實證醫學病例討論報告

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臨床場景(clinical scenario)

- A 43 y/o female had bilateral lower limbs edema for one week
- Past history: systemic lupus erythematosus diagnosed for 10+ years
- No medication for recent 2 months

- U/R: Protein (4+), RBC: 0-2/HPF
- Serum Alb: 1.8 g/dL, Chol/TG: 306/256 mg/dL

Asking (提出臨床問題)

Background question

- Q1: What kind of renal disease does SLE related?
- Q2: How to treat SLE related renal diseases?

Question 1: spectrum of renal disease

- 資料出處：Uptodate
- Key word: Systemic lupus erythematosus
- Topic: Types of renal disease in SLE (06, 2008)
- Answer:
  - Minimal mesangial lupus nephritis (class I), Mesangial proliferative lupus nephritis (class II), Focal lupus nephritis (class III), Diffuse segmental or global lupus nephritis (class IV), Membranous lupus nephritis (class V), Advanced sclerosing lupus nephritis (class VI)
  - There are three other forms of lupus renal disease: tubulointerstitial nephritis; vascular disease; and renal disease infrequently associated with drug-induced lupus.
  - Glomerular podocytopathy —diffuse epithelial cell foot process effacement without immune complex deposition, which is the classic histologic findings of minimal change disease

Question 2: therapy

- 資料出處：Uptodate
- Key word: Systemic lupus erythematosus
- Topic: Therapy of diffuse or severe focal proliferative or severe membranous lupus nephritis (06, 2008)
- Topic: Overview of the therapy and prognosis of lupus nephritis (06, 2008)
- Answer:
  - The optimal treatment of lupus nephritis (LN) is uncertain given the relative scarcity of randomized controlled trials
  - No specific therapy is indicated for class I and II lupus (minimal mesangial and mesangial proliferative LN)
  - Treatment is almost always indicated in patients with severe membranous LN (with severe nephrotic syndrome and/or rising creatinine, or associated with focal or diffuse proliferative changes) and severe focal and diffuse proliferative LN.
  - Prednisolone, cyclophosphamide, Mycophenolate, cyclosporine, tacrolimus, azathioprine, rituximab

Apply到我的病人身上

- Renal biopsy result:
  - normal LM
  - no IF immune complex deposition
- Final diagnosis:
  - Minimal change disease [Glomerular podocytopathy]
- Apply: not applicable

Foreground questions

- Question: Will Steroid alone or combined immunotherapy do more benefit to SLE with MCD cases?

Formulate A PICO Question

P	**Patient or population**	**Describes patient** **(age, sex, race, past medical history, etc)**	**A 45 year-old, female, SLE case with renal pathology of MCD presented as** **nephrotic syndrome**
I	**Intervention**	**What happens or is to be done; treatment, diagnostic test, exposure, screening**	**Steroid only**
C	**Comparison**	**Compared to what?** **Nothing, placebo, gold standard, another intervention**	**Combined immunotherapy**
O	**Outcomes**	**What is the effect of the intervention? (Be specific, mortality after a particular time period, hospitalizations)**	**Remission of proteinuria, rate of Cr progression, ESRD, Mortality**

搜尋最有用的資料

先從已經過評讀的database開始找起(system,synopses,synthesis)

最後再找尚未經過嚴格評讀的study

Up to date

ACP medicine

ACP pier

Ovid

ACP journal club

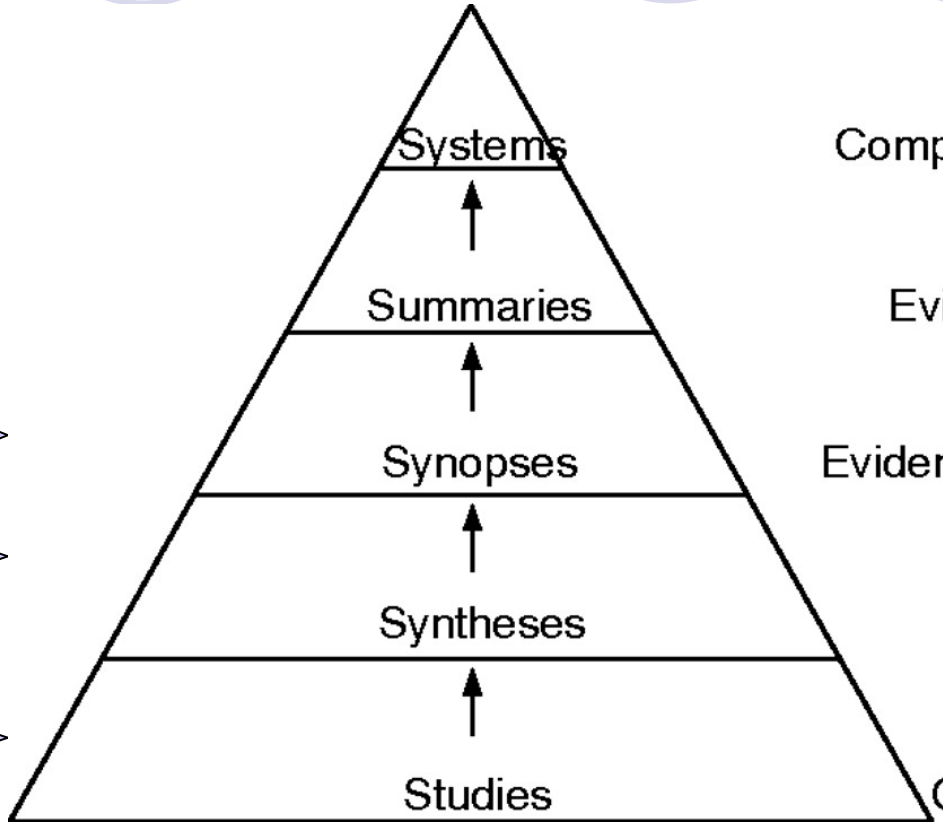
Evidence-Based Medicine(BMJ)

Cochrane Library

PubMed

SUMsearch

Google



Examples

Computerized decision support

Evidence based textbooks

Evidence based journal abstract

Systematic reviews

Original journal articles

搜尋Summaries

- 出處：UptoDate
- Key word: “systemic lupus erythematosus” AND “minimal change disease”

- Result:
  - Types of renal disease in systemic lupus erythematosus
  - Diagnosis and causes of minimal change disease in adults

Summaries搜尋到的文章標題

- Title: Types of renal disease in systemic lupus erythematosus
  - Ref: Glomerular podocytopathy in patients with systemic lupus erythematosus: 17/470 case series
- Title: Diagnosis and causes of MCD in adults
  - Although the relationship is unclear, there are reports of MCD occurring in association with the following glomerular or renal diseases: SLE, Type I DM, PKD, HIVAN
  - Ref: Secondary MCD: NDT 2003
  - Ref: MCD in SLE: Clin Nephrol 2002

⇨ **Title: Treatment of MCD in adults**

Summaries搜尋到的文章內容

- **Title: Treatment of MCD in adults**
  - Glucocorticoid therapy — The recommendation for initial therapy with prednisone in adults is based upon the beneficial results reported in several large prospective randomized trials in children, extensive observational studies in children and adults
  - A single randomized controlled trial in 31 adults that compared prednisone with no specific therapy

將Summaries搜尋的結果應用到我的病人

- 沒有直接討論lupus合併MCD (nephrotic syndrome)的治療

- 若nephrotic syndrome 的病因爲MCD,則steroid可以做爲第一線治療

搜尋Synopses，ACP Journal Club

- Key word: “systemic lupus erythematosus” AND “minimal change disease”
  - Result: no matches!
- Key word: “minimal change disease”, therapeutics
  - Result: 10 matches (1)
  - Interventions for minimal change disease in adults with nephrotic syndrome. (Cochrane Database Syst Rev, 2008)

搜尋 Syntheses, Cochrane Library

- Key word: “systemic lupus erythematosus” AND “minimal change disease”
  - Result: no matches!

- Key words: “minimal change disease”
  - Result: 6 matches (1)
  - Interventions for minimal change disease in adults with nephrotic syndrome. (Cochrane Database Syst Rev, 2008)

Synopses and Syntheses
搜尋到的文章標題

- Title:
  - **Interventions for minimal change disease in adults with nephrotic syndrome**
    Suetonia C Palmer, Kushma Nand, Giovanni FM Strippoli
  - Year: 2008

Synopses and synthesis
搜尋到的文章內容

- **Main results:**
  - This review identified three small studies (68 participants) :
    - 1) intravenous plus oral steroid treatment versus oral steroids;
    - 2) oral versus short-course intravenous steroid treatment;
    - 3) oral steroid treatment versus placebo.
  - Only oral steroid treatment (compared to short-course intravenous steroid treatment) showed an increase in the number of patients who achieved complete remission.
  - **No RCTs** were identified comparing regimens in adults with a steroid-dependent or relapsing disease course or comparing treatments **comprising alkylating agents, cyclosporine, tacrolimus, levamisole, or mycophenolate mofetil.**

- **Apply: only MCD, no SLE: not applicable to our cases!**

搜尋Studies, Pubmed

- Search via [Mesh]
- Key words: "Lupus Erythematosus, Systemic"[Mesh] AND "Nephrosis, Lipoid/drug therapy"[Mesh]

- Result: 14
  - 7 published after 1990, 1 in German
  - Only 2 matched papers

Studies搜尋到的文章標題

- Minimal change nephrotic syndrome associated with systemic lupus erythematosus..Nephrol Dial Transplant. 2006

- Minimal-change nephrotic syndrome associated with systemic lupus erythematosus.Am J Nephrol. 1995

- Both were case reports!
- Both case (2/2) respond to steroid therapy!

搜尋Studies, Pubmed

- Search via [Clinical Queries]
- Key words: "Lupus Erythematosus, Systemic"[Mesh] AND "Nephrosis, Lipoid/drug therapy"[Mesh]
  - Result: no matches!
- Key words: "Nephrosis, Lipoid/drug therapy"[Mesh]
  - Result: 0/11, not applicable!

By EBM searching method: No (or a few) matched finding!

Let’s try other strategies!

搜尋到的文章標題 in UptoDate

- Title: Types of renal disease in systemic lupus erythematosus
  - Ref: Glomerular podocytopathy in patients with systemic lupus erythematosus: 17/470 case series
- Title: Diagnosis and causes of MCD in adults
  - Although the relationship is unclear, there are reports of MCD occurring in association with the following glomerular or renal diseases: SLE, Type I DM, PKD, HIVAN
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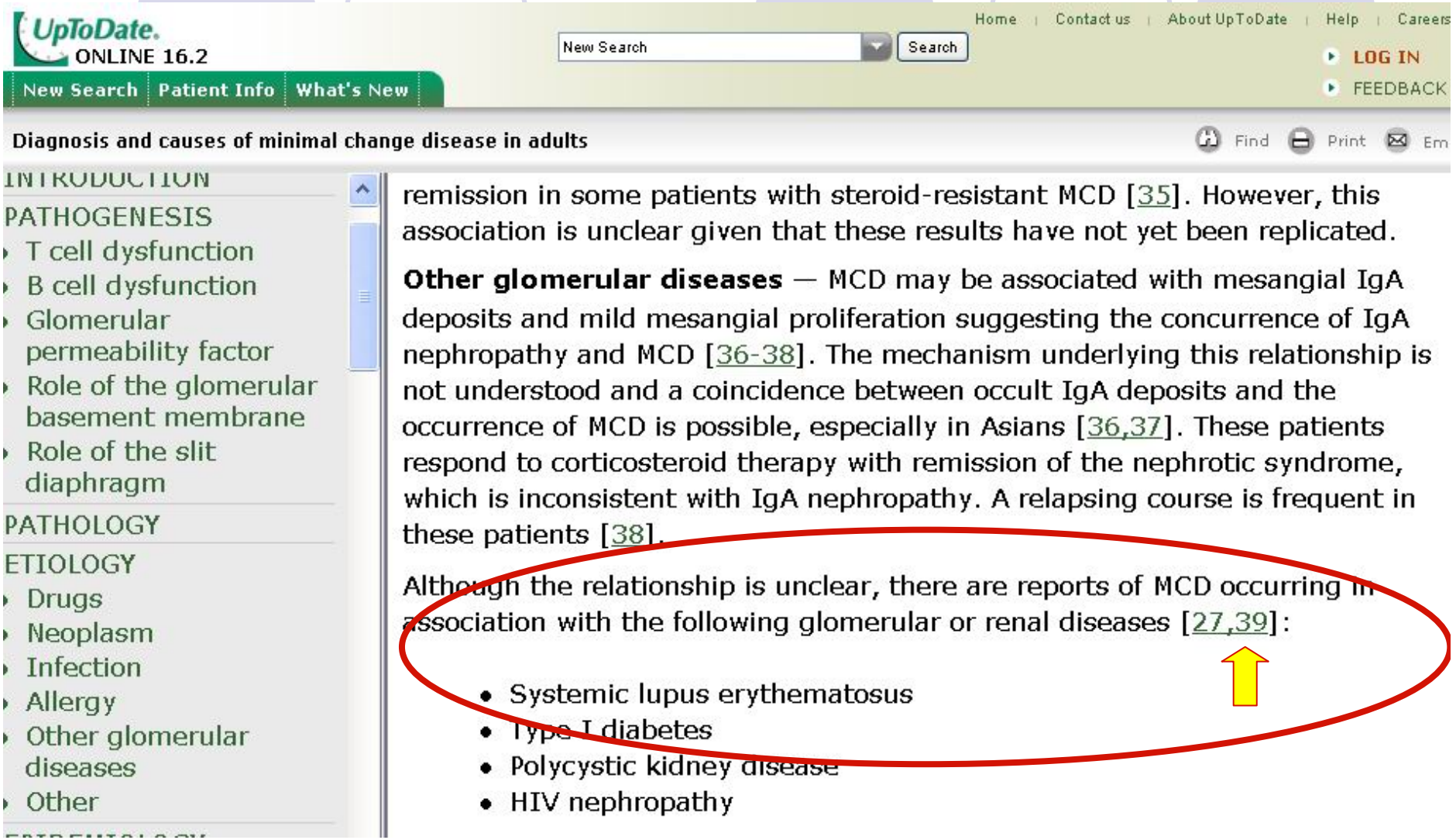
UpToDate.
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Search
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New Search | Patient Info | What's New
Diagnosis and causes of minimal change disease in adults
Find
Print
Em
INTRODUCTION
PATHOGENESIS
T cell dysfunction
B cell dysfunction
Glomerular permeability factor
Role of the glomerular basement membrane
Role of the slit diaphragm
PATHOLOGY
ETIOLOGY
Drugs
Neoplasm
Infection
Allergy
Other glomerular diseases
Other
remission in some patients with steroid-resistant MCD [35]. However, this association is unclear given that these results have not yet been replicated.
Other glomerular diseases — MCD may be associated with mesangial IgA deposits and mild mesangial proliferation suggesting the concurrence of IgA nephropathy and MCD [36-38]. The mechanism underlying this relationship is not understood and a coincidence between occult IgA deposits and the occurrence of MCD is possible, especially in Asians [36,37]. These patients respond to corticosteroid therapy with remission of the nephrotic syndrome, which is inconsistent with IgA nephropathy. A relapsing course is frequent in these patients [38].
Although the relationship is unclear, there are reports of MCD occurring in association with the following glomerular or renal diseases [27,39]:
Systemic lupus erythematosus
Type I diabetes
Polycystic kidney disease
HIV nephropathy

Medline ® Abstracts for References 27,39
of 'Diagnosis and causes of minimal change disease in adults'

27

TI Secondary minimal change disease.

AU Glassock RJ

SO Nephrol Dial Transplant. 2003 Aug;18 Suppl 6:vi52-8.

The great majority of patients identified as having a 'minimal change lesion' accompanying the nephrotic syndrome have a primary or 'idiopathic' disorder. Nevertheless, it is quite apparent that a similar or identical lesion can appear consequent to a growing number of underlying diseases; it is then known as 'secondary minimal change disease'. The predisposing conditions include neoplastic diseases, toxic allergic reactions to drugs, infections, auto-immune disorders and other miscellaneous entities. These disorders are reviewed and catalogue in this contribution.

AD The Geffen School of Medicine at UCLA, California, USA. glassock@cox.net

PMID 12953043

39

TI Minimal change disease in systemic lupus erythematosus.

AU Dube GK; Markowitz GS; Radhakrishnan J; Appel GB; D'Agati VD

SO Clin Nephrol 2002 Feb;57(2):120-6.

We report the clinical and pathologic findings in 7 patients with systemic lupus erythematosus and minimal change disease. All 7 patients presented with full nephrotic syndrome including peripheral edema, nephrotic range proteinuria (mean 9.6 g/day), and hypoalbuminemia (mean 1.8 g/dl). In all cases, renal biopsy revealed diffuse foot process effacement in the absence of significant peripheral capillary wall immune deposits, findings consistent with minimal-change disease. In addition, 5 cases displayed mesangial electron-dense deposits, with without associated mesangial proliferation, consistent with underlying lupus nephritis class II. In all cases, steroid therapy induced a rapid remission of nephrotic syndrome. Minimal change disease is an underrecognized and readily reversible form of nephrotic syndrome in syste

1: Clin Nephrol. 2002 Feb;57(2):120-6.

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Department of Pathology, Columbia University, New York Presbyterian Hospital, NY, USA.

We report the clinical and pathologic findings in 7 patients with systemic lupus erythematosus and minimal change disease. All 7 patients presented with full nephrotic syndrome including peripheral edema, nephrotic range proteinuria (mean 9.6 g/day), and hypoalbuminemia (mean 1.8 g/dl). In all cases, renal biopsy revealed diffuse foot process effacement in the absence of significant peripheral capillary wall immune deposits, findings consistent with minimal-change disease. In addition, 5 cases displayed mesangial electron-dense deposits, with or without associated mesangial proliferation, consistent with underlying lupus nephritis class II. In all cases, steroid therapy induced a rapid remission of nephrotic syndrome. Minimal change disease is an underrecognized and readily reversible form of nephrotic syndrome in systemic lupus erythematosus. Because it may occur superimposed on mild mesangial proliferative lupus nephritis, this entity may be misinterpreted as an atypical presentation of lupus nephritis class II. Proper recognition of this entity requires careful integration of the renal biopsy immunofluorescence and electron microscopic findings.

PMID: 11863121 [PubMed - indexed for MEDLINE]

Related Articles

- Emerging minimal-change nephrotic syndrome in a patient with [Intern Med. 200
- Glomerular podocytopathy in patients with systemic lupus ery [J Am Soc Nephrol. 200
- [A case of systemic lupus erythematosus associated w [Nippon Jinzo Gakkai Shi. 199
- [A case report of lupus nephritis associated with minimal [Nippon Jinzo Gakkai Shi. 199
- C1q nephropathy: a variant of focal segmental glomerulosclero [Kidney Int. 200

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Dis y Summary Show 20 Sort By Send to

All: 655 | Review: 60

Items 1 - 20 of 655

Page 1 of 33 Next

1: Dube GK, Markowitz GS, Radhakrishnan J, Appel GB, D'Agati VD. Related Articles, Links

Minimal change disease in systemic lupus erythematosus.

Clin Nephrol. 2002 Feb;57(2):120-6.
PMID: 11863121 [PubMed - indexed for MEDLINE]

2: Deji N, Sugimoto T, Kanasaki M, Aoyama M, Tanaka Y, Sakaguchi M, Nishio Y, Uzu T, Kashiwagi A. Related Articles, Links

Emerging minimal-change nephrotic syndrome in a patient with chronic mesangial proliferative lupus nephritis.

Recent Activity

Turn Off Clear

- Related Articles for PubM... (655)
- Related Articles for PubM... (655)
- Emerging minimal-change nephrotic syndrome in a patient with chronic mesangial proliferative lupus n...
- Minimal change disease in systemic lupus erythematosus.

Limit: [Related article] AND [Limit]

- all related articles (655)
- Limit: Human, English, all Adult (317)
- Humans, English, all Adult, clinical trial, meta-analysis, practice guideline, RCT, core clinical journals (0)
- Humans, English, all Adult, core clinical journals (71)

- Matched finding: some Case reports!

Topic: Minimal change disease in systemic lupus erythematosus.

- Dube GK; Markowitz GS; Radhakrishnan J; Appel GB; D'Agati VD
- Clin Nephrol 2002 Feb;57(2):120-6.
-
- We report the clinical and pathologic findings in 7 patients with systemic lupus erythematosus and minimal change disease. In all cases, steroid therapy induced a rapid remission of nephrotic syndrome.

- Result: 7/7 cases response to steroid therapy!

Appraisal (嚴格評讀)

對找到的文章
進行critical appraisal

證據等級

Oxford Centre for Evidence-based Medicine Levels of Evidence (May 2001)

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; Ecological studies	"Outcomes" Research		Ecological studies	Audit or outcomes research
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"

Produced by Bob Phillips, Chris Ball, Dave Sackett, Doug Badenoch, Sharon Straus, Brian Haynes, Martin Dawes since November 1998.

Grades of Recommendation

A	consistent level 1 studies
B	consistent level 2 or 3 studies ***or*** extrapolations from level 1 studies
C	level 4 studies ***or*** extrapolations from level 2 or 3 studies
D	level 5 evidence ***or*** troublingly inconsistent or inconclusive studies of any level

使用work sheet嚴格評讀

Critical Appraisal of Therapy Study

- Are the results of the trial valid (效度如何)？
  - Was the assignment of patients to treatment randomised (是隨機分配嗎)？ No!
  - Were the groups similar at the start of the trial (試驗開始時兩組條件是否相似)？ No!
  - Aside from the allocated treatment, were groups treated equally (兩組其他治療條件一樣)？No!
  - Were all patients who entered the trial accounted for and were they analysed in the groups to which they were randomised (所有進入試驗者皆列入統計，並依所分配的組別計算)？No!
  - Were measures objective or were the patients and clinicians were blinded (結果的測量客觀，受試者及醫師都不知道所接受的治療爲何)？No!
- What were the results (結果爲何)？
  - How large was the treatment effect (治療效果有多大)？Yes!
  - How precise was the estimate of the treatment effect (治療效果的預測多準確)？Unknown!
- Will the results help me in my patient care (適用於我的病人嗎)？Yes!