

# 實證醫學

改善照護品質與運用手法

2015

**Evidence-Based Health Care**  
**Evidence-Based Medicine**

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# Medical Practice and Education in the New Century

- 醫學人文教育
- 生物資訊
- 以病人為中心的照護 (Q&A?)
- 以問題為導向的學習 (PBL)
- 以實證為基礎的治療 (EBM, EBHC)



# Bell's Facial Palsy

- 貝爾氏麻痺(Bell's palsy) (暫時性的顏面神經麻痺)



N Engl J Med. 2007 Oct 18;357(16):1598-607

[Cochrane Database Syst Rev. 2015 Jul 1;7:CD001869. \[Epub\]](#)

# Evidence-Based Health Care

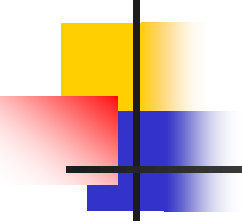
## Evidence-Based Medicine

※ 實證健康照護 定義: Use of **current best evidence** in making decisions about the care of individual patients.

※ 三方面整合: EBM is the **integration** of best research **evidence** with clinical **expertise** and **patients'** unique biology, values and circumstances (**expectation**). **(3E)**  
*(Evidence-based Practice)*

1. 依循最佳證據
2. 專業建議 [告知]
3. 病患同意 [知情]

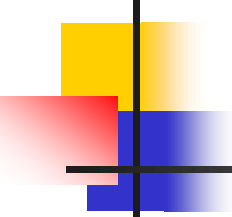




# Scenario 臨床情境

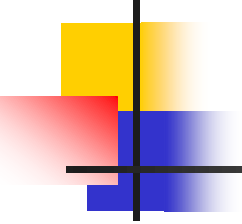
: Ask ~ PICO (Q&A)

- 腰椎穿刺後，需不需要評躺8小時，減少頭痛的發生？
- PRP (濃縮血小板) 治療退化性關節炎？
- 益生菌減少新生兒過敏氣喘？
- 嬰幼兒術前禁食之時間多寡？
- 不同消毒方式降低感染率的差異？
- 維骨力可不可以減少關節退化與疼痛？
- 腫瘤標誌篩檢異常的意義？檢驗ANA假陽性 5%
- ...



# 臨床問題類型

- 診斷 (Diagnosis)
  - Sensitivity, specificity 敏感度、特異度
  - Predictive value (PPV, NPV) 陽性預測值、陰性預測值
  - ROC curve, Likelihood ratio (**LR+**, **LR-**) 概似比
- 治療 (Therapy) 隨機分配對照臨床試驗
  - Clinical trial (Randomized Controlled Trial, **RCT**)
- 預後 (Prognosis)
  - Prediction model (Survival analysis, **HR** 風險比)
- 危險因子探討 (Risk factor)
  - 世代研究 Cohort study (Relative Risk, **RR** 相對風險比)
  - 病例對照 Case-control study (Odds Ratio, **OR** 勝算比)



# Dr. Sydney Burwell, Dean of Harvard Medical School

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- Half of what you are taught as medical students will in ten years have been shown to be wrong.
- And the trouble is, none of your teachers knows which half.

✂ 醫療處置的不確定性

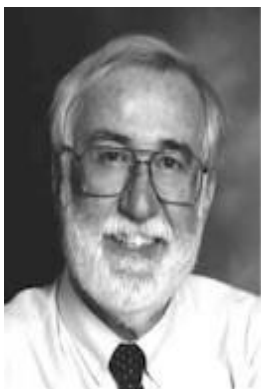
✂ UpToDate, Dynamed, PubMed, Cochrane...



# 資料庫搜尋 Database (Internet, Intranet)



# 發展趨勢與臨床應用



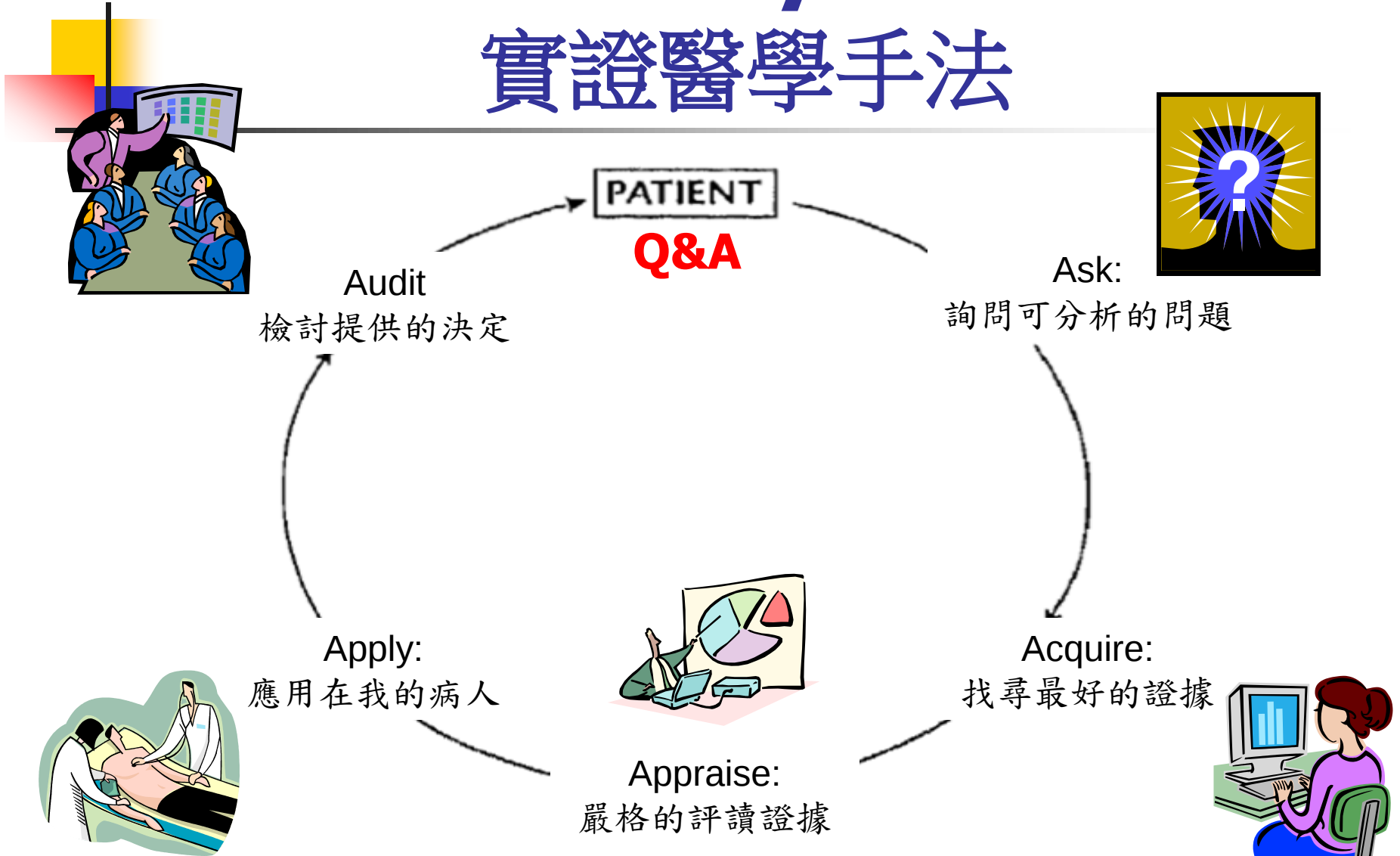
Dave Sackett





# Evidence Cycle "5 A"

## 實證醫學手法





# 實證醫學的五大進行步驟

## Five Steps to Practice EBM (5As)

---

- 1. Formulate an answerable question. ~ Ask**  
提問：由個案的臨床資料提出可回答的臨床問題
- 2. Track down the best evidence. ~ Acquire**  
尋找最佳的實證文獻〔各種文獻資料庫，包括發表及未發表的資料〕
- 3. Critically appraise the evidence for validity, impact, and applicability. ~ Appraisal**  
評估最佳實證醫學文獻的可信度、臨床重要性，以及可應用性
- 4. Integrate with our clinical expertise and patient values.**  
整合並應用於實際患者的治療決策～告知同意〔臨床應用〕～ Apply
- 5. Evaluate our effectiveness and efficacy. 效果評估 ~ Audit**  
溝通：用簡單且病人可以聽懂的語言，對病患告知診療的決策

# Scenario 臨床情境

: Ask ~ PICO

- 如何降低外科手術傷口感染率，嬰幼兒術前禁食之時間長短
  - 治療預後、病人安全問題 Q&A:手術前需不需剃除毛髮，手術前剃除毛髮會增加或減少手術部位感染的風險？
- 退化關節炎的老年人，應服用維骨力嗎
  - 治療問題
- 腰椎穿刺後需平躺8小時，減少頭痛發生？
  - 治療預後問題
- 下背痛患者，抽血HLA B27結果如何判讀
  - 診斷問題

# Bell's Facial Palsy

- 貝爾氏麻痺(Bell's palsy) (暫時性的顏面神經麻痺)



# 資料庫搜尋 Database (Internet, Intranet)



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COLLABORATION®



ACP JOURNAL CLUB

Evidence-Based Medicine for Better Patient Care



helping doctors make better decisions



Evidence - Based  
**MEDICINE** for Primary Care and Internal Medicine



National Guideline Clearinghouse  
www.guideline.gov



Medscape  
EDUCATION

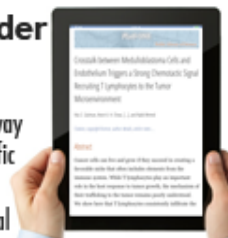


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Bell's palsy

Search

### Clinical Study Categories

Category: Therapy

Scope: Narrow

### Systematic Reviews

### Medical Genetics

Topic: All

#### Results: 5 of 63

[Comparison on efficacy and the safety evaluation on peripheral facial paralysis treated with electroacupuncture of different waveforms].

Liu LA, Zhu YH, Li QH, Yu ZL.

Zhongguo Zhen Jiu. 2012 Jul; 32(7):587-90.

The effect of prednisolone on sequelae in Bell's palsy.

Bylund N, Marsk E, Jonsson L, Kanerva M, Hultcrantz M, Engström M.

Arch Otolaryngol Head Neck Surg. 2012 May; 138(5):445-9.

Zoster sine herpette causing facial palsy.

Lee HY, Kim MG, Park DC, Park MS, Byun JY, Yeo SG.

Am J Otolaryngol. 2012 Sep-Oct; 33(5):565-71. Epub 2012 Mar 22.

Prognosis of nerve recovery in Bell's palsy using

#### Results: 5 of 73

Evidence-based guideline update: steroids and antivirals for Bell palsy: report of the Guideline Development Subcommittee of the American Academy of Neurology.

Gronseth GS, Paduga R, American Academy of Neurology.

Neurology. 2012 Nov 27; 79(22):2209-13. Epub 2012 Nov 7.

Familial Bell's Palsy: A Case Report and Literature Review.

Kubik M, Robles L, Kung D.

Case Report Neurol Med. 2012; 2012:674981. Epub 2012 Aug 5.

A systematic review of the clinimetric properties of habitual physical activity measures in young children with a motor disability.

Ofstedal S, Bell KL, Mitchell LE, Davies PS, Ware RS, Boyd RN.

Int J Pediatr. 2012; 2012:976425. Epub 2012 Aug 9.

#### Results: 5 of 70

Zoster sine herpette causing facial palsy.

Lee HY, Kim MG, Park DC, Park MS, Byun JY, Yeo SG.

Am J Otolaryngol. 2012 Sep-Oct; 33(5):565-71. Epub 2012 Mar 22.

Bell's palsy. A prospective, longitudinal, descriptive, and observational analysis of prognosis factors for recovery in Mexican patients.

Sánchez-Chapul L, Reyes-Cadena S, Andrade-Cabrera JL, Carrillo-Soto IA, León-Hernández SR, Paniagua-Pérez R, Olivera-Díaz H, Baños-Mendoza T, Flores-Mondragón G, Hernández-Campos NA.

Rev Invest Clin. 2011 Jul-Aug; 63(4):361-9.

A cell culture model of facial palsy resulting from reactivation of latent herpes simplex type 1.

Kuhn MA, Nayak S, Camarena V, Gardner J, Wilson A, Mohr I, Chen MY, Roehm PC.

Am J Med 2013;126:336–41.

## Steroid-antiviral Treatment Improves the Recovery Rate in Patients with Severe Bell's Palsy

Ho Yun Lee, MD, Jae Yong Byun, MD, Moon Suh Park, MD, Seung Geun Yeo, MD, PhD

*Department of Otorhinolaryngology, School of Medicine, Kyung Hee University, Seoul, Korea.***Table 3** Results of Multiple Logistic Regression Analysis for Complete Recovery

| Variable                    | Odds Ratios (95% Confidence Interval) | P Value |
|-----------------------------|---------------------------------------|---------|
| Favorable EMG               | 2.2 (1.1-4.5)                         | .034    |
| Steroid-antiviral treatment | 2.6 (1.3-5.1)                         | .006    |

EMG = electromyography.

Further reading: Cochrane Database Syst Rev. 2015 Jul 1;7:CD001869. [Epub]

**Table 1** Patient Characteristics

| Variable                  | Steroid Only    | Combination Therapy | <i>P</i> Value |
|---------------------------|-----------------|---------------------|----------------|
| Total n (%)               | 107 (51.9)      | 99 (48.1)           |                |
| Age                       |                 |                     |                |
| Mean $\pm$ SD             | 48.6 $\pm$ 15.1 | 46.7 $\pm$ 16.2     | .381           |
| Range                     | 16-77           | 16-76               |                |
| Sex, n (%)                |                 |                     |                |
| Male                      | 51 (47.7)       | 50 (50.5)           | .780           |
| Female                    | 56 (52.3)       | 49 (49.5)           |                |
| EMG, n (%)                |                 |                     |                |
| Favorable                 | 85 (79.4)       | 75 (75.8)           | .616           |
| Unfavorable               | 22 (20.6)       | 24 (24.2)           |                |
| ENoG, n (%)               |                 |                     |                |
| Poor                      | 5 (4.7)         | 9 (9.1)             | .271           |
| Good                      | 102 (95.3)      | 90 (90.9)           |                |
| Onset of treatment, n (%) |                 |                     |                |
| Within 3 days             | 84 (79.2)       | 67 (67.7)           | .081           |
| 3-7 days                  | 22 (20.8)       | 32 (32.3)           |                |
| Final facial grade, n (%) |                 |                     |                |
| Mean $\pm$ SD             | 2.1 $\pm$ 1.1   | 1.9 $\pm$ 0.8       | .216           |
| I                         | 42 (39.3)       | 31 (31.3)           | .221           |
| II                        | 29 (27.1)       | 51 (51.5)           |                |
| III                       | 26 (24.3)       | 12 (12.1)           |                |
| IV                        | 7 (6.5)         | 5 (5.1)             |                |
| V                         | 2 (1.9)         | 0 (0.0)             |                |
| VI                        | 1 (0.9)         | 0 (0.0)             |                |
| Recovery rate (%)         | 66.4            | 82.8                | .010           |





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UpToDate

專案事前報備資料

腎病防治中心收案

## 組織檢體查詢

曲線圖

### 專科手繪圖

## 中醫檢查

急診觀察區等住院病患

病歷未完成

手術報告未完成

## 呼吸道隔離病患

呼吸照護

醫師別預住院病患

### 醫師別出院病患

## 醫師管制藥品使用執照

醫師代號

會診值班醫師

科別預住院病患

科別空床

病患異動明細

標準住院日數

## 病歷書寫規範

## 特殊符號表

危險營養因子查詢

外傷登錄查詢

性別 女 主治醫師

護理站

使用者 余光輝

3 年齡 53 科 別 風濕過敏科

生日 1956/04/10

0 身份 

病歷總覽

SOAP 逾1日以上未寫SOAP M 麻疹 T 團隊診療 @ 傳染病 HR 建議照會轉介服務 Prob 2日內未寫

| 號   | 入院日期            | 時間    | 入院診斷              | CASE | 達成率 |
|-----|-----------------|-------|-------------------|------|-----|
| 254 | SOAP 2009/03/01 | 11:12 | 全身紅斑性狼瘡           |      |     |
| 925 | SOAP 2009/02/01 | 10:50 | 其他蜂窩組織炎及膿瘍，未明示位置者 |      |     |
| 968 | SOAP 2009/03/01 | 15:40 | 其他蜂窩組織炎及膿瘍，未明示位置者 |      |     |
| 251 | SOAP 2009/03/01 | 13:59 | 泌尿道感染，未明示位置者      |      |     |

**6 S: 連結個別病歷的臨床資訊與支援決策系統 (Computerized decision support) (ACP J Club. 2006;145:A8) 檢驗報告結合藥囑系統，由資訊系統進行控管，協助醫師臨床決策。 E.g. HLA-B\*1502, 5801**

第1次呼叫  
危OPD[1/2]:[0625  
/09:40]:莊[REDACTED]  
7160809],HLA-B[HLA-B\*  
15(15:02) &],.

今辨明出病患：

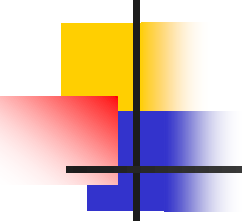


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Web Resources

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|-----------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------|------------|-----------------------------------|----------------------------|------------------------------------------------------------------------------------------------------|
| 1         |   | <a href="#">Ambulatory Pediatrics</a>                                    | Journal    | SDOS                              | 2001-2008/1                | JCR 北院區 南院區  聯合目錄 |
| 2         |   | <a href="#">Ambulatory Surgery</a>                                       | Journal    | Science Direct                    | 1995-2006                  | 北院區 南院區  聯合目錄     |
| 3         |   | <a href="#">American Annals of the Deaf</a>                              | Journal    | ProQuest                          | 1997-                      | 北院區 南院區  聯合目錄     |
| 4         |   | <a href="#">American Family Physician</a>                                | Journal    | MD Consult                        | 1999-                      | JCR 北院區 南院區  聯合目錄 |
| 5         |   | <a href="#">American Family Physician</a>                                | Journal    | American Academy Family Physician | 1998-                      | JCR 北院區 南院區  聯合目錄 |
| 6         |   | <a href="#">American Health</a>                                          | Journal    | ProQuest                          | 1988/1-1993/12             | 北院區 南院區  聯合目錄     |
| 7         |   | <a href="#">American Heart Journal</a>                                   | Journal    | Ovid                              | 1995-2005/5                | JCR 北院區 南院區  聯合目錄 |
| 8         |   | <a href="#">American Heart Journal</a>                                   | Journal    | MD Consult                        | 1995-                      | JCR 北院區 南院區  聯合目錄 |
| 9         |   | <a href="#">American Heart Journal</a>                                   | Journal    | Science Direct                    | 1995-                      | JCR 北院區 南院區  聯合目錄 |
| 10        |   | <a href="#">American Indian and Alaska Native Mental Health Research</a> | Journal    | ProQuest                          | 1998-1999                  | 北院區 南院區  聯合目錄     |
| 11        |   | <a href="#">American Journal of Audiology</a>                            | Journal    | ProQuest                          | 1998/3-2009/12             | 北院區 南院區  聯合目錄     |
| 12        |   | <a href="#">American Journal of Cardiology</a>                           | Journal    | MD Consult                        | 2001-                      | JCR 北院區 南院區  聯合目錄 |
| 13        |   | <a href="#">American Journal of Cardiology</a>                           | Journal    | Science Direct                    | 1995-                      | JCR 北院區 南院區  聯合目錄 |



# 實證醫學於診療之應用

## 實證健康照護

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- 學習並保持最新的診療知識
- 有效率的選取有價值的資訊
- 判斷資訊是否正確減少偏差



← Childrens hospital

← Wards 28 - 31

Accidents and  
emergencies →

Blood test →

Fracture clinic →

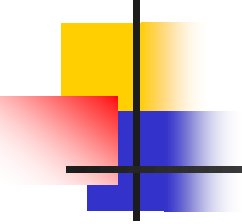
Pharmacy →

X-ray →

# 1. Asking Answerable Clinical Question (PICO)

|                                   |                   |
|-----------------------------------|-------------------|
| <b>P</b> atient/Problem<br>病人問題   | 孕婦 (有氣喘家族史)       |
| <b>I</b> ntervention<br>介入處置 (檢查) | 吃益生菌 (probiotics) |
| <b>C</b> omparison<br>對照的處置       | 不吃益生菌             |
| <b>O</b> utcomes<br>臨床結果          | 減少新生嬰兒氣喘的<br>發生率  |

Step 1. 提出問題的要點：\* **As specific as possible!**



# 1. Asking Answerable Clinical Question (PICO)

P

- A child with appendicitis

I

- Laparoscopic appendectomy

C

- Open appendectomy

O

- Prognosis and complications

# 1. Asking Answerable Clinical Question (PICO)

Question: 罹患退化性膝關節炎的老年男性持續服用葡萄糖胺是否能改善其關節疼痛症狀？

| Patient and/or problem<br>病人或問題  | 退化性膝關節炎的老年男性       |
|----------------------------------|--------------------|
| Intervention<br>介入處置             | 葡萄糖胺 (Glucosamine) |
| Comparison intervention<br>對照的處置 | 安慰劑 (Placebo)      |
| Outcomes<br>臨床結果                 | 關節疼痛改善             |

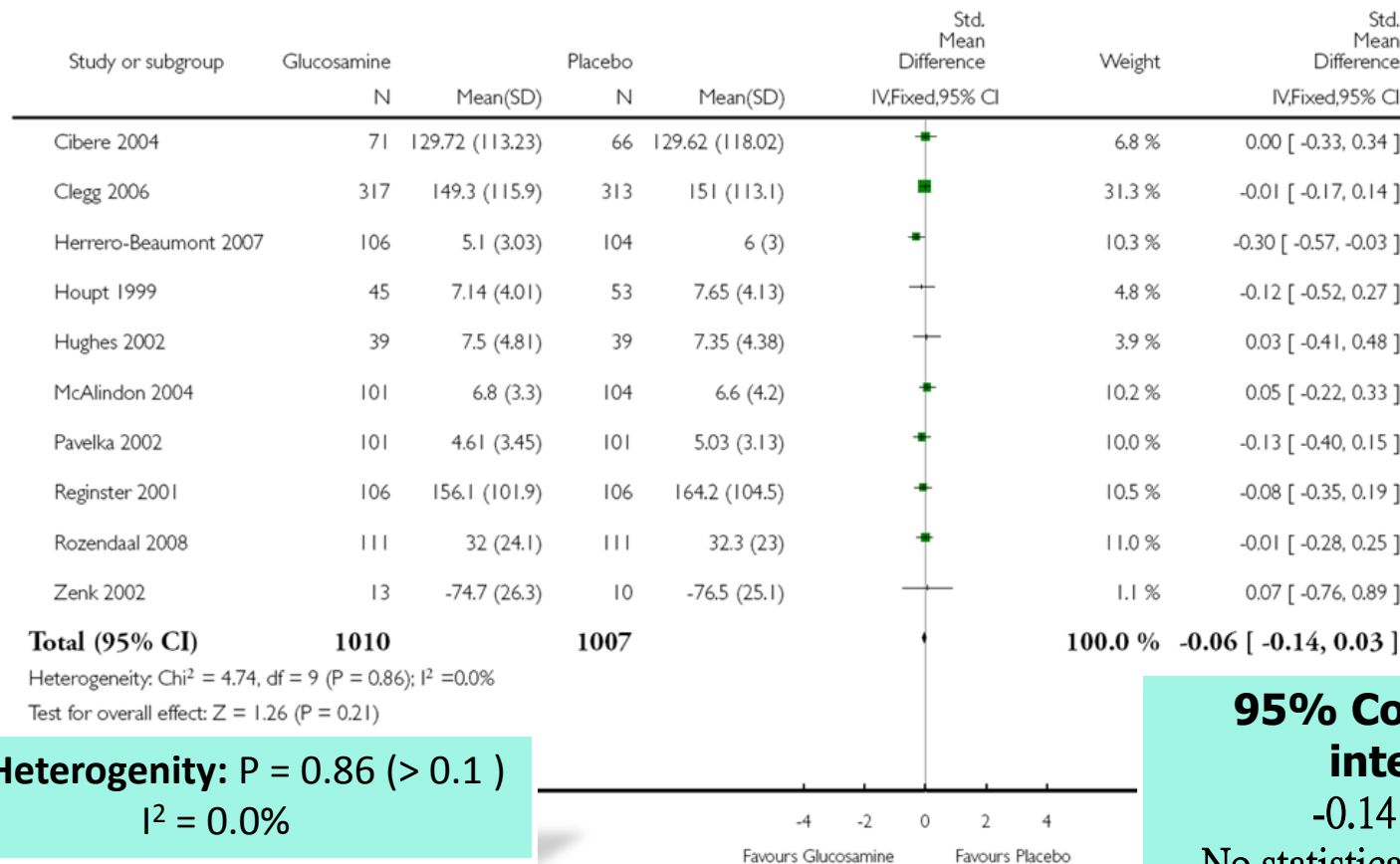
# Conclusion

**Cochrane** Database Syst Rev. 2005 Apr 18;CD002946  
**BMJ**. 2010 Sep 16;341:c4675. Effects of glucosamine, chondroitin, or placebo in patients with osteoarthritis of hip or knee: network meta-analysis.



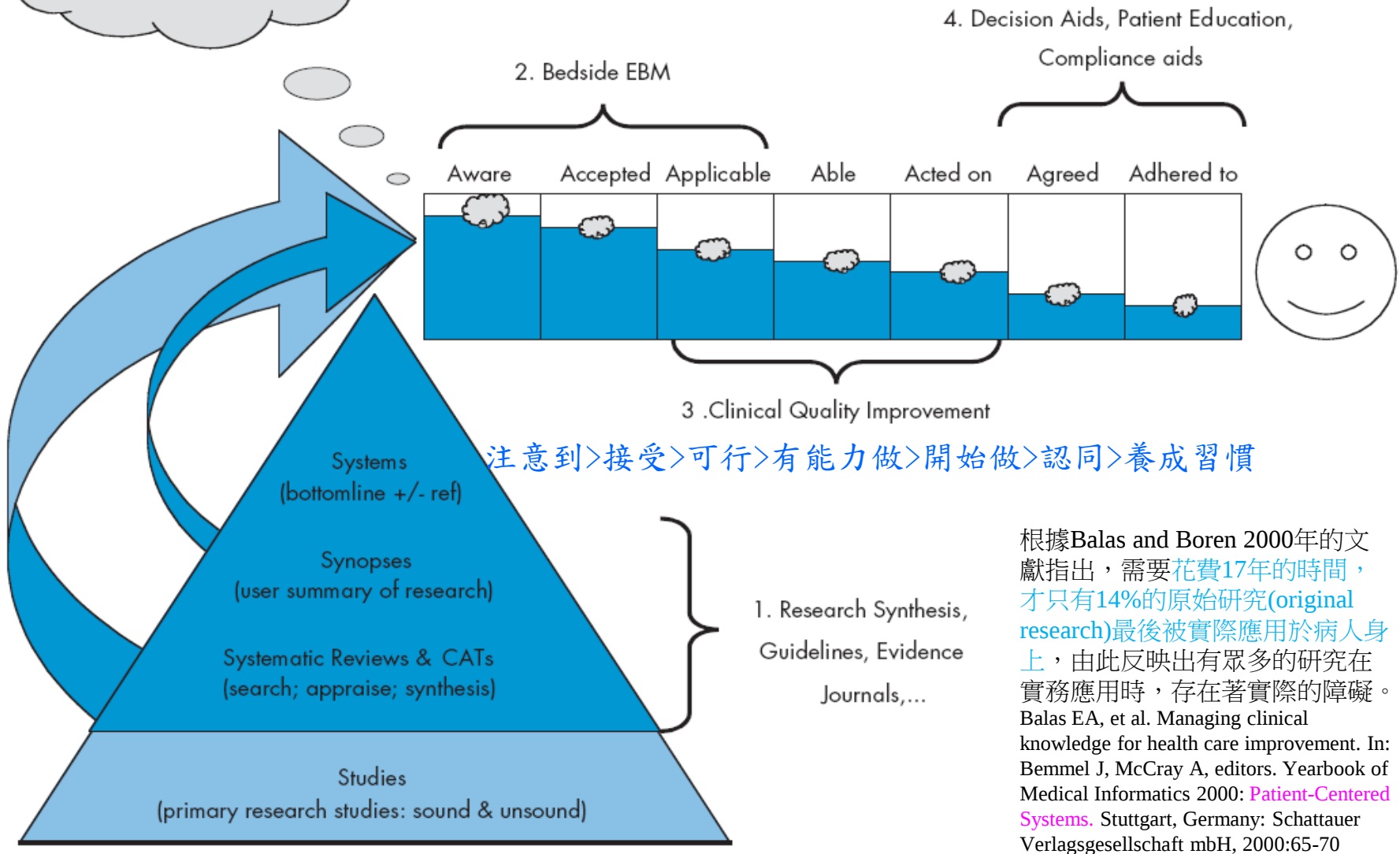
**Compared with placebo, glucosamine do **NOT** reduce joint pain or have an impact on narrowing of joint space.**

## Analysis 3.4. Comparison 3 Glucosamine versus placebo (adequate allocation concealment), Outcome 4 WOMAC Pain Subscale.

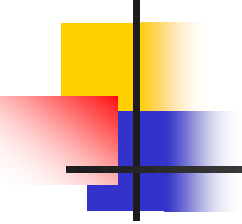




# 實證健康照護：從研究到實踐



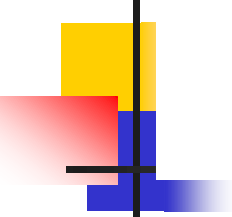
The research-to-practice pipeline. New research, of varying soundness, is added to the expanding pool and enters practice both directly or is reviewed, summarised, and systematised (delay) before entering practice, with leakage occurring at each of several stages between awareness and patient outcome. Different knowledge translation disciplines focus on different parts of the pipeline (1-4).



# 實證健康照護：從研究到實踐 知識轉譯過程

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- Paul Glasziou 稱這個應用模式為：證據管道 (evidence pipeline)，由左邊的實證資料庫進入到右側的應用端，主要有7個應用階段 (7 “A”)，分別為
  - 注意到 (aware)
  - 接受 (accepted)
  - 可行 (applicable)
  - 有能力做 (able)
  - 開始做 (acted on)
  - 認同 (agreed)
  - 養成習慣 (adhered to)



# Preoperative Hair Removal— a Systematic Literature Review

## **RECOMMENDATIONS FROM THE US AGENCY FOR HEALTHCARE POLICY AND RESEARCH**

| <b>Level</b> | <b>Type of documentation</b>                                                                                                                                    |
|--------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Ia           | Meta-analyses                                                                                                                                                   |
| Ib           | Randomized controlled trials                                                                                                                                    |
| IIa          | Controlled studies (eg, prospective observational studies with sequential switchover)                                                                           |
| IIb          | Quasi-experimental studies (eg, prospective studies comparing groups in which the allocation was not randomized)                                                |
| III          | Nonexperimental observational studies (eg, series of patients receiving treatment compared with historical controls, case control studies, correlation studies) |
| IV           | Documentation from expert groups or review articles                                                                                                             |
| 0            | Irrelevant studies                                                                                                                                              |



## Surgical site infections (SSIs)

1970s and 1980s Cruse et al.

1999 CDC guidelines (Mangram et al. Clipper, before surgery)

2006 Cochrane meta-analysis (Tanner et al. 2011 Update)

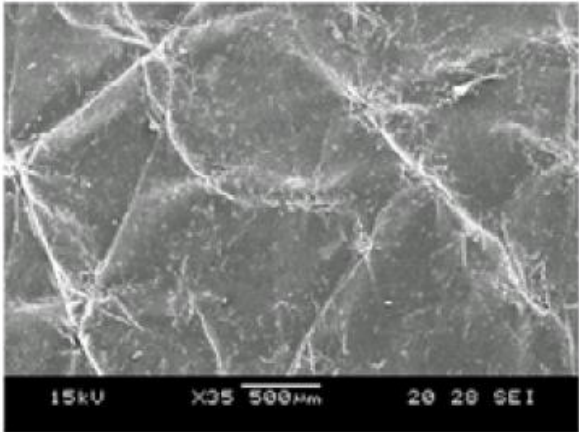
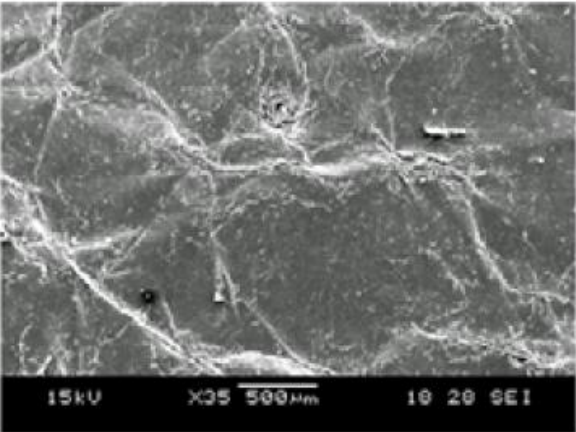
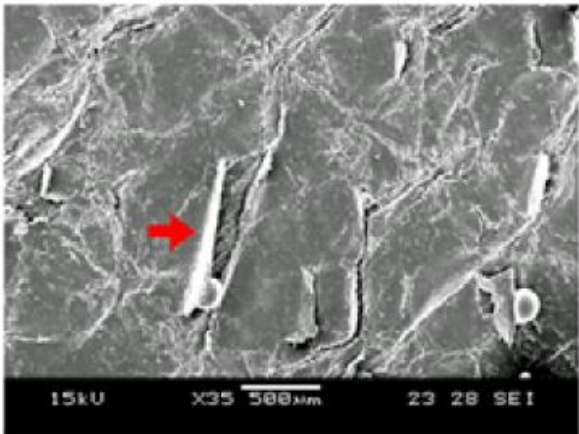
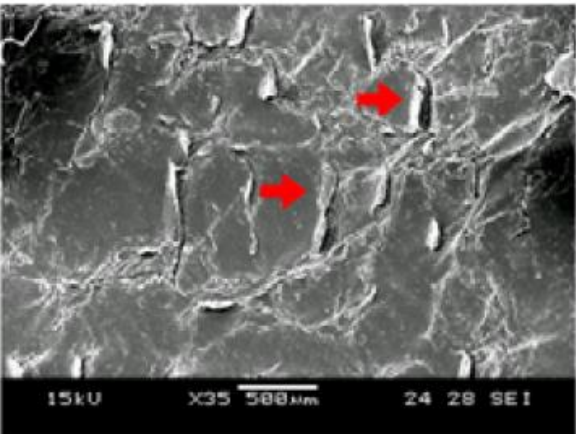
Cruse et al. **A five-year prospective study of 23,649 surgical wounds.** Arch Surg 1973;107:206-10 (SSI- Shaven 2.3% vs. Clipped 1.7% vs. No shaving 0.6%)

Cruse et al. The epidemiology of wound infection. A 10-year prospective study of 62,939 wounds. Surg Clin North Am 1980;60:27-40

Hamilton et al. **Preoperative hair removal.** Can J Surg 1977;20:269-71,274-5

Kjonnixsen et al. Preoperative hair removal -- a systematic literature review.

AORN J 2002;75:928-38

| Use                                                  | Skin magnified photo after two time shaving                                        |                                                                                     | Result                                                    |
|------------------------------------------------------|------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------|-----------------------------------------------------------|
| E C<br>l i<br>e p<br>c p<br>t p<br>r e<br>i c<br>a l |   |   | No skin irritation and damage                             |
| P r<br>e p<br>R a<br>z o<br>r                        |  |  | Skin irritation and damage can be seen<br><br>(    →    ) |

## PREOPERATIVE HAIR REMOVAL: IMPACT ON SURGICAL SITE INFECTIONS

# Surgical hand antisepsis to reduce surgical site infection (Review)

Tanner J, Swarbrook S, Stuart J



**THE COCHRANE  
COLLABORATION®**

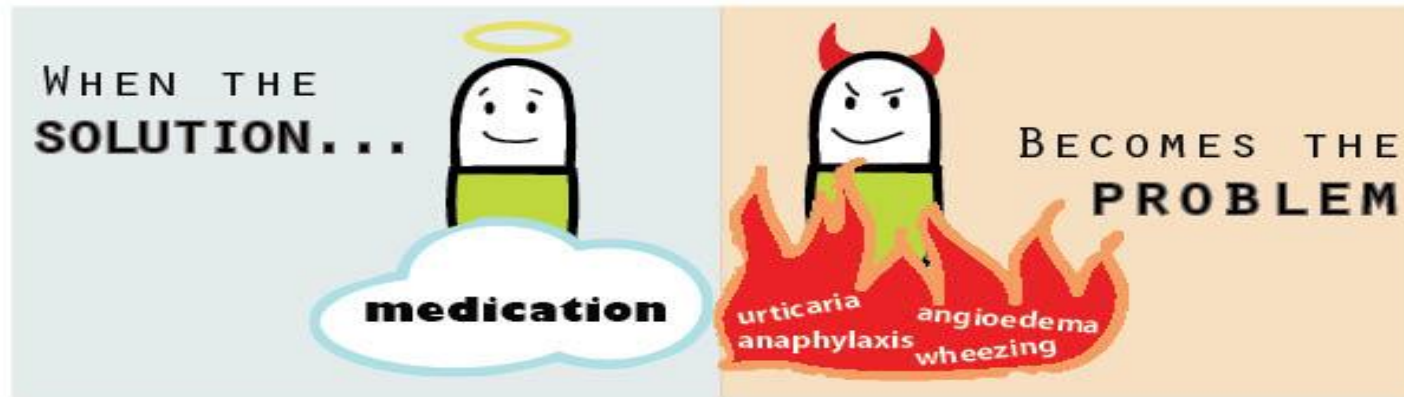
# Preoperative hair removal to reduce surgical site infection (Review)

Tanner J, Norrie P, Melen K

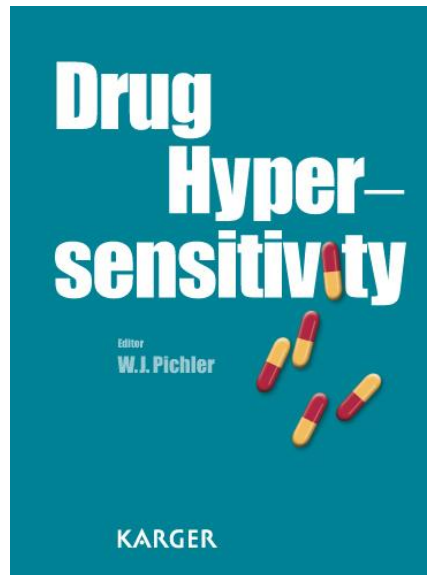


**THE COCHRANE  
COLLABORATION®**

# DRUG ALLERGY



## 藥物過敏



The exact **incidence** of SJS and TEN is unknown. SJS is estimated to affect **1–6 patients per million population per year**, and it is up to three times more common than TEN (Roujeau JC. N Engl J Med 1995; Rzany B. Br J Dermatol 1996).

Prevalence: 0.2-0.4% for Allopurinol

## 藥害救濟給付案之可疑藥品前六名 (1999-2011/10)

| 藥品學名          | 案例數 |
|---------------|-----|
| Allopurinol   | 96  |
| Carbamazepine | 89  |
| Phenytoin     | 82  |
| Isoniazid     | 51  |
| Pyrazinamide  | 49  |
| Rifampin      | 46  |

第1~150次審議會



# 婦吃痛風藥過敏破皮如燙傷

## 誘發史帝文森強生症 嚴重恐致死



**小心服藥**  
痛風藥，因對成分過敏，竟兩度引發史帝文森強生症候群，全身皮膚破皮、流血、疼痛，症狀嚴重猶如燒燙傷。衛生署去年統計顯示，申請藥物傷害救濟的死亡給付案中，以史帝文森強生症候群約佔六成的比率最高。醫師提醒，領藥前應主動告知藥物過敏史，服藥後須謹慎觀察。

**接獲** 獲此個案的台安醫院藥劑科高姓婦人服用醫師開立的痛風藥後，全身皮膚出現燒燙傷般的潰爛，到台安醫院就醫檢查發現，她對痛風藥中的Allopurinol成分過敏，因而誘發史帝文森強生症候群，住院治療三周才漸漸痊癒。

請藥物傷害救濟的死亡給付案為二十八件，其中十七件即為史帝文森強生症候群申請案，比率約佔六

其症狀輕微時，會導致眼睛、嘴巴等部位的黏膜潰瘍，皮膚出現紅疹、水泡，嚴重時皮膚即開始潰爛，狀況有如燒燙傷，病況危急時，易造成全身感染而導致敗血症，致死率約三成。

**主動告知過敏病史**

潘企岳提醒，抗癲癇、降尿酸等藥物較易導致史帝文森強生症候群，若對藥物過敏或需服用此類藥物者，應特別注意，若服藥後皮膚出現紅疹、發癢等症狀，甚至出現燙傷般脫皮，應盡速就醫。

郭浩藥師也提醒，有藥物過敏病史患者應主動告知醫師、藥師，避免開立相同成分藥物，並確認健保IC卡上藥物過敏史欄位，有詳細註記藥物過敏史，確保用藥安全。

資料來源：郭浩藥師 潘企岳醫師

衛生署去年統計顯示，民眾申



■高姓婦人服用痛風藥，全身皮膚破皮、流血。 郭浩藥師提供

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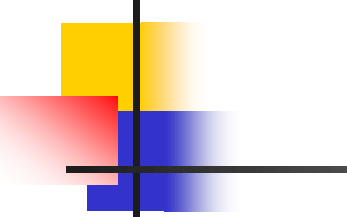
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Taiwan: 台灣族群帶有HLA-B\*5801 基因型 (15-18%)

A&R 2012;64: New Zealand 54 cases (1998-2010) in 3 Million population

# 藥害救濟給付案之可疑藥品前十名

(1999-2015.1)第1~217次審議會

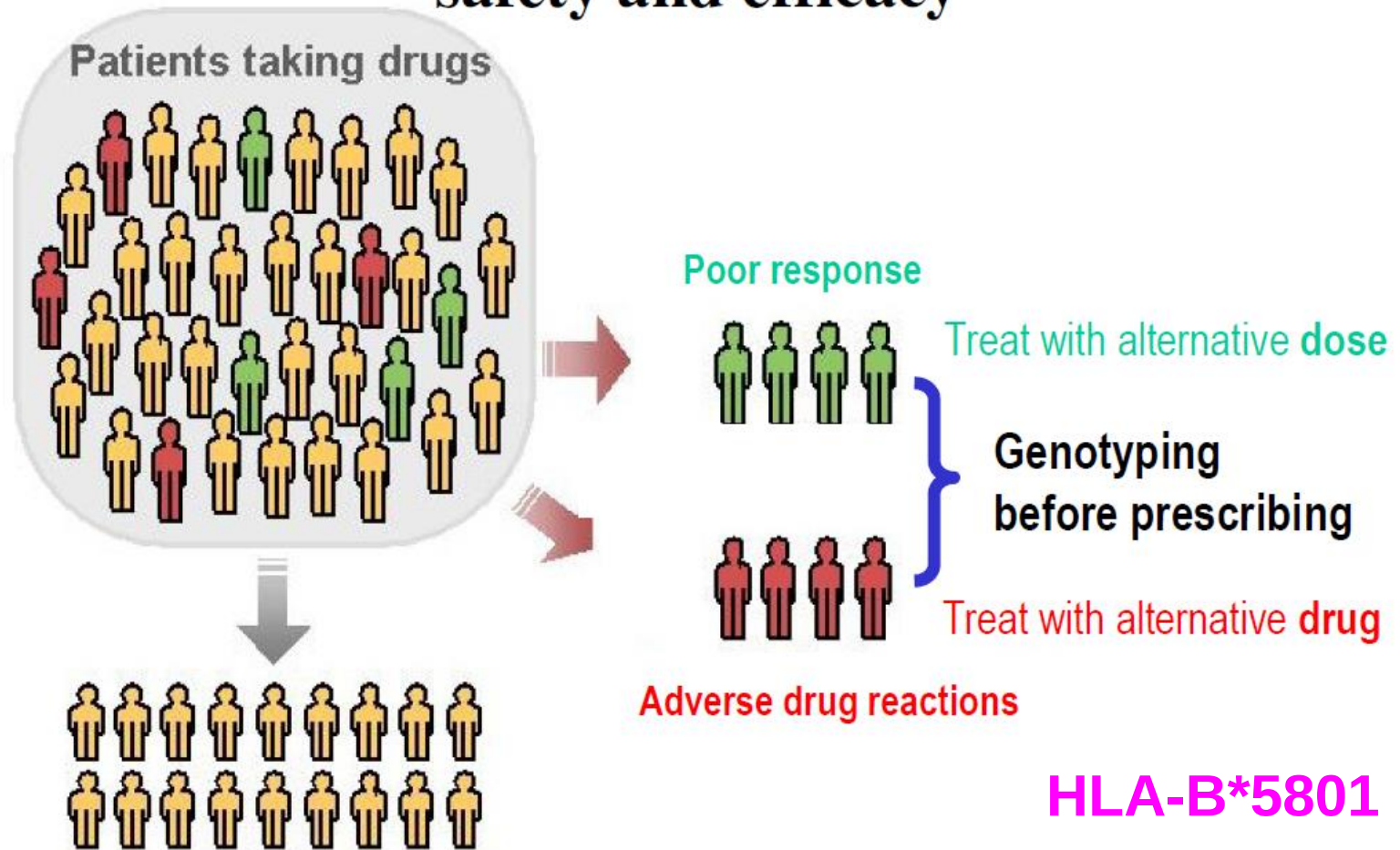


| 排名 | 藥物名稱                            | 案例數      |
|----|---------------------------------|----------|
| 1  | Allopurinol                     | 205      |
| 2  | Phenytoin                       | 132      |
| 3  | Carbamazepine                   | 113      |
| 4  | Rifampin/Isoniazid/Pyrazinamide | 73/70/68 |
| 5  | Diclofenac                      | 58       |
| 6  | Lamotrigine                     | 38       |
| 7  | Co-trimoxazole                  | 37       |
| 8  | Mefenamic acid                  | 34       |
| 9  | Ibuprofen                       | 33       |
| 10 | Cefazolin                       | 29       |

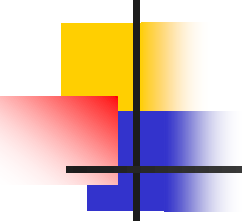
財團法人藥害救濟基金會88至104年1月藥害救濟統計資料

降尿酸、抗癲癇及非類固醇類消炎止痛藥最多，其案例數佔總給付案近半數。根據健保資料庫統計，**每一千人服用Allopurinol的人，即有2~3人會發生SJS/TEN。**

# Using Pharmacogenomics to improve drug safety and efficacy



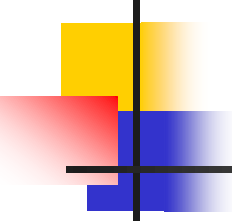
# HLA-B\*1502 or 5801 test performance



| DRUG          | HLA Allele | HLA Carriage Rate                     | Prevalence of diagnosis | Negative Predictive Value | Positive Predictive Value | NNT to prevent One Case |
|---------------|------------|---------------------------------------|-------------------------|---------------------------|---------------------------|-------------------------|
| Allopurinol   | B*5801     | 9-11% Han Chinese<br>1-6% Caucasian   | 1/250-1/1000            | 100% in Han Chinese       | 3%                        | 250                     |
| Carbamazepine | B*1502     | 10-15% Han Chinese<br><0.1% Caucasian | <1-6/1000               | 100% in Han Chinese       | 3%                        | 1000                    |

J ALLERGY CLIN IMMUNOL 2011;127:S60-S66

Even with 'strongly associated' medications such as carbamazepine or allopurinol, SCARs are actually very rare. Incidences are in the range of 1/10,000 to 1/1000 for DRESS.



# Uncertainty

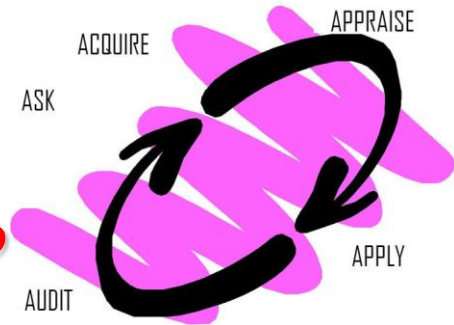
- EBM 應用於處理醫療的不確定性

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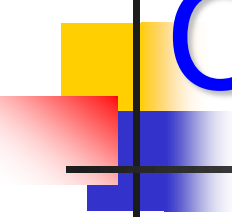
- 未來的健康照護有兩大重點：
  - Communication skills
  - Doctor-patient relationship
    - 告知、知情同意
- EBM to deal with this **Changing**

# 學習目標

## “Learning by Doing”



- **Five steps in practicing EBM (手法: 5A步驟)**
  - Formulate clinical question ~ **PICO** principle
    - **Search database**
      - Cochrane database, **CCTR**, DARE, ACP journal club
      - UpToDate
      - **PubMed** - **Clinical queries** (high quality filter) etc.
      - Micromedex, CINHAL...
    - **Judge level of evidence (研究設計), critical appraisal** (VIP principle, RAMbo, Critical appraisal sheet, CASP...)
- **Calculate NNT, NNH**
  - number needed to treat (**NNT** =  $1/ARR$ )
  - number needed to harm (**NNH** =  $1/ARI$ )
  - **Read forest plot (meta-analysis)**
- **Practice**
  - 積極主動自我學習 Attitude and behavior change (尋找資料 引用文獻)
  - **apply to patient care and chart record (cite reference!).**



# Case Scenario

---

- **Patient's Problem**
- **Raise Question**
- **Perform Five Steps in EBM (5 As)**
  - 問 **Ask**: ask a clinical question (PICO)
  - 找 **Acquire**: search database (cite references)
  - 評 **Appraisal** (VIP): Valid? Important? Practical?
  - 用 **Apply**: to patient's problem
  - 審 **Audit**: effectiveness

**Record in Chart**

Search: PubMed

[Limits](#) [Advanced search](#) [Help](#)**Search**

Clear

## PubMed

PubMed comprises more than 20 million citations for biomedical literature from MEDLINE, life science journals, and online books. Citations may include links to full-text content from PubMed Central and publisher web sites.

### Using PubMed

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### PubMed Tools

[Single Citation Matcher](#)[Batch Citation Matcher](#)[Clinical Queries](#)[Topic-Specific Queries](#)

### More Resources

[MeSH Database](#)[Journals Database](#)[Clinical Trials](#)[E-Utilities](#)[LinkOut](#)

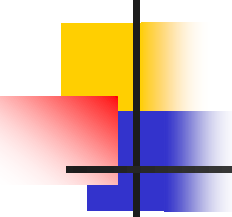
**UpToDate, Dynamed, Cochrane, PubMed-clinical queries...**

謝謝聆聽 敬請指教

Thank you!



Yu K.H.  
Taiwan



以下為 補充附件

---

# The Evidence Pyramid

原始文獻：以研究方法區分

隨機對照+雙盲之試驗研究

隨機對照試驗研究

世代研究

病例對照研究

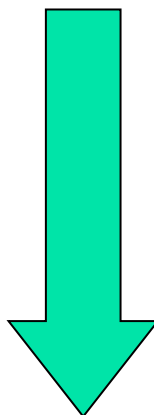
病例系列研究

病例報告

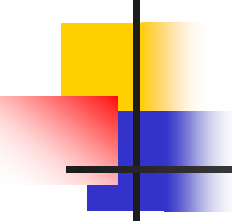
專家意見

動物實驗

試管試驗



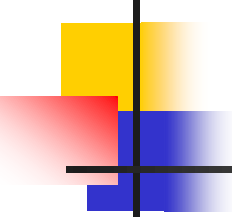
研究設計與證據強度 (Bias, or Robust)



# 實證醫學的五大進行步驟

## Five Steps to Practice EBM (5 As)





# 1. Asking Answerable Clinical Questions ~ use PICO format ~

---

There Are Four Elements of a Well-formulated Question

**P**atient ~ Who is the patient or what is the problem being addressed?

病人問題

**I**ntervention ~ What is the intervention? **(A)**

介入處置 或 檢驗

**C**omparison ~ What are the alternatives? **(B)**

對照的處置 或 檢驗 (其它的處置選擇)

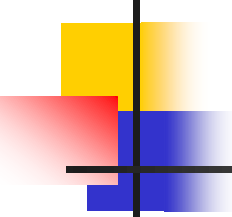
**O**utcome ~ What are the outcomes?

重要的臨床結果、指標

# Scenario 臨床情境

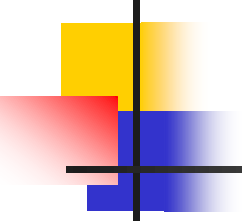
: Ask ~ PICO

- 如何降低外科手術傷口感染率，嬰幼兒術前禁食之時間長短
  - Q&A: 手術前需不需剃除毛髮，手術前剃除毛髮會增加或減少手術部位感染的風險？治療預後、病人安全問題
- 退化關節炎的老年人，應服用維骨力嗎
  - 治療問題
- 腰椎穿刺後需不需平躺8小時減少頭痛發生
  - 治療預後問題
- 下背痛患者，抽血HLA B27結果如何判讀
  - 診斷問題



# 風濕免疫常見疾病之實證醫學範例

| 疾病                      | PICO 問題                                                              |
|-------------------------|----------------------------------------------------------------------|
| 1. SLE lupus nephritis  | WHO第四型狼瘡腎炎，使用 <b>Cyclophosphamide</b> 與使用 <b>steroid</b> 之差別         |
|                         | WHO第四型狼瘡腎炎，使用Cyclophosphamide與使用Mycophenolate之差別                     |
| 2. Rheumatoid arthritis | 關節炎患者，使用 <b>COX 2 inhibitor</b> 與傳統 <b>NSAID</b> 止痛藥物，對產生心血管疾病風險之差異？ |
| 3. Gout                 | 急性痛風關節炎時，使用高劑量或低劑量之秋水仙素？                                             |
| 4. Dermatomyositis      | 嚴重皮肌炎患者，使用免疫球蛋白治療？                                                   |
| 5. Scleroderma          | 硬皮症患者，使用高劑量或低劑量之D-penicillamine治療？                                   |
| 6. Osteoarthritis       | 退化關節炎患者，使用維骨力治療以減少疼痛及退化速度？                                           |



## 2. Searching The Best Evidence 尋找最佳實證資料

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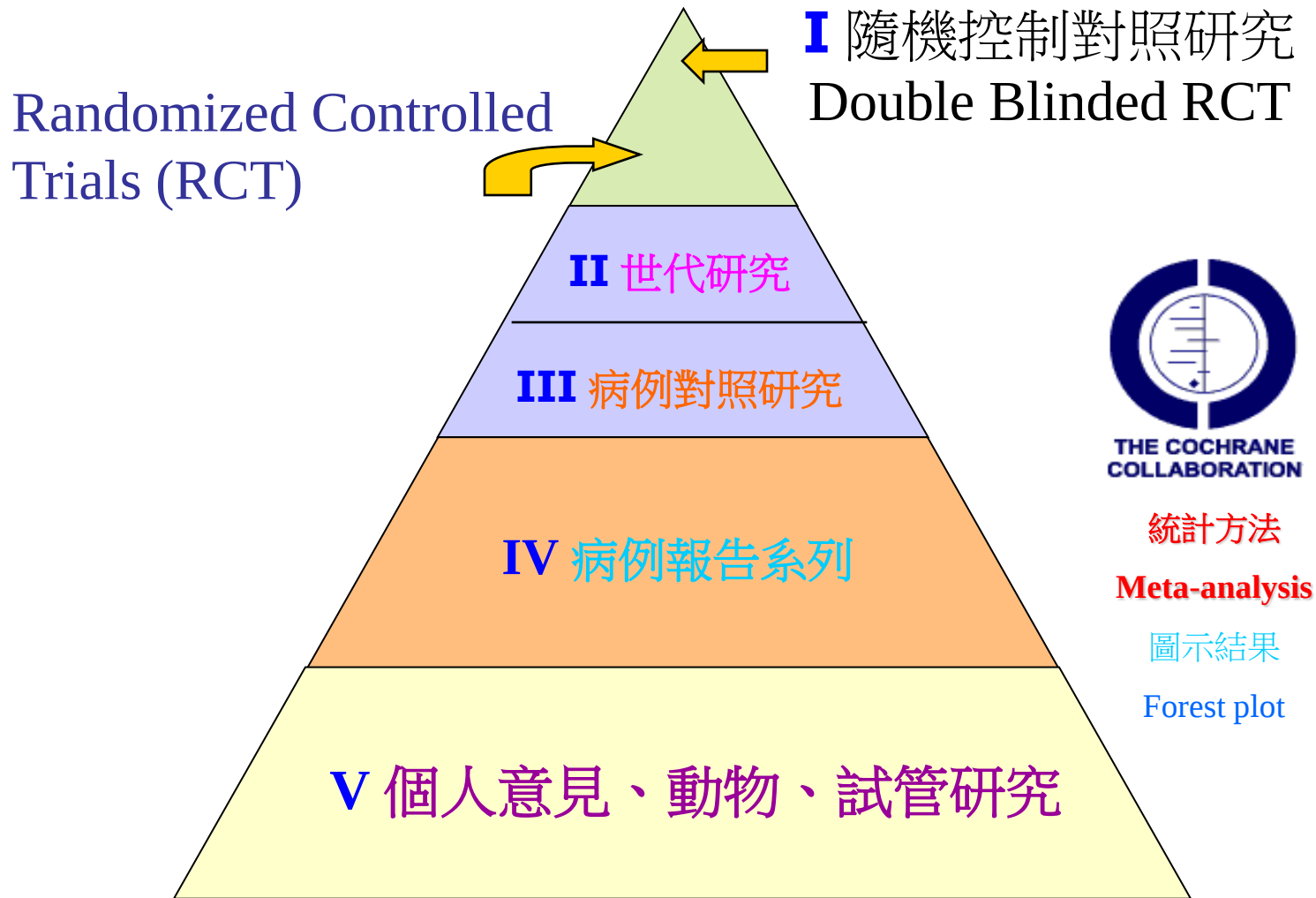
- 直接使用實證醫學資料庫 (**secondary journals or databases**) ~ ACP journal club, Cochrane database, CINAHL (**Cumulative Index to Nursing and Allied Health Literature**), Micromedex...
- 或是找研究論文資料庫 (**primary journals or databases**) ~ 如 Medline, NEJM, Lancet...
- **原則**：搜尋與病人問題相同或類似且**證據等級(level of evidence – 由上往下 top down)** 較高之文獻，再謹慎評讀與評估此文章的證據在此問題的適用性。

# 資料庫搜尋 Database (Internet, Intranet)



# The Evidence Pyramid

Level of Evidence: I~V

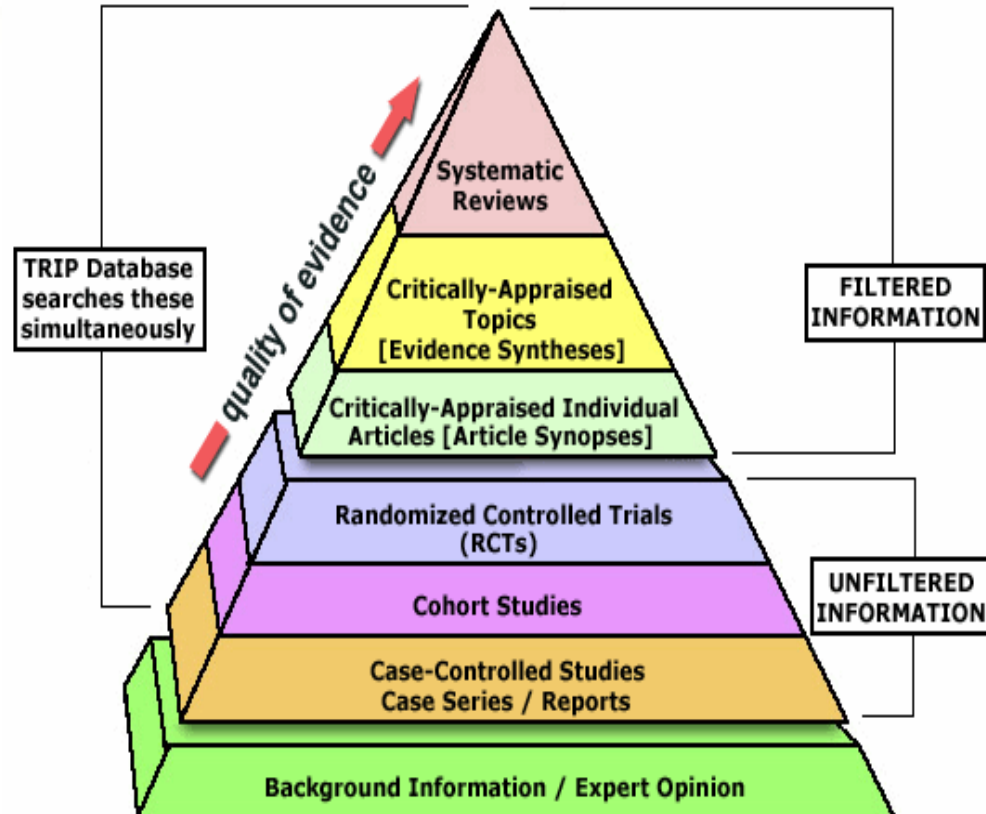


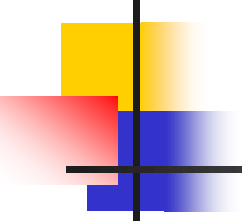
Meta - analysis

研究設計與證據強度 (Bias, Robust)

Hierarchy of evidence: arranges study designs by their susceptibility to bias.

# Search- and EBM-pyramids





# Treatment of Class III-IV Lupus Nephritis

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## Meta-Analysis (統合分析) (pooling studies)



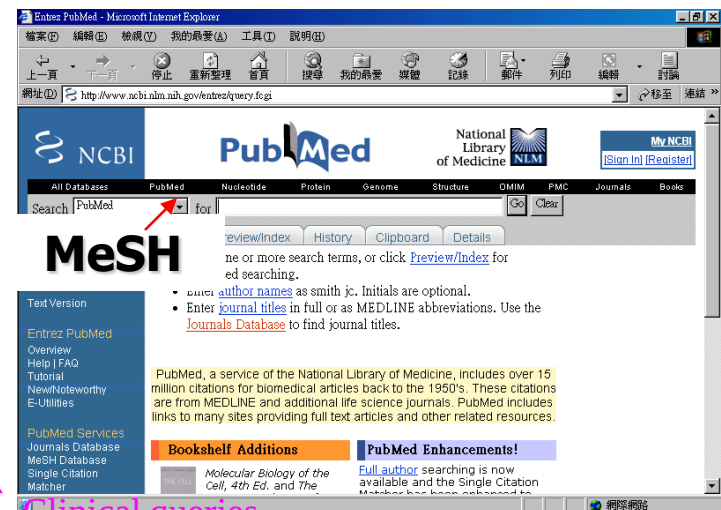
**Treatment of diffuse proliferative lupus nephritis: A meta-analysis  
of randomized controlled trials**

Am J Kidney Dis. 2004;43:197-208.

*Cochrane Renal Group Cochrane Database of Systematic  
Reviews. 1, 2004.*

# Search the Best Evidence

- 1. Cochrane library, CCTR\*, ACP journal club, DARE
- 2. UpToDate, Dynamed, MD consult
- 3. PubMed, Medline, CINAHL
  - *Meta-analysis*
  - *Systematic review*
  - *Cochrane (keyword 關鍵字)*
  - *Clinical queries\* (高品質)*
- Clinical evidence
- Best evidence
- Guidelines Clearinghouse ...
- (Evidence is never enough)



Free: [http://www.mrw.interscience.wiley.com/cochrane/cochrane\\_search\\_fs.html](http://www.mrw.interscience.wiley.com/cochrane/cochrane_search_fs.html)

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Display Summary

All: 2 Review: 1

**Keywords: xxx and xxx and (Cochrane or meta-analysis or Systematic review)**

1: [Baun](#)

2: [Woo](#)

glucosamine and osteoarthritis (Cochrane or meta-analysis or systematic review)

Search Clear

Results: 1 to 20 of 179

- Antioxidants and antiinflammatory dietary supplements for osteoarthritis and rheumatoid arthritis. Rosenbaum CC, O'Mathuna DP, Chavez M, Shields K. Altern Ther Health Med. 2010 Mar-Apr;16(2):32-40. Review. PMID: 20232616 [Published - indexed for MEDLINE]
- QARS recommendations for the management of hip and knee osteoarthritis: part III. Changes in evidence following systematic cumulative update of research published through January 2009. Zhang W, Nuki G, Moskowitz RW, Abramson S, Altman RD, Arden NK, Bierma-Zeinstra S, Brandt KD, Croft P, Doherty M, Dougados M, Hochberg M, Hunter DJ, Kwoh K, Lohmander LS, Tugwell P. Osteoarthritis Cartilage. 2010 Apr;18(4):476-99. Epub 2010 Feb 11. PMID: 20170770 [Published - in process]
- Choosing nonopioid analgesics for osteoarthritis: clinician summary guide. Agency for Healthcare Research and Quality U.S. Department of Health and Human Services. J Pain Palliat Care Pharmacother. 2009;23(4):433-57. PMID: 19947847 [Published - indexed for MEDLINE]
- The clinical effectiveness of glucosamine and chondroitin supplements in slowing or arresting progression of osteoarthritis of the knee: a systematic review and economic evaluation. Black C, Clar C, Henderson R, MacEachern C, McNamee P, Quayyum Z, Royle P, Thomas S. Health Technol Assess. 2009 Nov;13(52):1-148. Review. PMID: 19903416 [Published - indexed for MEDLINE]

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Review (165)

Free Full Text (34)

Titles with your search terms

- Glucosamine long-term treatment and the progression of knee o (Ann Pharmacother. 2005)
- Glucosamine and chondroitin for treatment of osteoarthritis: a systematic qu (JAMA. 2000)
- Structural and symptomatic efficacy of glucosamine and chon (Arch Intern Med. 2003)

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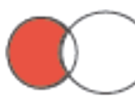
- Evaluation of symptomatic slow-acting drugs in osteoarthritis (BMC Musculoskelet Disord. 2005)
- Review: Glucosamine hydrochloride for the treatment of osteoarthritis (Cin Interv Aging. 2007)

# Search Strategy

## 搜尋策略 1



### 布林邏輯 (Boolean logics)

| 運算元 | 例舉                | 圖示                                                                                   | 作用                        |
|-----|-------------------|--------------------------------------------------------------------------------------|---------------------------|
| AND | H1N1 AND Tamiflu  |   | 1. 縮小檢索範圍;<br>2. 用於相異概念詞彙 |
| OR  | H1N1 OR Swine flu |   | 1. 擴大檢索範圍;<br>2. 用於相似概念詞彙 |
| NOT | H1N1 NOT bird flu |  | 排除不相關的範圍                  |

|   | Primary Term |    | Synonym 1   |    | Synonym 2 |  |
|---|--------------|----|-------------|----|-----------|--|
| P | ( H1N1       | OR | Swine flu   | OR | ) AND     |  |
| I | ( Tamiflu    | OR | Oseltamivir | OR | ) AND     |  |
| C | (            | OR |             | OR | ) AND     |  |
| O | (            | OR |             | OR |           |  |

# 1. Asking Answerable Clinical Question (PICO)

|                                   |                   |
|-----------------------------------|-------------------|
| <b>P</b> atient/Problem<br>病人問題   | 孕婦 (有氣喘家族史)       |
| <b>I</b> ntervention<br>介入處置 (檢查) | 吃益生菌 (probiotics) |
| <b>C</b> omparison<br>對照的處置       | 不吃益生菌             |
| <b>O</b> utcomes<br>臨床結果          | 減少新生嬰兒氣喘的發生率      |

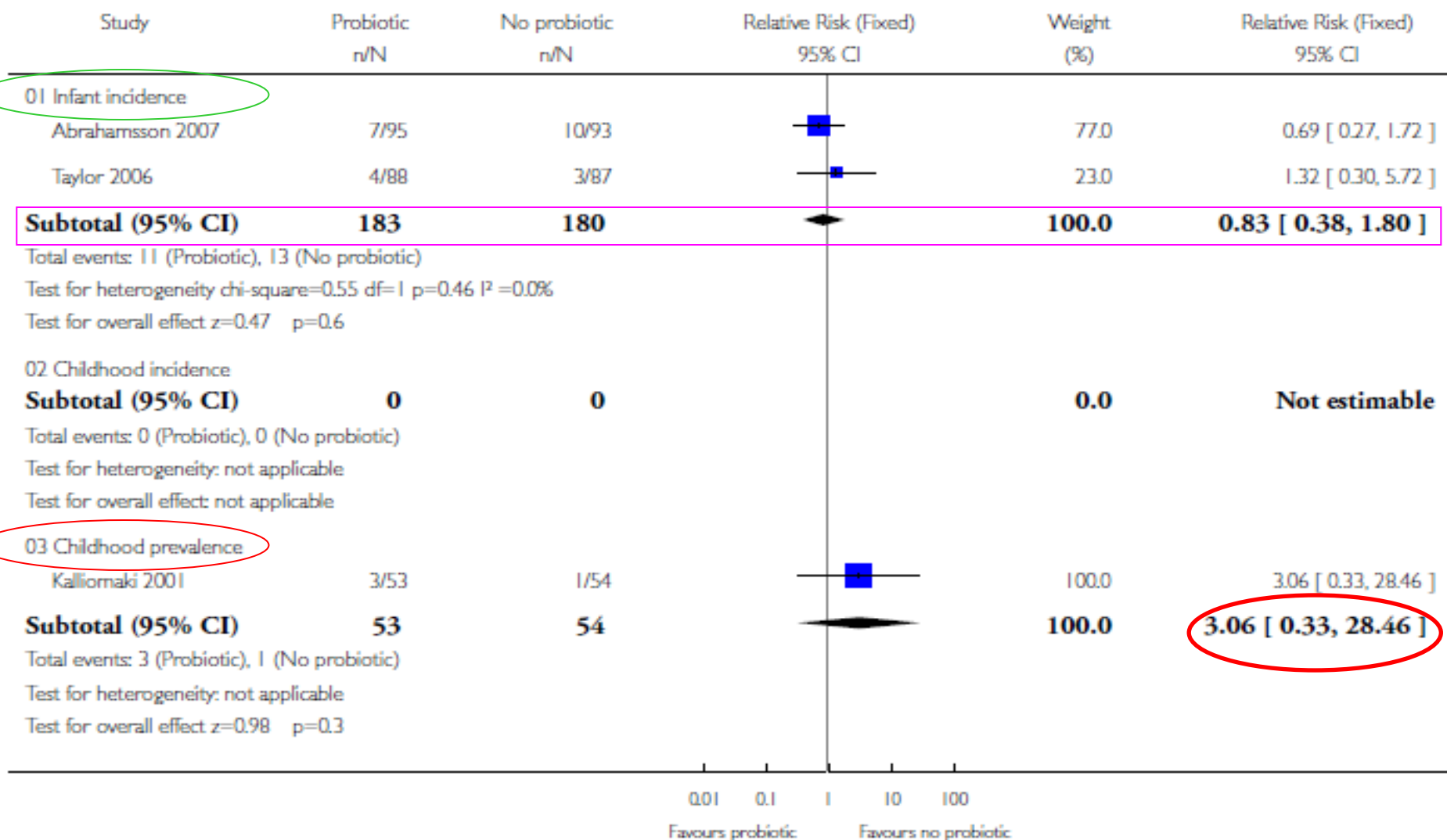
Step 1. 提出問題的要點：\* **As specific as possible!**

## Analysis 01.04. Comparison 01 Probiotic versus no probiotic - all infants, Outcome 04 Asthma

Review: Probiotics in infants for prevention of allergic disease and food hypersensitivity

Comparison: 01 Probiotic versus no probiotic - all infants

Outcome: 04 Asthma



# Randomized, Double-Blind, Placebo-Controlled Trial of Probiotics for Primary Prevention: No Clinical Effects of *Lactobacillus* GG Supplementation

Matthias Volkmar Kopp, MD, Isabell Hennemuth, MD, Andrea Heinzmann, MD, Radvan Urbanek, MD

University Children's Hospital, Freiburg, Germany

The authors have indicated they have no financial relationships relevant to this article to disclose.

## What's Known on This Subject

Epidemiologic data show that children with allergy have a different intestinal flora from healthy children. Based on these data, "harmless" microbial agents, that is, probiotics, have been tested for their efficacy in the prevention of allergy in infants. However, the value of probiotics for primary prevention is controversial.

## What This Study Adds

Supplementation with *Lactobacillus* GG during pregnancy and early infancy did not reduce the incidence of atopic dermatitis or alter the severity of atopic dermatitis in affected children but was associated with an increased rate of recurrent episodes of wheezing bronchitis. Therefore, *Lactobacillus* GG cannot be recommended generally for primary prevention.

## ABSTRACT

**BACKGROUND.** The value of probiotics for primary prevention is controversial. Published trials vary considerably in study design and the applied probiotics, thereby limiting comparability of the results.

**OBJECTIVE.** The purpose of this trial was to study the preventive effect of the probiotic *Lactobacillus* GG on the development of atopic dermatitis.

**METHODS.** In a double-blind, placebo-controlled prospective trial, 105 pregnant women from families with  $\geq 1$  member (mother, father, or child) with an atopic disease were randomly assigned to receive either the probiotic *Lactobacillus* GG (American Type Culture Collection 53103;  $5 \times 10^9$  colony-forming units of *Lactobacillus* GG twice daily) or placebo. Ninety-four families (89.5%) completed the trial. The supplementation period started 4 to 6 weeks before expected delivery, followed by a postnatal period of 6 months. The primary end point was the occurrence of atopic dermatitis at the age of 2 years. Secondary outcomes were severity of atopic dermatitis, recurrent episodes of wheezing bronchitis, and allergic sensitization at the age of 2 years.

**RESULTS.** Atopic dermatitis was diagnosed in 14 (28%) of 50 in the *Lactobacillus* GG group and in 12 (27.3%) of 44 in the placebo group. The risk of atopic dermatitis in children on probiotics relative to placebo was 0.96 (confidence interval 0.38–2.33). Severity of atopic dermatitis was comparable between the 2 groups. Notably, children with recurrent ( $\geq 5$ ) episodes of wheezing bronchitis were more frequent in the *Lactobacillus* GG group (26%;  $n = 13$ ), as compared with the placebo group (9.1%;  $n = 4$ ). No difference was observed between both groups in total immunoglobulin E concentrations or numbers of specific sensitization to inhalant allergens.

**CONCLUSIONS.** Supplementation with *Lactobacillus* GG during pregnancy and early infancy neither reduced the incidence of atopic dermatitis nor altered the severity of atopic dermatitis in affected children but was associated with an increased rate of recurrent episodes of wheezing bronchitis. Therefore, *Lactobacillus* GG cannot be generally recommended for primary prevention.

[www.pediatrics.org/cgi/doi/10.1542/peds.2007-1492](http://www.pediatrics.org/cgi/doi/10.1542/peds.2007-1492)

doi:10.1542/peds.2007-1492

We affirm that the study has been registered at a qualified national registry, the registry for clinical studies at the University of Freiburg. Registration number is UKF000505.

### Key Words

allergy, prevention, probiotics, *Lactobacillus* GG, atopic dermatitis, neonates

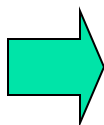
### Abbreviations

Th—T helper  
LGG—*Lactobacillus* GG  
AD—atopic dermatitis  
IgE—immunoglobulin E  
CI—confidence interval  
OR—odds ratio

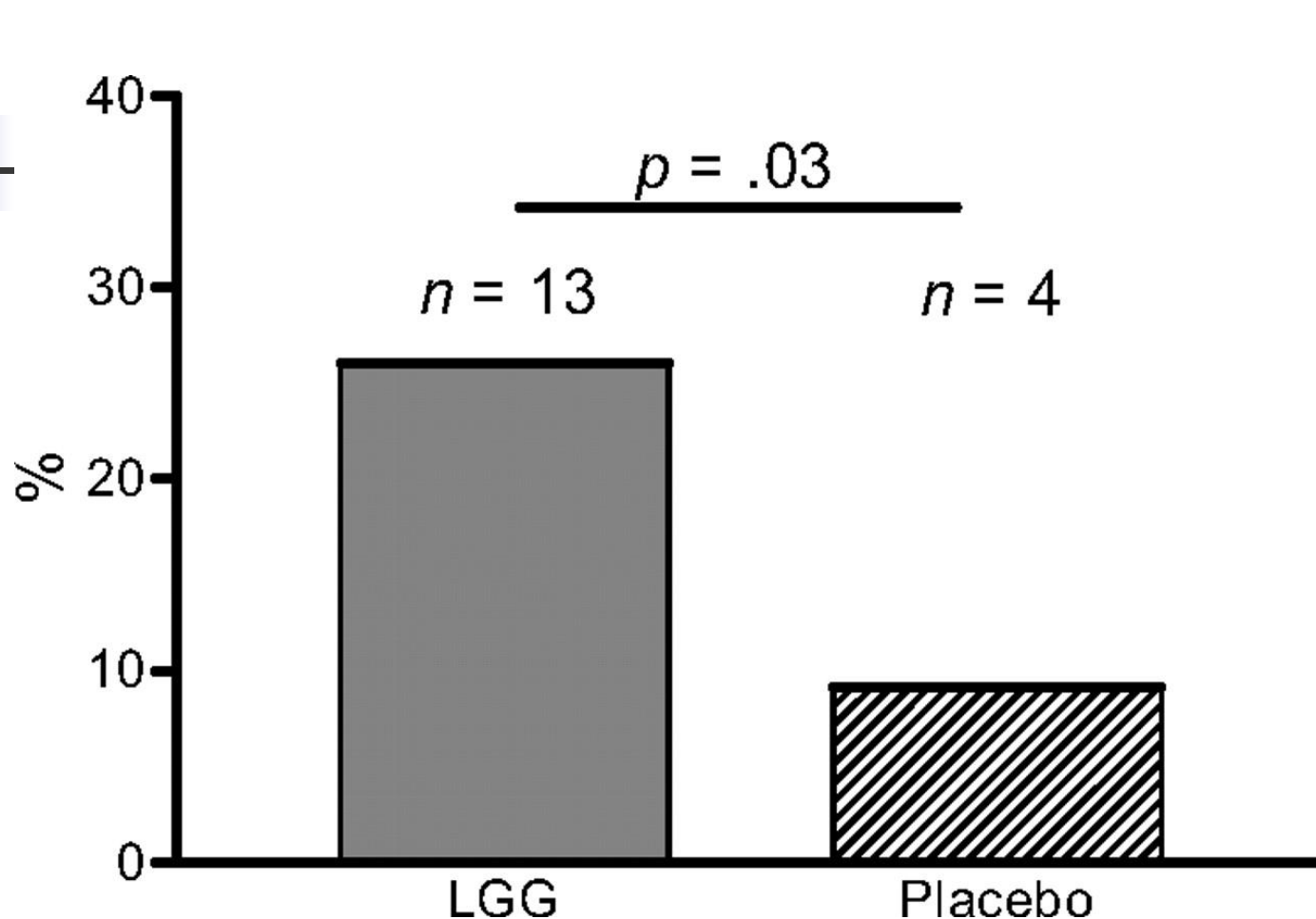
Accepted for publication Sep 21, 2007

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PEDIATRICS (ISSN Numbers: Print, 0031-4005; Online, 1098-4275). Copyright © 2008 by the American Academy of Pediatrics



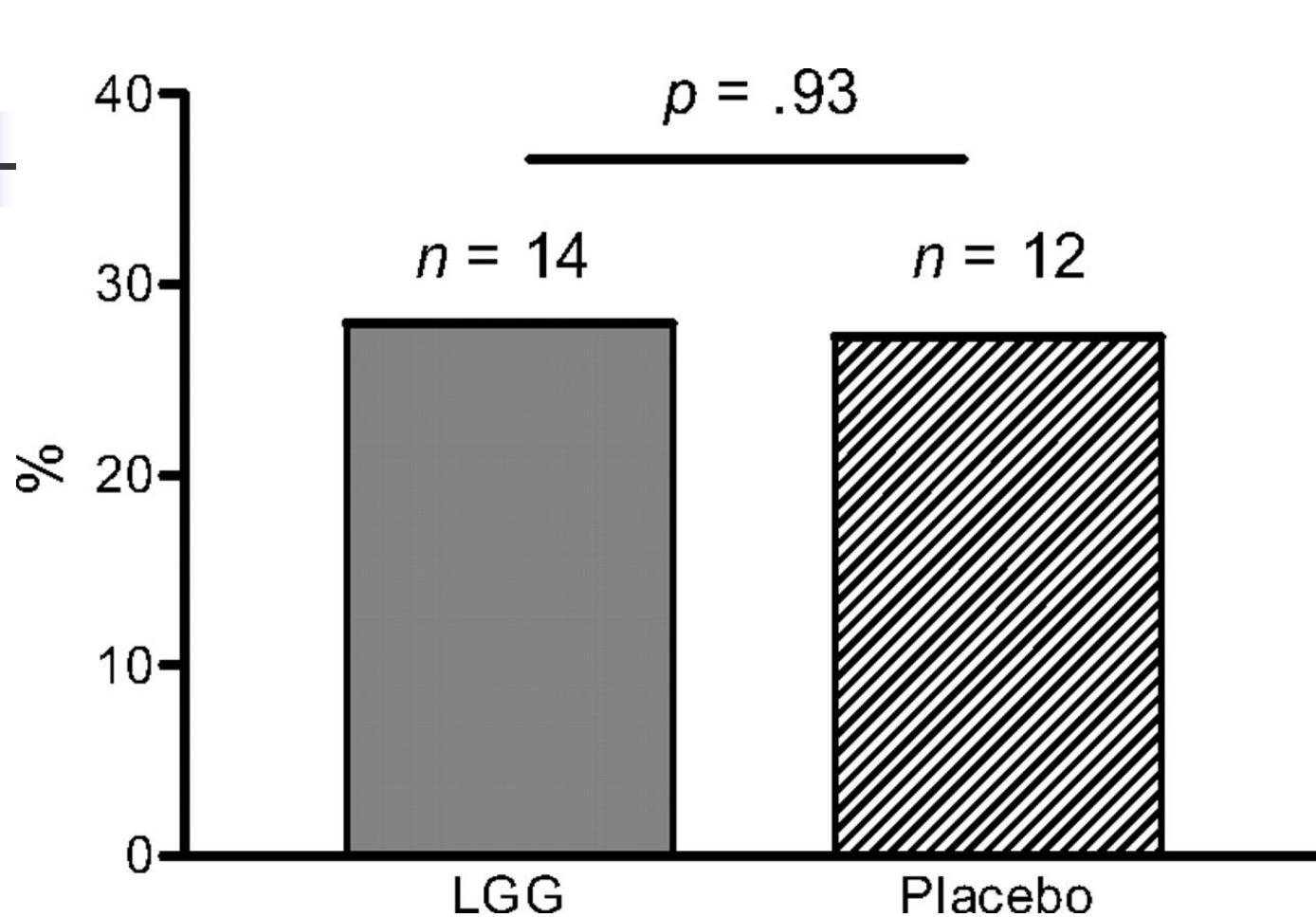
**FIG 4. Treatment effect of LGG on atopic diseases showing the proportion of children with  $\geq 5$  episodes of wheezing bronchitis during the first 2 years of life**



Kopp M. V. et al. Pediatrics 2008;121:e850-e856

**Critical appraisal:  
Not ITT analysis**

**FIG 2. Treatment effect of LGG on atopic diseases showing the proportion of 2-year-old children with Atopic Dermatitis (Eczema)**



**Kopp M. V. et al. Pediatrics 2008;121:e850-e856**

# 3. 如何評讀論文

可以應用到我的病人嗎？

How do I apply the results to the care of my patients? (**VIP**: both 1 & 2)

1. Are the result **Valid**? (文獻的結果可信嗎? Truth?)
2. What is the **Impact**? (效果大小 Size of the effect: **NNT**)
3. Practical in **Practice**? (**VIP**)

### 3. Critically Appraising the Evidence

## 治療文獻 論文評讀 重點

### 評估文章的可信度(Validity)和實用性(\*注意研究選入病人的條件是否相似)

1. 病人的分組是隨機分派的嗎？(random allocation) Yes or No
2. 分派的方法是否保密？(concealment of allocation) Yes or No
3. 追蹤是否完整？(follow-up duration) (rate > 80%) (失聯者少於20%為佳)
4. 治療方法對病患、醫護人員、研究者是否blinded？(雙盲，盲性客觀評估)
5. 是否利用意圖治療分析intention-to-treat analysis (ITT)？ vs. per protocol
6. 除了研究治療項目以外，其他的治療在各組間是否相同？(same)
7. 兩組在治療開始時的基礎條件(baseline)是否相似？(Table 1)

■ 閱讀每一篇文章時，要注意是否符合以上基本原則，如果沒有，是為什麼沒有，對於結果有沒有影響？

■ 當有了一個可信的結果，還要考慮文章的結果對病人實際上的意義為何？重不重要 (Impact: size of the effect, NNT, NNH)？

文章常以RRR (Relative risk reduction)來表示療效，但以 NNT (益一治療數 Number Needed to Treat)，及 NNH (Number needed to harm) 來表達更為直接。

- Validity: consider selection bias, information bias, confounding factor
- Reliability of measurement: intraobserver (similarity over time), interobserver, internal consistency
  - SD, variance, 95% CI (confidence interval~ wide or narrow),  $p$  value (> or < 0.05)

# Treatment of Proliferative lupus nephritis

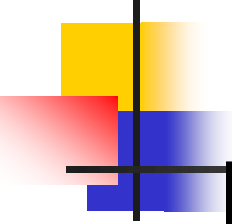
嚴格評讀 ~ 研究方法的品質：如 隨機產生方式、隱密性，盲性，ITT及失聯比率。

(評讀的 Checklist: Jadad score, Grade method, VIP, RAMbo, CAT, CASP...)

Table 3. Quality assessment of RCTs Included in This Systematic Review

| Reference                    | Year | Allocation<br>Concealment | Blinding                                             | Intention-to-Treat<br>Analysis | Lost to Follow-Up* |
|------------------------------|------|---------------------------|------------------------------------------------------|--------------------------------|--------------------|
| Austin et al <sup>14</sup>   | 1986 | Unclear                   | No                                                   | No                             | 4/107 (3.7)        |
| Balletta et al <sup>16</sup> | 1992 | Unclear                   | No                                                   | Yes                            | 0/10 (0.0)         |
| Barron et al <sup>12</sup>   | 1982 | Inadequate                | No                                                   | No                             | 0/22 (0.0)         |
| Belmont et al <sup>21</sup>  | 1995 | Unclear                   | Investigators,<br>participants,<br>outcome assessors | Yes                            | 0/14 (0.0)         |
| Boletis et al <sup>25</sup>  | 1999 | Unclear                   | No                                                   | Yes                            | 0/14 (0.0)         |
| Boumpas et al <sup>17</sup>  | 1992 | Unclear                   | No                                                   | Yes                            | 0/65 (0.0)         |
| Cade et al <sup>5</sup>      | 1973 | Inadequate                | No                                                   | No                             | 4/54 (7.4)         |
| Chan et al <sup>26</sup>     | 2000 | Unclear                   | No                                                   | Yes                            | 0/42 (0.0)         |
| Clark et al <sup>11</sup>    | 1981 | Unclear                   | No                                                   | No                             | 0/12 (0.0)         |
| Clark et al <sup>13</sup>    | 1983 | Unclear                   | No                                                   | No                             | 3/39 (7.7)         |
| Derksen et al <sup>15</sup>  | 1988 | Unclear                   | No                                                   | Yes                            | 0/20 (0.0)         |
| Donadio et al <sup>7</sup>   | 1974 | Inadequate                | No                                                   | No                             | 1/19 (5.2)         |
| Donadio et al <sup>10</sup>  | 1978 | Unclear                   | No                                                   | Yes                            | 0/50 (0.0)         |
| Doria et al <sup>19</sup>    | 1994 | Unclear                   | No                                                   | Yes                            | 0/18 (0.0)         |
| Fries et al <sup>6</sup>     | 1973 | Unclear                   | No                                                   | Yes                            | 0/10 (0.0)         |
| Fu et al <sup>23</sup>       | 1998 | Adequate                  | No                                                   | No                             | 0/40 (0.0)         |
| Ginzler et al <sup>9</sup>   | 1976 | Unclear                   | No                                                   | No                             | 0/14 (0.0)         |
| Gourley et al <sup>22</sup>  | 1996 | Unclear                   | No                                                   | Yes                            | 5/82 (6.1)         |
| Hahn et al <sup>8</sup>      | 1975 | Unclear                   | No                                                   | No                             | 2/24 (8.3)         |
| Houssiau et al <sup>27</sup> | 2002 | Adequate                  | No                                                   | Yes                            | 1/90 (1.1)         |
| Lewis et al <sup>18</sup>    | 1992 | Adequate                  | No                                                   | Yes                            | 1/86 (1.2)         |
| Nakamura et al <sup>28</sup> | 2002 | Unclear                   | No                                                   | Yes                            | 0/20 (0.0)         |
| Sesso et al <sup>20</sup>    | 1994 | Unclear                   | No                                                   | Yes                            | 2/29 (6.9)         |
| Steinberg et al <sup>4</sup> | 1971 | Unclear                   | Investigators,<br>participants,<br>outcome assessors | No                             | 2/15 (13.3)        |
| Wallace et al <sup>24</sup>  | 1998 | Unclear                   | No                                                   | No                             | 1/19 (5.2)         |

\*Values expressed as number/total number (percent).



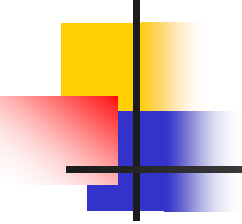
# Asking Answerable Clinical Question ~ **NNT, NNH**

|                         |                                                  |
|-------------------------|--------------------------------------------------|
| <b>P</b> atient/Problem | Insulin-dependent<br>diabetics                   |
| <b>I</b> ntervention    | Intensive insulin<br>regimen <b>(A)</b>          |
| <b>C</b> omparison      | Regular insulin<br>regimen <b>(B)</b>            |
| <b>O</b> utcomes        | 1. Retinopathy<br>2. Symptomatic<br>hypoglycemia |

# Treatment Effects

## NNT

- Occurrence of **diabetic retinopathy** at 5 years among insulin-dependent diabetic in the DCCT trial
  - Usual insulin regimen (**CER**: control event rate): **38%**
  - Intensive insulin regimen (**EER**: experimental event rate): **13%**
- **Risk reduction (calculation): NNT**
  - Absolute risk reduction (**ARR**)  
$$= | \text{CER} - \text{EER} | = 38\% - 13\% = \mathbf{25\%}$$
  - Relative risk reduction (RRR)  
$$= | \text{CER} - \text{EER} | / \text{CER} = 25\% / 38\% = \mathbf{66\%}$$
  - **Number needed to treat (NNT)**  
$$= \mathbf{1/ARR} = 1 / 25\% = \mathbf{4} \text{ patients}$$
  - **NNT: The number of patients that need to be treated to prevent one bad outcome or get one good outcome.**
  - 增加一位病患得到某種處置好處所需的治療病人數= $\mathbf{1/ARR}$ ,即與對照組療法相比而言,使一位病人達到實驗組治療之有利結果(或預防產生不利結果)所需治療的病人數目。**(NNT 越少越好)**



# Harm: NNH

- The proportion of patients with at least one episode of **symptomatic hypoglycemia**
  - Usual insulin regimen (CER: control event rate): 23%
  - Intensive insulin regimen (EER: experimental event rate): 57%

## Risk increase (calculation): NNH

- Absolute risk increase (ARI) =  $| \text{EER} - \text{CER} | = 57\% - 23\% = 34\%$
- Relative risk increase (RRI) =  $| \text{EER} - \text{CER} | / \text{CER} = (57\% - 23\%) / 23\% = 148\%$
- **Number needed to harm (NNH) =  $1 / \text{ARI} = 1 / 0.34 = 3$  patients (整數)**
  - **NNH: The number of patients that need to be treated to cause one bad outcome (being harmed).**
  - 增加一位受試者罹患某種醫源性傷害的治療病人數：即對多少病人進行實驗組治療〔與對照組療法做比較〕會有多一個病人產生不良副作用。  
(NNH 數目, 越大越好)

# From **RRR** to **ARR** and **NNT**

治療效果有多大？

Measures of the effects of treatment: RRR, **ARR**

|                    | CER  | EER   | <b>RRR</b>           | <b>ARR</b> | <b>NNT</b>   |
|--------------------|------|-------|----------------------|------------|--------------|
| <b>Treatment A</b> | 50%  | 39%   | 22% $= (50-39) / 50$ | 11%        | <b>9 人</b>   |
| <b>Treatment B</b> | 5.0% | 3.9%  | 22%                  | 1.1%       | <b>90 人</b>  |
| <b>Treatment C</b> | 0.5% | 0.39% | 22%                  | 0.11%      | <b>900 人</b> |

**\*RRR can not discriminate huge treatment effects from small ones!**

# How large was the treatment effect

## 治療效果有多大？

某研究治療追蹤二年，對照組死亡率15%，治療組死亡率10%，  
結果呈現的方式有下列幾種：

| 呈現的方式                                                                                                                                               | 代表的意義                                                                                     |
|-----------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------|
| <b>Relative Risk (相對風險) (RR)</b><br><br>$RR = 0.10 / 0.15 = 0.67$                                                                                   | 治療組發生風險相對於對照組的倍數。RR=1 兩組無差別，<br>RR < 1 治療可降低風險， RR > 1 治療會增加風險<br><br>RR < 1 表示治療可降低死亡的風險 |
| <b>Absolute Risk Reduction (ARR)</b><br>(絕對危險性降低)<br><br>$ARR = 0.15 - 0.10 = 0.05 \text{ or } 5\%$                                                 | 治療組與對照組發生風險的絕對差異<br><br>治療的益處是(絕對值)降低5%的死亡率                                               |
| <b>Relative Risk Reduction (RRR)</b><br>(相對風險性降低)<br><br>$RRR = 0.05 / 0.15 = 0.33 \text{ or } 33\%$<br>or $RRR = 1 - 0.67 = 0.33 \text{ or } 33\%$ | 相對於對照組，治療組降低風險的比率<br>(最常見的呈現方式)<br><br>相對於對照組，治療可以降低死亡的機率 33%                             |
| <b>Number Needed to Treat (NNT)</b><br>(益一需治數)<br><br>$NNT = 1 / ARR = 1 / 0.05 = 20$                                                               | 要預防一位病人不良結果發生，所必需治療的病人數<br><br>治療20位病人2年，才能預防1人死亡                                         |

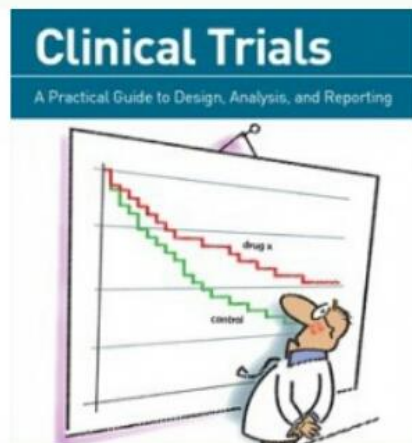
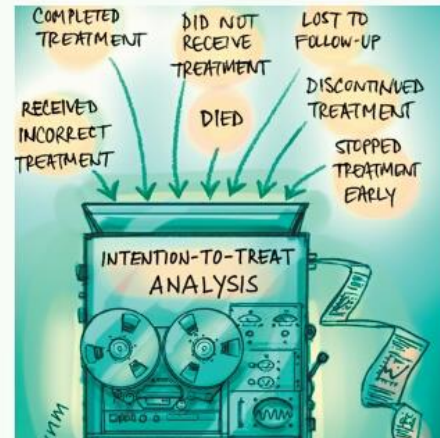


Fig. 3 A double-blind placebo-controlled clinical trial for CAM



# Appraisal

(VIP - Validity, Impact, and Applicability)

☒ Yes

☒ No

☐ ? Unclear

文獻 #2, Kopp MV, Individual RCT “查看 Method 和 Result 的敘述”

## 隨機對照試驗文獻可信度評估表格

評讀

☒

1. 這些病人的分組是隨機分派的嗎？

是

2. 分派的方法是否保密？

是

3. 分派的兩組在治療開始時的baseline是否相似？若不相似，是否用統計的方法來修正，或增加被研究者的數目，這些代表隨機分配的方法是否適當？

是

4. 除了研究治療項目以外，其他的治療在各組間是否相同？

是

5. 治療方法對病患、醫護人員、研究者是否blinded (double blinded)？

是

6. 追蹤是否完整？(loss follow up reason)

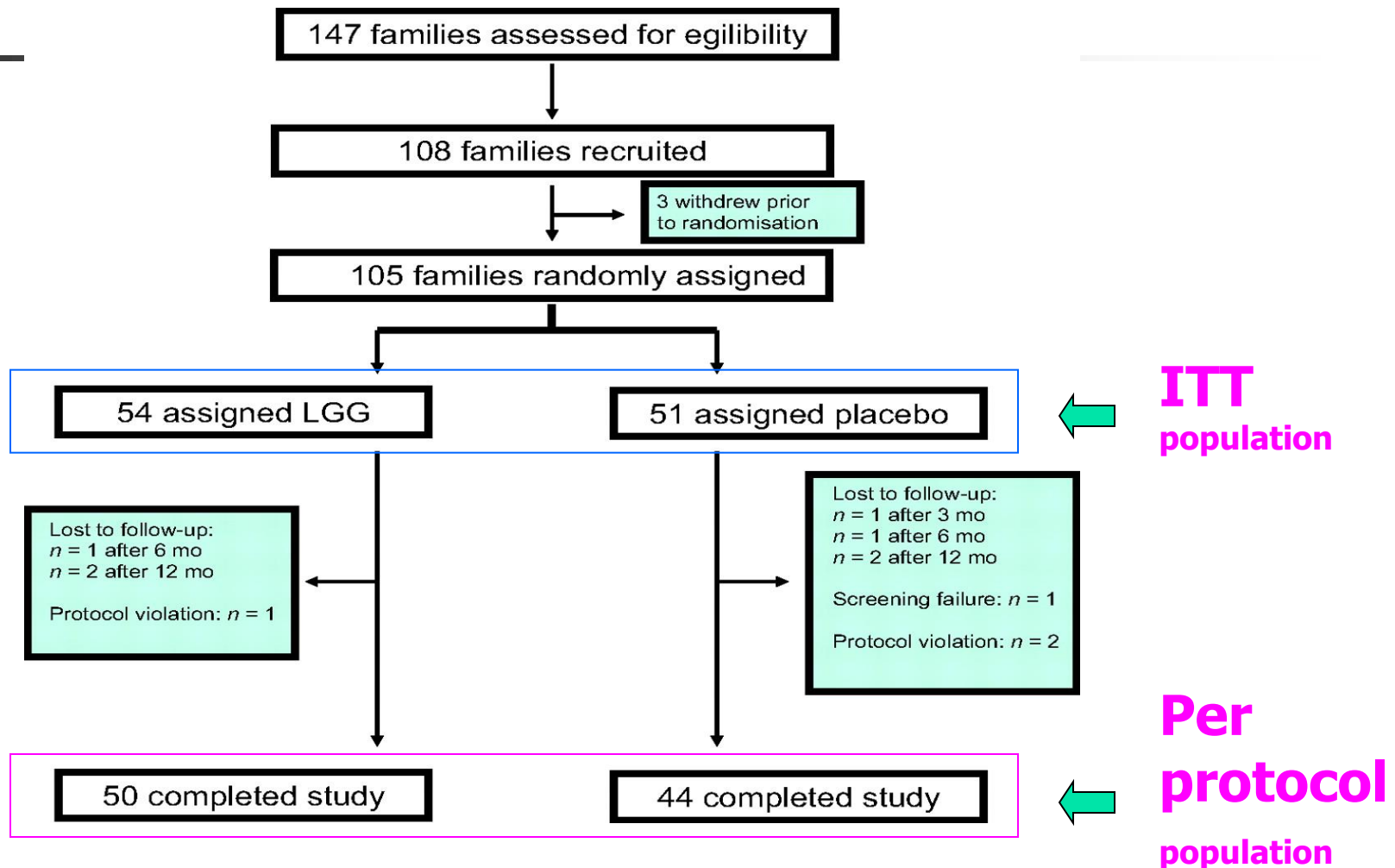
2年

7. 分析時是否利用intention-to-treat analysis分析？

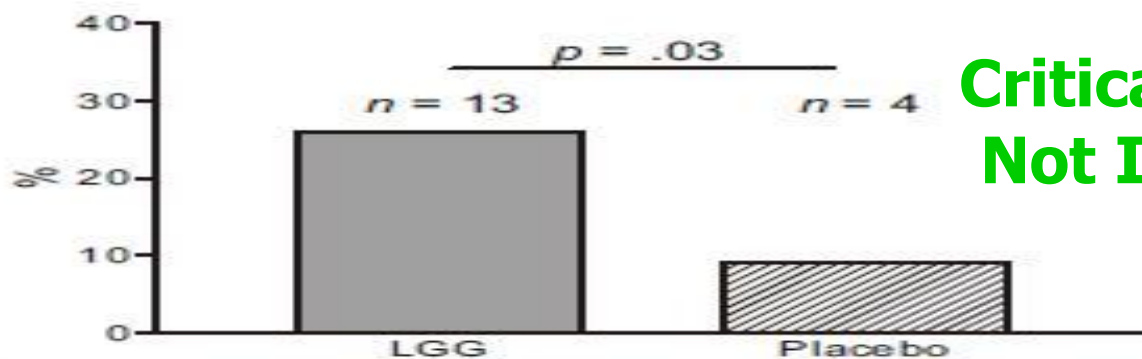
否 ☒

# Randomized, Double-Blind, Placebo-Controlled Trial of Probiotics for Primary Prevention: No Clinical Effects of *Lactobacillus* GG Supplementation

Matthias Volkmar Kopp, MD, Isabell Hennemuth, MD, Andrea Heinzmann, MD, Radvan Urbaneek, MD



# 臨床重要性評估 **NNH = 6 (95% CI: 3-48)**



**Critical appraisal:  
Not ITT analysis**

FIGURE 4

Treatment effect of LGG on atopic diseases showing the proportion of children with  $\geq 5$  episodes of wheezing bronchitis during the first 2 years of life.

**50**

**44**

## CAT maker

Kopp M. V. et al. Pediatrics 2008;121:e850-e856

練習

嬰兒在2歲的時候有氣喘的比例

**Not ITT 分析**

吃安慰劑

Control Event  
Rate

**CER**

吃益生菌

Experimental  
Event Rate

**EER**

Relative Risk  
Increase  
(RRI)

$|EER - CER| / CER$

**186%**

Absolute  
Risk  
Increase  
(ARI)

$|EER - CER|$

**16.9%**

Number Needed  
to Harm  
(NNH)

$1 / ARI$

**6 [95% CI 3-48]**

**4/44 = 9.1%**

**13/50 = 26%**

Use Control-C to copy selected text, Control-V to paste and Control-X to cut.



# *making a CAT* diagnosis



Your  
Question

the Study  
Patients

the Study  
Evidence

the Bottom  
Line

the Other  
Stuff

Analysis 1 of 1

|                                      |          | TARGET DISORDER      |                      | 95% Confidence<br>Intervals |
|--------------------------------------|----------|----------------------|----------------------|-----------------------------|
|                                      |          | Present              | Absent               |                             |
| TEST                                 | Positive | <input type="text"/> | <input type="text"/> |                             |
|                                      |          | a                    | b                    |                             |
|                                      | Negative | <input type="text"/> | <input type="text"/> |                             |
|                                      |          | c                    | d                    |                             |
| SENSITIVITY                          |          | $a / (a+c)$          |                      | %                           |
| SPECIFICITY                          |          | $d / (b+d)$          |                      | %                           |
| Pre-test Probability ("Prevalence"): |          | $(a+c) / (a+b+c+d)$  |                      | %                           |
| Positive Predictive Value:           |          | $a / (a+b)$          |                      | %                           |
| Negative Predictive Value:           |          | $d / (c+d)$          |                      | %                           |
| LIKELIHOOD RATIO +                   |          | $sens / (1 - spec)$  |                      |                             |
| LIKELIHOOD RATIO -                   |          | $(1 - sens) / spec$  |                      |                             |



Analyse another test in this same study

restart

show formulae

calc

previous

next

Please enter the numbers in each group for the diagnostic test in the study. When you're ready, click the CALC button to work out Sensitivity, Specificity, Likelihood Ratios, etc.



# 診斷檢驗

## Diagnostic test

指標 : Sensitivity, Specificity, PPV, NPV, LR, ROC curve

|              |                  | 疾病<br>(Disease) |               |
|--------------|------------------|-----------------|---------------|
|              |                  | 有<br>(Present)  | 無<br>(Absent) |
| 檢查<br>(Test) | 陽性<br>(Positive) | 真陽性<br>TP a     | 偽陽性<br>b FP   |
|              | 陰性<br>(Negative) | 偽陰性<br>c FN     | d 真陰性<br>TN   |

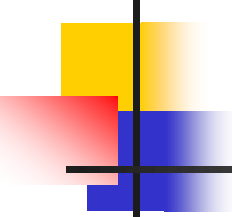
An estimated 5% of medical errors are related to misinterpretation of laboratory test results.<sup>10</sup>

# 4. 實證醫學的五大進行步驟

## Five Steps to Practice EBM

- Step 1. Converting the need for information (about prevention, diagnosis, prognosis, therapy, causation, etc.) into an answerable **question**. **(PICO)**
- Step 2. **Searching** the best evidence with which to answer that question. **(cite reference)**
- Step 3. Critically **appraising** the evidence for its validity (closeness to the truth), impact (size of the effect), and applicability (usefulness in our clinical practice). **(VIP)**
- **Step 4. Integrating** the **evidence** with our **clinical expertise** and **patients'** unique biology, values and circumstances (**expectation**). **(3E)**
- **Step 5. Evaluating** our effectiveness and efficiency in executing steps 1-4 and seeking ways to improve them both for next time.

**重點：** 用簡單且病人可以聽懂的语言，對病患告知診療的決策

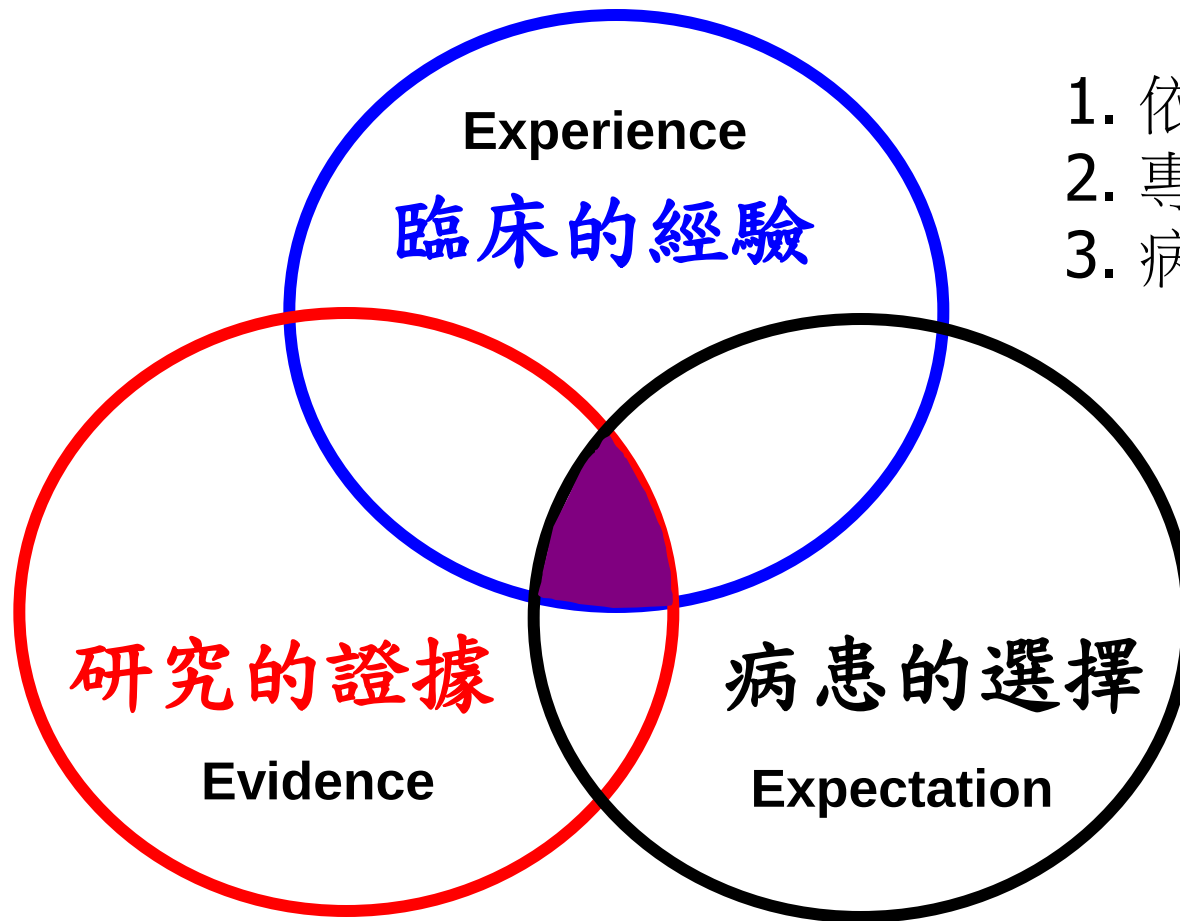


# Two Fundamental Principles of EBM

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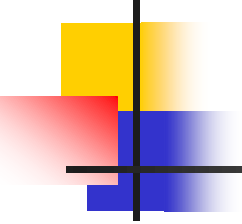
- EBM posits a hierarchy of evidence to guide clinical decision making. (Level of evidence)
  - **Evidence** alone is never sufficient to make a clinical decision. **3E:**
    - Consider the patient's value (**Expectation of the Patient**) 告知同意：用病人可以聽得懂的語言 (explain)
    - Integrate clinical expertise (**Expert opinion**)
      - Trade the benefits and risks (NNT, NNH)
      - Costs (\$)
      - Inconvenience
1. (尋找並且)依循證據
  2. (告知選擇)專業建議
  3. 病患同意(醫病溝通)

# 實證醫學的精神 “3 E”



1. 依循證據
2. 專業建議
3. 病患同意



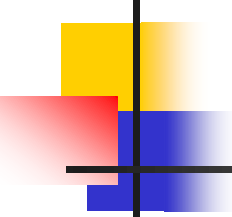


# Take Home Message

## EBM (EBHC)

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- **Patient's Clinical Problem**
    - raise clinical question - 許我一個 **PICO**
  - **Perform Five Steps in EBM (5 As)**
    - **A**sk (**PICO**): ask a clinical question (P-I-C-O)
    - **A**cquire: search database (cite reference)
    - **A**ppraisal (**VIP**): **V**alid? **I**mportant? **P**ractical?
    - **A**pply: to patient's problem (**3E** evidence, experience, expectation)
    - **A**udit: effectiveness (**Explain** treatment options to you patient)
- 記載於病歷 **Record in Chart**



# 實證健康照護: 從研究到實踐

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- 醫策會每年舉辦舉辦全國EBM比賽
- 比賽的臨床應用組，有許多是醫療機構裡成功執行實證醫學的經驗

醫品圈  
JCI評鑑  
品質改善

# The growing needs for EBHC teaching

