實證醫學 病例討論報告

Evidence-Based Medicine

職級：R1
姓名：鄭功全
報告日期: 101.06.04

Outline

- Clinical scenario-臨床場景
- Asking-提出問題
- Acquire- 搜尋資料
- Appraisal-嚴格評讀
- Apply-臨床應用
- Audit-自我評估

Clinical scenario

PATIENT'S PROFILE

- This 55 y/o male had history of:
  - Ascending colon cancer, adenocarcinoma with liver metastases, suspect lung metastases.
    (Stage IV. pT4bN2bM1)
    - s/p right hemicolectomy + venous port implantation on 100/10/10.
    - s/p 8 course of radiotherapy and FOLFOX4 and 6 course of Erbitux since 100/11/15.
- This time, he was admitted because of abdominal cramping pain with nausea and vomiting for 2 days.
- Impression: adhesion ileus

AFTER ADMISSION...

- Abdominal CT on 101-04-20:
  - partial mechanical ileus with transitional zone in the distal jejunum. Susp/adhesion.
- Operation on 101-04-28
  - Enterolysis + segmental resection of small intestine + end-to-end anastomosis
  - Pathology report:
    - Cytomegaloviral cytopathic change is noted on the endothelial cells of granulation tissue
    - CMV stain highlights the nuclei of infected cells
  - Pathologic diagnosis: cytomegaloviral ileitis
  - Serum CMV IgG(+, >256), IgM(-), CMV PP65(-)

ASKING

Background question

Q1: What's the prevelence of CMV infection in our population?

- The proportion of humans with evidence of prior CMV infection varies throughout the world, with seroprevalence rates ranging between 40-100% of the adult population .
- Seroprevalence generally correlates inversely with a country's socioeconomic development, with highest rates observed in developing countries throughout Africa and Asia.

Q2: What organs would be affected by CMV infection?

- **Gastrointestinal manifestations:** CMV colitis
- **Hepatic manifestations** : Liver function abnormalities
- **Neurologic manifestations:** Encephalitis, Guillain-Barré syndrome
- **Cardiovascular manifestations:** Pericarditis, Myocarditis, Venous thrombosis

ASKING

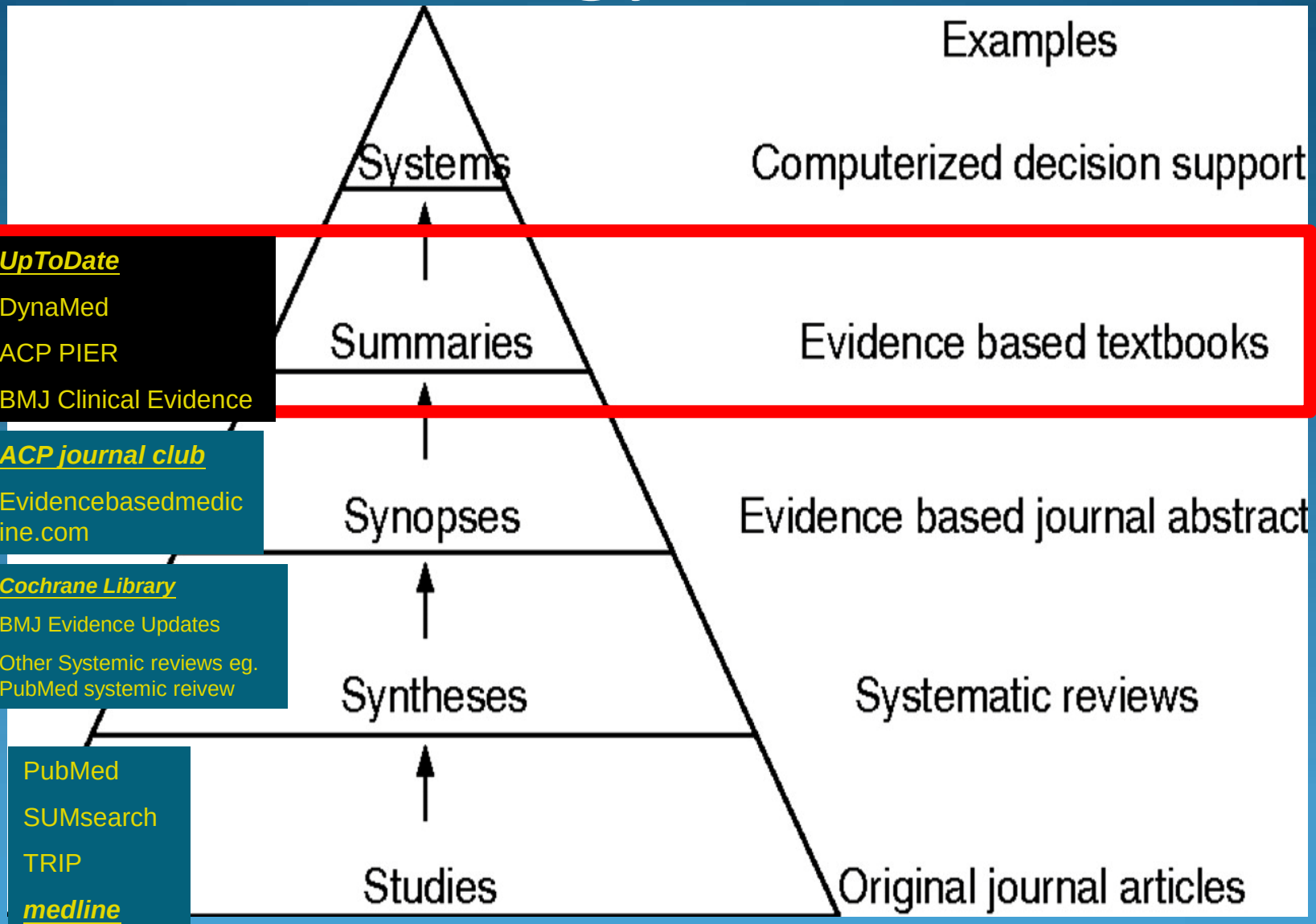
Foreground question

Is CMV infection a poor prognosis factor in immunocompetent patients?

PICO

Patient	1. 55 y/o • Ascending colon cancer, Stage 4 IV
Intervention	CMV infection
Comparison	Without CMV infection
Outcome	Mortality rate, Length of hospital stay

Search strategy: 5S model



搜尋 UpToDate

- Key words
  - Cytomegaloviral infection

Summaries search results~

UpToDate. CMV infection | All Topics Search

News from UpToDate | Contact Us | Ab

New Search | Patient Info | What's New | Calculators

Search Results for **"CMV infection"**

- **All Topics**
- **Adult**
- **Pediatric**
- **Patient**
- **Graphics**

- **Epidemiology, clinical manifestations, and treatment of cytomegalovirus infection in immunocompetent hosts**
- Diagnosis of cytomegalovirus
- Cytomegalovirus infection and disease in newborns, infants, children and adolescents
- Cytomegalovirus infection in renal transplant recipients
- Cytomegalovirus infection in pregnancy
- Cytomegalovirus infection as a cause of pulmonary disease in HIV-infected patients
- Clinical manifestations, diagnosis, and treatment of cytomegalovirus infection in lung transplant recipients
- AIDS-related cytomegalovirus gastrointestinal disease
- Viral load testing for cytomegalovirus in solid organ transplant recipients
- AIDS-related cytomegalovirus neurologic disease
- Prevention of cytomegalovirus infection in lung transplant recipients
- Overview of TORCH infections
- Pathogenesis, clinical manifestations, and diagnosis of AIDS-related cytomegalovirus retinitis
- Causes of rhabdomyolysis
- Prophylaxis of infections in hematopoietic cell transplant recipients
- Treatment of AIDS-related cytomegalovirus retinitis
- Infectious complications in liver transplantation

Topic Outline

INTRODUCTION

INFECTION, LATENCY AND REACTIVAT

IMMUNOLOGY

EPIDEMIOLOGY

TRANSMISSION

CMV MONONUCLEOSIS
- Differences between EBV and CMV mononucleosis
- Laboratory abnormalities

ORGAN-SPECIFIC COMPLICATIONS
- Gastrointestinal manifestations
- Hepatic manifestations
- Neurologic manifestations
  - Encephalitis
  - Guillain-Barré syndrome
  - Other
- Pulmonary manifestations
- Ocular manifestations
- Cardiovascular manifestations
  - Pericarditis and myocarditis
  - Atherosclerosis
  - Venous thrombosis

REACTIVATION IN CRITICALLY ILL PATI

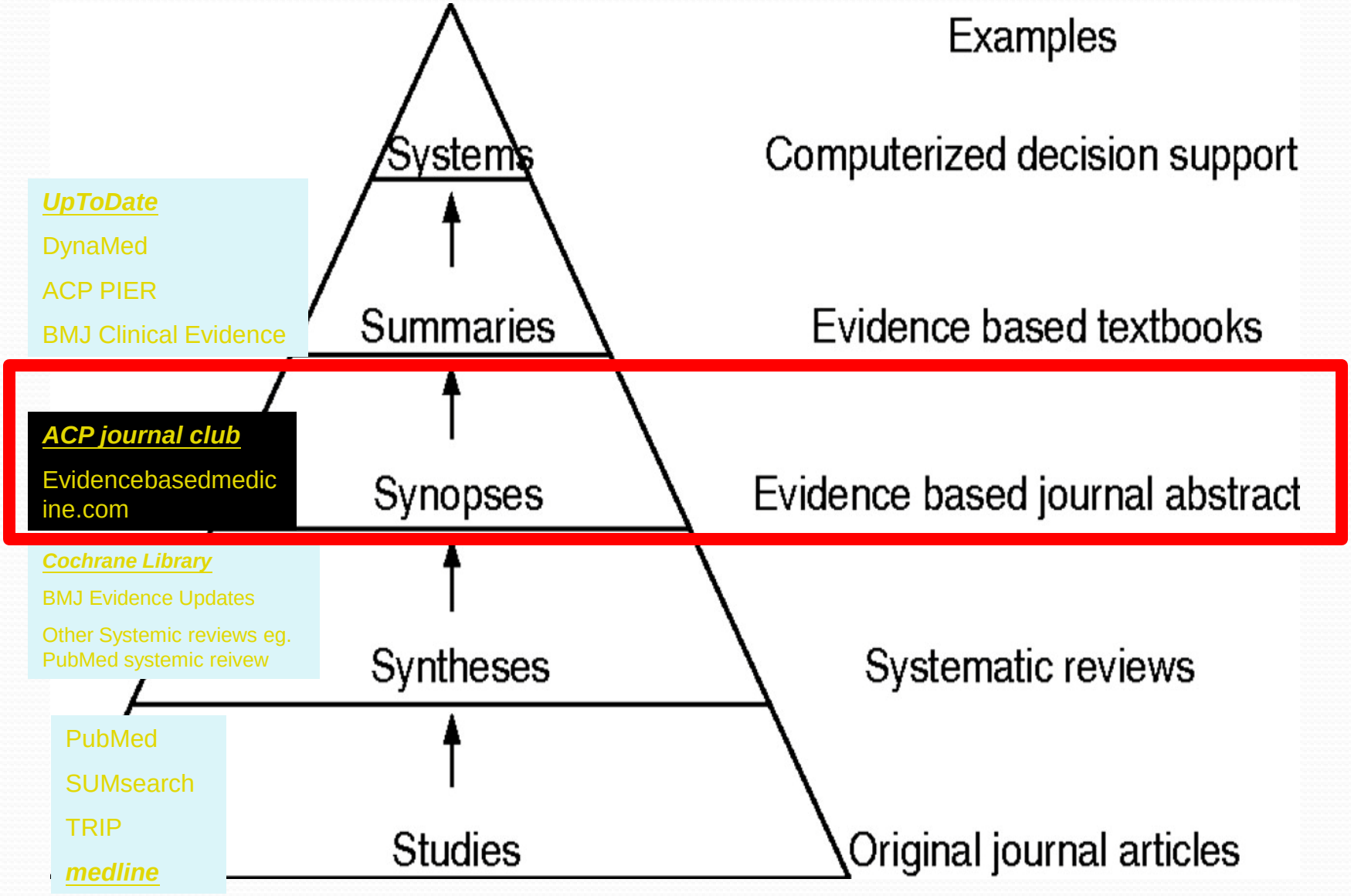
ASSOCIATION BETWEEN SEROPOSITI OUTCOMES

- In a population-based study of 1468 Latino adults 60 years and older, all-cause mortality was 1.43 times higher among individuals with cytomegalovirus (CMV) IgG antibody titers in the highest quartile compared with lower quartiles.
- In a retrospective study that evaluated the impact of CMV serostatus on outcomes in immunocompetent ICU patients, on multivariable analysis, there was no association between CMV seropositivity and ICU mortality which was the primary end point of the study,

將Summaries搜尋的結果應用到我的病人

- 根據summaries的結果，目前對於non-immunocompromised的病人，CMV對於prognosis的影響並無定論。

Search strategy: 5S model



搜尋 ACP Journal Club

- Key words
  - CMV
  - Cytomegalovirus

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Cytomegalovirus Search

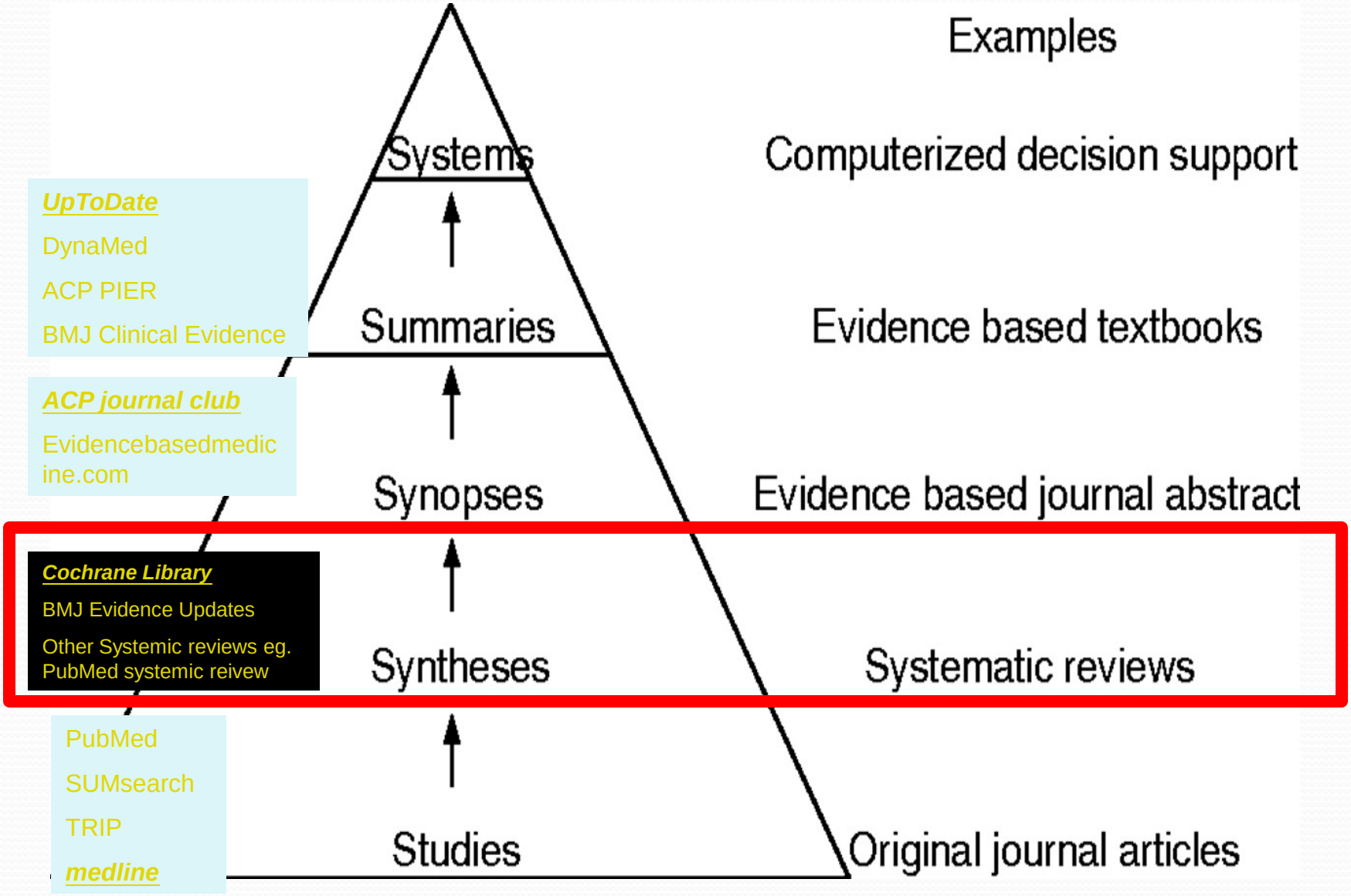
Search Help

Your search - **Cytomegalovirus** - did not match any documents.

Suggestions:

- Make sure all words are spelled correctly.
- Try different keywords.
- Try more general keywords.

Search strategy: 5S model



搜尋 Cochrane Library

- Key words
  - CMV

Search Results

Show Results in:

Cochrane Reviews [13] | Other Reviews [2] | Trials [697] | Methods Studies [4] | Technology Assessments [1] | Economic Evaluations [4] | Cochrane Groups [0]

There are **13** results out of **7272 records** for: "**CMV** in **Title, Abstract or Keywords** in **Cochrane Database of Systematic Reviews**"

Save Search

Edit Search

View: **1-13**

Export All Results

Record Information — Issue: Current | **All** — Restrict to: Reviews | Protocols — Sort by: Record Title | **Match %** | Date

- [ ] **Antiviral medications for preventing cytomegalovirus disease in solid organ transplant recipients**
  Elisabeth M Hodson, Jonathan C Craig, Giovanni FM Strippoli, Angela C Webster
  April 2010
  Review

- [ ] **Immunoglobulins, vaccines or interferon for preventing cytomegalovirus disease in solid organ transplant recipients**
  Elisabeth M Hodson, Cheryl A Jones, Giovanni FM Strippoli, Angela C Webster, Jonathan C Craig
  April 2010
  Review

- [ ] **Antenatal interventions for preventing the transmission of cytomegalovirus (CMV) from the mother to fetus during pregnancy and adverse outcomes in the congenitally infected infant**
  Fergus P McCarthy, Michelle L Giles, Shelley Rowlands, Kara J Purcell, Cheryl A Jones
  March 2011
  Review

- [ ] **Pre-emptive treatment for cytomegalovirus viraemia to prevent cytomegalovirus disease in solid organ transplant recipients**
  Giovanni FM Strippoli, Elisabeth M Hodson, Cheryl A Jones, Jonathan C Craig
  February 2010
  Review

- [ ] **Positive end expiratory pressure for preterm infants requiring conventional mechanical ventilation for respiratory distress syndrome or bronchopulmonary dysplasia**
  Nicolas Bamat, David Millar, Sanghee Suh, Haresh Kirpalani
  January 2012
  Review

- [ ] **Synchronized mechanical ventilation for respiratory support in newborn infants**
  Anne Greenough, Gabriel Dimitriou, Michael Prendergast, Anthony D Milner
  October 2008
  Review

- [ ] **Interleukin 2 receptor antagonists for kidney transplant recipients**
  Angela C Webster, Lorenn P Ruster, Richard McGee, Sandra L Matheson, Gail Y Higgins, Narelle S Willis, Jeremy R Chapman, Jonathan C Craig
  March 2010
  Review

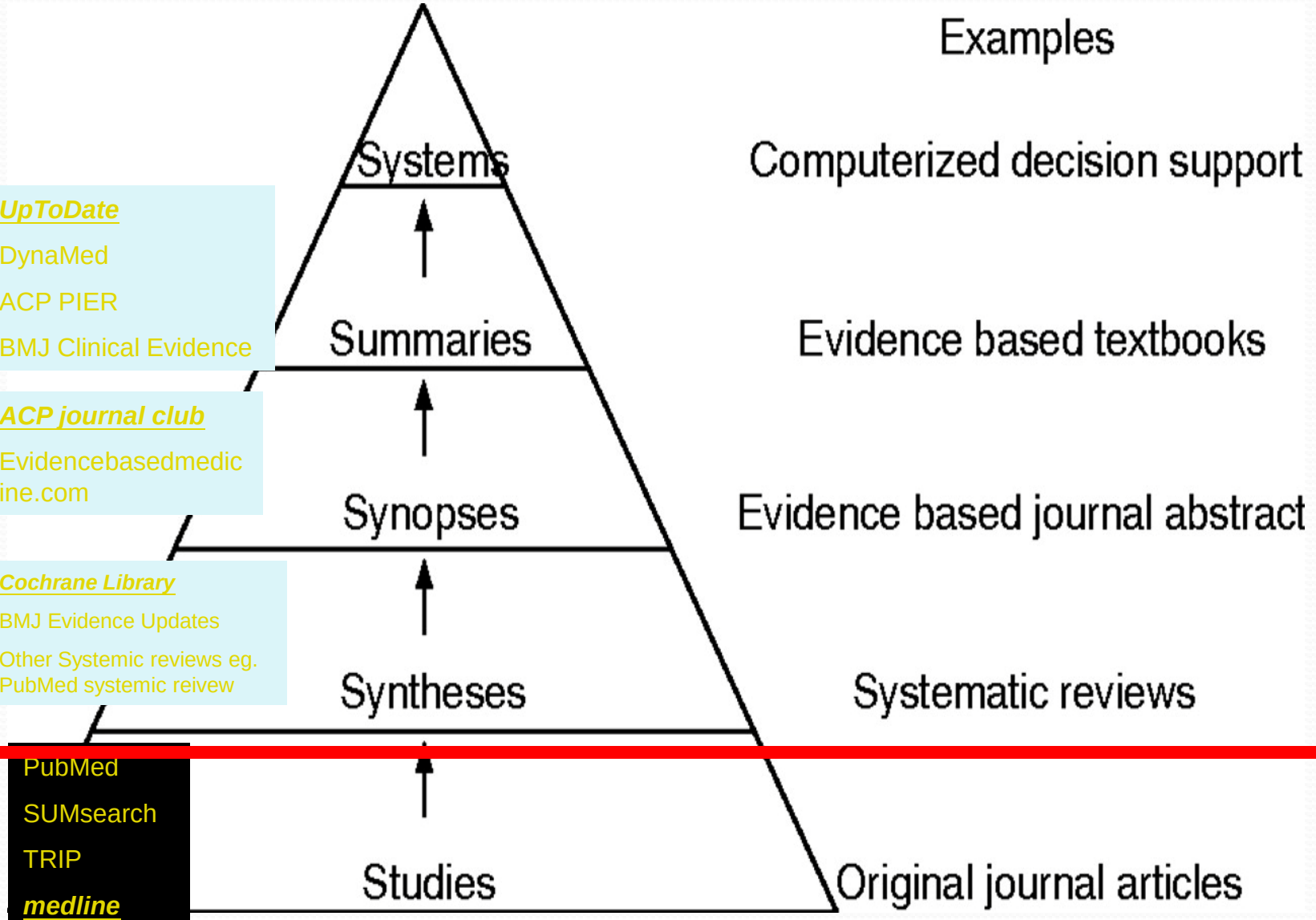
- [ ] **Alemtuzumab for patients with chronic lymphocytic leukaemia**
  Nicole Skoetz, Kathrin Bauer, Thomas Elter, Ina Monsef, Verena Roloff, Michael Hallek, Andreas Engert
  February 2012
  Review

- [ ] **Antiviral agents for treating CMV infection of the nervous system in people with HIV**
  Diana S Klajn, Alejandro Basnak, Viviana Rodriguez, Sergio Nogueira
  January 2009
  Protocol

- [ ] **Antiviral therapy for symptomatic congenital cytomegalovirus infection in neonates and infants up to 3 months of age**
  Cheryl A Jones, Karen S Walker, David J Henderson-Smart

- No article mentions about our question.

Search strategy: 5S model



搜尋 PubMed

- Key words
  - Cytomegalovirus
  - Immunocompetence

PubMed.gov

Cytomegalovirus serostatus and outcome in nonimmunocompromised critically ill patients*

Greet De Vlieger, MD; Wouter Meersseman, MD, PhD; Katrien Lagrou, PharmD, PhD; Pieter Wouters, MSc; Alexander Wilmer, MD, PhD; Willy E. Peetermans, MD, PhD; Greet Van den Berghe, MD, PhD; Eric Van Wijngaerden, MD, PhD

Crit Care Med 2012 Vol. 40, No. 1

Cytomegalovirus serostatus and outcome in nonimmunocompromised critically ill patients

- ***Objective:***
  The impact of cytomegalovirus reactivation duringcritical illness remains unclear and studies investigating prophylaxis in cytomegalovirus seropositive patients are being considered. This study investigates the association between cytomegalovirus seropositivity and outcome in a large population of nonimmunocompromised critically ill patients

Cytomegalovirus serostatus and outcome in nonimmunocompromised critically ill patients

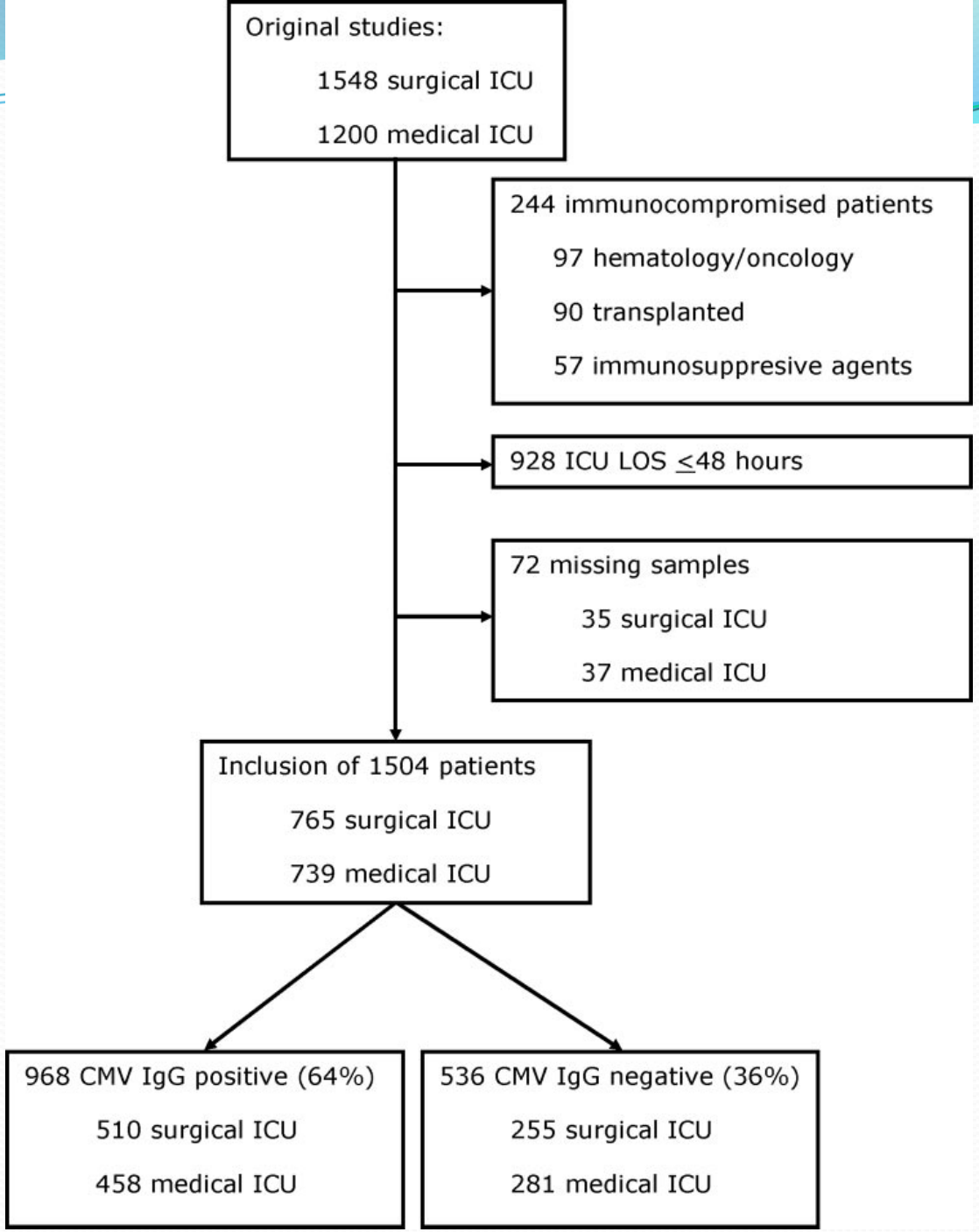
- ***Design:***
  Cytomegalovirus serostatus was determined on prospectively collected serum samples. The primary end point was intensive care unit mortality. The secondary end points were in-hospital mortality, time to alive discharge from intensive care unit and hospital, time to alive weaning from mechanical ventilation, and need for renal replacement therapy.

Cytomegalovirus serostatus and outcome in nonimmunocompromised critically ill patients

- ***Setting:***
  This retrospective study was performed in a 17-bed medical and 56-bed surgical intensive care unit in a 1,900-bed referral hospital.

Cytomegalovirus serostatus and outcome in nonimmunocompromised critically ill patients

- ***Patients:***
  We analyzed serum of 1,504 nonimmunocompromised critically ill patients with an intensive care unit length of stay of 3 days or more. Patients with hematologic malignancy, transplantation, immunosuppressive therapy (calcineurin inhibitors, antitumor necrosis factor- drugs, antilymphocyte antibodies, or chemotherapeutic agents), or a do-not-resuscitate order were excluded.


Original studies:
1548 surgical ICU
1200 medical ICU
244 immunocompromised patients
97 hematology/oncology
90 transplanted
57 immunosuppresive agents
928 ICU LOS ≤48 hours
72 missing samples
35 surgical ICU
37 medical ICU
Inclusion of 1504 patients
765 surgical ICU
739 medical ICU
968 CMV IgG positive (64%)
510 surgical ICU
458 medical ICU
536 CMV IgG negative (36%)
255 surgical ICU
281 medical ICU

Cytomegalovirus serostatus and outcome in nonimmunocompromised critically ill patients

- ***Interventions:***
  None.
- ***Measurements and Main Results:***
  Sixty-four percent of the studied patients were cytomegalovirus seropositive. Multivariable analysis revealed no associated risk for intensive care unit or hospital mortality, or for time to alive discharge from intensive care unit or hospital. The risk for alive weaning from mechanical ventilation and the need for renal replacement therapy were also comparable in seropositive and seronegative groups

Cytomegalovirus serostatus and outcome in nonimmunocompromised critically ill patients

- ***Conclusion:***
  No association was found between the cytomegalovirus serostatus and the studied major clinical outcomes. Based on these results, the design of an intervention study assessing the impact of cytomegalovirus prophylaxis in all cytomegalovirus seropositive critically ill patients appears premature.

Cytomegalovirus serostatus and outcome in nonimmunocompromised critically ill patients

Table 1. Risk profile of the cytomegalovirus immunoglobulin G negative and positive patients

Patient Characteristics	Cytomegalovirus Seronegative	Cytomegalovirus Seropositive	p^a
Age (years) (mean ± SD)	59.2 ± 15.7	67.2 ± 13.3	<.0001
Gender, male	70.9%	62.1%	<.001
Body Mass Index (kg/m^2)			.14
≤19	41.4%	58.6%	
20–25	33.3%	66.7%	
26–30	31.6%	68.4%	
≥31	37.7%	62.3%	
History of diabetes	12.3%	16.6%	.03
History of malignancy	17.0%	17.8%	.72
Medical intensive care unit	52.4%	47.3%	.06
Acute Physiology and Chronic Health Evaluation II score	17 ± 10.0	17 ± 9.1	.82
Sepsis at admission	58.8%	59.1%	.22
Unit packed cells/week intensive care unit	0.77 ± 1.14	0.73 ± 1.05	.45
Intensive insulin treatment	49.1%	50.5%	.63
Steroids	40.3%	36.1%	.11
Norepinephrine	55.4%	55.8%	.91
Mechanical ventilation	86.0%	90.7%	<.01
Admission diagnostic category			<.001
Abdominal	17.4%	16.0%	
Cardiovascular	27.6%	35.8%	
Thoracic	28.9%	30.2%	
Other	26.1%	18.0%	

Appraisal

Step 1：分析文章等級

Step 2：使用**work sheet**評讀文章價值

Oxford Centre for Evidence-based Medicine Levels of Evidence

Level	Therapy/Prevention, Aetiology/Harm	Prognosis	Diagnosis
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
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
2c	"Outcomes" Research; Ecological studies	"Outcomes" Research	
3a	SR (with homogeneity*) of case-control studies		SR (with homogeneity*) of 3b and better studies
3b	Individual Case-Control Study		Non-consecutive study; or without consistently applied reference standards

PROGNOSIS WORKSHEET (Sackett Jane)

- **Are the results of this prognosis study valid?**
  - Was a defined, representative sample of patients assembled at a common (usually early) point in the course of their disease?
    這篇研究收集了MICU與SICU共1504個病 人，並排除住院時間<48小時的病人，足以代表病程嚴重的病人。
  - Was patient follow-up sufficiently long and complete?
    Yes.

PROGNOSIS WORKSHEET (Sackett Jane)

- **Can you apply this valid, important evidence about prognosis in caring for your patient?**
  - Were the study patients similar to your own?
    Yes.
  - Will this evidence make a clinically important impact on your conclusions about what to offer or tell your patient?
    直覺上我們會認爲high CMV IgG level代表CMV reaction，這類的病人可能病況較嚴重、預後較差。然這篇文章告訴我們影響病程的還是以underlying爲主，CMV seropositive/negative 影響較少。

總結與討論

目前已知道CMV infection對immunocompromised patients有所影響，但對於critical ill immunocompetence的病人，CMV infection究竟是造成病程惡化的原因，或只是co-incident、對於病程沒有影響這個問題到目前爲止仍沒有答案。這篇文章統計了ICU內共1504位病患，並說明了六成以上的病患CMV IgG(+)，但此種seropositive對prognosis沒有任何影響。

AUDIT（自我評估）

提出臨床問題上之困難

- 我提出的問題是否具有臨床重要性？普通
- 我是否明確的陳述了我的問題？ 有
- 我的foreground question 是否可清楚的寫成PICO？可以
- 我的background question是否包括what, when, how, who等字根？是
- 我是否清楚的知道自己問題的定位？（亦即可以定位自己的問題是屬於診斷上的、治療上的、預後上的或流行病學上的），並據以提出問題？知道,屬於預後上的
- 對於無法立刻回答的問題，我是否有任何方式將問題紀錄起來以備將來有空時再找答案？有

搜尋時最佳證據上方面

- 我是否已盡全力搜尋？盡力了...
- 我是否知道我的問題的最佳證據來源？知道
- 我是否從大量的資料庫來搜尋答案？是
- 我工作環境的軟硬體設備是否能支援我在遇到問題時進行立即的搜尋？是
- 我是否在搜尋上愈來愈熟練了？尚待練習
- 我會使用「斷字」、布林邏輯、同義詞、MeSH term，限制（limiters)等方法來搜尋？會

嚴格評讀文獻：方面

- 我是否了解worksheet每一項的意義？多能瞭解
- 評讀後，我是否做出了結論？是

應用到病人身上之方面

- 我是否將搜尋到的最佳證據應用到我的臨床工作中？是
- 當搜尋到的最佳證據與實際臨床作爲不同時，我如何解釋？瞭解不同國家的醫療現況以及病人能配合治療的實際情形。

改變「醫療行為」方面

- 當最佳證據顯示目前臨床策略需改變時，我是否遭遇任何阻止改變的阻力？目前無
- 我是否因此搜尋結果而改變了原來的治療策略？做了那些改變？沒有

感想報告

- 這篇報告，我總共花了多少時間？兩個晚上
- 我是否覺得這個進行實證醫學的過程是值得的？值得，雖然累，但搜尋資料的過程比以前上手,也有很多收穫。

Thanks for your attention!