BMJ | Knowledge

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Making evidence accessible to clinicians

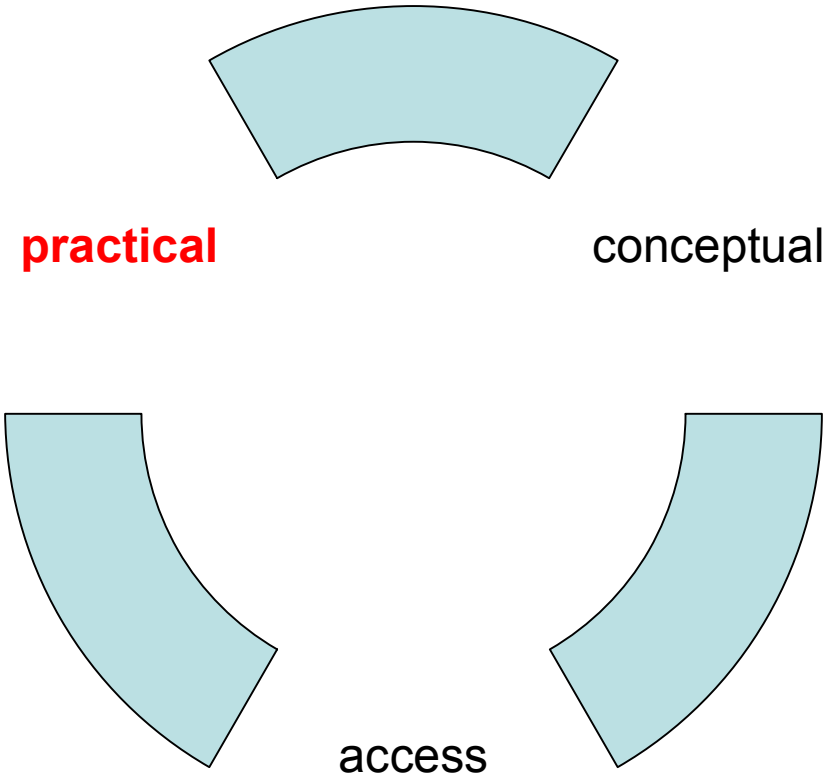
Dr Charles Young
Editor, *BMJ Clinical Evidence*

Why bother?

- Canadian observational study of *BMJ Clinical Evidence* integrated into a computerised physician order entry system
- Antibiotic use before and after integration (334 children; 2 weeks – 2 years)
- Children receiving antibiotics fell from 35% - 22% (P=0.016)
- Readily accessible clinical evidence at the point of care associated with a significant reduction in antibiotic use.

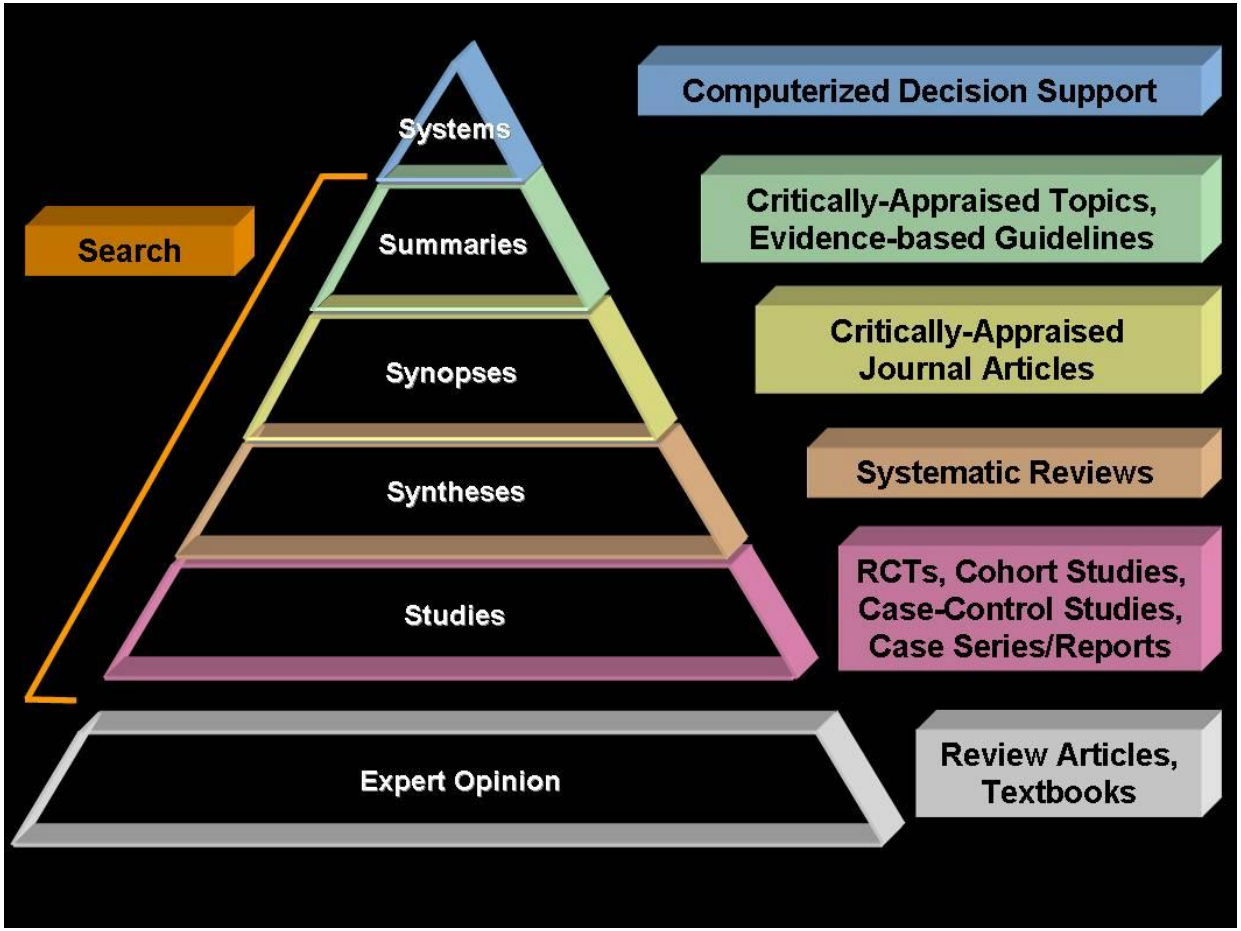
King WJ, Le Saux N, Sampson M, Gaboury I, Norris M, Moher D. **Effect of point of care information on inpatient management of bronchiolitis.** *BMC Pediatrics* 2007. Jan 24 7

Practical versus Conceptual



Progress

Practical issues



Haynes RB, ACP J Club 2006; 145(3):A8

Why publish the full paper?

"most readers of medical journals don't read the original articles. They may scan the abstract, but it's the rarest of beasts who reads an article from beginning to end, critically appraising it as he or she goes."

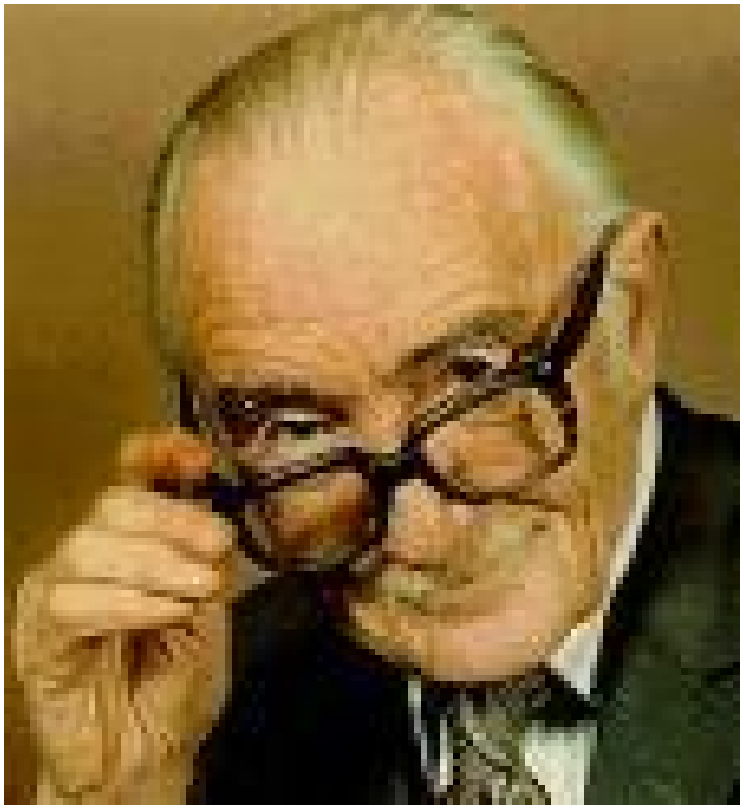
Smith R. BMJ 2004;328 (19 June), doi:10.1136/bmj.328.7454.0-h

But……

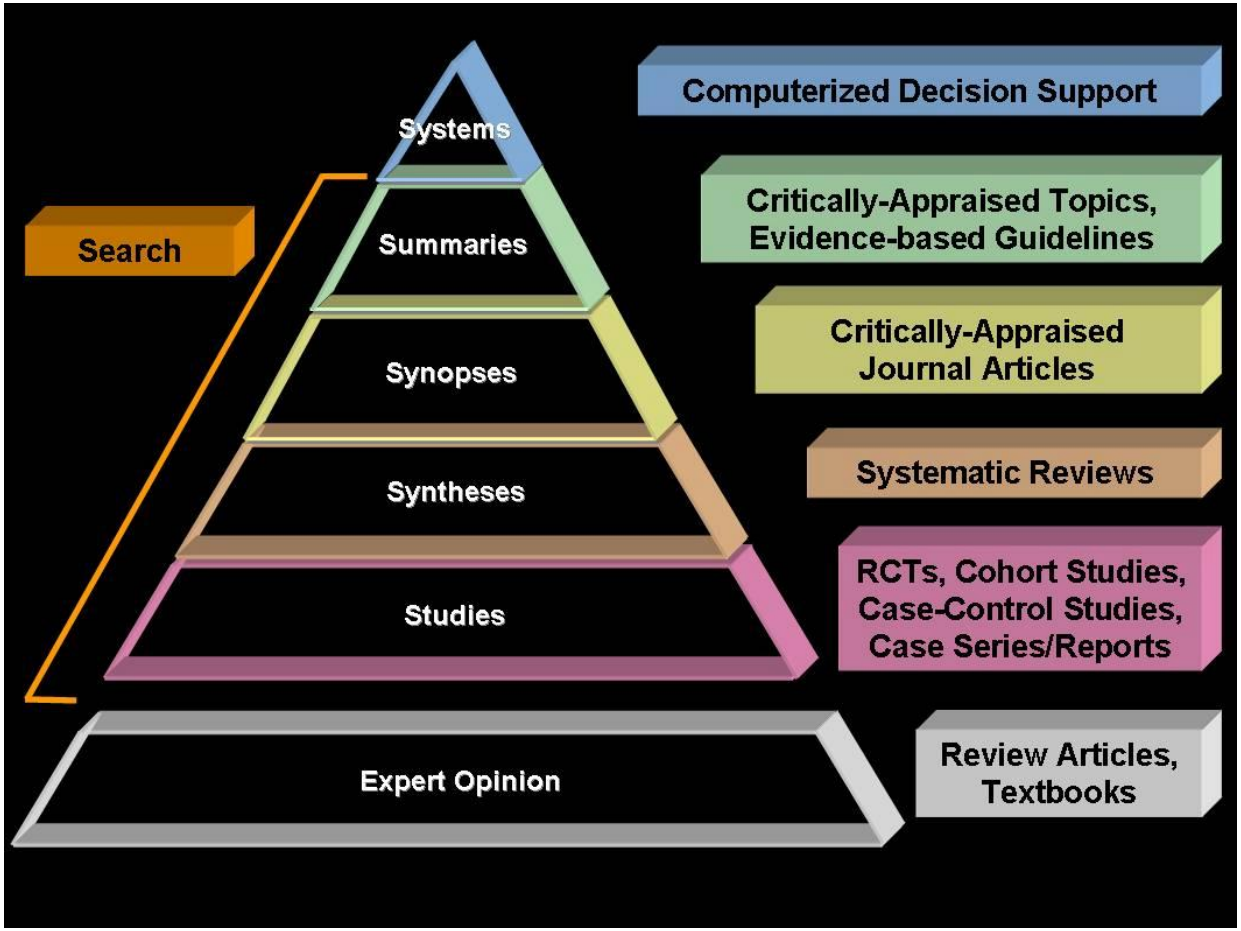
"Significant results in abstracts are common but should generally be disbelieved. "

Gøtzsche P C. BMJ 2006;333:231-234 (29 July), doi:10.1136/bmj.38895.410451.79

Progress



Practical issues

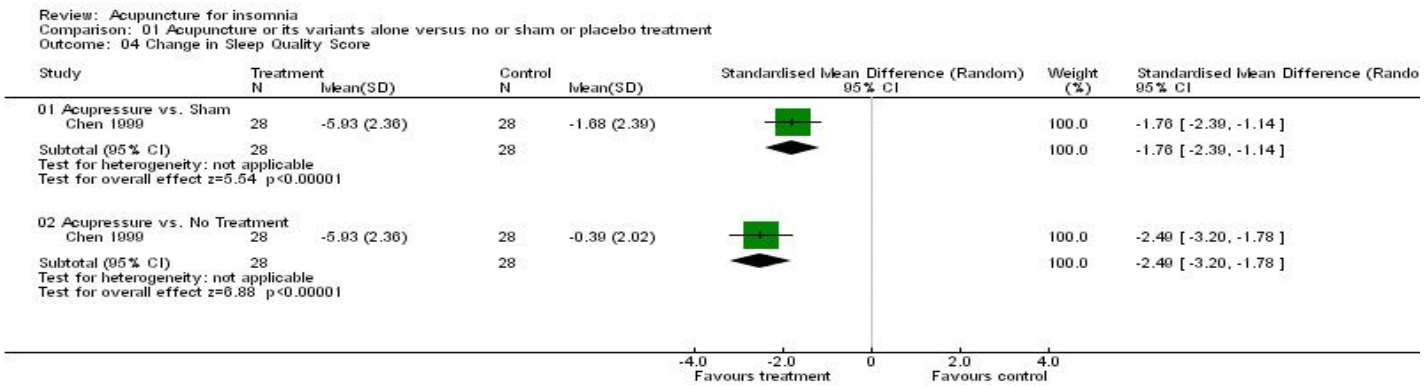


Haynes RB, ACP J Club 2006; 145(3):A8

Words, numbers, or pictures?

Authors' conclusions
The small number of randomised controlled trials, together with the poor methodological quality and significant clinical heterogeneity, means that the current evidence is not sufficiently extensive or rigorous to support the use of any form of acupuncture for the treatment of insomnia. Larger high quality clinical trials employing appropriate randomisation concealment and blinding with longer follow-up are needed to further investigate the efficacy and safety of acupuncture for the treatment of insomnia.

Sleep quality (primary outcome)
Two studies reported an outcome of post-treatment sleep quality (Tsay 2003; Tsay 2004) that was better in the treatment group, and the combined result reached statistical significance (**SMD = -0.55, 95% CI = -0.89 to -0.21, p=0.002**) (Figure 01.03). A change in sleep quality score was reported by Chen 1999 that was significantly better in the treatment group (**SMD = -2.49, 95% CI = -3.20 to -1.78, p<0.00001**) (Figure 01.04).



Cheuk D, Yeung W, Chung K, Wong V. Cochrane Database Syst Rev. 2007 Jul 18;(3):CD005472.

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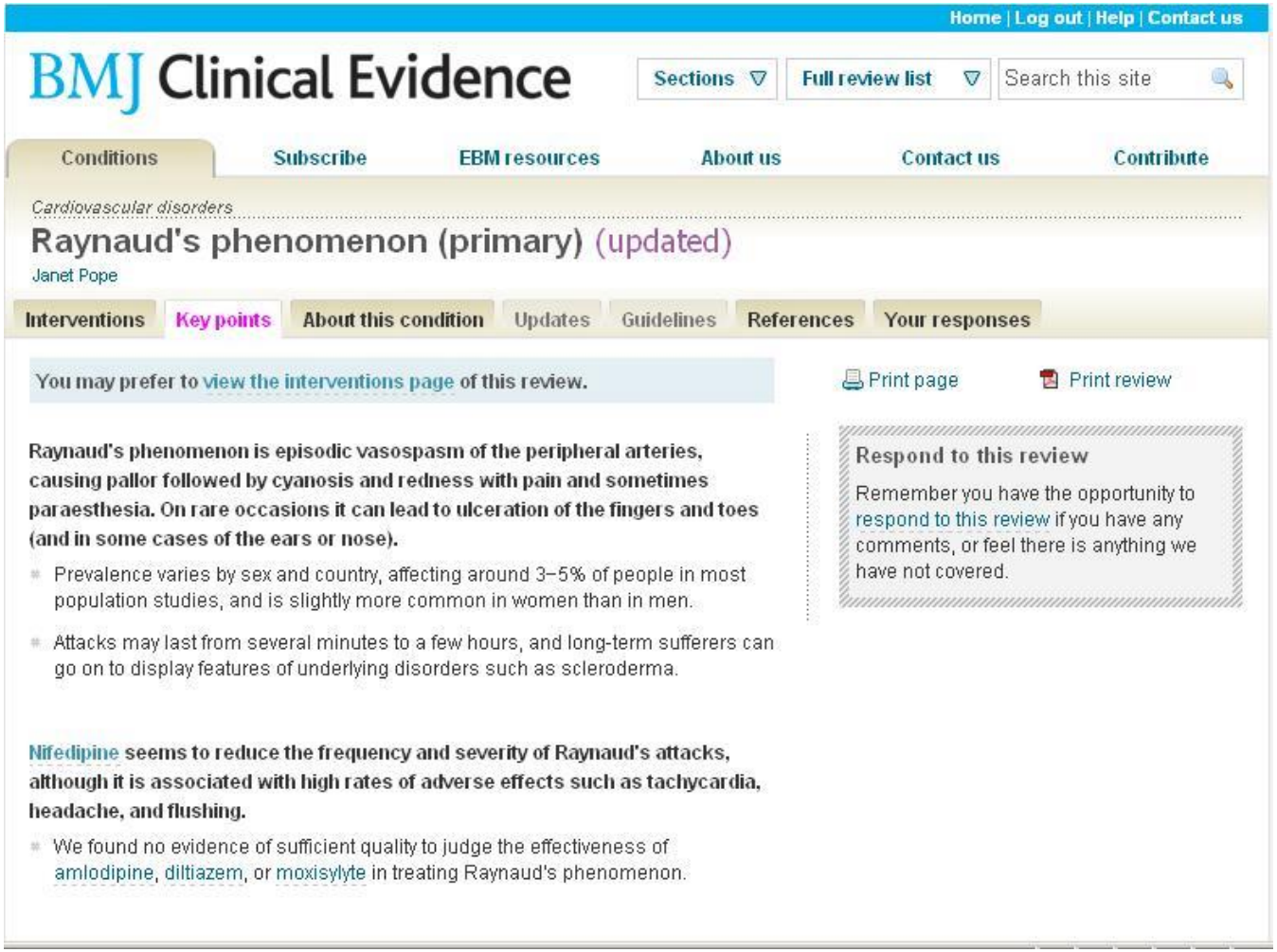
Doubt



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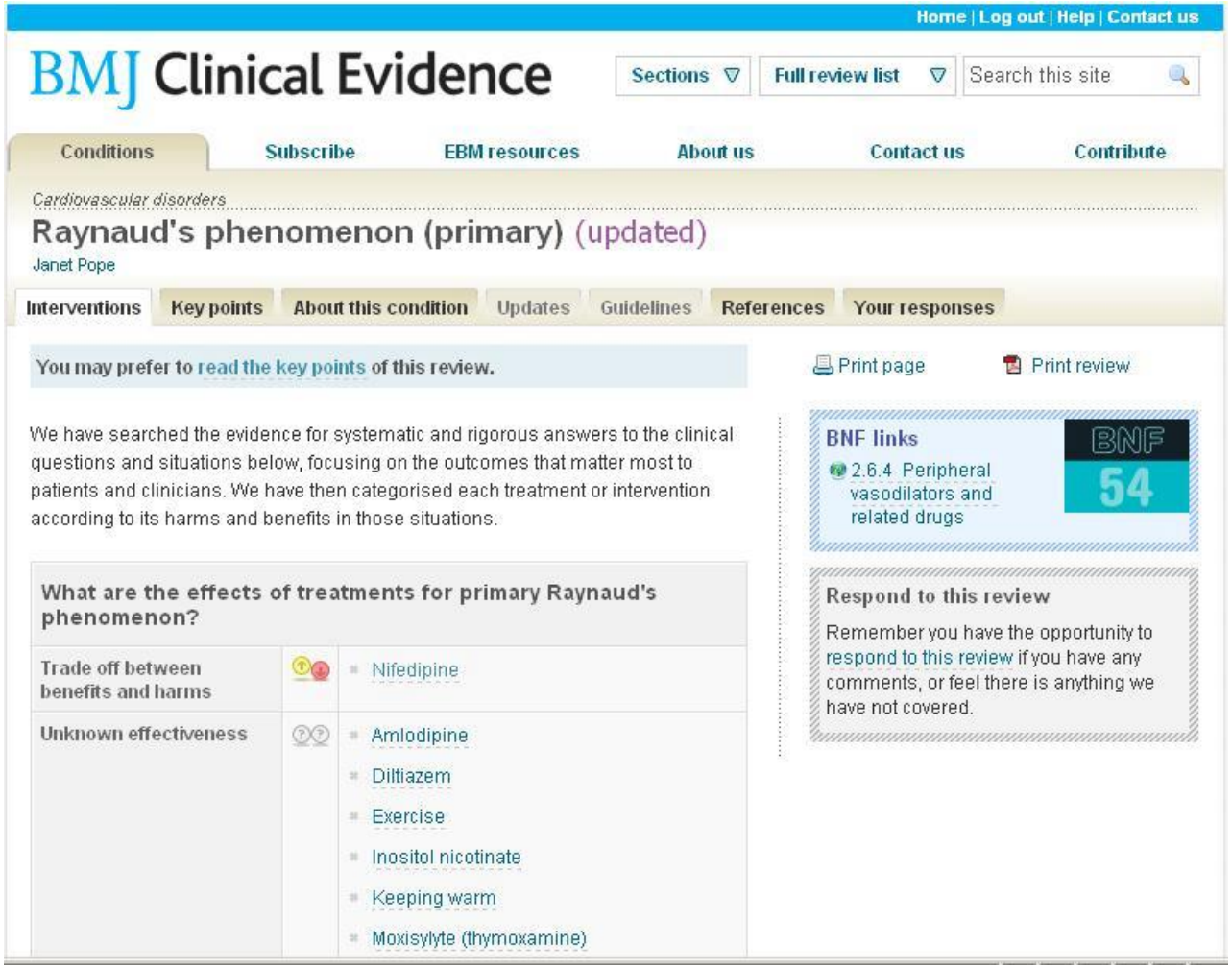
Doubt



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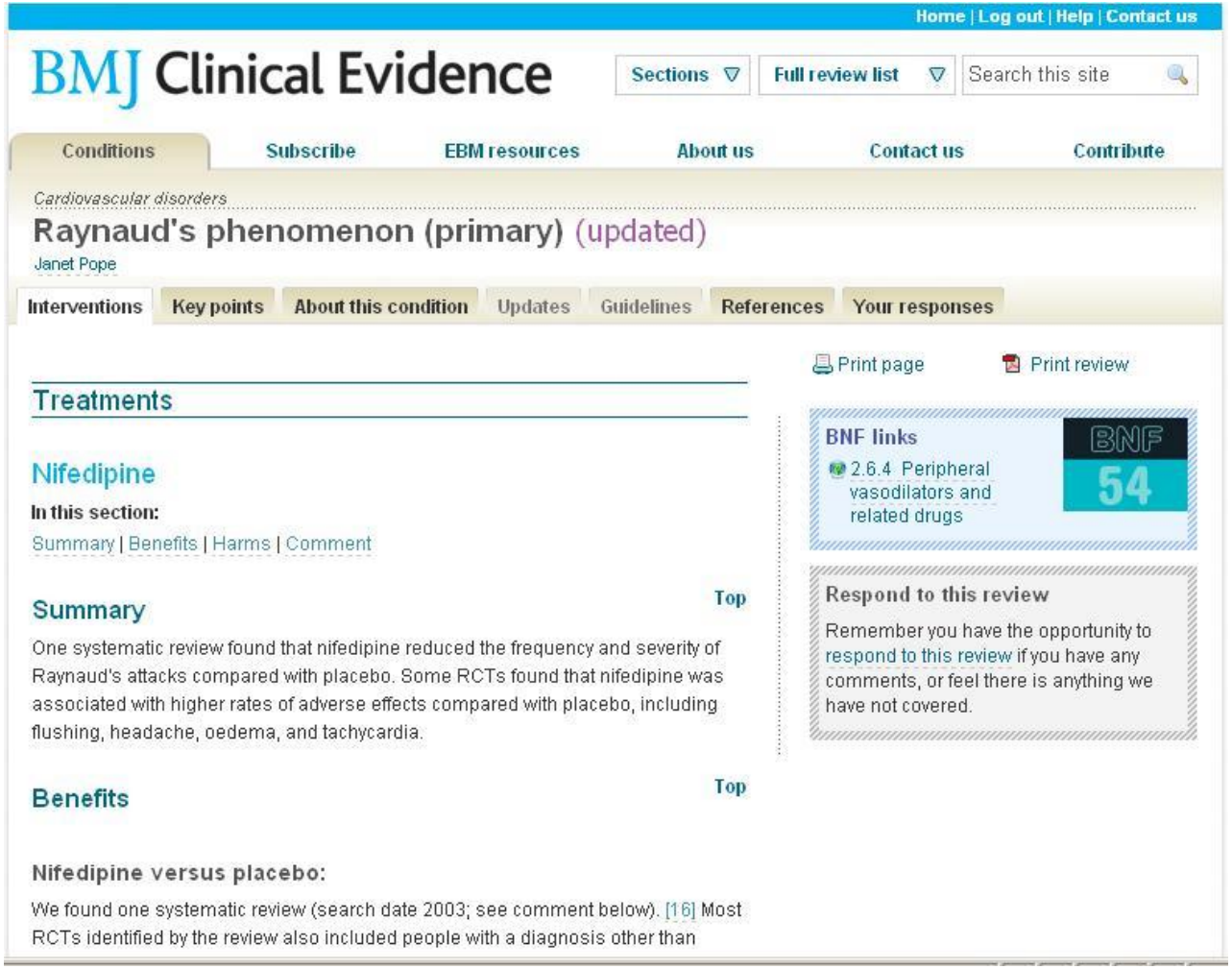
Doubt



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Doubt

Benefits

Top

Nifedipine versus placebo:

We found one systematic review (search date 2003; see comment below). [16] Most RCTs identified by the review also included people with a diagnosis other than primary Raynaud's phenomenon. In such cases, the review included the RCT if a subset of people with primary Raynaud's phenomenon could be identified separately and their outcome assessed independently, or if more than 75% of people had primary Raynaud's. The review included 13 RCTs which compared nifedipine versus placebo, of which 11 RCTs were crossover in design. Most RCTs were small, and the number of people included in each RCT with primary Raynaud's phenomenon ranged from three to 130 people (8 RCTs included 21 people or fewer with primary Raynaud's). The review found that nifedipine significantly reduced both the frequency and severity of ischaemic attacks compared with placebo (frequency of ischaemic attacks: 10 RCTs, absolute numbers not provided, WMD –6.05, 95% CI –0.19 to –11.19, P = 0.04; severity [measured on a 10 cm visual analogue scale]: 5 RCTs, absolute numbers not provided, WMD –1.81, 95% CI –0.54 to –3.08, P = 0.005). [16] It found that nifedipine significantly improved ischaemic attacks measured on a five-point scale compared with placebo (scale not further defined: WMD –1.11, 95% CI –0.85 to –1.38). [16] The review noted that most RCTs included people with or without primary Raynaud's phenomenon, so the meta-analysis could be regarded as a subset analysis of the original RCTs, which could be biased if randomisation was not stratified in people with primary Raynaud's. It also noted that most RCTs were small, crossover in design, and did not report pre-crossover results. Results after crossover may not allow for confounding factors such as inadequate washout, and the naturally variable course of Raynaud's phenomenon.

Harms

Top

The review did not report on harms in the included RCTs. [16] The six largest RCTs included in the review included data on adverse effects. [17] [18] [19] [20] [21] [22] The first RCT found that significantly more people taking nifedipine compared with placebo had oedema (24% with nifedipine *v* 0% with placebo; P < 0.01) or flushing

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Doubt

Harms

Top

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Comment

Top

The review included RCTs with a drop-out rate of up to 35%. [16] It noted that many of the included RCTs were of short duration (median 2 weeks, range 1 to 10 weeks) and used relatively low doses of nifedipine. [16] The review also compared calcium channel blockers as a group versus placebo. The meta-analysis included 12 RCTs of nifedipine, 2 RCTs of nisoldipine, 2 RCTs of nicardipine, and 1 RCT of diltiazem. It found that calcium channel blockers as a group significantly reduced the frequency and the severity of attacks compared with placebo (frequency of ischaemic attacks: 17 RCTs, WMD –2.08, 95% CI –1.70 to –3.90; severity [measured on a 10 cm visual analogue scale]: 8 RCTs, WMD –1.39, –0.58 to –2.20). [16] However, the majority of

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GRADE - categories

- High-quality evidence
- Moderate-quality evidence
- Low-quality evidence
- Very low-quality evidence

GRADE - components

- Type of study: RCT or not?
- Quality: sparse data, methodology
- Consistency: do all studies agree?
- Directness: are results generaliseable?
- Effect size: does it make a big difference to outcomes?

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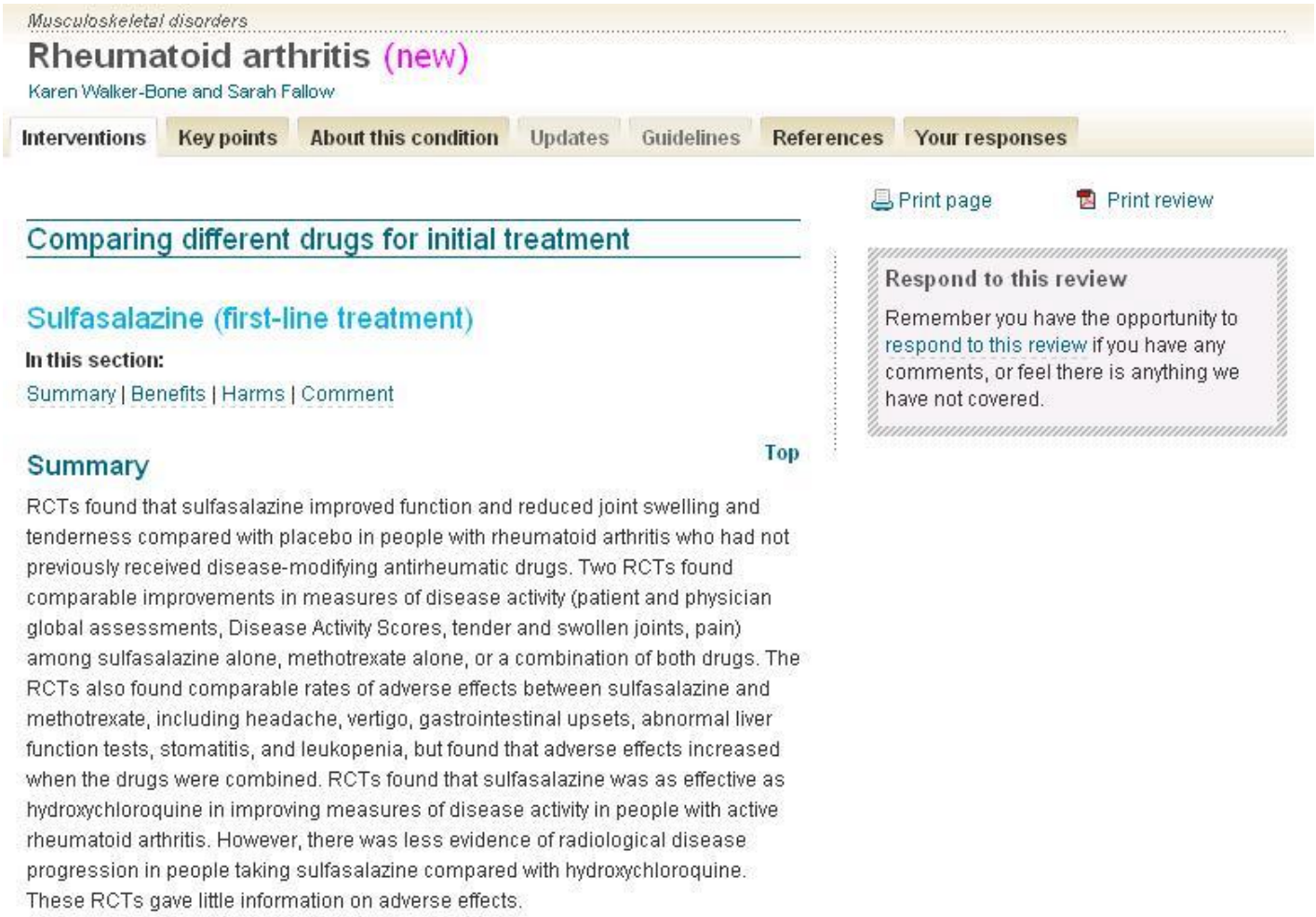
GRADE



Musculoskeletal disorders

Rheumatoid arthritis (new)

Karen Walker-Bone and Sarah Fallow

Interventions | Key points | About this condition | Updates | Guidelines | References | Your responses

Print page Print review

Comparing different drugs for initial treatment

Sulfasalazine (first-line treatment)

In this section:

Summary | Benefits | Harms | Comment

Top

Summary

RCTs found that sulfasalazine improved function and reduced joint swelling and tenderness compared with placebo in people with rheumatoid arthritis who had not previously received disease-modifying antirheumatic drugs. Two RCTs found comparable improvements in measures of disease activity (patient and physician global assessments, Disease Activity Scores, tender and swollen joints, pain) among sulfasalazine alone, methotrexate alone, or a combination of both drugs. The RCTs also found comparable rates of adverse effects between sulfasalazine and methotrexate, including headache, vertigo, gastrointestinal upsets, abnormal liver function tests, stomatitis, and leukopenia, but found that adverse effects increased when the drugs were combined. RCTs found that sulfasalazine was as effective as hydroxychloroquine in improving measures of disease activity in people with active rheumatoid arthritis. However, there was less evidence of radiological disease progression in people taking sulfasalazine compared with hydroxychloroquine. These RCTs gave little information on adverse effects.

Respond to this review

Remember you have the opportunity to respond to this review if you have any comments, or feel there is anything we have not covered.

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GRADE

OPTION SULFASALAZINE (FIRST-LINE TREATMENT) New

abridged-title: Sulfasalazine (first-line treatment)
intervention-title: Sulfasalazine (first-line treatment) [efficacy: beneficial]
substantive-change: No description. [status: new-option]

disorders

Disease severity
Compared with placebo Sulfasalazine may not improve overall disease severity compared with placebo as first-line therapy in people with rheumatoid arthritis who had not previously received disease-modifying antirheumatic drugs (very low quality evidence).

Compared with methotrexate Sulfasalazine may be as effective as methotrexate at reducing disease activity over 12 months as first-line treatment in people with rheumatoid arthritis (low quality evidence).

Compared with sulfasalazine plus methotrexate Sulfasalazine alone may be as effective as sulfasalazine plus methotrexate at reducing disease activity over 12 months as first-line treatment in people with rheumatoid arthritis (low quality evidence).

Compared with hydroxychloroquine Sulfasalazine is as effective as chydroxychloroquine at improving symptoms and function in people with rheumatoid arthritis (moderate quality evidence).

Joint pain and tenderness
Compared with placebo Sulfasalazine may reduce joint pain and tenderness compared with placebo after 6-12 months as first-line therapy (low quality evidence).

Adverse effects
The risk of adverse effects seems to be similar with sulfasalazine and methotrexate , including headache, vertigo, gastrointestinal upsets, abnormal liver function tests, stomatitis, and leukopenia. Adverse effects may increase when the drugs are combined.

Benefits:

Sulfasalazine versus placebo:
We found no systematic review but found three RCTs in adults with early active rheumatoid arthritis (< 12 months since diagnosis) who had not previously received disease-modifying antirheumatic drugs (DMARDs). [8] [9] [10] The first RCT (105 people aged 22–78 years with early non-erosive rheumatoid arthritis) compared sulfasalazine 2 g daily versus placebo over 6 months. [8] Corticosteroid use was not allowed during the trial. In total, 65 people (62%) completed the trial; analysis was by intention to treat for all outcomes except radiological progression. The RCT found that sulfasalazine significantly improved joint tenderness measured by the Ritchie articular index and the number of swollen and tender joints compared with placebo (see table 2, p 36). It found

GRADE

TABLE 1 GRADE evaluation of interventions for rheumatoid arthritis

Important outcomes	Disease activity, pain, swollen joints, functional status, mortality, adverse effects								
Number of studies (participants)	Outcome	Comparison	Type of evidence	Quality	Consistency	Directness	Effect size	GRADE	Comment
What are the effects of drug treatments in people with rheumatoid arthritis who have not previously received any disease-modifying antirheumatic drug treatment?									
2 (310) [Dougados 1999][Haagsma 1997]	Disease activity	Methotrexate v sulfasalazine v methotrexate plus sulfasalazine	4	0	-1	-1	0	Low	Consistency point deducted for conflicting results. Directness point deducted for inconsistent use of corticosteroids
3 (371) [Australian multicentre CT group 1992][Hannonen 1993][Williams 1988]	Joint pain or tenderness	Sulfasalazine v placebo	4	-1	0	-1	0	Low	Quality point deducted for poor follow up. Directness point deducted for inconsistent use of corticosteroids
3 (371) [Australian multicentre CT group 1992][Hannonen 1993][Williams 1988]	Disease severity (patient/physician global assessment)	Sulfasalazine v placebo	4	-2	-1	-1	0	Very low	Quality point deducted for poor follow up and incomplete reporting of results. Consistency point deducted for conflicting results. Directness point deducted for inconsistent use of corticosteroids
1 (60) [Nuver-Zwart 1989]	Disease severity	Sulfasalazine v hydroxychloroquine	4	-1	0	0	0	Moderate	Quality point deducted for sparse data
2 (145) [Clark 1993][Anon 1995]	Joint pain/tender-	Hydroxychloroquine v placebo	4	-1	0	-1	0	Low	Quality point deducted for sparse data. Directness point

Updating

- What does updating mean to us and our users?
- How do update schedules fit into clinical practice?
- Do we really have to recreate the entire review each time?

St Thomas' Hospital ED

St Thomas' ED

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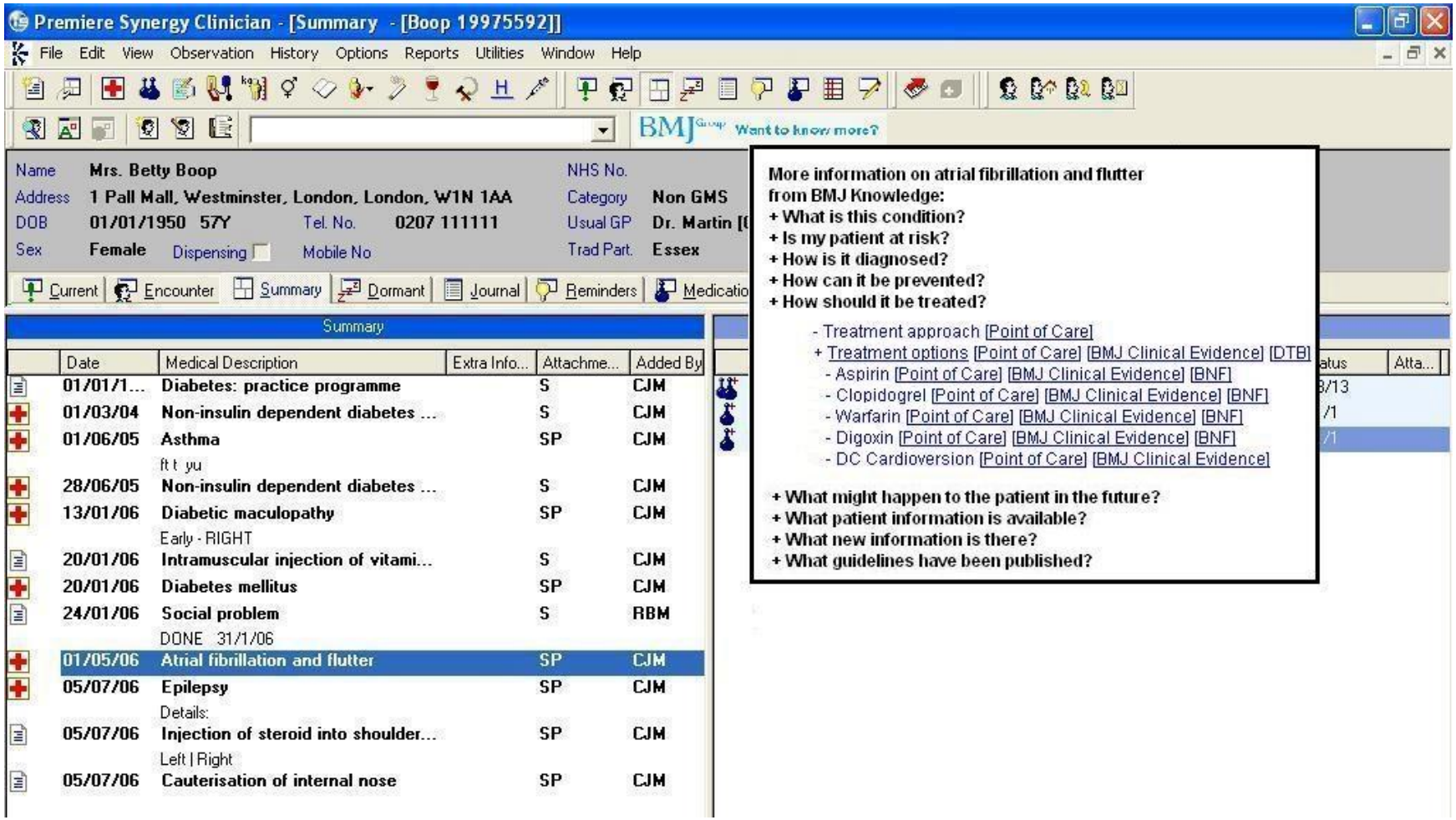
Integration



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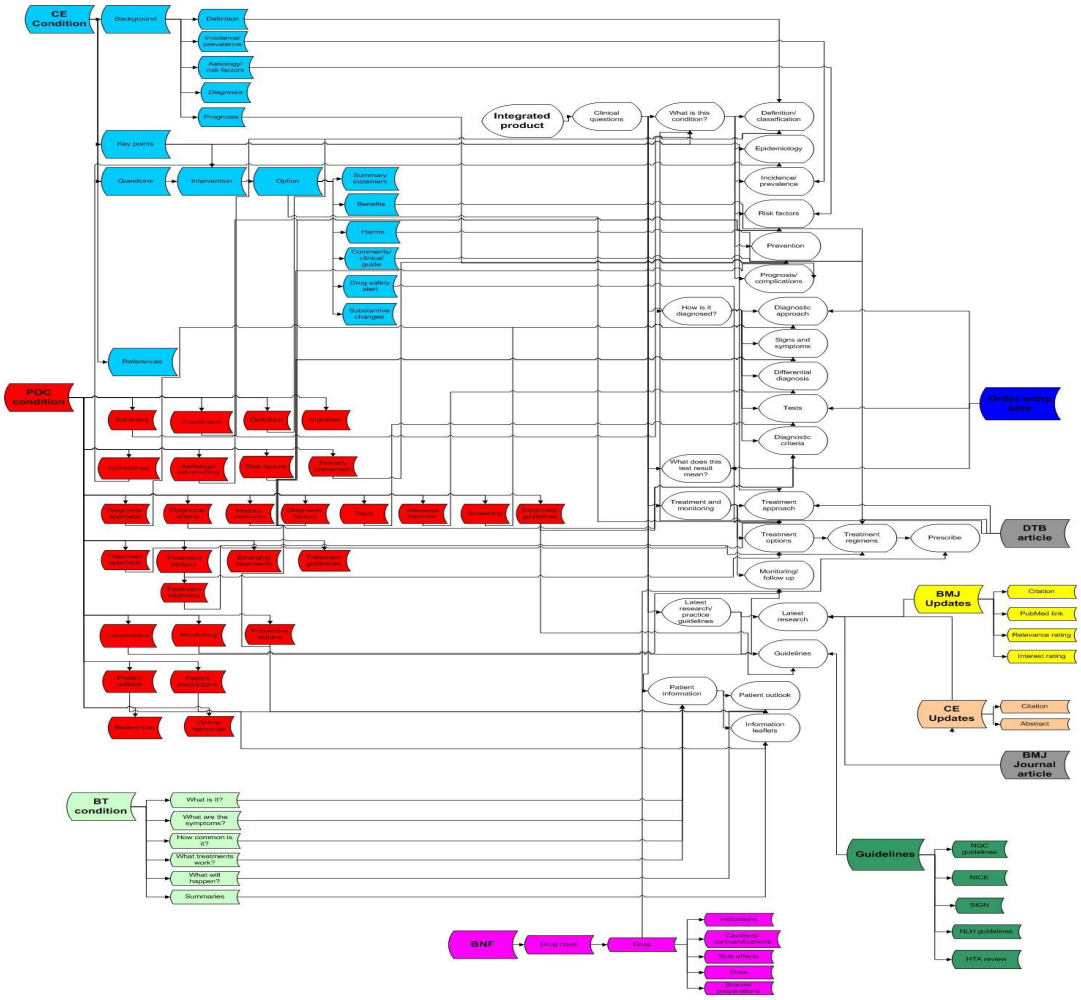
Integration



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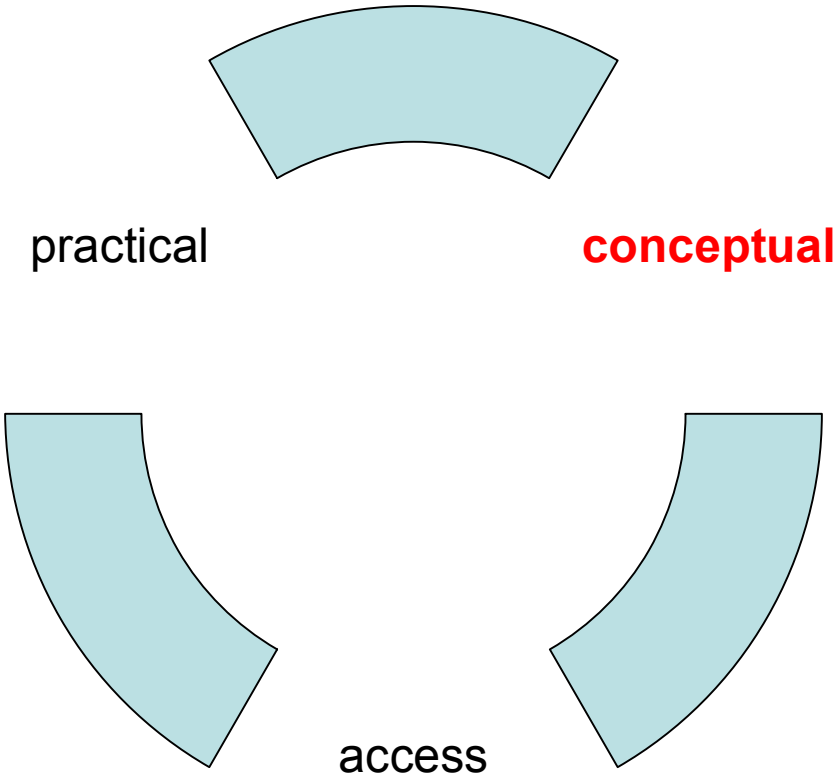
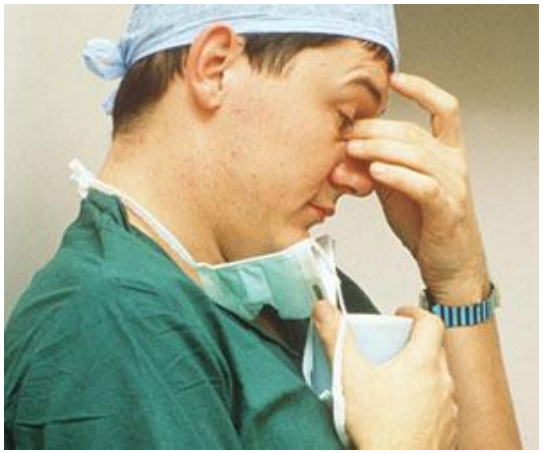
Practical versus Conceptual



Spot the odd one out?



‘Drug 'ends need for mastectomy’

‘Herceptin eradicates aggressive tumors: study’

Conclusion

- How do we convey doubt?
- How do we update?
- How do we integrate knowledge?