Importance)?
■ 文獻是否適合應用在您病人身上?

P **EBM五步驟**

○ 嚴格判讀 (Critical appraisal)-有深度判讀
○ P（Practice/Applicability）臨床適用性。
   如果我們相信這個研究，它的結果是否可以應用在我們的病患身上？"其中要考量的是病患的差異、可運用的資源以及病患的偏好。在這個部份我們可以考量病患的生物因素（biologic issues）即是"同樣的治療應用在不同的病患族群是否有不同的反應？"

■ 文獻研究收集個案方式是否嚴謹，是否具有效度(Validity)?
■ 文獻統計方法是否正確，結果是否具有重要性(Importance)?
■ 文獻是否適合應用在您病人身上?

EBM五步驟

○ 恰當運用 (Evidence application

■ *Evidence is never enough*
   證據，永遠是不足的
■ Can the results be applied to my patient?
   –有效且重要的證據能實際應用到我照顧的病人身上嗎？
■ *Evidence Applicability* –證據適用性

■ 實際應用到你的病人
■ 將證據"外推"，應用於個案？
■ 個案自己的價值觀與喜好？

EBM五步驟

○ 恰當運用 (Evidence application

■ 病人與研究文獻所收錄的病人，有無明顯差異？
   – 研究族群為60-70歲有效，但是你的病人為40歲
■ 評估病人接受與研究文獻所施行相同的治療（或處置），所得益處（及害處）將有多大？
   –應用到您的個案前，需先藉此修正文獻結果
   –單位或是你自己是否有能力（資源）施行相同的治療（或處置）？執行品質為何？

■ 實際應用到你的病人
■ 將證據"外推"，應用於個案？
■ 個案自己的價值觀與喜好？

EBM五步驟

○ 恰當運用 (Evidence application

■ 是否清楚與個案（及家屬）說明溝通？

■ 個案對治療（或處置）的遵從性？

■ 實際追蹤你的個案的成果（outcome）

■ 實際應用到你的病人
■ 將證據"外推"，應用於個案？
■ 個案自己的價值觀與喜好？

EBM五步驟

○ 評估結果 (Outcome evaluation)

■ Self – Evaluation （自我評估）
   –所遇到的臨床問題是可以回答的嗎？
   –搜尋文獻及評讀證據的速度夠快嗎？
   –這些證據應用在適當的臨床病人嗎
■ Evaluation (Audit) by Expert or peer
   –專家監督或同儕彼此評估

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Thank's for your attention

Evidence-Based Medicine

科別：影像醫學科

報告人：蔡政宏

製作人：蘇逸欣.夏啟皓.鄭安傑.蔡政宏

日期：103.10.18

Outline

☐ **提出問題 (Question formulation)**

☐ 搜尋證據 (Evidence search)

☐ 嚴格判讀 (Critical appraisal)

☐ 恰當運用 (Evidence application)

☐ 評估結果 (Outcome evaluation)

Question formulation

◆ Scenario(臨床情境)

　　臉部外傷病人，因被懷疑zygomatic arch fracture，而執行一般X光檢查，有時因病人某些特殊狀況，如

➡ 嬰幼兒發育未完全　➡ 病人躁動無法配合

➡ 病人佩帶頸圈　➡ 病人無法使頭轉正

造成檢查影像無法完整判斷zygoma有無fracture，在不做CT的情況下，想要知道使用ultrasound診斷的可行性

3

Question formulation

◆ Ask(形成問題)

　　病人被懷疑**zygomatic arch fracture**，是否可使用**ultrasound** 代替一般 X-ray 的檢查，並提供足夠的**診斷準確率**並**減低輻射劑量**？

This is a **diagnostic** problem

4

Question formulation

◆ PICO

P Patient/Problem	R/O zygomatic arch fracture
I Intervention	Ultrasound examination
C Comparison	Routine X-ray examination
O Outcome	Diagnostic accuracy

5

Outline

☐ 提出問題 (Question formulation)

☐ **搜尋證據 (Evidence search)**

☐ 嚴格判讀 (Critical appraisal)

☐ 恰當運用 (Evidence application)

☐ 評估結果 (Outcome evaluation)

Evidence search

◆ Database source(資料庫資源)

PubMed (www.ncbi.nlm.nih.gov/pubmed)

ClinicalKey (https://www.clinicalkey.com/)

7

Evidence search

◆ Search key word(搜尋關鍵字)

➢ diagnosis

➢ sonography

➢ zygomatic arch fracture

8

Evidence search

◆ Search result(搜尋結果)
➢ PubMed search
Key word：
Diagnosis and sonography and zygomatic fracture →17篇
Article Type：
Systematic Reviews → 2篇
Search time：
103.10.10

9

Evidence search

◆ Search result(搜尋結果)
➢ ClinicalKey search
Key word：
Diagnosis , sonography , zygomatic arch fracture → 1965篇
Study Type：
Systematic reviews → 3篇
Search time：
103.10.10

10

Outline

☐ 提出問題 (Question formulation)
☐ 搜尋證據 (Evidence search)
☐ 嚴格判讀 (Critical appraisal)
☐ 恰當運用 (Evidence application)
☐ 評估結果 (Outcome evaluation)

Critical appraisal

◆ Papers appraised(評審文獻)
◎篇名：
A systematic review of the diagnostic role of ultrasonography in maxillofacial fractures

W. L. Adeyemo, O. A. Akadiri: A systematic review of the diagnostic role of ultrasonography in maxillofacial fractures. Int. J. Oral Maxillofac. Surg. 2011; 40: 655–661.

◎文獻等級：
Systematic reviews ＋Randomized controlled trial
→ **Level 1**

12

Critical appraisal

V

◆ **Materials and methods**：

Step 1：

搜尋 systematic reviews(系統性回顧)和 meta-analyse(統合分析)的文獻

Step 2：

運用多種資料庫，以 ultrasound and maxillofacial fractures 的相關關鍵字，運用布林(Boolean)運算子'and'交互搜尋，縮小範圍

13

Critical appraisal

V

◆ **Materials and methods**：

Step 3：手動搜尋滿足兩個條件

1. 運用 CT or conventional radiography or intraoperative findings 等方法跟 ultrasonography 比較

2. 運用 sensitivity and specificity 等統計方法來呈現結果

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Critical appraisal

!

◆ **Summary-Patients**：

→maxillofacial fractures

→midfacial fractures

→**zygomatic complex fractures**

→nasal bone fractures

→orbital fractures

→mandibular fractures

15

Critical appraisal

!

◆ **Summary-Intervention**：

→ultrasound

◆ **Summary-Comparison**：

→CT or conventional radiography

16

Critical appraisal

!

◆ **Summary-Outcome**：

Specificity：100%

Sensitivity：94%

Limits：

→Detailed bony imaging may be precluded in acute situations with **extensive facial oedema**, and **emphysema**

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Critical appraisal

!

◆ **Summary-Conclusion**：

※The use of **diagnostic ultrasonography** in zygomatic arch fractures has been well investigated and it is found **very accurate** in all cases of **displaced arch fractures**.

※Ultrasonography may not be sufficient to diagnose **complex maxillofacial fractures**, such as **multiple or pan facial fractures**, and the use of **CT** in such cases is **obligatory**.

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Outline

- ☐ 提出問題 (Question formulation)
- ☐ 搜尋證據 (Evidence search)
- ☐ 嚴格判讀 (Critical appraisal)
- ☐ **恰當運用 (Evidence application)**
- ☐ 評估結果 (Outcome evaluation)

Evidence application

◆ 回答臨床問題：

　　顴骨弓骨折可以使用超音波診斷，有94%的敏感度和100%的特異度，如果診斷後發現有骨折，幾乎能**確定有骨折**，即可以不進行一般X光的檢查，減少輻射的曝露，但如果發現沒有，卻仍然懷疑有骨折的可能，就建議使用一般X光或電腦斷層檢查來做更進一步的確認。

20

Evidence application

◆ 優缺點：
- •優點：
  1. 可**減少該類病患醫療輻射曝露**，尤其針對**嬰幼兒、懷孕婦女**等，需減低或不可接受輻射曝露之患者
  2. 超音波檢查**時間較短、便利性高**且**成本低**
  3. 對於**躁動病患與繫帶頸圈的頸椎骨折患者**，相較於一般X光檢查，超音波可提供較好的診斷價值

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Evidence application

◆ 優缺點：
- •缺點：
  1. 有**偽陰性**的狀況存在
  2. 只能針對僅顴骨弓骨折的**少數群體**
  3. 超音波影像**解析度較差**
  4. 受操作者的**經驗與技術**影響其成像與診斷
  5. 需壓迫病患傷處，可能造成**病人不適感提升**

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Evidence application

◆ 醫療建議：

　　針對僅懷疑zygomatic arch fracture的病患，可使用ultrasound做為初步的診斷工具，如無法確認，再進行routine X-ray或CT等更高階的檢查，以合理抑低病患醫療輻射劑量，並提高檢查成功率和診斷準確性

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Outline

- ☐ 提出問題 (Question formulation)
- ☐ 搜尋證據 (Evidence search)
- ☐ 嚴格判讀 (Critical appraisal)
- ☐ 恰當運用 (Evidence application)
- ☐ **評估結果 (Outcome evaluation)**

Outcome evaluation

◆ **本篇EBM的自我評估：**

•優點：

1. 列出<u>正確的PICO</u>，訂定良好的<u>搜尋策略</u>，很快的縮減搜尋的結果，並找到需要的文獻
2. 找到符合問題的<u>系統性回顧</u>文獻，作者運用嚴密的篩選，是可評為<u>level 1</u>的文獻內容
3. 文獻運用<u>良好的統計</u>呈現出結果，並給出能回答問題的結論
4. 可以回答臨床問題，並<u>可應用在臨床</u>適當的病人身上

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Outcome evaluation

◆ **本篇EBM的自我評估：**

•缺點：

　　文獻中共有17篇回顧性文章，但只有**其中1篇**的結果可回答此臨床問題，其餘16篇為其它面部骨折部位的統計與結果

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Thanks for your attention

實證醫學-臨床問題討論紀錄單 (EBM)

日期：　　　　　　　　機構：

姓名：　　　　　　　　單位：

職級：□R__ □PGY1 □Intern□放射師□醫檢師

□復健師□心理師□社工師□呼吸治療師

□物理治療師□職能治療師□護理 N__

□藥師 □其他_____

臨床情境：

步驟 1：提出臨床問題：

實證 PICO 問題類型：□治療/預防 □診斷 □危害/病因 □預後 □其他：

P:

I:

C:

O:

步驟 2：搜尋證據：

資料庫資源：□ACP Journal Club □Cochrane □PubMed □UpToDate □其他（請說明）：

搜尋關鍵字及搜尋策略：

文獻：

研究設計：□RCT □Cohort study □Case control study □Case series study □Systematic review □其他（請說明）：

步驟 3：文獻評讀：**VIP**

V:有效性：

(1)□非隨機□隨機（如何達成?）

(2)追蹤完整性?（%）

(3)□非雙盲□盲法（如何達成?）

I:重要性（*P* value, 95% CI, ARR, NNT…）

P:臨床適用性：是否可以應用在我們的病患身上？

證據等級（Level 1~5）：

文獻主要結論：

步驟 4：恰當運用： 您如何將文獻結論應用於您的病人身上？

步驟 5：評估結果：

(1)Self － Evaluation （自我評估）
- – 所遇到的臨床問題是可以回答的嗎？
- – 搜尋文獻及評讀證據的速度夠快嗎？
- – 這些證據應用在適當的臨床病人嗎

(2)Evaluation (Audit) by Expert or peer－專家監督或同儕彼此評估（若無專家監督或同儕彼此評估，則可以不呈現此項目）

搜尋日期：	執行 EBM 者：

實證醫學

尋找*EBM*教學適用教材-
資料庫搜尋與應用

影像醫學科
品管教學組長 陳嘉宏

1

Learning Objectives

To 學習臨床問題轉換「PICO」要領

To 利用Search工具，有效尋找能解決問題的文獻

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引言

- 臨床上面臨的問題有許多不確定性，這種不確定性是以**機率**來表示。

- 機率的估計可以來自個人以往的經驗，免不了有某種程度的**偏差**。

- 沒有任何一位臨床醫師擁有**完全足夠**的臨床經驗，可以辨識大部分慢性病之間細微又長期的互動關係。

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EBM 五大步驟 (5A)

- Asking — 問問題 (可以回答的問題)
- Accessing — 找資料 (可獲得最好的證據資訊)
- Appraising — 分析判斷 (文獻效度與重要性)
- Applying — 臨床應用 (整合四大層面)
- Auditing — 評估成果 (執行EBM的效率)

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PICO & SEARCH

- 1.能分辨**前景**問題與**背景**問題之不同

- 2.能掌握臨床問題之類別

- 3.能提出一個**前景**的臨床問題

- 4.能分析問題的結構

- 5.資料庫 & 基本搜尋技巧

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臨床問題由何而來？ 醫護

- 1.臨床發現(clinical findings)
- 2.病因(etiology)
- 3.疾病的臨床表徵(clinical manifestations of disease)
- 4.鑑別診斷及診斷檢查(DDx & diagnostic test)
- 5.治療(prevention)
- 6.預後(prognosis)
- 7.預防措施(prevention)
- 8.自我進步(self-improvement)

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臨床問題由何而來？ 家屬

- 1.是什麼疾病(differential diagnosis)
- 2.如何檢查(diagnostic tests)
- 3.為什麼會發生(etiology)
- 4.對我會有什麼影響(prognosis)
- 5.如何治療(therapy)
- 6.如何避免(prevention)
- 7.是否會再發生(meaning) 7

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背景問題 VS 前景問題

背景問題	前景問題
• 高血壓用藥有哪幾大類？ • 輻射線對人體的傷害？	• 用正子攝影或細針穿刺，哪一種檢查對甲狀腺腫瘤有較高診斷率

實證醫學是完全著眼在解決前景問題的一套思考邏輯與方法學。

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背景問題 (Background questions)

- 詢問有關疾病的一般知識性問題

A question root (who、what、where、when、how、why)	A disorder or an aspect of disorder

- Background resources：textbook、UpToDate

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前景問題 (Foreground questions)

- 詢問有關處理病人所需特別知識的問題

Ask for specific knowledge about managing patients with a disorder

- 「PICO」helps to formulate the question

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前景問題 (Foreground questions)

包括性質、狀況及疾病的特定性質

P Patient / population / problem

針對病人做何種處置（治療、診斷、觀察）

O Outcome

I Intervention

相對的效果為何(如致病、死亡或併發症)

C Comparison

對上述intervention的方法是否有其他選擇(如placebo)

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前景問題的種類

- 1.診斷 (diagnosis)
- 2.預測 (predict)
- 3.預防 (prevent)
- 4.治療 (therapy)
- 5.併發症
- 6.預後 (prognosis)

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診斷類型

- Q：Does a normal ECG rule out a serious elevation of potassium？

Population	Inspected hyperkalemia
Indicator	Does a normal ECG
Comparator	
Outcome	Rule out hyperkalemia

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預測類型

- Q：戒菸門診病人一年戒菸成功率與性別有無差異？

Population	門診之戒菸病人
Indicator	男性 (或女性)
Comparator	女性 (或男性)
Outcome	戒菸成功率

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預防類型

- Q：對臍帶未脫落的嬰兒，每天用95%酒精塗抹和自然晾乾，肚臍感染率及脫落時間有無差別？

Population	臍帶未脫落的嬰兒
Indicator	每天用95%酒精塗抹臍帶
Comparator	自然晾乾
Outcome	肚臍感染率及脫落時間

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預後類型

- Q：How about the prognosis of Salmonella bacteremia？

Population	Child and salmonella
Ind	背景問題
Com	
Outcome	prognosis

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Learning Objectives

To	學習臨床問題轉換「PICO」要領

To	利用Search工具，有效尋找能解決問題的文獻

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如何蒐尋最佳的臨床證據

- 1.以**PICO**原則提問題
- 2.認識**資料庫**，包括EBM database、各種網路資訊等
- 3.設定**關鍵字**進行資料搜尋(依據問題)
- 4.判斷文獻**證據等級**

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實證醫學資料庫查詢優點

- 1.文獻資料可經由網路快速查詢，最新的醫學進展可立即見於網路，比傳統教科書更update。
- 2.以實證醫學特有的文獻格式，表達資料取得方法及重要結果，不需花很多時間便能了解其要旨。
- 3.利用這些資源，可以節省閱讀大量文獻的時間。

實證醫學=臨床流行病學+醫學資訊學+團隊合作

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5S-Evolution of Information Resources

系統 systems	Computerized decision support system
綜結 Summaries	Evidence based textbooks(UptoDate)
精要 synopses	Evidence based journals (EBM)
統整 syntheses	Systematic review (Cochrane)
研究 studies	Original articles、PubMed

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Searching for the best evidence

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搜尋答案

資料庫		
Uptodate	建議先 search	background
Cochrane Library		2nd database
EBMR		2nd database
PubMed (Clinical Queries)		1st database
Medline		1st database
遠距圖書		本土期刊

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Searching for the best evidence

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UptoDate 資料庫

- 由3,000多位專業醫師執筆撰寫，資料涵蓋6,000多個內科及次專門科主題評論，並涉及家醫科、小兒科及婦產科，提供up-to-date實證醫學及臨床醫療資訊，以協助醫師進行診療上的快速判斷與決策，內容也包含160,000筆醫學摘要、Lexi-Comp 藥物資料庫，以及病人宣傳手冊。

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The Cochrane Library

- The Cochrane Library為一個實證醫學全文型資料庫，製作單位為 The Cochrane Collaboration。其下又分為7個資料庫，由Cochrane專業團體或國際組織對文獻進行系統性評論、控制實驗與生統分析。

  - The Cochrane Database of Systematic Reviews (Cochrane Reviews) - 提供超過1,800種完整的評論 (Reviews)

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Searching for the best evidence

```
            Searching
            evidence
          /          \
   Medical            Internet
   database        search engine
   /      \              \
prefiltered  unfiltered   Google
                          Yahoo
   |            |
UptoDate     PubMed
MDCONSULT    Medline
Cochrane Library
```

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Medline

- 美國國家醫學圖書館NLM 於1964建立了全國性醫學文獻網路其中最重要且發展最早的為 MEDLINE 生物醫學資料庫。
- 收錄自1966 至最新月份的完整MEDLINE 資料庫。
- 即時獲取每月所屬專科最新資料。
- 具超強連結功能，可與全文資料庫及實證醫學資料庫（EBMR）相互搭配使用，立即查到全文資料及臨床實證資訊。

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PubMed

- 收錄年限：西元**1950**年至今
- 更新頻率：週更新
- 出版機構：美國國家醫學圖書館的國家生技資訊中心**(NCBI)** National Center for Biotechnology Information
- 資料類型：醫學期刊文獻、即將出版的醫學論文
- **PubMed Central** 典藏的**full-text**
- 收錄主題：生物醫學、生命科學、生化學、
  行為科學為主；也有收錄資訊科學、
  航太科學等等。

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PubMed與Medline之差異

- PubMed 除MEDLINE的內容外，還包括：

  由出版社以電郵方式提供的引文，其刊登的期刊仍未被選定為MEDLINE索引，故不被歸類為MEDLINE的引文。

  仍未被更新為目前詞彙索引的OLD MEDLINE引文(刊出時間自1948～1965年間，大多沒有摘要，約190萬份)。

  寄到 PubMed Central 內被NLM審核過的某些生命科學期刊的全文文獻。

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實例介紹

使用何種準備方式可以讓胃部CT掃描時具有最佳的擴張效果

比較**發泡劑**與**傳統口服顯影劑**讓胃部在進行電腦斷層掃描時，具有**最佳擴張效果**（腫瘤偵測率）

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臨床問題轉換PICO

UGI
effervescent (gas powder) **I**
gastric (stomach) **P**
carcinoma (tumor)
buscopan
ampulla vater
Duodenal
Contrast (oral) **C**

一般原則是
先放「P」與「I」，
「C」與「O」視搜
尋結果決定

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PubMed使用

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(Slide 33: PubMed search for "effervescent", Results: 1 to 20 of 633)

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(Slide 34: PubMed search for "effervescent gastric", Results: 1 to 20 of 129)

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(Slide 35: PubMed search for "effervescent gastric carcinoma", Results: 8)

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(Slide 36: PubMed search for "effervescent "gastric carcinoma"", Results: 4)*

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Slide 43 — Google 學術搜尋: "effervescent gastric carcinoma"

Slide 44 — Google 學術搜尋: "effervescent gastric carcinoma buscopan"

Slide 45 — Google 學術搜尋設定

搜尋技巧(2)

OR	尋找包含某特殊字眼或片語的研究。如,「child OR adolescent」會找到包含「child」或「adolescent」的所有文章。
AND	尋找同時包含兩個特殊字眼或片語的研究。如,「child AND adolescent」會找到包含「child」和「adolescent」的所有文章。
NEAR	類似AND 的功能,必須同時包含兩個字,而且這兩個字中間的距離間隔,不能超過五個字。
NOT	排除包含某特殊字眼或片語的研究。如,「child NOT adolescent」表示要找包含「child」一詞、但不包括「adolescent」一詞的所有文章。較少使用。
Limits	可以經由在某些方面加以限制,而找到想要找到的文章。如,日期、語言、及是否提供摘要等。
( )	利用括號組合文字。如,"(child OR adolescent) AND (hearing OR auditory)",會找到包括"child"或"adolescent"以及"hearing"或"auditory"的文章。
*	截斷字;"*"為萬用字元,代表任何字母。如,child*為child 加任何字母,相當於(child OR child's OR children OR childhood)。
[ti]or : ti	尋找標題中有該字眼的研究。如,hearing〔ti〕(in PubMed)及hearing:ti (in Cochrane)會找到標題中有hearing 這個字的研究。
[so]or : so	尋找特定來源的研究,如,hearing AND BMJ〔so〕會找到BMJ 中與hearing 有關的研究。
MeSH	MeSH 為Medical Subject Headings 的縮寫,是關鍵字的特殊語彙,通常用在PubMed 或Cochrane。同時使用MeSH 及內文(text words),經常會很有用。

Slide 46

搜尋工具介紹

* **MeSH Database**:
  可幫助找到需要的MeSH詞彙來連接作
  PubMed的文章搜尋。

* **Clinical Queries**:
  為一預先建構的搜尋工具,能幫助你縮少搜尋
  範圍在與臨床有關的文章上。

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Slide 47

控制字彙之檢索:MeSH

醫學圖書館標題表(Medical Subject Headings)

* 是 NLM 針對生物醫學資料所整理出的主題詞彙。對同一概念採用固定的詞彙表達方式,以達到控制詞彙目的,方便生物醫學領域的學者或從業人員彼此間的溝通,更可用以陳述資料內容的主題意涵並提供檢索。

* 它的制定可協助做為主題編目選用標目之依據,以為讀者查檢館藏目錄時的檢索點之一。 美國醫學標題表的內容分成兩個部分:字母順序標題表及樹狀結構標題表。

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Slide 55

PubMed Clinical Queries

Results of searches on this page are limited to specific clinical research areas. For comprehensive searches, use PubMed directly.

effervescent (gastric or carcinoma)　　　Search

Clinical Study Categories
Category: Diagnosis
Scope: Narrow

Results: 1 of 1
Multidetector CT and virtual endoscopy in the evaluation of the esophagus.
Mazzeo S, Caramella D, Gennai A, Giusti P, Neri E, Melai L, Cappelli C, Bertini R, Caprio A, Rossi M, et al.
Abdom Imaging. 2004 Jan-Feb; 29(1):2-8.
See all (7)

This column displays citations filtered to a specific clinical study category and scope. These search filters were developed by Haynes RB et al. See more filter information.

Systematic Reviews

Results: 0 of 0

This column displays citations for systematic reviews, meta-analyses, reviews of clinical trials, evidence-based medicine, consensus development conferences, and guidelines. See filter information or additional related sources.

Medical Genetics
Topic: All

Results: 0 of 0

This column displays citations pertaining to topics in medical genetics. See more filter information.

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Slide 56 — 檢索策略

- 找到關鍵字(keyword) **PICO**
- 判斷問題類型 –
  etiology、diagnosis、therapy、prognosis
- 使用布林邏輯 –
  and、or、not …
- 快速查詢較高證據文獻 –
  Clinical Queries

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Slide 57 — Troubleshooting

Too many reference	Too few reference
Use *specific* MeSH term	Use *broader* term
Use *limit*	Use "*OR*" with other term
Restrict *ti* only	*Combine* MeSH and Text word searching
Selective specific *subheading*	Select "*include all subheading*"
Add terms and use "*AND*"	on MeSH term

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Slide 58

Thanks for your Attention

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Slide 1
Evidence-Based Medicine

醫用輻射線，胎兒的天敵？

影像醫學科
品管教學組長 陳嘉宏

Slide 2
臨床情境

前幾天照X光，現在又照，會不會對身體有影響？

常常照，會不會得到癌症？

小朋友這麼小，照X光不會有問題嗎？

照完X光，需要吃什麼東西補充營養嗎？

圖片來源:health.oeeee.com、www.canstockphoto.hk
嘉義基督教醫院

Slide 3
臨床情境

- 一位懷孕八週婦女因急性腹痛到急診室求診，理學及超音波檢查無特殊發現。臨床醫師解釋腹部電腦斷層檢查也可提供其它資訊以幫忙確診，但病人擔心輻射線對胎兒會有不良影響，甚至造成畸形。請您提供病人意見，若接受腹部電腦斷層輻射線會不會導致畸胎？

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Slide 4
認識輻射~ 原子能委員會 http://www.aec.gov.tw/

01.什麼是輻射？

嘉義基督教醫院

Slide 5
認識輻射~

嘉義基督教醫院

Slide 6
認識輻射~

07.游離輻射對健康的影響

嘉義基督教醫院

認識輻射～

一般游離輻射劑量比較圖

註：1 西弗 = 1000 毫西弗

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嘉義基督教醫院

認識輻射～

註：1 西弗 = 1000 毫西弗

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嘉義基督教醫院

EBM 五大步驟 (5A)

- Asking 問問題(可以回答的問題)
- Accessing 找資料(可獲得最好的證據資訊)
- Appraising 分析判斷(文獻效度與重要性)
- Applying 臨床應用(整合四大層面)
- Auditing 評估成果(執行EBM的效率)

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嘉義基督教醫院

前景問題 (Foreground questions)

- 一位**懷孕八週婦女**因急性腹痛到急診室求診，理學及超音波檢查無特殊發現。臨床醫師解釋腹部電腦斷層檢查也可提供其它資訊以幫忙確診，但病人擔心**輻射線**對**胎兒**會有不良影響，甚至造成畸形。請您提供病人意見，若接受**腹部電腦斷層輻射線**會不會導致**畸胎**？

	中文	英文
P	懷孕八週婦女、胎兒	(early) pregnant、fetus
I	腹部電腦斷層檢查	Abdomen CT、radiation
C		background radiation
O	畸胎	teratogenesis、teratogen、teratogenicity

一般原則是先放「P」與「I」，「C」與「O」視搜尋結果決定

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嘉義基督教醫院

UptoDate 資料庫

- 由3,000多位專業醫師執筆撰寫，資料涵蓋6,000多個內科及次專門科主題評論，並涉及家醫科、小兒科及婦產科，提供up-to-date實證醫學及臨床醫療資訊，以協助醫師進行診療上的快速判斷與決策，內容也包含160,000筆醫學摘要、Lexi-Comp 藥物資料庫，以及病人宣傳手冊。

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嘉義基督教醫院

UptoDate 資料庫

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嘉義基督教醫院

UptoDate 資料庫

UpToDate®

Diagnostic imaging procedures during pregnancy   ▾ All Topics   🔍   ▸ Contents

Search Results for **"Diagnostic imaging procedures during pregnancy"**

◉ **All Topics**
○ Adult
○ Pediatric
○ Patient
○ Graphics 🖼

Diagnostic imaging procedures during pregnancy
- Issues by type of diagnostic imaging procedure
- Effects of ionizing radiation on the fetus
- Summary and recommendations
- Fetal exposure from common procedures
- Guidelines
- 🔹 Fetal radiation exposure (Tables)
- 🔹 The developing fetus (Figures)

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UptoDate 資料庫

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UptoDate 資料庫

Estimated average fetal radiation exposure from selected imaging studies performed on the mother during pregnancy

Procedure	Fetal dose (mrad) for an average study
Chest radiograph (PA and lateral)	<1
Abdominal plain film	100 to 300
Intravenous pyelogram	400 to 900
Barium enema	700 to 1600
Cervical spine radiograph	<1
Dorsal spine radiograph	<1
Lumbar spine radiograph	400 to 600
Lumbosacral area	200 to 600
Upper GI series	50 to 400
Hip and femur radiograph	100 to 400
Dental radiograph	0.01
Mammography	Negligible
Cerebral angiography	<10
CT of the chest	30
CT of the abdomen	250
Perfusion lung scan with 99Tc	6 to 12
Ventilation lung scan	1 to 19
Pulmonary angiography via femoral route	221 to 374
Pulmonary angiography via brachial route	<50

PA: posterior-anterior; GI: gastrointestinal; CT: computed tomography; 99Tc: technitium-99.

Data from: Bentur Y. Ionizing and nonionizing radiation in pregnancy. In: Maternal-fetal toxicology, 2nd ed, Koren G (Ed), Marcel Dekker, New York, 1994, p.515, and Guidelines on diagnosis and management of acute pulmonary embolism. Task Force on Pulmonary Embolism, European Society of Cardiology. Eur Heart J 2000; 21:1301.

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UptoDate 資料庫

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The Cochrane Library

- The Cochrane Library為一個實證醫學全文型資料庫，製作單位為 The Cochrane Collaboration。其下又分為7個資料庫，由Cochrane專業團體或國際組織對文獻進行系統性評論、控制實驗與生統分析。

  - The Cochrane Database of Systematic Reviews (Cochrane Reviews) - 提供超過1,800種完整的評論(Reviews)

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Cochrane Search

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Cochrane Search

Search	Query	Items found
#7	#5 and #6	4
#6	Teratogen*	124
#5	(#1 or #2) and (#3 or #4)	1001
#4	CT [ti,ab,kw]	35338
#3	radiation [ti,ab,kw]	9874
#2	fetus [ti,ab,kw]	1947
#1	Pregnan* [ti,ab,kw]	26181

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Cochrane Search

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PubMed Search

Search	Query	Items found
#4	#3 and free full text[sb]	21
#3	#2 and ("last 10 years" [PDat] and humans[Mesh])	127
#2	#1 and Teratogen*	572
#1	(Pregnan* or fetus) and (radiation or CT)	17704

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PubMed Search

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決定問題的型態

- 治療或預防
  - 服用阿斯匹林是否可以預防中風？
- 傷害或病因
  - 停經婦女使用荷爾蒙治療是否會增加乳癌的機率？
- 診斷
  - McBurney's sign診斷急性盲腸炎的敏感性及特異性為何？
- 預後
  - 利用 Ranson's criteria 預測急性胰臟炎死亡率為何？

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依問題的型態決定研究設計

Type of question	Suggested best type of study
Therapy	RCT > Cohort > Case Control > Case Series
Diagnosis	Prospective, blind comparison to gold standard
Etiology/Harm	RCT > Cohort > Case Control > Case Series
Prognosis	Cohort Study > Case Control > Case Series
Prevention	RCT > Cohort Study > Case Control > Case Series
Clinical Exam	Prospective, blind comparison to gold standard
Cost analysis	economic analysis

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低

證據等級高低

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低

Oxford Centre for Evidence-Based Medicine 2011 Levels of Evidence

OCEBM Levels of Evidence Working Group*. "The Oxford 20...

不要忘記研究倫理道德

- 此研究問題不適合用前瞻性的研究設計，較適合用回溯性的研究設計。
  - Case control, case series, case report

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回溯性的文獻：以此篇為例

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其摘要 (1)

- For the first time, dose estimates have been related to small head circumference induced by exposure in utero to the atomic bomb.
- There was a progressive increase with dose in the frequency of the abnormality among persons whose mothers were exposed before the eighteenth week of pregnancy.

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其摘要 (2)

- In Hiroshima the minimum dose-producing effect was 10-19 rad, but in Nagasaki no effect was observed under 150 rad.
- At maternal doses of 150 rad or more in both cities, small head circumference was often accompanied by mental retardation.
- The observations at low doses in Hiroshima are not directly applicable to medical radiology because of the possible influence of neutrons (nil in Nagasaki) and perhaps to interactions with other environmental disturbances, more widespread in Hiroshima than in Nagasaki.

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結論

- 含輻射線之診斷檢查需依ALARA (As Low As Reasonably Achievable)的原則。
- 游離輻射效應分為stochastic effect及 deterministic effect。
- 容易因游離輻射產生畸胎的孕期約為2-20週，懷孕8週是位於游離輻射易感期內。
- 標準的腹部電腦斷層檢查對胎兒的劑量約為1-4.6 rad，以 deterministic effect來說，未達致畸胎閾值(5 rad)。以stochastic effect來說，雖然機率很低，仍無法完全排除致畸胎可能。

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結論

- 在理學檢查或超音波仍無法對腹部急症的懷孕婦女有初步的診斷或排除嚴重或致死性疾病時，電腦斷層檢查對媽媽來說，還是一個必須要考慮的選項。
- 因為倫理道德考量，不應該做有關游離輻射效應的人體試驗和研究。因此搜尋後所找到的文獻，其證據等級不會太高。在研究方法的限制之下，只能根據目前有限的證據和強度，對病患和家屬據實以告，協助他們做最適合的決定。

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Evidence-Based Medicine

Speaker：Yu-Xuan Lin

Date：2016.04.17

進撃のEBM

attack on EBM

Two fundamental questions…

- What is the purpose of medicine?
- How do I decide what to do?

You have to know where you're going before deciding how to get there…

What is the purpose of medicine?

- Patient care
- Public health
- Research

➤ *Improving the quality of patients' lives…*

What is "Evidence-Based Medicine?"

Evidence based medicine is…

 ➢ Tracking down the best external evidence with which to answer our clinical questions…

Evidence-based medicine is the conscientious explicit and judicious use of current best evidence in making decisions about the care of individual patients.

J Trauma Acute Care Surg. 2013 Dec;75(6):927-35.

引用一位哈佛醫學院院長對畢業生的一段演講：”恭喜各位同學順利畢業，但是我有二個壞消息要告訴大家：第一個是你們現在所學的知識，有三分之一在五年後會變成過時的，甚至是錯誤的；第二個是，到底是哪三分之一，需要靠大家去發現。

Introduction Evidence Based Medicine

☐ Evidence-based medicine is the integration of best research evidence with clinical expertise and patient values. (Sackett et al., 2000)

✓ Evidence-based medicine, EBM
✓ Evidence-based nursing, EBN
✓ Evidence-based Health Care, EBHC
✓ Evidence-based ?, EB?

Best research evidences

EBM

Clinical expertise

Patient expectations

The core mechanisms in EBM include the following four steps

➢ Formulate a clear clinical question from a patient's problem.
➢ Search the literature for relevant clinical articles.
➢ Evaluate (critically appraise) the evidence for its validity and usefulness.
➢ Implement useful findings in clinical practice.

The core mechanisms in EBM include the following four steps

- **Formulate a clear clinical question from a patient's problem.**
- Search the literature for relevant clinical articles.
- Evaluate (critically appraise) the evidence for its validity and usefulness.
- Implement useful findings in clinical practice.

How to ask clinical question you can answer ?

P.I.C.O. Model for Clinical Questions

P	**P**atient, Population, or Problem	How would I describe a group of patients similar to mine?
I	**I**ntervention, Prognostic Factor, or Exposure	Which main intervention, prognostic factor, or exposure am I considering?
C	**C**omparison or Intervention (if appropriate)	What is the main alternative to compare with the intervention?
O	**O**utcome you would like to measure or achieve	What can I hope to accomplish, measure, improve, or affect?
	What type of question are you asking?	Diagnosis, Etiology/Harm, Therapy, Prognosis, Prevention
	Type of study you want to find	What would be the best study design /methodology?

進撃のEBM
attack on EBM

100年

- 我有一位65歲阿姨最近要去美國看她剛出生沒多久的孫子，這是她第一次坐飛機長途飛行，因此她很緊張，到處詢問長途飛行的注意事項。她找到雜誌上一篇有關的報導，其中有提到穿彈性襪可以預防長途飛行產生腳部靜脈栓塞，因此她打電話問我她要不要買來穿？

101年度院內EBM競賽　　臨床情境2

25歲男性病人，沒有任何過去病史。昨天開始覺得上腹部不舒服，自行服用胃藥後症狀仍沒有緩解，隔天持續性右下腹疼痛、噁心、發燒、沒有食慾，因而到急診求診。血液檢查有白血球增加，會診一般外科醫師後，因高度疑似急性闌尾炎(acute appendicitis)，建議開刀手術治療。

病人請求是否可以進一步做電腦斷層檢查以確診？再則因為一星期後他要結婚，擔心開刀恢復期較長，婚期必須延期，詢問可否不要開刀或用內視鏡開刀以縮短復原期。

如果你(妳)是病人家屬，請問你的建議為何？

2014 年底，台北政壇掀起一陣「柯P旋風」，除了引起大家對醫生能力讚嘆外，也引起大眾對於「自閉症」的關注。蔡小弟，今年六歲，剛上小學，出現一些情況包括不理人，不和人講話等無法和同學相處的情況，課堂上常常只專注於自己有興趣的事物，對老師的教導也常常沒有反應。一開始媽媽以為只是單純的適應不良，後來在老師的協助下，看了兒童心智科的醫師。仔細詢問起來，蔡小弟從小各項能力的發展包括：社交、互動、語言能力發展就比同年齡小孩慢，後來經醫師依據精神疾病診斷與統計手冊第四版（DSM-IV）的定義確診為輕度兒童自閉症（autism spectrum disorder, ASD）。對於蔡小弟的狀況，蔡媽媽相當擔心，想詢問醫師有沒有甚麼方法治療？是否一定要吃藥？哪些藥物有效呢?因為聽說一些治療藥物都有副作用包括姿勢性低血壓、嗜睡、噁心、嘔吐、體重增加…等，所以媽媽不太想讓小孩吃藥。另外，蔡媽媽在網路上找了一些新聞，聽說音樂治療對這類的小孩也有幫忙，想詢問醫師，網路消息可不可信？除了音樂治療以外，她還有甚麼樣的非藥物治療可以選擇?按摩可以嗎？有沒有哪些食物可以幫忙改善孩子的情況?使用這些非藥物治療的方法，對小孩的溝通能力、親子關係、學習成果…等指標效果好不好？有無幫忙?

2015 HQLC Topic

進擊のEBM

The core mechanisms in EBM include the following four steps

➢ Formulate a clear clinical question from a patient's problem.
➢ Search the literature for relevant clinical articles.
➢ Evaluate (critically appraise) the evidence for its validity and usefulness.
➢ Implement useful findings in clinical practice.

Search for the Best Evidence

5S EBM Resources (非關證據強弱!)

1. **Systems** — 連結個別病歷的臨床知識與支援決策系統

Pre-filtered Secondary

2. **Summaries** — 整合證據提供特定臨床問題之概述與建議
ACP PIER
BMJ Clinical Evidence
DynaMed
MDconsult
UpToDate

3. **Synopses** — 對單篇研究或回顧性文獻作摘要評述
ACP Journal Club, Evidence-Based Medicine
(PubMed, Ovid Medline)

4. **Syntheses** — 特定臨床問題的系統性評論文獻
Cochrane Database of Systematic Reviews
Database of Abstracts of Reviews of Effects
(PubMed, Ovid Medline): Systematic Reviews

Primary

5. **Studies** — 原始文獻 original studies
(*PubMed*, Ovid Medline, CINAHL, EMBASE
Cochrane CENTRAL, Google Scholar
CEPS中文電子期刊, 中文期刊篇目索引)

Model from: Haynes, R. B. (2006). Of studies, syntheses, synopses, summaries, and systems: the "5S" evolution of information services for evidence-based health care decisions. ACP Journal Club, 145(3), A8.

Ann Intern Med.2009;151:JC3-2

Search for the Background

説明疾病
好發族群
常見病因與危險因子
目前治療方式

Search for the Best Evidence

Search for the Best Evidence

More than 23,000 medical journals
"the literature"

Ask experts

Smaller journals
Unpublished research

Cochrane

PubMed

MEDLINE

EMBASE™

How to choose the right format for your research?

➢ Here are some tips to help you choose the right format for your research.

    ✓ **Know** that the types of publications are different fields.
      Example :
            -social sciences > Empirical study

    ✓ **Remember** that not all journals publish all types of articles.

    ✓ **Look** at the journal's author guidelines for details about the types of articles accepted.

    ✓ **Speak** to your supervisors or senior colleagues for advice.

Study Type of Evidence Level

Type of question	Suggested best type of study
Therapy	RCT > Cohort > case control > case series
Diagnosis	Prospective, blind comparison to a gold standard
Etiology/Harm	Cohort > case control > case series
Prognosis	Cohort study > case control > case series
Prevention	RCT > Cohort > case control > case series
Clinical Exam	Prospective, blind comparison to a gold standard
Cost	Economic analysis

Definition of Cohort Study

✓ More clearly established temporal sequence between exposure and disease.

Type of review

Type of review articles-Systematic reviews

What authors DO

Identify the issue and determine the question

Write a plan for the review *(protocol)*

Search for studies

Sift and select studies

Extract data from the studies

Assess the quality of the studies

Combine the data *(synthesis or meta-analysis)*

Discuss and conclude overall findings

Systematic Review

Dissemination

✓ Are more structured and rigorous than literature reviews.

✓ Address a clearly formulated question about the literature reviewed.

✓ Include reviews of published studies as well as gray literature (unpublished studies, reports , dissertations, conference papers and abstracts, governmental research, ongoing clinical trails.. .etc.

Definition of Meta-analysis

Meta-analysis is a quantitative approach for systematically combining results of previous research to arrive at conclusions about the body of research.

- Quantitative：numbers
- Systematic：methodical
- Combining：putting together
- Previous research：what's already done
- Conclusions：new knowledge

In a Meta-analysis, each study becomes a subject in the new study. Therefore, the mean of study one becomes the score for subject one and so on.

Meta-analysis

Study 1   Study 2   Study 3   Study 4

Overall Effect Size

進撃のEBM

Narrative reviews, systematic reviews and Meta-Analysis

✓ Narrative Reviews : traditional expert review subjective, no formal rules in selecting studies, no standard statistical methods for combing studies.

✓ Systematic Review : review in which there is a comprehensive search for relevant studies on a specific topic and those identified are then appraised and synthesized according to a predetermined and explicit method.

✓ Meta-Analysis : systematic review that employs statistical methods (a quantitative summary) to combine and summarize the results of several studies.

Definition of Randomized controlled trial

RCT are quantitative, comparative, controlled experiments in which investigators study two or more interventions in a series of individuals who receive them in random order.

Blinding

ITT or PP

BMJ. 2010; 340: c332.

The RCT is one of the simplest and most powerful tools in clinical research.

What is a blinded study?

➢ This approach avoids bias because when people know what they are taking, it might change the way they react.

- In a single blinded study, the patient does not know which arm of the protocol they have been assigned to.

- Double blinded studies are those studies where neither the patient or the research physician know whether the patient is receiving the actual study drug or standard drug.

Illustration: Hans Møller, mollers.dk

What is Bias?

Any trend in the collection, analysis, interpretation, publication or review of data that can lead to conclusions that are systematically different from the truth.   Last, 2001

A process at any state of inference tending to produce results that depart systematically from the true values.   Fletcher et al, 1988

Systematic error in design or conduct of a study.   Szklo et al, 2000

Bias

✓ Selection bias

✓ Performance bias

✓ Attrition bias

✓ Detection bias

Intention to treat (ITT) analysis and Per-protocol (PP) analysis

The core mechanisms in EBM include the following four steps

- Formulate a clear clinical question from a patient's problem.
- Search the literature for relevant clinical articles.
- **Evaluate (critically appraise) the evidence for its validity and usefulness.**
- Implement useful findings in clinical practice.

Critically Appraise the 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.

How to cite the Levels of Evidence Table
OCEBM Levels of Evidence Working Group*. "The Oxford 2011 Levels of Evidence".
Oxford Centre for Evidence-Based Medicine. http://www.cebm.net/index.aspx?o=5653
* OCEBM Table of Evidence Working Group = Jeremy Howick, Iain Chalmers (James Lind Library), Paul Glasziou, Trish Greenhalgh, Carl Heneghan, Alessandro Liberati, Ivan Moschetti, Bob Phillips, Hazel Thornton, Olive Goddard and Mary Hodgkinson

牛津實證醫學中心證據等級表 2011 (翻譯 by EGRD Office)

臨床問題	建議等級 A	建議等級 B		建議等級 C	建議等級 D
	證據等級 1*	證據等級 2*	證據等級 3*	證據等級 4*	證據等級 5*
此臨床問題多常見？	區域及當代隨機樣本的(人口)普查	切合當地環境普查的系統性回顧**	區域性非隨機樣本調查**	系列病例報告**	n/a
診斷或監測工具正確嗎？(診斷)	使用一致的參考(黃金)標準及盲化的斷代研究的系統性回顧	使用一致的參考(黃金)標準及盲化的斷代研究	非連續性研究 或 沒有使用一致的參考(黃金)標準的研究**	病例對照試驗，低品質或 無獨立參考標準的研究**	基於基本原理的推斷
如果不治療會有什麼後果？(預後)	初期(inception)世代研究的系統性回顧	初期(inception)世代研究	世代研究 或 隨機對照研究的控制組**	系列病例報告，病例對照試驗 或 低品質的預後型世代研究**	n/a
這個介入治療有幫助嗎？(治療益處)	隨機對照試驗(RCT) 或隨機序列治療試驗(n-of-1)[a]的系統性回顧	隨機對照試驗 或 有顯著療效的觀察型研究	非隨機控制的世代/追蹤研究**	系列病例報告，病例對照試驗 或 歷史對照試驗**	基於基本原理的推斷
介入治療的常見害處？(治療傷害)	隨機對照試驗(RCT), 巢式病例對照試驗, 隨機序列治療試驗(n-of-1)[a]或 有顯著療效的觀察型研究的系統性回顧	隨機對照試驗 或 有顯著傷害[b]的異常觀察型研究	非隨機控制的世代/追蹤研究 (上市後監測) 提供足夠的樣本數去排除常見之危害 (關於長期危害，需有足夠的追蹤時間)**	系列病例報告，病例對照試驗 或 歷史對照試驗**	基於基本原理的推斷
介入治療的罕見害處？(治療傷害)	隨機對照試驗(RCT) 或隨機序列治療試驗(n-of-1)[a]的系統性回顧	隨機對照試驗 或 有顯著傷害的異常觀察型研究			
值得早期診斷嗎？(篩檢)	隨機對照試驗(RCT)的系統性回顧	隨機對照試驗	非隨機控制的世代/追蹤研究**	系列病例報告，病例對照試驗 或 歷史對照試驗**	基於基本原理的推斷

*如果研究品質差、不精確 (95% 信賴區間大)、PICO 和我們的臨床情境不盡相符，或是證據間沒有一致性、絕對效果 (absolute effect size) 小，證據等級需酌情降級！反之，如果絕對效果顯著，證據等級可考慮升級！ **系統性回顧文獻優於單一研究文獻。

(a) 不同的治療方式 (A or B) 依隨機方式依序施行於同一個病人身上，一組為 A-B 序列治療組，另一組為 B-A 序列治療組。

(b) 有顯著危害是指超過 20%的受試者有此傷害反應。

如何引用這個證據等級表：

OCEBM Levels of Evidence Working Group*. "The Oxford 2011 Levels of Evidence". Oxford Centre for Evidence-Based Medicine. http://www.cebm.net/index.aspx?o=5653

* OCEBM Table of Evidence Working Group = Jeremy Howick, Iain Chalmers (James Lind Library), Paul Glasziou, Trish Greenhalgh, Carl Heneghan, Alessandro Liberati, Ivan Moschetti, Bob Phillips, Hazel Thornton, Olive Goddard and Mary Hodgkinson.

Teammate

進擊のEBM

奇行種進擊隊

鯛民

過份樂觀

按部就班

文獻評讀

臨床決策

文獻搜尋

For further reading and referents…

Characteristics of Clinical Trail

➢ Usually medical or clinical studies on human volunteers, these investigations follow a pre-determined research protocol.

Can be of two broad types :
-**Observational** (investigators observe the participants)
-**Interventional** (participants receive specific treatments or interventions)

實證醫學

教學評估及回饋-
嚴謹文獻評讀方式介紹

影像醫學科
品管教學組長 陳嘉宏

Learning Objectives

To 了解文獻設計型態，搜尋適合臨床問題之證據

To 嚴謹評讀文獻之分析判斷技巧 V.I.P.

Type of Study Design

Case Series / Report

Cross Sectional Study

Case Control Study

Cohort Study

Randomized Control Trial

Type of Study Design

- **Case Series / Report**

Case Series report new diseases or health related problems

They may provide some descriptive data on exposures to potential causal factors

---

Type of Study Design

- **Cross Sectional Study** — Prevalence

existing disease and current exposure levels

some indication of the relationship between the disease and exposure or non-exposure

sample at one point in time

Type of Study Design

- **Cross Sectional Study**

Advantages	Disadvantages
• **cheap** and simple • can study multiple exposures or multiple outcomes or diseases • **ethically** safe	• not a useful type of study for establishing **causal** relationships • only **prevalence** can be estimated (incidence)

Type of Study Design

- **Case Control Study** — Odds ratio

identify existing disease and look back in previous years to identify previous exposures to causal factors

Analyses examine if exposure levels are different between the groups

Case	Control
those who have a disease	those without a disease

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Type of Study Design

- **Case Control Study**

Advantages	Disadvantages
• Best design for **rare diseases** • cheap and quick • **ethically** safe	• Can **not calculate incidence**, population relative risk or attributable risk • high potential for **bias**

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Type of Study Design

- **Cohort Study** — Incidence / Relative risk

subjects with an exposure to a causal factor are identified and the incidence of a disease over time is compared with that of controls

subjects are followed over time with continuous or repeated monitoring of risk factors or health outcomes, or both

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Type of Study Design

- **Cohort Study**

Advantages	Disadvantages
• estimate overall and specific disease rates (**incidence**) • lower potential for bias - **no** recall bias	• blinding is **difficult** • randomization not present • **large sample size** or **long follow-up** is necessary

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Type of Study Design

- **Comparison**

Past	Now	Future

Exposure → Disease — Cohort Study

Exposure ← Disease — Case Control Study

Disease

Exposure — Cross Sectional Study

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Type of Study Design

- **Randomized Controlled Trial** — NNT / Confidence Interval

An experimental comparison study in which participants are allocated to treatment/intervention or control/placebo groups using a random mechanism

Best for study the effect of an intervention

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Type of Study Design

Randomized Controlled Trial

Advantages	Disadvantages
• unbiased distribution of confounders • **blinding** more likely • randomization facilitates **statistical analysis**	• **expensive** （time、money） • volunteer bias • ethically problematic at times

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Study Design Tree

What was the aim of the study?

When were the outcomes determined?

Was the intervention randomly allocated?

All Studies

Descriptive

Analytic

Experimental

Observational

Randomized (parallel group)

Randomized (crossover)

Cohort Study

Cross Sectional

Case-Control Study

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Level of Evidence

Systematic Review

RCT

Cohort studies

Case Control studies

Case Series / Reports

Editorials/Expert Opinion

15

Type of Study Design

Question type	Study design
Diagnostic test	Prospective、blinded cross-sectional study comparing with gold standard
Prognosis	Cohort study > Case control study > Case series
Etiology	Cohort study > Case control study > Case series
Therapy	Randomized Controlled Trial
Prevention	Randomized Controlled Trial

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分析判斷(文獻效度與重要性)

Validity 效度/信度
• Can we believe it？研究方法的探討

Importance 重要性
• We believe it！But does it matter? 研究結果的分析

Practicability 臨床適用性
• If we believe it - does it apply to our patients?

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分析判斷(文獻效度與重要性)

Validity 效度/信度

- 研究族群是否隨機 randomize
- 評估者是否blind

Were patients aware of group allocation?
Were clinicians aware of group allocation?
Were outcome assessors aware of group allocation?

- 追蹤率 > 80%
  (Intention-to-treat analysis)

Was follow-up complete ?

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Level of Evidence

Systematic Review

RCT

Cohort studies

Case Control studies

Case Series / Reports

Editorials/Expert Opinion

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Levels of Evidence

Oxford Centre for Evidence-Based Medicine 2011 Levels of Evidence

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Levels of Evidence

Level	Therapy / Prevention, Aetiology / Harm	Prognosis	Diagnosis	Differential diagnosis / symptom prevalence study	Economic and decision analyses
1a	SR (with homogeneity*) of RCTs	SR (with homogeneity*) of inception cohort studies; CDR† validated in different populations	SR (with homogeneity*) of Level 1 diagnostic studies; CDR† with 1b studies from different clinical centres	SR (with homogeneity*) of prospective cohort studies	SR (with homogeneity*) of Level 1 economic studies
1b	Individual RCT (with narrow Confidence Interval‡)	Individual inception cohort study with > 80% follow-up; CDR† validated in a single population	Validating** cohort study with good††† reference standards; or CDR† tested within one clinical centre	Prospective cohort study with good follow-up****	Analysis based on clinically sensible costs or alternatives; systematic review(s) of the evidence; and including multi-way sensitivity analyses
1c	All or none§	All or none case-series	Absolute SpPins and SnNouts††	All or none case-series	Absolute better-value or worse-value analyses †††††
2a	SR (with homogeneity*) of cohort studies	SR (with homogeneity*) of either retrospective cohort studies or untreated control groups in RCTs	SR (with homogeneity*) of Level >2 diagnostic studies	SR (with homogeneity*) of 2b and better studies	SR (with homogeneity*) of Level >2 economic studies
2b	Individual cohort study (including low quality RCT; e.g., <80% follow-up)	Retrospective cohort study or follow-up of untreated control patients in an RCT; Derivation of CDR† or validated on split-sample§§§ only	Exploratory** cohort study with good††† reference standards; CDR† after derivation, or validated only on split-sample§§§ or databases	Retrospective cohort study, or poor follow-up	Analysis based on clinically sensible costs or alternatives; limited review(s) of the evidence, or single studies; and including multi-way sensitivity analyses
2c	"Outcomes" Research;	"Outcomes" Research		Ecological studies	Audit or outcomes research

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Levels of Evidence

Level	Therapy / Prevention, Aetiology / Harm	Prognosis	Diagnosis	Differential diagnosis / symptom prevalence study	Economic and decision analyses
3a	SR (with homogeneity*) of case-control studies		SR (with homogeneity*) of 3b and better studies	SR (with homogeneity*) of 3b and better studies	SR (with homogeneity*) of 3b and better studies
3b	Individual Case-Control Study		Non-consecutive study; or without consistently applied reference standards	Non-consecutive cohort study, or very limited population	Analysis based on limited alternatives or costs, poor quality estimates of data, but including sensitivity analyses incorporating clinically sensible variations
4	Case-series (and poor quality cohort and case-control studies§§)	Case-series (and poor quality prognostic cohort studies***)	Case-control study, poor or non-independent reference standard	Case-series or superseded reference standards	Analysis with no sensitivity analysis
5	Expert opinion without explicit critical appraisal, or based on physiology, bench research or "first principles"	Expert opinion without explicit critical appraisal, or based on physiology, bench research or "first principles"	Expert opinion without explicit critical appraisal, or based on physiology, bench research or "first principles"	Expert opinion without explicit critical appraisal, or based on physiology, bench research or "first principles"	Expert opinion without explicit critical appraisal, or based on economic theory or "first principles"

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Levels of Evidence 簡易版

證據力等級	治療, 病因, 預防	預後	診斷	鑑別診斷, 症狀盛行率研究	經濟分析, 決策分析
Level 1	RCT 的系統性回顧；或 Confidence Interval 窄的 RCT	世代研究 的系統性回顧；或達到80% 比例的世代研究；或 經驗證的臨床指引	系統性回顧 Level 1文獻；或以公認標準驗證的世代研究；或臨床指引	前瞻世代研究之系統性回顧；或追蹤完整之前瞻世代研究	系統性回顧 Level 1 證據；或比較好壞方向的研究
Level 2	世代研究的系統性回；或 低品質的 RCT或追蹤小於 80% 或預後研究%	回溯性世代研究；或追蹤 RCT 中未治療的對照組；或由小族群推測或驗證的 臨床指引；或預後研究	系統性回顧 Level 2文獻；或偏在小族群驗證的臨床指引	回溯世代研究之系統性回顧；或追蹤不全之回溯世代研究；或生態(ecological)研究	系統性回顧 Level 2 文獻；或重要臨床方法或成本的單一研究；或預後研究
Level 3	有對照組 (controlled study)		系統性回顧 Level 3文獻；或不連續或缺乏公認標準驗證的研究	不連續或小族群的世代研究	其他臨床方法或成本的研究，包括敏感度 (sensitivity) 分析
Level 4	病例系列	病例系列	對照病例研究 (case- control study)	病例系列	未分析敏感度
Level 5	專家意見	專家意見	專家意見	專家意見	專家意見

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評讀證據

- 先從文獻的Topic找研究方法
- 若文獻的Topic沒有說明,再從Abstract的method中去判斷

嘉義基督教醫院

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1 1a
2 1b
3 2a
4 2b

Post-operative radiotherapy for ductal carcinoma in situ of the breast.

Goodwin A, Parker S, Ghersi D, Wilcken N.

Cancer Genetics, Westmead Hospital, Hawksberry Road, Westmead, NSW, Australia, 2145.

BACKGROUND: The addition of radiotherapy (RT) following breast conserving surgery (BCS) was first shown to reduce the risk of ipsilateral recurrence in the treatment of invasive breast cancer. Ductal carcinoma in situ (DCIS) is a pre-invasive lesion. Recurrence of ipsilateral disease following BCS can be either DCIS or invasive breast cancer. Randomised controlled trials (RCTs) have shown that RT can reduce the risk of recurrence, but assessment of potential long-term complications from addition of RT following BSC for DCIS has not been reported for women participating in RCTs. OBJECTIVES: To summarise the data from RCTs testing the addition of RT to BCS for treatment of DCIS to determine the balance between the benefits and harms. SEARCH STRATEGY: We searched the Cochrane Breast Cancer Group Specialised Register (January 2008), Cochrane Central Register of Controlled Trials (CENTRAL) (The Cochrane Library 2008, Issue 1), MEDLINE (February 2008), and EMBASE (February 2008). Reference lists of articles and handsearching of ASCO (2007), ESMO (2002 to 2007), and St Gallen (2005 to 2007) conferences were performed. SELECTION CRITERIA: RCTs of breast conserving surgery with and without radiotherapy in women at first diagnosis of pure ductal carcinoma in situ (no invasive disease present). DATA COLLECTION AND ANALYSIS: Two authors independently assessed each potentially eligible trial for inclusion and its quality. Two authors also independently extracted data from published Kaplan-Meier analysis (survival curves) and reported summary statistics. Data were extracted and pooled for four trials. Data for planned subgroups were extracted and pooled for analysis.There were insufficient data to pool for long-term toxicity from radiotherapy. MAIN RESULTS: Four RCTs involving 3925 women were identified and included in this review. All were high quality with minimal risk of bias. Three trials compared the addition of RT to BCS. One trial was a two by two factorial design comparing the use of RT and tamoxifen, each separately or together, in which participants were randomised in at least one arm. Analysis confirmed a statistically significant benefit from the addition of radiotherapy on all ipsilateral breast events (hazards ratio (HR) 0.49; 95% CI 0.41 to 0.59, P < 0.00001) and ipsilateral DCIS recurrence (HR 0.64; 95% CI 0.41 to 1.01, P = 0.05). Pooled analysis for invasive recurrence did not reach statistical significance. All the subgroups analysed benefited from addition of radiotherapy. No significant long-term toxicity from radiotherapy was found. No information about short-term toxicity from radiotherapy or quality of life data were reported. AUTHORS' CONCLUSIONS: This review confirms the benefit of adding radiotherapy to breast conserving surgery for the treatment of all women diagnosed with DCIS. No long-term toxicity from use of radiotherapy was identified.

[此篇文獻,是將多篇原始文獻RCT經過 SYSTEMIC REVIEW的過程做出來的]

1 1a
2 1b
3 2a
4 2b

Meta-analysis of N-acetylcysteine to prevent acute renal failure after major surgery.

Ho KM, Morgan DJ.

Intensive Care Unit, Royal Perth Hospital, Perth, WA 6000, Australia. kwok.ho@health.wa.gov.au

BACKGROUND: Acute renal failure after major surgery is associated with significant mortality and morbidity that theoretically may be attenuated by N-acetylcysteine. DESIGN: Meta-analysis of relevant studies sourced from the Cochrane Controlled Trial Register (2007 issue 4), EMBASE, and MEDLINE databases (1966 to February 1, 2008) without language restriction. SETTING & POPULATION: Adult patients undergoing major surgery without the use of radiocontrast. SELECTION CRITERIA FOR STUDIES: Randomized controlled studies comparing N-acetylcysteine with a placebo perioperatively. DATA ANALYSIS: Categorical variables are reported as odds ratio (OR) with 95% confidence interval (CI), and continuous variables are reported as weighted-mean-difference (WMD) with 95% CI. OUTCOME MEASURES: Effects of N-acetylcysteine on mortality and acute renal failure requiring dialysis were the main outcomes of interest. Additional outcome measures included an incremental increase in serum creatinine concentration greater than 25% above baseline, surgical reexploration for bleeding, amount of allogeneic blood transfusion, and length of intensive care unit stay. RESULTS: 10 studies involving a total of 1,193 adult patients undergoing major surgery were considered. N-Acetylcysteine use was not associated with a decrease in mortality (OR, 1.05; 95% CI, 0.58 to 1.92), acute renal failure requiring dialysis (OR, 1.04; 95% CI, 0.45 to 2.37), incremental increase in serum creatinine concentration greater than 25% above baseline (OR, 0.84; 95% CI, 0.64 to 1.11), or length of intensive care unit stay (WMD in days, 0.46; 95% CI, -0.43 to 1.36). N-acetylcysteine did not appear to increase the risk of surgical reexploration for bleeding (OR, 1.16; 95% CI, 0.57 to 2.38) or amount of allogeneic blood transfusion required (WMD in units, 0.31; 95% CI, -0.21 to 0.84). LIMITATIONS: Most studied patients had cardiac surgery and normal renal function preoperatively. CONCLUSIONS: There is no current evidence that N-acetylcysteine used perioperatively can alter mortality or renal outcomes when radiocontrast is not used.

[此篇文獻,是將多篇原始文獻(都是RCT)經過 META-ANALYSIS 的過程做出來的]

Utility of N-acetylcysteine to prevent acute kidney injury after cardiac surgery: a randomized controlled trial.

Adabag AS, Ishani A, Koneswaran S, Johnson DJ, Kelly RF, Ward HB, McFalls EO, Bloomfield HE, Chandrashekhar Y.

1 1a
2 1b
3 2b
4 3b

Division of Cardiology, Veterans Affairs Medical Center, University of Minnesota, Minneapolis, MN 55417, USA. adaba001@umn.edu

BACKGROUND: Acute kidney injury (AKI) after heart surgery is associated with increased mortality. We sought to determine whether prophylactic perioperative administration of N-acetylcysteine (NAC) prevents postoperative AKI in patients with chronic kidney disease undergoing cardiac surgery (clinical trials.gov identifier NCT00211653). METHODS: In this prospective, randomized, placebo-controlled, double-blinded clinical trial, 102 patients with chronic kidney disease who underwent heart surgery at the Minneapolis Veterans Affairs Medical Center were randomized to either NAC (n = 50) 600 mg PO twice daily or placebo (n = 52) for a total of 14 doses (3 preoperative). The primary outcome was maximum change in creatinine from baseline within 7 days after surgery. Secondary outcome was AKI (ie, >0.5 mg/dL or >or=25% increase in creatinine from baseline). RESULTS: Creatinine increased in both groups (0.45 +/- 0.7 mg/dL in NAC vs 0.55 +/- 0.9 mg/dL in placebo, P = .53) and peaked on postoperative day 5. Acute kidney injury occurred in 41 patients (22 NAC vs 19 placebo, P = .44) by postoperative day 5, but persisted in only 14 (7 NAC vs 7 placebo, P = .94) by day 30. In multivariable analysis, perioperative NAC was unassociated with AKI (relative risk 1.2, 95% CI, 0.8-1.9, P = .34). Five patients (3 NAC vs 2 placebo, P = .68) underwent hemodialysis, and 5 (2 NAC vs 3 placebo, P = 1.0) died perioperatively. There was no difference in lengths of stay in the intensive care unit (4.9 +/- 7 days in NAC vs 6.5 +/- 9 days in placebo, P = .06) and the hospital (13.2 +/- 13 days in NAC vs 16.7 +/- 17 days in placebo, P = .12). CONCLUSION: Prophylactic perioperative NAC administration does not prevent AKI after cardiac surgery.

[此篇文獻從Topic 發現是屬 原始文獻的RCT，單篇]

Glucose-added dialysis fluid prevents asymptomatic hypoglycaemia in regular haemodialysis. 1 1a
                                                                                              2 1b
Burmeister JE, Scapini A, da Rosa Miltersteiner D, da Costa MG, Campos BM.   3 2b
                                                                                              4 3b
Unidade de Medicina Renal, Hospital Universitário, Universidade Luterana do Brasil, R. Alvaro Alvim, 400 90420-020, Porto Alegre, RS, Brazil. burmeister@via-rs.net

BACKGROUND: Hypoglycaemia (HG) has been demonstrated during chronic haemodialysis (HD). These events may become more frequent with the current use of glucose-free bicarbonate dialysis solution, the standard formula in most dialysis facilities in the last decade. On the other hand, HG-related symptoms are unusual among patients during or just after dialysis sessions. The aim of this study was to evaluate the occurrence of HG in diabetic (DM) and non-diabetic (NDM) end-stage renal failure patients during HD using dialysis solution without and with glucose. METHODS: Forty-two chronic renal failure patients-21 DM and 21 NDM-randomly selected among the 97 in our dialysis unit were submitted to an HD session with glucose-free bicarbonate solution (phase 1). Serum glucose was measured at 30, 60, 150 and 240 min. In eight patients (four DM and four NDM) glucose was also measured in fluid leaving the dialyser at 30, 60 and 150 min. After a week, all procedures were repeated in the same patients, this time with a 90 mg/dl glucose-added bicarbonate solution (phase 2). We compared the glucose levels and the number of symptomatic and asymptomatic HG events in each group in phases 1 and 2, using bivariate analysis methods with confidence limit of 0.95%. RESULTS: Data were expressed as mean+/-SD. No patient presented any clinical evidence of HG. For all patients, the mean plasma glucose level (mg/dl) was significantly higher in phase 2 than in phase 1 (138.2+/-96.3 vs 120.7+/-75.9; P=0.0392). This occurred in DM (171.1+/-104.5 vs 132.5+/-71.0; P=0.0067), but not in NDM (101.3+/-19.4 vs 95.2+/-21.2; P=0.06). With glucose-free HD solution, 10 patients (five DM, five NDM) presented 18 measures of glycaemia under 70 mg/dl, and with glucose-added solution, only one (DM) presented two measures under 70 mg/dl-P=0.0045 (number of patients); P=0.0003 (number of HG measures). Among DM patients, values for HG measures in phase 1 (49.1+/-16.2 mg/dl) were significantly lower than in phase 2 (65.0+/-1.4 mg/dl)-P=0.0139. For all patients, glucose was lost in HD fluid leaving the dialyser at lower values in phase 2 (5.2+/-2.9 g/h) than in phase 1 (16.7+/-10.9 g/h)-P<0.0001. CONCLUSIONS: Asymptomatic HG was frequent during HD when glucose-free dialysis solution was used. Glucose was lost in dialytic fluid leaving the dialyser in significantly lower amounts when using glucose-added solution than glucose-free solution. Glucose-added dialysis solution at 90 mg/dl significantly reduced the number and severity of HG episodes and although it caused higher mean glycaemia in DM patients during HD, its use seems advisable in all patients.

此篇文獻的Topic沒有說明,只好再從Abstract的 method中去判斷,此篇文獻為低等級的RCT

CONCLUSIONS: Asymptomatic HG was frequent during HD when glucose-free dialysis solution was used. Glucose was lost in dialytic fluid leaving the dialyser in significantly lower amounts when using glucose-added solution than glucose-free solution. Glucose-added dialysis solution at 90 mg/dl significantly reduced the number and severity of HG episodes and although it caused higher mean glycaemia in DM patients during HD, its use seems advisable in all patients.

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The Lancet, Volume 300, Issue 7781, Pages 784 - 787, 14 October 1972
doi:10.1016/S0140-6736(72)92145-9 ( ) Cite or Link Using DOI

What are the RARE harms?
(Treatment Harms)
Llevel 4

SMALL HEAD SIZE AFTER IN-UTERO EXPOSURE TO ATOMIC RADIATION

RobertW. Miller , WilliamT. Blot [1]

Abstract

For the first time, dose estimates have been related to small head circumference induced by exposure in utero to the atomic bomb. There was a progressive increase with dose in the frequency of the abnormality among persons whose mothers were exposed before the eighteenth week of pregnancy. In Hiroshima the minimum dose-producing effect was 10-19 rad, but in Nagasaki no effect was observed under 150 rad. At maternal doses of 150 rad or more in both cities, small head circumference was often accompanied by mental retardation. The observations at low doses in Hiroshima are not directly applicable to medical radiology because of the possible influence of neutrons (nil in Nagasaki) and perhaps to interactions with other environmental disturbances, more widespread in Hiroshima than in Nagasaki.

a Epidemiology Branch, National Cancer Institute, Bethesda, Maryland, U.S.A.
b and Atomic Bomb Casualty Commission, Hiroshima, Japan

不要忘記研究倫理道德

■ 此研究問題不適合用前瞻性的研究設計,較適合用回溯性研究設計。
   Case control, case series, case report

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分析判斷(文獻效度與重要性)

Importance 重要性

- How **large** was the treatment effect?

- How **precise** was the treatment effect?

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分析判斷(文獻效度與重要性)

Importance 重要性

■ **研究常用統計**

*顯著水準(significance level,p value)
*信賴區間(confidence interval,CI)
*相對危險性(relative risk,RR)
*危險對比值(odds ratio,OR)
*相對危險性降低度(relative risk reduction,RRR)
*絕對危險性降低度(absolute risk reduction,ARR)
*治療需要數(number needed to treat,NNT)
*傷害需要數(number needed to harm,NNH)

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分析判斷(文獻效度與重要性)

Importance 重要性

■ **NNT** (Number Need to Treat) 治療需要數

～ 要預防一位不良結果發生所需治療的病人數

	一年的死亡人數	一年的存活人數	
接受某治療	300	700	實驗組事件發生率(EER) = 300 / (300+700) = 30%
不接受某治療	800	200	對照組事件發生率(CER) = 800 / (800+200) = 80%

相對危險性,風險比(Risk ratio. RR)= EER / CER = 0.3 / 0.8 = 0.375
絕對危險性降低度(ARR)= CER-EER = 80% - 30% = 50%
相對危險性降低度(RRR)=(CER-EER) / CER= (80%-30%) / 80% = 62.5%
NNT = 1 / ARR = 1/50% = 20 (每治療20位,會有1位存活)

EER:Experimental event rate   ARR:Absolute risk reduction
CER:Control event rate   RRR:Relative risk reduction

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分析判斷(文獻效度與重要性)

Importance 重要性

某一研究追蹤二年，對照組死亡率20%，治療組死亡率10%，結果的呈現方式有：

呈現方式	代表的意義
Relative Risk (相對風險性) RR = 0.10 / 0.20 = 0.5	治療組發生風險相對於對照組的倍數 (EER/CER) RR=1兩組無差別，RR<1治療可降低風險，RR>1治療會增加風險 **RR<1表示治療可降低死亡的風險**
Absolute Risk Reduction (絕對危險性降低度) ARR = 0.20 – 0.10 = 0.10 or 10%	治療組與對照組發生風險的絕對差異(EER-CER) **治療的益處是降低10%的死亡率**
Relative Risk Reduction (相對風險降低度) RRR = 1 – 0.50 = 0.50 or 50%	相對於對照組，治療組降低風險的比率 (1 – RR) (最常見的呈現方式) **相對於對照組，治療可以降低死亡的的機率50%**
Number Needed to Treat (益一需治數) NNT = 1 / ARR = 1 / 0.10 = 10	要預防一位不良結果發生所必需治療的病人數 **必需治療10位病人2年才能預防1人死亡**

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分析判斷(文獻效度與重要性)

Importance 重要性

- CI (Confidence Interval) 95%信賴區間

  45% (CI：40% ~ 50%)

  45% (CI：1% ~ 99%)　信心區間太寬，可能是樣本數太少。

  45% (CI：-2% ~ 53%)　信心區間跨越原點0，不具統計意義。

- CI 的寬度代表該研究的精確度(precision)，如果CI 越窄，代表我們越有信心評估治療的療效
- 如果研究顯示該治療的確有顯著療效，且CI 的下限仍有臨床意義，則可確定該治療具有重要的臨床價值

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分析判斷(文獻效度與重要性)

Practicability 臨床適用性

- How can I apply the results to my patient care？

  *Were the study patients similar to my patient？

  *Were all patient-important outcomes considered?

  *Are the likely benefits worth the potential harms and costs?

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分析判斷(文獻效度與重要性)

Practicability 臨床適用性

- 可否用來照顧我的病人？
  回頭看文章的PICO，是否和臨床問題相符？

- 4E：Evidence、Expectation、Experience、Environment

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Applying、Auditing

- 在實證醫學的執行過程中，您的表現如何？
  您可做下列自我評估：

  *提出可以回答的問題
  *發現最佳外部證據
  *審慎評讀證據的正確性與實用性
  *專業知識的整合及應用的臨床的務實變醫療
   行為

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Thanks for your Attention

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Evidence-Based Medicine
What are the major database?

Speaker：Yu-Xuan Lin

Date：2016.04.17

Big data is like teenage sex：

　everyone talks about it, nobody really knows how to do it, everyone thinks everyone else is doing it, so everyone claims they are doing it…
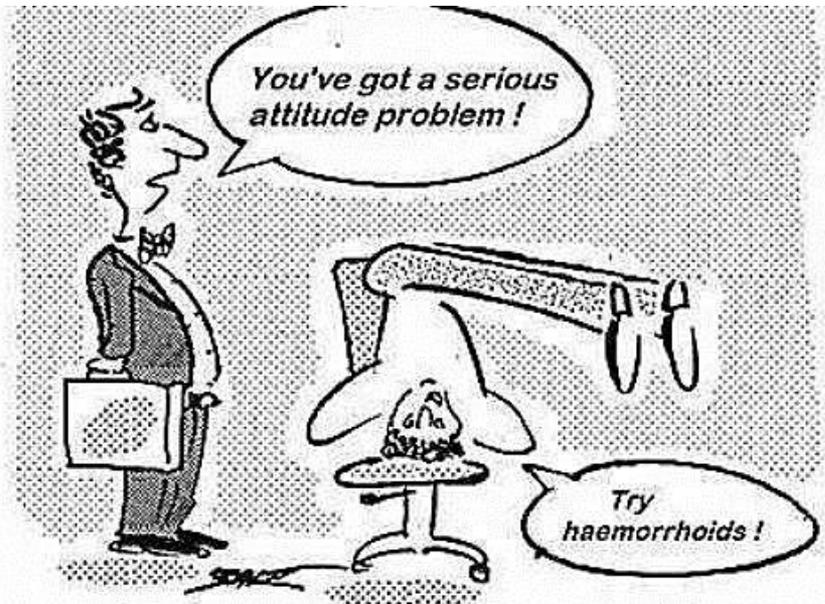
Dan Ariely

大數據就像青少年談性：每個人都在說，卻不知道誰做了。每個人都認為別人在做，所以每個人都聲稱自已在做。這是Dan Ariely的在Face book中的一句玩笑話，卻道出了實際的情況。真正在作大數據的企業並不多，但是大家多躍躍欲試。

The core mechanisms in EBM include the following four steps

➢ Formulate a clear clinical question from a patient's problem.
➢ Search the literature for relevant clinical articles.
➢ Evaluate (critically appraise) the evidence for its validity and usefulness.
➢ Implement useful findings in clinical practice.

What is the Statistics…

Statistics　　**Input**　　**Produce**　　**Output**

$$S \;=\; \boxed{I} \longrightarrow \boxed{P} \longrightarrow \boxed{O}$$

統計　　數據資料　資料處理　有意義的資訊

What's difference between Statistics and Biostatistics?

統計學(Statistics)
　　對觀察或測量到的資料，如何加以處理分析，而分析後的結果如何加以利用，以協助研究者或實務者做判斷及推論

數理統計、商用統計… vs. 生物統計
　　生物統計學(Biostatistics)特指應用於醫學研究、健康問題、或其他健康相關領域的統計分析方法，意即處理或分析的對向是有關生物的事務或現象

Appraisal

➢ **V (Valid/Reliability):**
   Are the results of the review valid?

➢ **I (Important/Impact):**
   What were the results?

➢ **P (Practice/Applicability):**
   Will the results help me in clinical practice?

PHARMACOLOGICAL DRUG TRIAL RESULTS

OUR TRIALS SHOW THAT THE NEW DRUG PERFORMS NO BETTER THAN PLACEBO
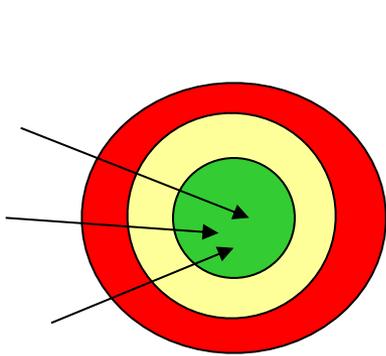
MAYBE WE SHOULD INVEST IN PLACEBOS
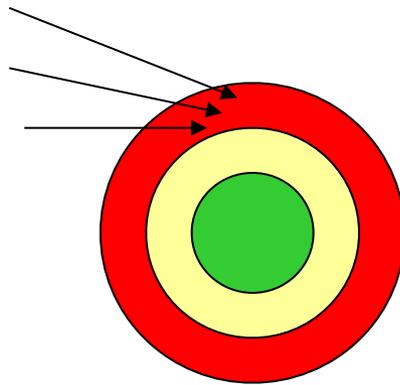
CHRIS MADDEN

VIP

Validity and Reliability

- 效度（Validity）：測量的正確性，指測驗或其他測量工具確能測得其所欲測量的特質或功能之程度。
  - 測量的效度愈高，表示測量的結果愈能顯現其所欲測量對象的真正特徵。
  - 效度可由敏感度(Sensitivity)和特異度(Specificity)來表示。

- 信度 (Reliability)：是指測驗結果的一致性和穩定性。
  - 一致性（Consistency）─表示測驗內部試題間是否相互符合。
  - 穩定性（Stability）─不同的測驗時點下，測驗分數前後一致的程度。
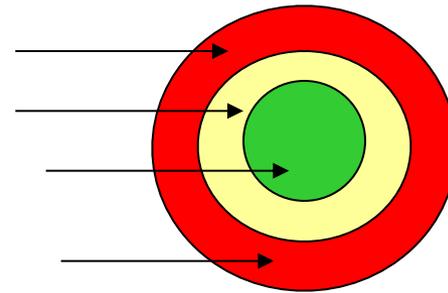
信度與效度的關係

- 信度是效度的必要條件，但非充分條件。一個測驗要有效度，必須要有信度，但是，有信度並不能保證有效度。

兼具信度和效度　　　　　　有信度但無效度　　　　　　無信度亦無效度

Appraisal

➢ **V (Valid/Reliability):**

   Are the results of the review valid?

➢ **I (Important/Impact):**

   What were the results?

➢ **P (Practice/Applicability):**

   Will the results help me in clinical practice?

不同類型的研究結果分析

Therapy/prevention	Harm/Etiology	Diagnosis	Prognosis
✓ Relative risk reduction (RRR)相對風險性降低度 ✓ Absolute risk reduction (ARR)絕對風險性降低度 ✓ Number needed to treat (NNT)益一需治數	✓Relative risk (RR)相對風險 ✓Odds ratio (OR)勝算比 ✓Number needed to harm (NNH)害一需治數	✓Sensitivity 敏感度 ✓Specificity特異度 ✓Positive predictive value 陽性預測值 ✓Negative predictive value 陰性預測值 ✓Likelihood ratio 相似比	✓Event rate事件發生率 ✓Odds ratio (OR)勝算比

Odds Ratio (OR)勝算比：	➤ 意即實驗組中發生某事件的人數與控制組中發生該事件人數的比值。 ➤ **1≥OR≤1。** **(理想狀態為<1)**
Relative Risk (RR)相對風險： • RR$=\dfrac{risk\ in\ exposed}{risk\ in\ non\ exposed}$ $=\dfrac{EER}{CER}$ EER=experimental event rate CER=control event rate	➤ 意即治療組發生風險相對於對照組之間產生的倍數。 ➤ RR=1-risk is same in exposed and unexposed groups。 RR>1-risk is greater in exposed group。 **RR<1-reduction in risk in exposed group**。

Absolute Risk Reduction (ARR)絕對危險降低度： • ARR＝CER-EER	➤ 意即告訴我們絕對差在兩組間事件的比率和存在的基本風險、治療效果的指示。 ➤ 當ARR=0，表示二組間並無不同，因此治療並無效果。
Relative Risk Reduction (RRR)相對風險降低度： • RRR＝1-RR＝$\frac{CER-EER}{CER}$	➤ 意即相對於對照組，治療組降低風險的比率。 ➤ 最常見的呈現方式，同時也是RR(相對風險)的補充。

RR : Relative Risk
CER : Control Event rate
EER : Experimental Event Rate

Number Need to Treat (NNT)益一需治數： • $NNT = \dfrac{1}{ARR}$	➢ 意即相對於對照組，我們需要去治療多少病人才會得到一個有正向回饋治療效果的病人。 ➢ **NNT值介於1~∞，且為一個整數。(理想狀態為1)**
Number Need to Harm (NNH)害一需治數： • $NNH = \dfrac{1}{AR}$	➢ 意即平均多少人曝露在特定危險因子後，就會有一個人產生副作用。 ➢ **NNH值介於1~∞，且為一個整數。(理想狀態為∞)**

ARR：Absolute Risk Reduction
AR：Absolute Risk

休息一下…

▸ 你知道什麼叫做「EBM」嗎？

▸ Evidence-based medicine (EBM)，全世界都在流行 EBM，世界各國的說法都不同..

「循證醫學」 🇨🇳 　「 根拠に基づいた医療」 ●
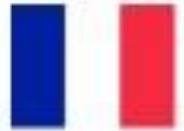
「 Medicina basada en la evidencia 」 🇩🇪 　「 Medicina basata su prove di efficacia 」 🇫🇷

「 Medicina baseada em evidências 」 🇵🇹 　「 پزشکی مبتنی بر شواهد 」 🇮🇷

Appraisal

> ## **V (Valid/Reliability):**
>   Are the results of the review valid?

> ## **I (Important/Impact):**
>   What were the results?

> ## **P (Practice/Applicability):**
>   Will the results help me in clinical practice?

Homogeneity and Heterogeneity

同質性 (Homogeneity)：
　-整合分析相同主題的多個文章之中，各個研究皆為個別獨立的研究，若收集樣本的**條件及結果都相似**，則稱為同質性高。

異質性 (Heterogeneity)：
　-整合分析中相同主題的多個文章之中，各個研究皆為個別獨立的研究，但是收集樣本的**條件有些不相似**或者**結果不相似**，則稱為異質性。

How to look for Heterogeneity?

Visually

- Forest plot：可經由每筆研究之間的信賴區間重疊度來判讀彼此之間的異質性及統合其研究差異與效果.
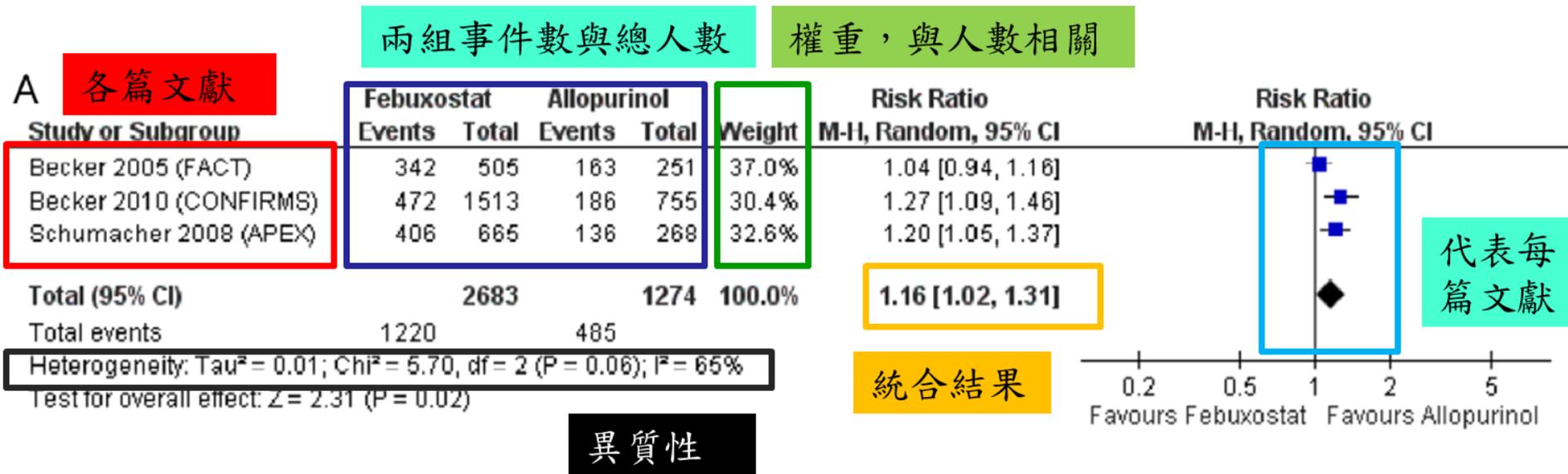
Statistically

- 從統計學上判斷（有無異質性）
  - Chi-square test
  - P<0.1:異質性存在之可能性高
  - P>0.1:異質性存在之可能性低
    - Q/df>1:異質性存在之可能性高
    - Q/df<1:異質性存在之可能性低

- I^2 test（異質性程度）
  - 0-40%:無異質性
  - 40-60%:中度異質性
  - 60-90%:中高度異質性
  - 90-100%:高度異質性

注意!!!
一般統計顯著是以p<0.05，
而異質性是p<0.1

How to read a Forest Plot?

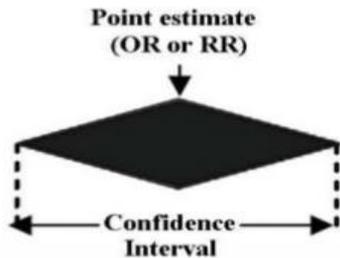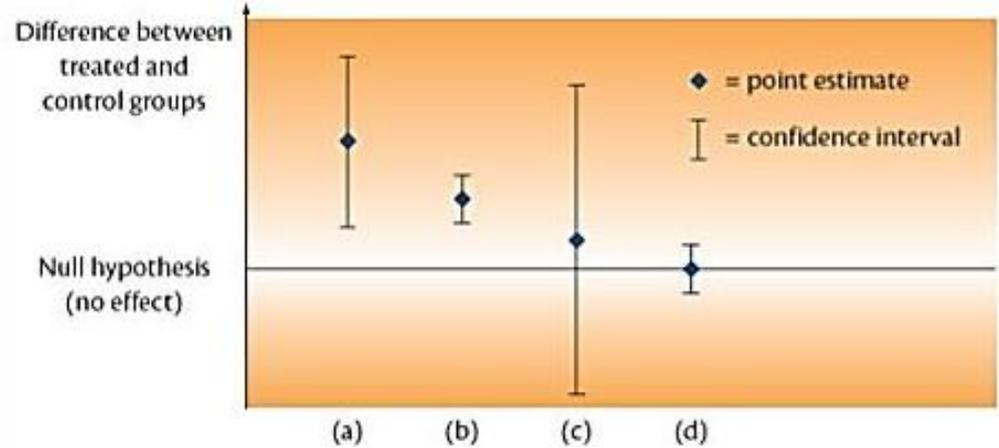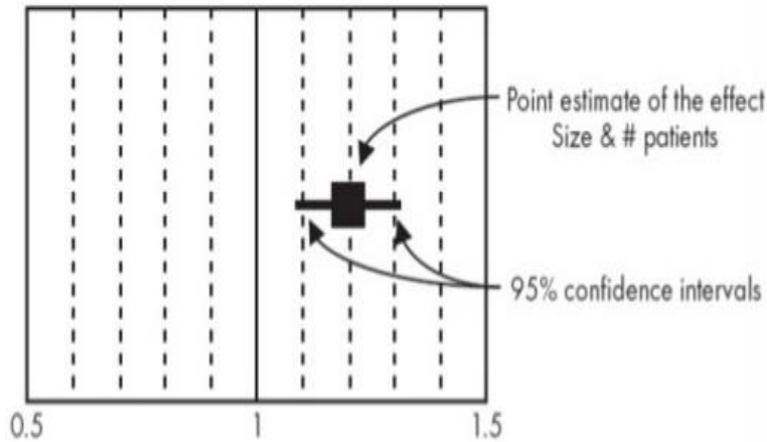➤ The graphical display of results from individual studies on a common scale is a forest plot.

☐ In the forest plot each study is represented by a black square and a horizontal line (CI : 95%).

☐ A logarithmic scale should be used for plotting the Relative Risk (RR).

What are Confidence Intervals (CI) and P values?

1. 對一個處理其影響量的信賴區間計算，是用以顯示此處理真正影響性的範圍。

2. p值的計算是用以評估試驗的結果，只是單純的機率數值（假設新方法與舊方法無真正不同，而且這些試驗都是在完善規劃下完成）。

3. 信賴區間的判別結果比p值更有意義，信賴區間可以告知真實值可能的影響範圍。

4. 在信賴區間被用以解釋是否有顯著差異之前，必須先評估偏差值（Bias）。甚至在非常大的樣本數目與非常窄的信賴區間，只要有偏差存在，評估結果都可能誤導。

5. 非顯著性不代表「無影響」。在一些處理真正有顯著影響，但是因為樣本很小，經常被判斷為無顯著影響。
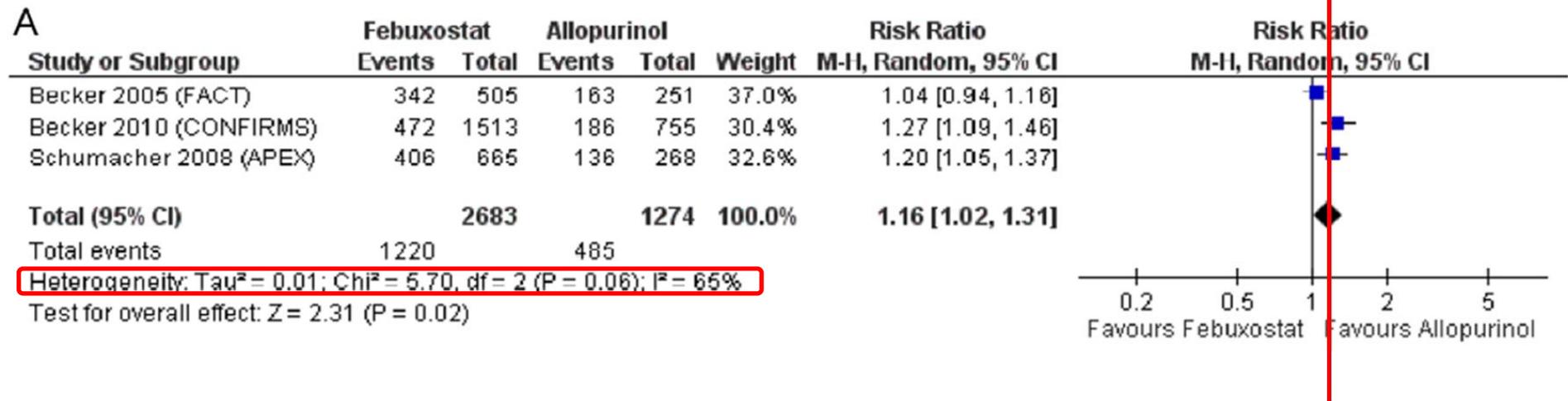
6. 統計上的顯著性並不一定代表此影響是真實存在。有二十分之一的機率使得研究結果為偽證（spurious）。

Statistical significance and Confidence Intervals (CI)

(a) Statistically significant, low precision
(b) Statistically significant, high precision
(c) Not statistically significant, low precision
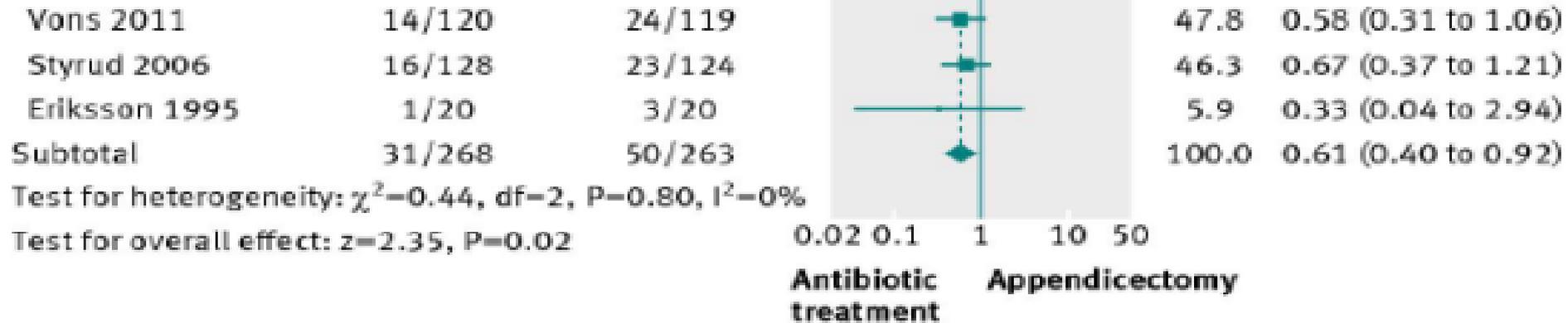(d) Not statistically significant, high precision

Glasziou P er al. Evidence based practice workbook. Blackwell. 2 en edtion.2007

Eyeball test on forest plot

A	Febuxostat		Allopurinol			Risk Ratio		Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI		M-H, Random, 95% CI
Becker 2005 (FACT)	342	505	163	251	37.0%	1.04 [0.94, 1.16]		
Becker 2010 (CONFIRMS)	472	1513	186	755	30.4%	1.27 [1.09, 1.46]		
Schumacher 2008 (APEX)	406	665	136	268	32.6%	1.20 [1.05, 1.37]		
Total (95% CI)		2683		1274	100.0%	1.16 [1.02, 1.31]		
Total events	1220		485					

Heterogeneity: Tau² = 0.01; Chi² = 5.70, df = 2 (P = 0.06); I² = 65%
Test for overall effect: Z = 2.31 (P = 0.02)

0.2 0.5 1 2 5
Favours Febuxostat   Favours Allopurinol

- **P=0.06 (P<0.1)**
- **Q/df:5.7/2=2.8,大於1,表示可能有異質性存在**
- **I²:65%,表示中等程度的異質性**

Eyeball test on forest plot
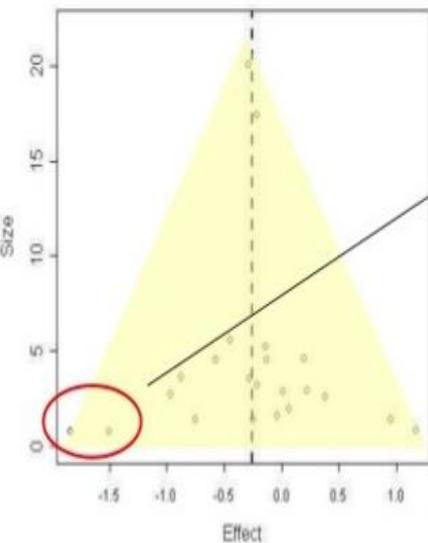

Adapted from BMJ. 2012; 344: e2156.

(A) 沒有一個單一研究顯示使用抗生素相較於外科手術，可以顯著降低併發症風險

(B) 這張森林圖是以線性 (linear) 指標畫的

(C) 相對風險 (relative risk) 低於"1.0"代表使用抗生素 相較於 外科手術，受試者發生併發症風險較低

(D) 這項綜合分析結果顯示使用抗生素 相較於 外科手術，可以下降31%併發症風險

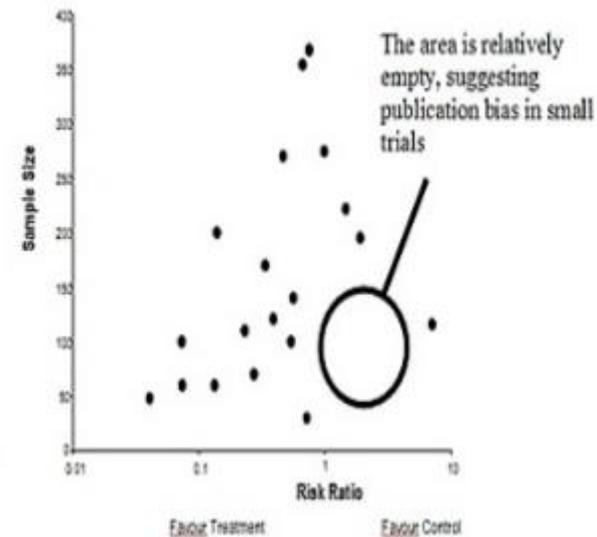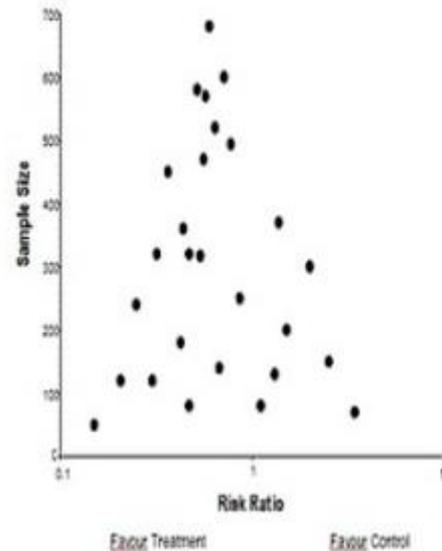(E) 收納研究的相對風險之間並沒有顯著異質性 (heterogeneity)

Funnel analysis

➢ The presence of bias should be examined in funnel plots.

➢ It is graphical test for any type of bias that is associated with sample size.

➢ Results from small studies will scatter widely at the bottom of the graph.

To study a funnel plot, look at its LOWER LEFT corner, that's where negative or null studies are located

If EMPTY, this indicates "PUBLICATION BIAS"

Note that here, the plot fits in a funnel, and that the left corner is not all that empty, but we cannot rule out publication bias

The area is relatively empty, suggesting publication bias in small trials

Take home message

Knowledge is of two kinds：

We know a subject ourselves or we know where

we can find information upon it.

Dr. Samuel Johnson.

For further reading and referents…

對於一個測量工具，使用者最常提出的問題是：

1. 「它準不準」（指效度問題）
2. 「它穩不穩定」（指信度問題）。

Effect of Therapy (治療效果)

	一年的死亡人數	一年的存活人數
接受某治療	300	700
不接受某治療	800	200

✞實驗組事件發生率 **(Experimental event rate, EER)**

EER = 300 / (300+700) = 30%

✞非實驗組事件發生率**(Control event rate, CER)**

CER = 800 / (800+200) = 80%

✞相對危險（**Relative risk, RR)**

RR = EER / CER = 30% / 80% = 0.375

✞絕對危險性降低度 **(Absolute risk reduction, ARR)**

ARR = CER – EER = 80% - 30% = 50%

✞相對風險性降低度 **(Relative risk reduction, RRR)**

RRR = CER – EER / CER = (80% - 30%) / 80% = 62.5%

相對風險性降低度 (RRR)與
絕對危險性降低度 (ARR)的比較

對照組的風險 CER	實驗組的風險 EER	相對風險性降低度 RRR	絕對危險性降低度 ARR
70%	35%	50%	35%
7%	3.5%	50%	3.5%
0.7%	0.35%	50%	0.35%

- 相對風險性降低度 (RRR)無法呈現實際風險降低程度，亦沒有考慮起始風險
- 絕對危險性降低度 (ARR)更準確表示治療效果，但亦不容易體會兩組的差別

Number Needed to Treat (NNT)
"益一需治數"

定義：為了預防一個不良結果或減少一人死亡所需治療的病人數。

NNT只是真實數值的估算，因此後面經常附註了95%的信賴區間(CI)。

NNT的解讀必須考慮其追蹤時間的長短 。

NNT = 1 / ARR = 1 / (CER – EER)

Effect of Harm (傷害影響)

	得病的人數	沒病的人數
暴露在某因子下	700	300
未暴露在某因子下	200	800

✟暴露組發病率 (**Exposure event rate, EER**)

 EER = 700 / (700+300) = 70%

✟非暴露組發病率(**Control event rate, CER**)

 CER = 200 / (200+800) = 20%

✟相對危險（**Relative risk, RR) = EER / CER = 70% / 20% = 3.5**

✟絕對危險度增加度（**Absolute risk increase, ARI**）= EER – CER

✟相對危險度增加度 （**Relative risk increase, RRI**）= (EER – CER) / CER

Effect of Harm (傷害影響)

	得病的人數	沒病的人數
暴露在某因子下	700	300
未暴露在某因子下	200	800

✝暴露組勝算 **(Experimental event odds)** = **700 / 300 = 2.33**

✝非暴露組勝算**(Control event odds)** = **200 / 800 = 0.25**

✝勝算比 **(Odds Ratio, OR)** ：(在病例對照研究中) 暴露組中發生疾病的勝算與非暴露組中發生疾病的勝算比值。

OR= Experimental event odds / Control event odds

= (700x800) / (300x200) = 9.33

Number Needed to Harm (NNH)
"害一需治數"

✞定義：多少人接受治療/暴露，就會有一位患者受到傷害。

✞任何介入與治療通常伴隨著一些負面效果。因此在做任何臨床決策時，我們不能只依賴其正面效果（NNT），還必須考慮並計算其負面效果（NNH）。

✞範例：追蹤的時間是6個月，其發生過敏反應的NNH為7（95％C.I.介於4～22間）。表示：在6個月當中，7個接受接受藥物治療的氣喘患者，就有一個發生過敏反應，而NNH真實數值可能最低為4，最高為22。

$$NNH = 1 / ARI = 1 / (CER - EER)$$

$$NNH = \frac{CER \times (OR - 1) + 1}{CER \times (OR - 1) \times (1 - CER)}$$

Confidence Intervals(信賴區間)

- ARR：信賴區間(CI)不包含「0」，表統計顯著。
- RR、OR：信賴區間(CI)不包含「1」，表統計顯著。

CI: 40% ~ 50%(A)

在**95%**的信心水準下，死亡率的平均 **ARR**值會介於 **40%~50%**之間。

CI: -2% ~ 53%(B)

CI太寬，可能樣本數太少，包含「**0**」，不具統計上顯著意義，但可能有臨床意義，有**2%**的機會反而提高死亡率。

CI: 1% ~ 99%(C)

CI太寬，可能樣本數太少或有極端值

0

Mean mortality <u>ARR</u>=45%

陽性預測值**(Positive predictive value, PPV)**

	真的有病（D+） （Disease Present）	真的沒病（D-） （Disease Absent）
檢測有病（T+） （Test Positive）	真陽性（**TP**） （**True Positive**）	偽陽性（**FP**） （**False Positive**）
檢測沒病（T-） （Test Negative）	偽陰性（**FN**） （**False Negative**）	真陰性（**TN**） （**True Negative**）

Sensitivity, Sn)

特異性(Specifi

陰性預測值**(Negative predictive value, NPV)**

Five step of EBM

☐ How to ask clinical question you can answer ?
☐ Search for the best evidence
☐ Critically appraise the evidence
☐ Individualize, based clinical expertise and patient concerns
☐ Evaluate your own performance