2008年4月21日
文献検索評価法

文献検索と評価の基本
:EBMの視点から(2)

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ペイシェント・クエッション
（Patient Question: PQ）

- 患者の視点で挙げられた療養（治療＆養生）に際する疑問。
- 生活上の留意点に関する疑問、治療法に関する情報を主治医と共有しようとする際に感じられる疑問など幅広く含む。
- そのうちのいくつかの項目は、多くの患者が共通に感じているもので、CQとしては挙げられにくいが、医療者と患者の情報共有を進めるため診療ガイドラインにおいて言及するのが望ましい場合もある。

疑問の定式化：PICO

1. ***Patient***
2. ***Intervention (Exposure)***
3. ***Comparison***
4. ***Outcome***

＋***Design***

＋***Setting***

- **現場での意思決定・・・少数のエビデンスレベルの高い文献を素早く検索、2次情報の活用。**
- **研究・・・腰をすえ、試行錯誤しながらじっくり検索。**

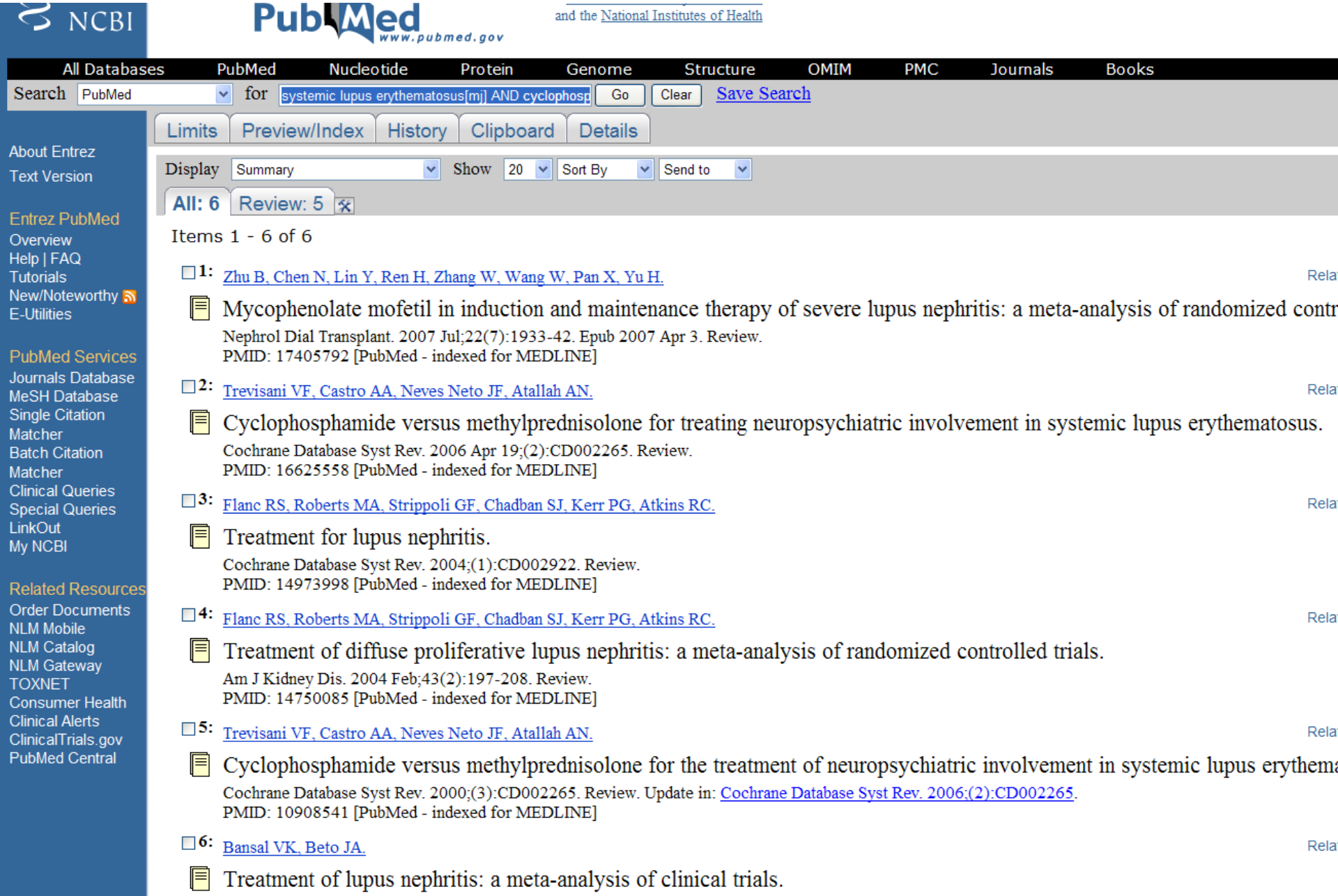
エビデンス検索の実際

- 30歳の女性、5年前全身性エリテマトーデス（SLE）の診断を受ける。
- ステロイドを服用しているが蛋白尿も見られ、自覚症状も思わしくない。
- サイクロフォスファマイド（エンドキサン）を試す価値はあるか？
- PICOへの当てはめ
  - Patient　　30歳女性、SLE（腎障害あり）
  - Intervention　　サイクロフォスファマイド
  - Comparison　　ステロイド
  - Outcome　　（自覚症状？）

SLEにおけるサイクロフォスファマイド

- 文献が多くないことが予想される課題では、指定が細かすぎるとヒット数0になる。
- まずはPとIの2要素で広めに検索。
- エビデンス・レベルの高い研究デザインを指定
  - 昔は先輩経験や症例報告、根拠となる文献引用の無い教科書が頼り）
- PubMedでの検索式 （全身性エリテマトーデス、SLE: systemic lupus erythematosus）
- systemic lupus erythematosus[mj] AND cyclophosphamide[mh] AND (Meta-Analysis [pt] OR Cochrane Database Syst Rev[ta])

検索日　2008年4月6日



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Items 1 - 6 of 6

1: Zhu B, Chen N, Lin Y, Ren H, Zhang W, Wang W, Pan X, Yu H. Rela

Mycophenolate mofetil in induction and maintenance therapy of severe lupus nephritis: a meta-analysis of randomized contr

Nephrol Dial Transplant. 2007 Jul;22(7):1933-42. Epub 2007 Apr 3. Review.
PMID: 17405792 [PubMed - indexed for MEDLINE]

2: Trevisani VF, Castro AA, Neves Neto JF, Atallah AN. Rela

Cyclophosphamide versus methylprednisolone for treating neuropsychiatric involvement in systemic lupus erythematosus.

Cochrane Database Syst Rev. 2006 Apr 19;(2):CD002265. Review.
PMID: 16625558 [PubMed - indexed for MEDLINE]

3: Flanc RS, Roberts MA, Strippoli GF, Chadban SJ, Kerr PG, Atkins RC. Rela

Treatment for lupus nephritis.

Cochrane Database Syst Rev. 2004;(1):CD002922. Review.
PMID: 14973998 [PubMed - indexed for MEDLINE]

4: Flanc RS, Roberts MA, Strippoli GF, Chadban SJ, Kerr PG, Atkins RC. Rela

Treatment of diffuse proliferative lupus nephritis: a meta-analysis of randomized controlled trials.

Am J Kidney Dis. 2004 Feb;43(2):197-208. Review.
PMID: 14750085 [PubMed - indexed for MEDLINE]

5: Trevisani VF, Castro AA, Neves Neto JF, Atallah AN. Rela

Cyclophosphamide versus methylprednisolone for the treatment of neuropsychiatric involvement in systemic lupus erythema

Cochrane Database Syst Rev. 2000;(3):CD002265. Review. Update in: Cochrane Database Syst Rev. 2006;(2):CD002265.
PMID: 10908541 [PubMed - indexed for MEDLINE]

6: Bansal VK, Beto JA. Rela

Treatment of lupus nephritis: a meta-analysis of clinical trials.

出所 http://www.ncbi.nlm.nih.gov/pubmed/

1: Cochrane Database Syst Rev. 2006 Apr 19;(2):CD002265.

Update of:
Cochrane Database Syst Rev. 2000;(3):CD002265.

Cyclophosphamide versus methylprednisolone for treating neuropsychiatric involvement in systemic lupus erythematosus.

Trevisani VF, Castro AA, Neves Neto JF, Atallah AN.

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BACKGROUND: Neuropsychiatric involvement in systemic lupus erythematosus is complex and several clinical presentations are related to this disease such as: convulsions, chronic headache, transverse myelitis, vascular brain disease, psychosis and neural cognitive dysfunction. This systematic review is an update of a review performed in 2000. OBJECTIVES: To assess the efficacy and safety of cyclophosphamide and methylprednisolone in the treatment of neuropsychiatric manifestations of systemic lupus erythematosus. SEARCH STRATEGY: We searched EMBASE, LILACS, Cochrane Central Register of Controlled Trials (CENTRAL) and MEDLINE up to and including May 2005. Additional articles were sought through handsearching in relevant journals. There were no language restrictions. SELECTION CRITERIA: All randomised controlled trials that compared cyclophosphamide to methylprednisolone were included. Patients of any age and gender were included as long as they fulfilled the criterion of the American College of Rheumatology for the diagnosis of systemic lupus erythematosus and presented with any one of the following neuropsychiatric events: convulsions, organic brain syndrome and cranial neuropathy. Outcome measures included the following: a) overall mortality (primary event); b) motor and psychiatric deficit (primary event); c) clinical improvement (secondary event). DATA COLLECTION AND ANALYSIS: Data was independently extracted by two reviewers and cross-checked. The methodological quality of each trial was assessed by the same two reviewers. Details of the randomisation (generation and concealment), blinding, and the number of patients lost to follow-up were recorded. Dichotomous data was presented as relative risks with corresponding 95% confidence intervals and a clinical relevance table was produced. MAIN RESULTS: We found one randomised controlled trial of 32 patients comparing cyclophosphamide versus methylprednisolone for the treatment of neuropsychiatric involvement in the systemic lupus erythematosus. A significantly greater number of people responded to treatment in the cyclophosphamide group. Treatment response was found in 94.7% (18/19) of patients using cyclophosphamide compared with 46.2% (6/13) in the methylprednisolone group at 24 months (RR 2.05, 95% CI 1.13, 3.73) The NNT for response to treatment is 2. Cyclophosphamide use was associated with a reduction in prednisone requirements. A significant decrease in the number seizures per month was observed in the cyclophosphamide group. All the patients in the cyclophosphamide group had electroencephalographic improvement. No significant differences in adverse effects between the groups were found. It was not possible to extract more data from the study because there was a small number of patients in the others clinical subgroups of neurological manifestations and the authors did not provide sufficient information for data extraction. AUTHORS' CONCLUSIONS: This systematic review found one randomised controlled trial with a small number of patients in the different clinical subgroups of neurological manifestation. It seems that cyclophosphamide is more effective in the treatment of neuropsychiatric involvement in systemic erythematosus lupus compared with methylprednisolone. However, properly designed randomised controlled trials that involve large, representative numbers of individuals, with explicit clinical and laboratory diagnosis criteria, sufficient duration of follow-up and description of

Cochrane Database Syst Rev. 2000;(3):CD002265.

- Trevisani VF, et al. Cyclophosphamide versus methylprednisolone for the treatment of neuropsychiatric involvement in systemic lupus erythematosus.
- MAIN RESULTS: We found no randomised controlled trials comparing cyclophosphamide versus methylprednisolone for the treatment of neuropsychiatric involvement in the systemic lupus erythematosus.
- REVIEWER'S CONCLUSIONS: Cyclophosphamide regimen treatment is a form of care in neuropsychiatric involvement in systemic lupus erythematosus with no evidence to prove better effectiveness and safety when compared with methylprednisolone. This systematic review found no randomised controlled trials and its findings must be interpreted as 'no evidence of effect' and not as 'evidence of no effect'.

Cochrane Database Syst Rev. 2006 Apr 19;(2):CD002265.

- Trevisani VF, et al. Cyclophosphamide versus methylprednisolone for the treatment of neuropsychiatric involvement in systemic lupus erythematosus.
- MAIN RESULTS: We found one randomised controlled trial of 32 patients comparing cyclophosphamide versus methylprednisolone for the treatment of neuropsychiatric involvement in the systemic lupus erythematosus.
- AUTHORS' CONCLUSIONS: This systematic review found one randomised controlled trial with a small number of patients in the different clinical subgroups of neurological manifestation. It seems that cyclophosphamide is more effective in the treatment of neuropsychiatric involvement in systemic erythematosus lupus compared with methylprednisolone. However, properly designed randomised controlled trials that involve large, representative numbers of individuals, with explicit clinical and laboratory diagnosis criteria, sufficient duration of follow-up and description of all relevant outcome measures are necessary to guide practice.
  - Cochrane Database Syst Rev. 2000;(3):CD002265.

Cochrane Database Syst Rev. 2004;(1):CD002922.

- Flanc RS, et al. Treatment for lupus nephritis.
- MAIN RESULTS: …Cyclophosphamide plus steroids reduced the risk of doubling of serum creatinine (RR 0.59, 95% CI 0.40 to 0.88) compared to steroids alone but had no impact on mortality (RR 0.98, 95% CI 0.53 to 1.82).
- REVIEWER'S CONCLUSIONS: Until future RCTs of newer agents are completed, the current use of cyclophosphamide combined with steroids remains the best option to preserve renal function in proliferative LN. The smallest effective dose and shortest duration of treatment should be used to minimise gonadal toxicity, without compromising efficacy.

簡単な注意書きによる改善
Centre for Clinical Effectivenessの試み

Centre for Clinical Effectiveness

ENHANCING PATIENT OUTCOMES THROUGH
CLINICAL APPLICATION OF THE BEST AVAILABLE EVIDENCE

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For staff of the Southern Health Care Network ONLY

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Our phone number: **9594 2726** **Our fax number:** **9594 6970**
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Email Address:	Work Phone:
Date of request:	Work Fax:

Instruction

Supplying a well-formulated question will assist us in processing your request with less delay. Please formulate your question so that each of the following components are clearly defined: (1) the **subjects** to which the answer will apply; (2) the type of **intervention / diagnostic test / prognostic factor** of interest; (3) the type of **comparison or control**; and (4) the **outcomes** of interest. We give you an example below (from Counsell, 1997):

A poorly formulated question:

Intervention — Subjects

Are anticoagulant agents useful in patients who have had stroke?

A well formulated question:

Intervention — Outcome — Subjects

Do anticoagulant agents improve survival in patients with acute ischaemic stroke compared with no treatment?

Comparison

Well-formulated question

- Poor
  - 脳卒中の既往のある患者に抗凝固薬は有効か？
- Well
  - 急性脳梗塞の患者に対して、抗凝固薬投与は投与しない場合に比べて、生命予後の改善（生存期間の延長）に有効か？

家庭医によるクリニカルクエスチョン

- 1996年4月から1997年12月
- ランダム抽出103名の家庭医
- 2日半、調査者が立会いクリニカルクエスチョン（CQ）を収集
- 1,101個のCQが生成され、69カテゴリーに分類可能。
- **64%**のCQはすぐに追求されなかった。
- 追求されたCQの**80%**は解答が得られた。
- 医師が解答を得るのに費やした時間は平均**2分**以下。
- ほとんどは印刷物あるいは他の医療従事者に聞くことによって解答を得ていた。

(Ely et al:Analysis of questions asked by family doctors regarding patient care. BMJ 2004;319:358)

家庭医によるCQ分類トップ10

(Ely et al:BMJ 2004;319:358)

CQ	%	追求%	解答%
症状Xの原因は何か？	9	9	50
薬剤Xの用量はいくつか？	8	85	97
疾患Xあるいは症状Xをどのようにマネージメントしたらいいか？	7	29	83
疾患Xあるいは症状Xをどのように治療したらいいか？	7	33	72
診察所見Xの原因は何か？	7	18	46
検査Xの結果の原因は何か？	4	40	72
この患者は疾患Xあるいは病態Xか？	4	14	67
Yの状況で検査Xは適応があるか？	4	29	83
病態Xに対してどの薬剤を選択すべきか？	3	47	76
病態Yにおいて薬剤Xは適応があるか？	3	25	78

用いられた情報源、時間、成功率

(Ely et al:BMJ 2004;319:358)

情報源	割合(%)	平均（SD)(秒）	成功率（%）*
人（医師、薬剤師など）	36	109（104）	79
添付文書以外の印刷物	32	100 (89)	52
添付文書	25	70 (66)	85
壁に貼られている文書	4	42 (34)	82
PC (CD-ROMやインターネット）	2	395 (552)	20
計	100	102 (137)	71

*回数に対する割合

クリニカルクエスチョンの分類

- John W Ely, et al. A taxonomy of generic clinical questions: classification study.　BMJ 2000;321:429-432
- **アイオワ（103名）とオレゴン（49名）のプライマリケア医が対象。**
- 1396 CQを64タイプに分類。
- 多いCQのタイプ
  - "What is the drug of choice for condition x?" (150 questions, 11%);
  - "What is the cause of symptom x?" (115 questions, 8%);
  - "What test is indicated in situation x?" (112 questions, 8%).
- **プライマリケア医のCQは限られたタイプに分類可能。**
- **分類（学）は、医師の情報ニーズに関する理解とそれへの対応を向上させることが期待される**

Generic questions derived from questions by primary care doctors in Iowa and Oregon and their frequencies

Question	Frequency					
	Iowa questions (n=1101)		Oregon questions (n=295)		Total questions (n=1396)	
	Rank	No (%) of questions	Rank	No (%) of questions	Rank	No (%) of questions
What is the drug of choice for condition x?	1st	112 (10)	1st	38 (13)	1st	150 (11)
What is the cause of symptom x?	2nd	106 (10)	11th	9 (3)	2nd	115 (8)
What test is indicated in situation x?	3rd	84 (8)	3rd	28 (9)	3rd	112 (8)
What is the dose of drug x?	4th	84 (8)	10th	10 (3)	4th	94 (7)
How should I treat condition x (not limited to drug treatment)?	7th	53 (5)	2nd	29 (10)	5th	82 (6)
How should I manage condition x (not specifying diagnostic or therapeutic)?	5th	62 (6)	19th	5 (2)	6th	67 (5)
What is the cause of physical finding x?	6th	61 (6)	16th	6 (2)	7th	67 (5)
What is the cause of test finding x?	8th	53 (5)	7th	11 (4)	8th	64 (5)
Can drug x cause (adverse) finding y?	10th	42 (4)	4th	17 (6)	9th	59 (4)
Could this patient have condition x?	9th	49 (4)	26th	2 (1)	10th	51 (4)

クリニカルクエスチョンの頻度と処理

(Am J Med 2000;109:218.)

- 米国　大学病院　64名のレジデント
- 1人の患者診察後に調査
  - **患者3人に対し2つのCQ　(0.7/pt)**
    - 治療　38%
    - 診断　27%
  - CQの**29%**が追求された
    - 教科書　31%
    - 原著　21%
    - 指導医　17%
  - CQを追求した理由
    - 患者が期待している
    - 医療訴訟を恐れて
  - CQを追求しなかった理由
    - 時間がない　60%
    - 忘れてしまった　29%

クリニカルクエスチョンの収集法による違い

(J Med Libr Assoc 2003;91:364.)

- 卒後平均15から19年の家庭医を中心とした調査
  - 1人の患者の診療後インタビュー（出口調査）VS 保持したカードに医師が記入（自己申告）
- 患者1人あたりのCQ数＝0.43 VS 0.16

診断	28.7%	23.1%
薬物療法	34.2	50.0
治療 (薬物以外あるいは一般的)	14.0	7.7
マネージメント (診断と治療)	9.4	5.7
疫学	7.5	5.7
非臨床	6.3	7.7

解答を得た情報源

コンサルタント	14.2%	18.7%
パートナー	10.6	9.5
教科書	10.0	12.2
卓上資料	13.3	22.6
MEDLINE以外のWebサイト	3.4	2.2
薬剤の添付文書	1.9	0.5
雑誌	2.7	3.0
MEDLINE	5.8	0.7

情報検索をしない理由1

- 患者に特異的な疑問に一般的な情報源で答えることが難しい。
- 患者からの情報が不十分で検索の焦点が絞れない。
- CQの関連領域が適切か良くわからない。補助的なCQも含むべきか良く分からない。
- 専門用語を用いた検索がうまく行かない。
- クリニカルクエスチョンの改変が検索を施行後必要なことが分かることがある。
- PI(E)CO形式にCQを合わせるのが難しい。
- 検索担当者とのコミュニケーションがうまく行かず、不要なCQの改変が行われる。

情報検索をしない理由2

- 関連した情報の存在に疑問を持っている。
- CQの重要性が情報検索を正当化するほど高くない。
- 検索を行う時間がない。
- コンサルテーションで容易に情報が得られるので、検索の必要が無い。
- どこに必要な情報があるかよく分からない。
- 情報検索のスキルが不十分で適切な検索ができない。
- どういう順に情報源を見るべきか良く分からない。

情報検索をしない理由3

- 必要な情報を失わないで、検索を絞込む方法が良く分からない。
- どの文献を熟読すべきか、どのように熟読すべきか良く分からない。
- 検索をどこでストップして良いかよく分からない。
- 検索結果がゼロの場合、改善すべき点が分からない。
- データベースのインデクシングの問題で、目的の語句がMeSHに無い。
- 情報源へのアクセスが不便。
- 知りたい情報がデータベースに含まれていない。
- etc.

Medline 検索のバリアー

(Int J Technol Assess Health Care 1999;15:281.)

1. 適切に作成したCQから始めていない。
2. 適切なMeSH (Medical Subject Headings)を使っていない。
3. 自分の考えと、検索式作成を適切につなげることができない。
4. 検索に適切なLimits（制限）をかけることができない。

プライマリケア医がCQを追求する動機

- Gorman PN, et al. Information seeking in primary care: how physicians choose which clinical questions to pursue and which to leave unanswered. Med Decis Making 1995;15:113-9.
- 約30%のCQしか解答を追及しない。なぜか？
- 49名のプライマリケア医の調査。
- 12因子の多変量解析の結果、2因子がCQの追及と有意に関連していた。
  - 確実な解答が存在すると信じられる
  - 患者の問題の緊急性が高い