實證醫學研討會
Evidence-Based Medicine Workshop

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Outline of workshop by NTUH team

- Introduction: Definition of EBM
- List the problem: PICO
- Strategies in searching
- Sources
- Examples
- Critical appraisal
- Special terms in EBM literature
- Suggested points to GP

Definition of EBM

- Conscientious, explicit, and judicious use of current best evidence in making decisions about individual patients
- Integrating individual clinical expertise with the best available external clinical evidence from systematic research

Five-step model for EBM practice

- Asking answerable clinical questions
- Searching for the evidence
- Critically appraising the evidence for its validity and relevance
- Making a decision, by integrating the evidence with clinical expertise and the patient's values
- Evaluating the performance

Paradigms between traditional and EBM

- 傳統醫學架構典範(traditional medical paradigm)之四個假設：
  - 個人臨床經驗為基礎，權威與經驗累積成正比
  - 病態生理學是臨床運用的基礎
  - 傳統的訓練及常識足夠使醫師評估新的檢查及治療
  - 臨床經驗是足以形成治療指導原則的基礎
- 實證醫學架構典範(Evidence-base medicine paradigm)之三個假設：
  - 臨床醫師儘可能地透過有系統、不偏頗且可重覆性的方法來對診斷及治療作有進步的了解。
  - 病態生理學並不足以回答臨床運用的所有基礎。
  - 了解特定的證據規則是有效且必須的手段來了解醫學文獻。

實證醫學的定義是對透過公正的認定，評估及運用相關的資訊來作醫療決策。

Strategy:

- PICO：利用PICO來建構一個特定的臨床問題
- 尋找證據的策略：
  - 由病人的問題開始：由照顧病人的過程引發的臨床問題
  - 將此臨床問題透過PICO翻譯成研究問題
  - 決定最適合的研究設計型式來回答問題
  - 針對適合的資源作文獻回顧

PICO

- P：Patient，population或problem
  - 包括性質、狀況及疾病的特定性質
- I : Intervention或Exposure
  - 要針對病人做何種處置(如治療、診斷或觀察？)
- C : Comparison intervention
  - 對上述阻介的方法是否有其他的選擇? (如Placebo，其他不同的藥物、手術)
- O : Outcome效果
  - 相關的效果為何(如致病、死亡或併發症等)

Element	Tips
Patient or Problem	Starting with your patient ask " How would I describe a group of patients similar as this patient?"
Intervention	Ask "Which main intervention am I considering?"
Comparison intervention	Ask "What is the main alternative to compare with the intervention?"
Outcome	Ask "What can I hope to accomplish?" or "What could the exposure really affect?"

Clinical scenarios -1:

- Your patient is a 72-year-old woman with osteoarthritis of the knees and moderate hypertension, accompanied by her daughter, a lab tech from the hospital.
- The daughter wants you to give her mother a prescription for one of the new COX-2 inhibitors.
- She has heard that they cause less GI bleeding. Her mother is concerned that the new drugs will mean more out of pocket costs each month.

PICO-1:

PATIENT/ PROBLEM	INTERVENTION	COMPARSION INTERVENTION	OUTCOME
72 year old woman with osteoarthritis of the knee and moderate hypertension	COX-2 Inhibitor	other NSAIDS	less BI bleeding pain control

Specific Question:
In a 72 year old woman with osteoarthritis of the knee, can COX-2 Inhibitor use decrease the risk of BI Bleeding compared with the NSAIDs?

Clinical scenarios -2:

- You have been treating a 54-year old woman for years and despite the excellence of fixed partial denture restorations, the intense routine maintenance by her periodontist, and good homecare,
- She has been experiencing a continued deterioration of her periodontal tissues. Her attempts to quit smoking have been unsuccessful; otherwise she is in good health and taking no medications. Because you are her primary care dentist, she has questioned you about her current dilemma.
- The periodontist has suggested a 3-week course of doxycycline therapy to control her latest exacerbation of periodontal disease, but she is concerned about Food and Drug Administration (FDA) reports asking for prudent use of antibiotics. How do you advise this patient?

PICO-2:

PATIENT/ PROBLEM	INTERVENTION	COMPARSION INTERVENTION	OUTCOME
54 year old woman with exacerbation of periodontal disease	doxycyline	no treatment	less gum bleeding stop recession

Specific Question:
For a 54 year old women with periodontal disease, how effective is the therapeutic use doxcyline decease gum bleeding and recession compared to no treatment?

Scenerio-3:

- 45歲男性
- 因上腹不適、解黑便及吐血到某醫院急診求診
- 經禁食及靜脈輸液後安排上消化道內視鏡檢查。
- 術中發現胃潰瘍併活動性出血，施以經內視鏡止血治療，並達到止血效果。
- 問題：是否使用氫離子幫浦阻斷劑（proton pump inhibitor）後續治療，以減少併發症？

PICO-3:

PATIENT/ PROBLEM	INTERVENTION	COMPARSION INTERVENTION	OUTCOME
45 y/o man, ulcer bleeding	Proton pump inhibitor	H2 blocker, antacid, no use	Rebleeding, morbidity, mortality

Specific Question:
For a 45 year old man with ulcer bleeding, how effective is the proton pump inhibitor compared to other treatment?

Scenario-4:

- A 51-year-old Chinese gentleman comes to your clinics because of chronic atrial fibrillation
- No other heart nor medical disorders
  - Question: Is the practice recommended by the current guideline suitable for this patient in INR between 2.0 and 3.0 v.s. INR >3.0 or INR < 2.0

PICO-4:

PATIENT/ PROBLEM	INTERVENTION	COMPARSION INTERVENTION	OUTCOME
51 y/o Chinese man, lone atrial fibrillation	Warfarin, INR 2-3	Other INR	Thromboembolism, morbidity, mortality

Specific Question:
For a 51 y/o Chinese man with lone atrial fibrillation, Can the alternative range of INR lead to lower mortality or morbidity from thromboembolism?

Scenario-5:

- 70-year-old woman undergoes a health examination, which shows bacteriuria. She does not have dysuria, urinary frequency or other discomfort
  - 老年女性發生無症狀之尿菌症(asymptomatic bacteriuria)時是否需要抗生素的治療?

PICO-5:

PATIENT/ PROBLEM	INTERVENTION	COMPARSION INTERVENTION	OUTCOME
70 y/o lady Asymptomatic bacteriuria	Antibiotics	No	Symptoms, morbidity, mortality

Specific Question:
For a 70 year-old lady with asymptomatic bateriuria, how effective is antibiotics treatment compared to no treatment?

Scenario-6:

- A 64-year-old man presents to the ER with acute dyspnea
- How to D/D CHF and/or COPD?
  - Brain Natriuretic Peptide (BNP) test

PICO-5:

PATIENT/ PROBLEM	INTERVENTION	COMPARSION INTERVENTION	OUTCOME
66 y/o male, acute dyspnea due to CHF and/or COPD	Brain Natriuretic Peptide (BNP) test	Symptoms/signs Echocardiography	Diagnosis of CHF vs. COPD

Specific Question:
For a 66 y/o man with dyspnea, what is the role of BNP as differential diagnosis of CHF vs. COPD?

Examples

性質	題目
治療	成年人使用乙狀阻斷器藥物與否對高血壓治療後，對冠心病及腦中風初級預防的效果是否有差別?
預後	成年人充血性心臟衰竭時伴隨心房顫動與否對預後是否有差別?
檢查篩檢	利用colonoscopy(大腸鏡)一般族群作直腸大腸良性瘤(adenoma)的篩檢對直腸大腸癌的發生及死亡的影響有何利弊?
治療	有成年族群發生急消化性潰瘍出血時，經過內視鏡治療後使用PPI (proton pump inhibitors)類的藥物是否有幫忙?
治療	成年人有小型肝癌(3公分以下)時，用酒精局部注射或手術切除兩種治療方式對預後的差異是否不同?
治療	華人單獨性心房顫動(lone Af)的情況下使用抗凝血劑治療(Anticoagulant therapy)的合理劑量為何?
治療	停經婦女骨質疏鬆的治療Vit D的劑量是否是以400 I μ或是更高?
治療	老年女性發生無症狀之尿菌症(asymptomatic bacteria)時是否需要抗生素的治療?
診斷工具	運動心電圖作為醫院成年人的冠狀動脈心臟病診所工具的利弊考量為何?

Types of question-1

- Clinical findings
  - How to interpret findings from the history and clinical examination
- Etiology
  - The causes of disease and their modes of operation
- Differential diagnosis
  - How to rank the possible causes likelihood, seriousness, and treat-ability

Types of question-2

- Therapy
  - Selection of treatments based on efficacy, cost, and values
- Prognosis
  - Course of disease over time and prediction of likely outcomes
- Prevention
  - Identifying primary and secondary risk factors,
- Outcomes
  - Cost-effectiveness, Quality of life

Finding the evidence: resources

- Levels of evidence
  - Good, fair, poor
- Electronic Sources
  - Primary database
  - Secondary database
- How to effectively search the sources?

Levels of evidence

- 1a: systematic review on multiple RCTs
- 1b: well designed, analyzed, RCT
- 1c: all or none
- 2a: systemic review on several cohort studies
- 2b: cohort study, poor designed RCT
- 2c: “outcomes” research; ecological studies
- 3a: systemic review on several case-control studies
- 3b: case-control study
- 4: one hospital experience, poor designed cohort or case-control studies
- 5: personal opinions, bench, animal data

Appendix Table 2. **U.S. Preventive Services Task Force Strength of Overall Evidence***

Grade	Definition
Good	Evidence includes consistent results from well-designed, well-conducted studies in representative populations that directly assess effects on health outcomes
Fair	Evidence is sufficient to determine effects on health outcomes, but the strength of the evidence is limited by the number, quality, or consistency of the individual studies; generalizability to routine practice; or indirect nature of the evidence on health outcomes
Poor	Evidence is insufficient to assess the effects on health outcomes because of limited number or power of studies, important flaws in their design or conduct, gaps in the chain of evidence, or lack of information on important health outcomes

* The U.S. Preventive Services Task Force (USPSTF) grades the quality of the overall evidence for a service on a 3-point scale (good, fair, poor).

次級入口的網站的性質優劣點: Secondary sources

入口網站	性質	優點	缺點
ACP Journal Club	Structured abstract	Best quality, most clinically useful recent data	Limited coverage,
Center for EBM, Oxford	Guidelines	CATs (Critically Appraised Topics) Nation-levels	Only one study per CAT; time-limited; quality control
Cochrane Collaboration Full Text		High-quality systematic reviews which cover a complete topic, over 1,000	Limited coverage, time lag, can be difficult to use One center, expertise, unknown quality control Time consuming

次級入口的網站的性質優劣點: Secondary sources

入口網站	性質	優點	缺點
UptoDate	Summary	Review	Registered, Expensive One center, expertise, unknown quality control
Agency for Healthcare Research and Quality (AHRQ)	USA	National levels	
Bandolier	Oxford	User-friendly, searchable collection of evidence-based summaries and commentaries	One center

次級入口的網站的性質優劣點: Secondary

入口網站	性質	優點	缺點
Best Evidence Resources - W K Kellogg Health Sciences Library		Pre-appraised summaries filtered for clinical relevance	Limited coverage
BMJ, Clinical Evidence	BMJ sponsored		

次級入口的網站的性質優劣點: Secondary

入口網站	性質	優點	缺點
National Guideline Clearinghouse, AHRQ	Platform for international guideline	Guideline, national level	Scanty data
MDConsult	summarized	Updated, detailed	membership
SIGN, Scottish Intercollegiate Guidelines Network	guideline	Complete guideline	Limited resource

次級入口的網站的性質優劣點: Secondary

入口網站	性質	優點	缺點
Health technology assessment (HTA)	Canadian	National level	Common drug review
National Institute for Clinical Excellence, NICE	UK	National level Good quality control	
New Zealand Guideline Group, NZGG	New Zealand, National levels	National level	

次級入口的網站的性質優劣點: Secondary

入口網站	性質	優點	缺點
SUMSearch	Free text	Specialized search engine, other sites, organized	
TRIP database		Linked to PubMed	subscription
e-MEDICINE	General, consumer health	Simple	Not for professionals, but for patients

初級入口的網站的性質優劣點: Primary, bibliographic databases

入口網站	性質	優點	缺點
PubMed Medline	US database for all clinical medicine	Original research articles, up-to-date, RCT database, original	Very detailed
MEDLINE®		Primary data	cost
CINAHL			Cost Difficult to search effectively, no quality filtering, bibliographic text
EMBASE	European equivalent of MEDLINE	Drugs and pharmacology	Cost, membership

初級入口的網站的性質優劣點: Primary, bibliographic databases

入口網站	性質	優點	缺點
Yahoo, Google	Free text	Ranking the outcome of search	Too diverse

初級及次級入口的網站的性質優劣點: Taiwan

入口網站	性質	優點	缺點
NTUH, Library, EBM-related	Library-related	Summarized	Semi-open Updated? Limited 僅開放醫學校區人士使用
彰基証據醫學	証據醫學中心的網路資訊	Specialist-oriented	-
萬芳醫院實證醫學中心	Various resources	News, updated	-

初級及次級入口的網站的性質優劣點: Other resources for cardiovascular fields

入口網站	性質	優點	缺點
Japan Cardiovascular Trial Database	Clinical Trials	Updated CV field, RCT, Worldwide, Special part in Japanese databases	Japanese, not English
中國循証醫學專題	From Chinese viewpoints	Updated news	Simple Chinese, membership

Strategies in PubMed: MEDLINE-1

Feature	Key	Explanation
Expand	Thesaurus (MeSH)	Use explosion and include all sub-heading to expand your search.
Truncation	*(or $)	analy* = analysis, analytic, analyse, etc.
Wildcards	?	Gyn?ecology = gynecology, gynecology; Randomi?*= randomization, randomization, randomized.
Boolean	AND	Article must include both terms.
	OR	Article can include either term.
	NOT	Excludes articles containing the term (for example econom* NOT economy picks up economic and economical but not economy).

Strategies in PubMed: MEDLINE-2

Feature	Key	Explanation
Proximity	NEAR	Terms must occur close to each other (for example within 6 words) (heart NEAR failure)
Limit	Variable	As appropriate, restrict by publication type (clinicaltrial.pt) year, language, possible by study characteristics, or by searching for terms in specific parts of the document (for example diabet* I ti will search for articles which have diabetes or diabetic I the title).
Related	Variable	Once you've found a useful article, this feature (for example in PubMed by clicking the "Related" hyperlink) searches for similar items in the database.

Strategies in Internet: Yahoo & Google

Feature	Key	Explanation
Truncation	*	Analy* = analysis, analytic, analytical, analyse, ect.
Adjacency	""	Words must be adjacent to each other: for example "heart attack"
AND	+	+natural+childbirth=documents must contain both words
Limits	t: u:	Words must occur I title of the document (t:natural childbirth) or words must occur in web address (u:uk)

Strategies in PubMed: MEDLINE

- Thesaurus searching
  - Subheading
  - Subject
  - category
- Textword searching
  - Free text

How to improve the search results: specificity

- Narrowing your question
- Using more specific terms
- Using Subject search rather than Free Text/Text word
- Selecting specific subheadings (drug therapy,…, etc.)
- Adding in terms (using AND) to represent other aspects of the question
- Limiting language of article, publication types, years

How to improve the search results: sensitivity

- Finding more search terms from relevant records and combining terms of related meanings (using OR)
- Using more general terms or categories
- Trying different combinations of terms
- Using Free Text/Text word and MeSH/Subject search
- Selecting all subheadings
- Using explore
- Using truncation (* or $) or Wildcard (?)

Dr. Huang's example

- 有成年族群發生急消化性潰瘍出血時，經過內視鏡治療後使用PPI (proton pump inhibitors)類的藥物是否有幫忙?
  - 45 year-old man suffered from peptic ulcer bleedings, after endoscopic therapy, what are the roles of PPIs for his treatment?

EBM 個案討論

- 臨床個案摘要
- PICO
- Source of evidence: primary database
- Searching strategy
- Appraisal strategy

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臨床個案摘要

- 45歲男性
- 因上腹不適、解黑便及吐血到某醫院急診求診
- 經禁食及靜脈輸液後安排上消化道內視鏡檢查。
- 術中發現胃潰瘍併活動性出血，施以經內視鏡止血治療，並達到止血效果。
- 問題：是否使用氫離子幫浦阻斷劑（proton pump inhibitor）後續治療，以減少併發症？

PICO

- Patient:
  - 45 y/o male, GU with active bleeding, s/p successful primary endoscopic hemostasis
- Intervention
  - Proton pump inhibitor (after endoscopic hemostasis)
- Comparison intervention
  - H2 blocker, antacid, placebo?
- Outcome
  - Rebleeding, morbidity, mortality
  - Others

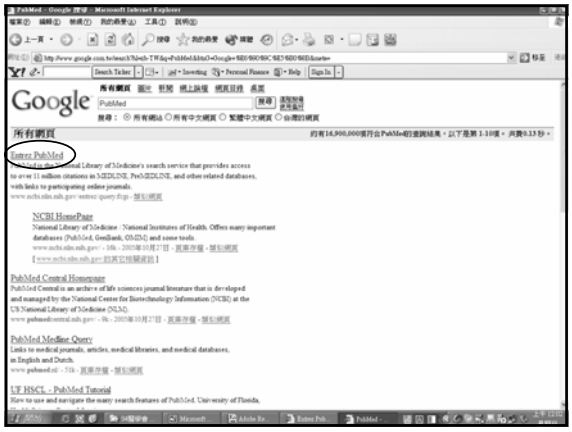
Source of evidence:

- Primary database
  - PubMed, Medline
- PubMed
  - Free online
  - Searching tools: simple & easy
  - Update: *[Epub ahead of print]*
  - Abstract and link to free full articles
  - Related articles
  - Extending searching

Searching strategy

- Primary or secondary database?
- *Thesaurus* or *textword* searching?
- Searching skills
- Expanding or focusing?
  - Purpose of searching
  - Strategy of limiting
  - Select papers of satisfactory quantity and quality
- **Practice and Try!**


Google
PubMed
Google 搜尋
好手氣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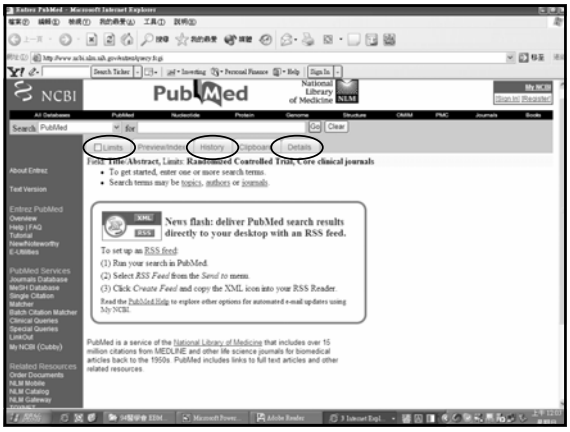
UF HSCL - PubMed Tutorial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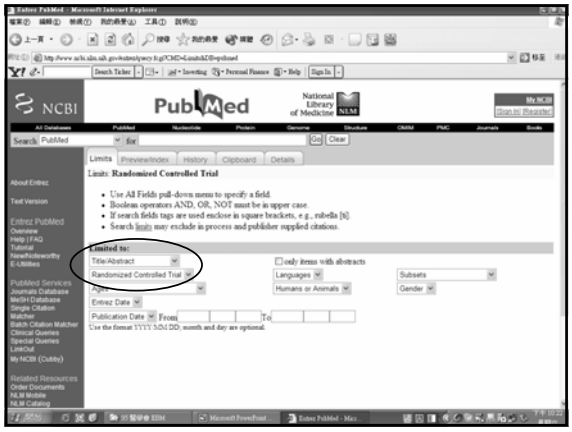
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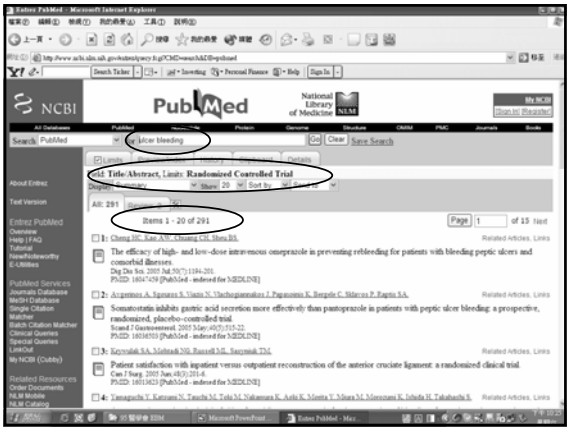
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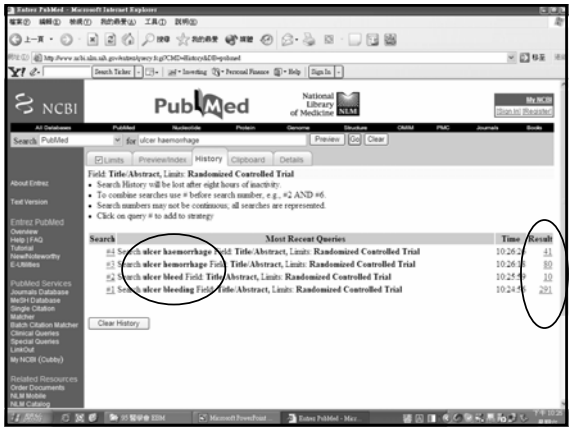
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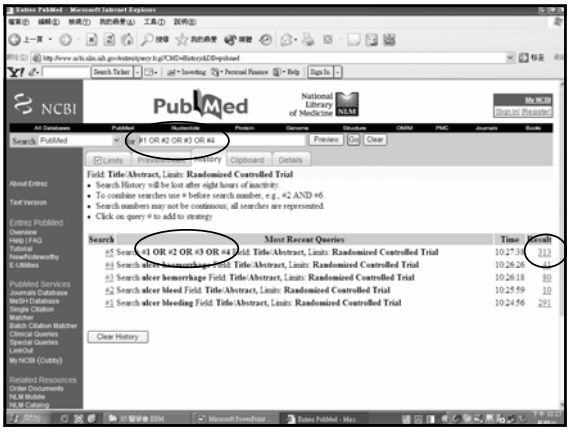

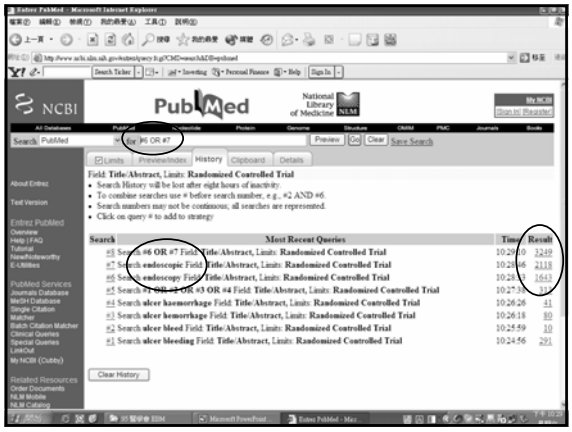

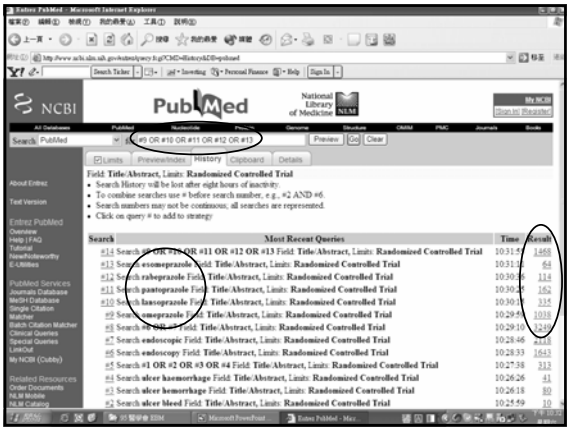

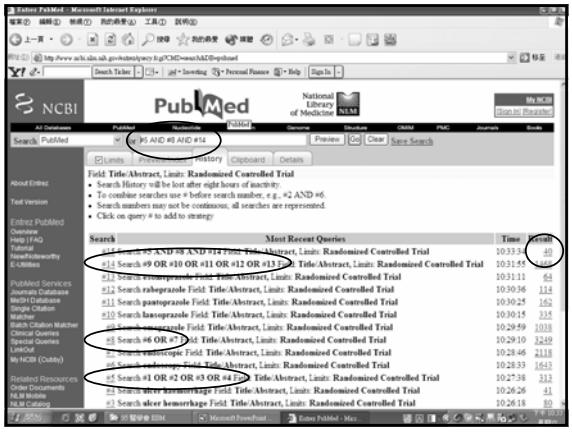

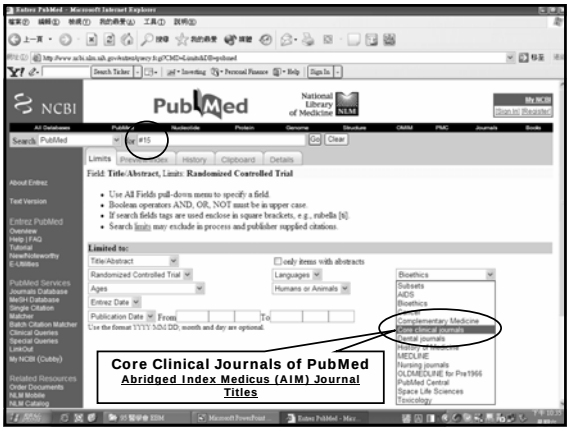
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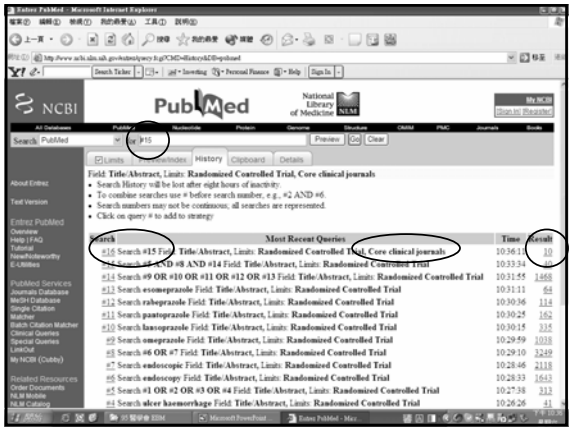
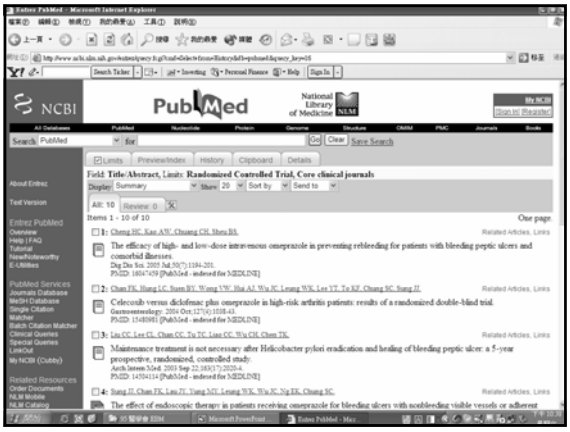
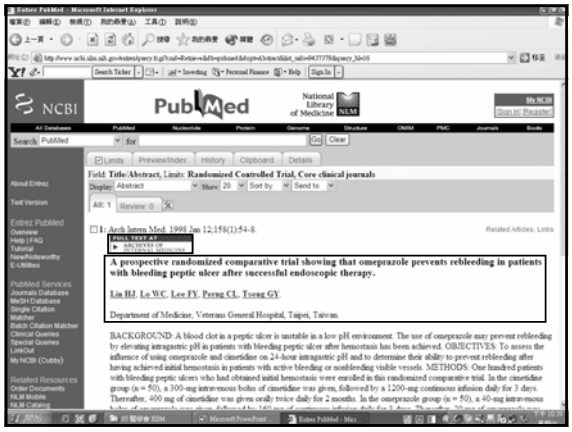
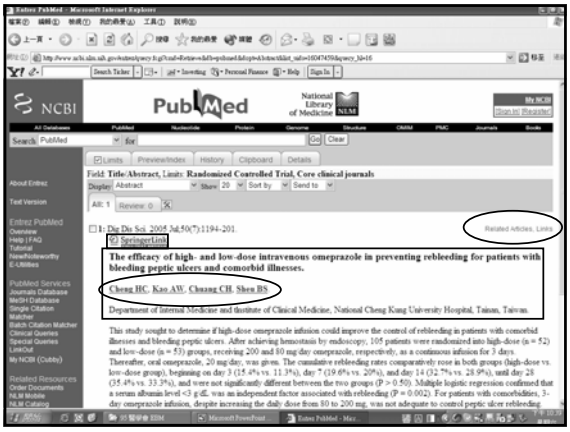
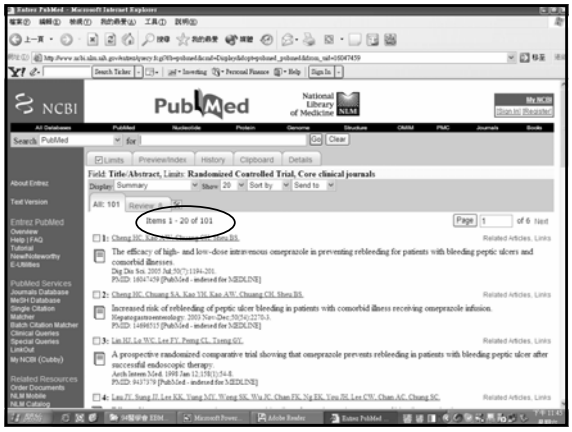
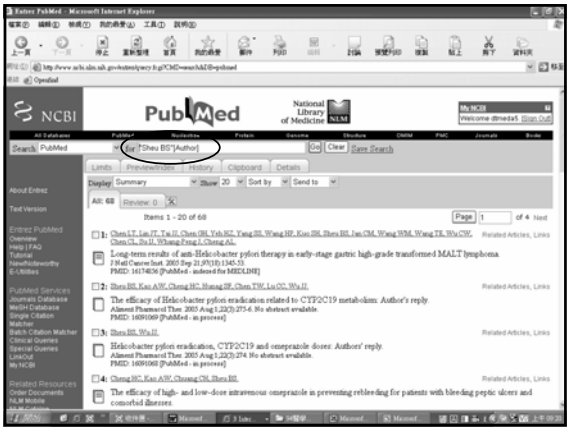


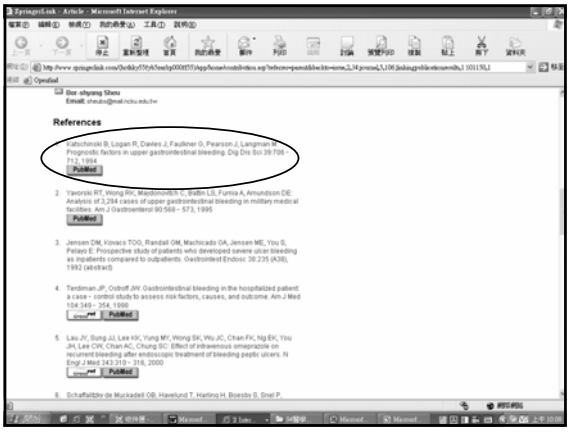


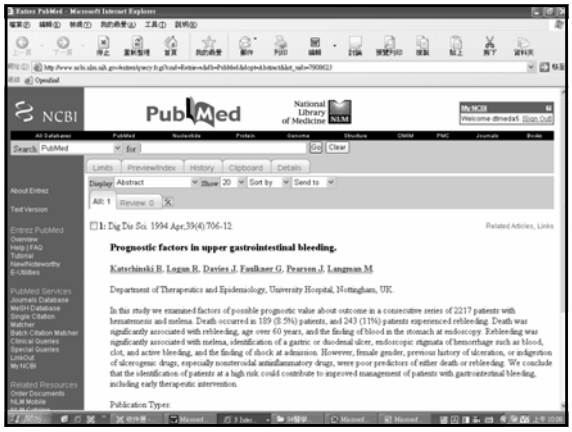












Appraisal strategy

Type of study (Study design):
- randomized controlled trial

Assessment of a randomized trial
- Description of evidence

Internal validity
- Non-causal explanations
- Positive features of causation

External validity
- External validity
- Other evidence

Description of evidence

- Intervention
  - Study and control (comparison)
- Outcome
  - Definition or determination of outcomes
- Design
  - Randomized controlled trial
- Study population
  - Characteristics (inclusion and exclusion criteria), age, gender, race, location
- Main result
  - Assessment of difference between study and control

Non-causal explanations

Are the results likely to be affected by
- Observation bias
  - Assessment of outcomes
- Confounding
  - Control of confounding by randomization
- Chance variation
  - Appropriate statistical tests
  - Appropriate time to test

Positive features of causation

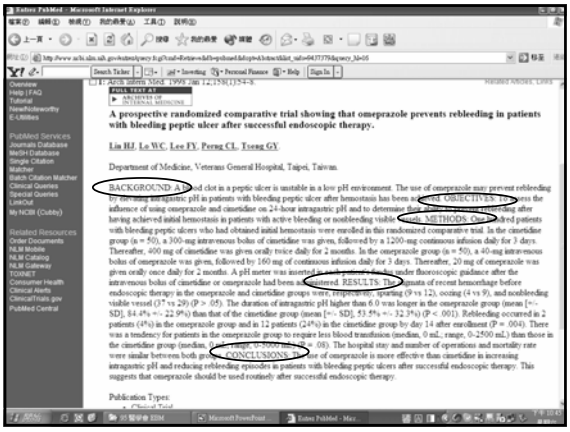
- Time relationship
- Strength
- Dose response
- Consistency
- Specificity

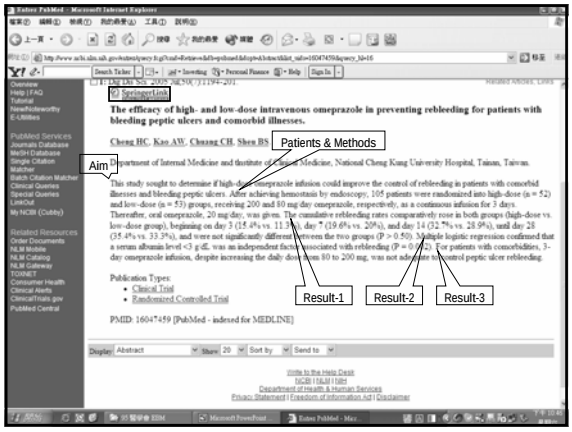
External validity

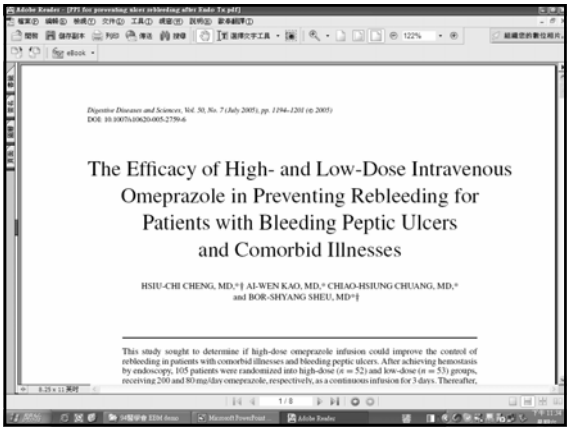
- To the eligible population
- To the source population
- To other population

Other evidence

- Consistency
- Specificity
- Plausibility
- Coherence







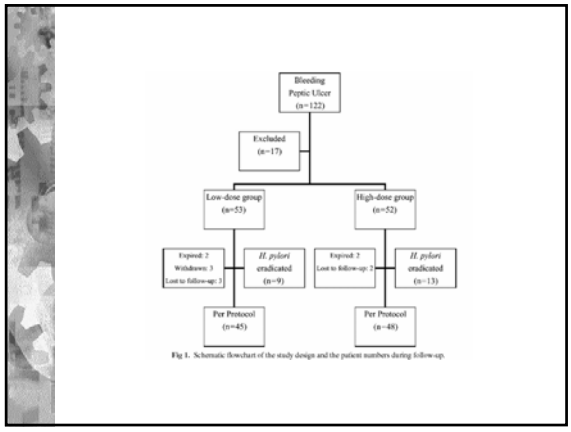


Fig 1. Schematic flowchart of the study design and the patient numbers during follow-up.

TABLE 1. BASELINE CHARACTERISTICS OF THE STUDY PATIENTS

Parameter	*High-dose group (n = 52)*	*Low-dose group (n = 53)*	P *value**
Female:male	16:36	22:31	0.35
Mean age (years)†	62.5 (12.5)	65.8 (13.8)	0.21
Location of ulcer (*n*),			
Stomach:duodenum:both	28:19:5	29:20:4	>0.50
SRH (*n*),			
major:minor	49:3	49:4	>0.50
Size of ulcer (cm)†	1.2 (0.8)	1.2 (1.0)	>0.50
H. pylori infection (%)	51.5	40.5	>0.50
NSAID user (%)	25.0	22.6	>0.50
Aspirin user (%)	1.9	5.7	>0.50
Anticoagulant user (%)	3.8	1.9	>0.50
Two more comorbid diseases (%)	4&1	34.0	0.20
ASA physical status classification (*n*),			
Class II:III:IV/V	7:26:19:1	4:29:19:0	>0.50
Hemoglobin (g/dL)†	8.9 (2.8)	9.1 (2.6)	>0.50
Platelet count (10^3/mm^3)†	230.6 (111.9)	232.3 (118.0)	>0.50
PT (sec)†	13.3 (4.3)	12.8 (2.4)	0.41
APTT (sec)†	32.1 (13.9)	33.0 (12.5)	>0.50
Albumin (g/dL)†	2.8 (0.8)	2.8 (0.6)	>0.50
Creatinine ≥ 1.5 mg/dL (%)	46.2	45.3	>0.50

Note. Major stigmata of recent hemorrhage (SRH)= spurting vessel, nonbleeding visible vessel, or fresh adherent clot. Minor SRH= old adherent clot or cherry red spot. NSAID, nonsteroidal anti-inflammatory drug; ASA, American Society of Anesthesiology; PT, prothrombin time; APTT, activated partial thromboplastin time. Hemoglobin: normal range, 13.5–17 g/dL. Platelet count: normal range, $136.1–353.4 \times 10^3$/cm^3. Albumin: normal range, 3.0–5.0 g/dL. Creatinine: normal range, 0.7–1.5 mg/dL.
*Chi-square test, employing Yates' correction for continuity.
†Mean (SD).

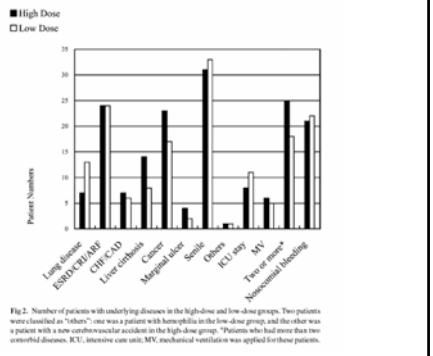


Fig 2. Number of patients with underlying diseases in the high-dose and low-dose groups. Two patients were classified as "others": one was a patient with hemophilia in the low-dose group, and the other was a patient with a new cerebrovascular accident in the high-dose group. *Patients who had more than two comorbid diseases. ICU, intensive care unit; MV, mechanical ventilation was applied for these patients.

TABLE 2. REBLEEDING RATES OF THE TWO STUDY GROUPS BY INTENTION-TO-TREAT (ITT) AND PER PROTOCOL (PP) ANALYSIS

	Rebleeding rate, % (n)			
	High-dose group	*Low-dose group*	P *value**	*Odds ratio [95% CI]†*
3 days	15.4 (8/52)	11.3 (6/53)	0.75	1.42 [0.46, 4.43]
7 days				
ITT	21.2 (11/52)	24.5 (13/53)	0.86	0.83 [0.33, 2.06]
PP	19.6 (10/51)	20 (10/50)	1.00	0.98 [0.37, 2.60]
14 days				
ITT	36.5 (19/52)	39.6 (21/53)	0.90	0.88 [0.40, 1.93]
PP	32.7 (16/49)	28.9 (13/45)	0.86	1.19 [0.50, 2.87]
28 days				
ITT	40.4 (21/52)	43.4 (23/53)	0.91	0.88 [0.41, 1.92]
PP	35.4 (17/48)	33.3 (15/45)	1.00	1.10 [0.47, 2.58]

Note. CI, confidence interval.
*Chi-square test, employing Yates' correction for continuity.

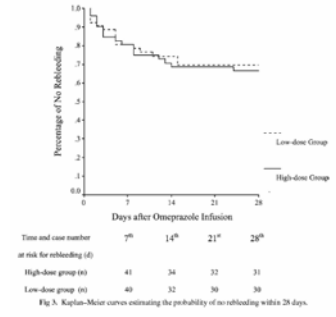


Fig 3. Kaplan–Meier curves estimating the probability of no rebleeding within 28 days.

TABLE 3. INTRAGASTRIC pH VALUES OF PATIENTS RECEIVING DIFFERENT DOSES OF OMEPRAZOLE INFUSION ON DAY 2

Patient	*Group*	*Median pH*	*Mean pH*	*Fraction of time pH >5.4 within 24 hr (%)*	*Rebleeding episode**
Case 1	High	7.3	7.1	>90	—
Case 2	High	7.4	7.5	>90	4th–14th day
Case 3	Low	7.3	7.3	>90	—
Case 4	Low	7.4	7.4	>90	—
Case 5	Low	6.0	6.0	80.3	3rd day

*Time of the rebleeding episode; (—) no rebleeding occurred during the 28 days.

TABLE 4. SIGNIFICANT UNIVARIATE FACTORS ASSOCIATED WITH REBLEEDING DURING THE INITIAL 3 DAYS, 4TH–14TH DAYS, 15TH–28TH DAYS, AND OVERALL STUDY PERIOD

Rebleeding rate of related factors		*Odds ratio (95% CI)**	P *value†*
Initial 3 days			
Creatinine ≥ 1.5 vs. < 1.5 mg/dL (%)	22.9 vs. 5.3	5.35 (1.40–20.51)	0.018
Albumin < 3.0 vs. ≥ 3.0 g/dL (%)	19.0 vs. 2.9	7.77 (0.98–62.6)	0.03
Days 15–28			
ESRD vs. non-ESRD (%)‡	25.0 vs. 1.8	18.33 (1.44–233.4)	0.039
Overall during 28 days			
Albumin <3.0 vs. ≥3.0 g/dL (%)‡	49.1 vs. 10.3	8.37 (2.27–30.80)	0.001
ESRD vs. non-ESRD (%)	62.5 vs. 28.6	4.17 (1.35–12.85)	0.021

Note. ESRD, end-stage renal disease.
*CI, confidence interval. This indicated that the range of 95% CIs included 1 and thus was defined as not significant.
†Chi-square test, employing Yates' correction for continuity.
‡An independent factor predictive of rebleeding by employing multiple logistic regression.

TABLE 5. MULTIVARIATE REGRESSION FOR THE INDEPENDENT FACTORS ASSOCIATED WITH REBLEEDING DURING THE INITIAL 3 DAYS, 4TH–14TH DAYS, 15TH–28TH DAYS, AND OVERALL STUDY PERIOD

Parameter	*Coefficient*	*SE*	*P value*	*95% CI*
Within 3 days				
Creatinine ≥1.5 vs. <1.5 mg/dL	1.251	0.708	0.077	0.873–13.980
Albumin <3.0 vs. ≥3.0 g/dL	1.856	1.075	0.084	0.778–52.613
Days 15–28				
ESRD vs. non-ESRD	2.909	1.298	0.025*	1.440–233.407
Overall during 28 days				
Albumin <3.0 vs. ≥3.0 g/dL	2.066	0.672	0.002*	2.112–29.468
ESRD vs. non-ESRD	1.072	0.634	0.091	0.844–10.123

*Statistically significant.

臨床個案結論

- 45歲男性
- 因上腹不適、解黑便及吐血到某醫院急診求診
- 經禁食及靜脈輸液後安排上消化道內視鏡檢查。
- 術中發現胃潰瘍併活動性出血，施以經內視鏡止血治療，並達到止血效果。
- 結論（1）：使用氫離子幫浦阻斷劑（proton pump inhibitor- omeprazole ）後續治療，相較於乙型組織胺拮抗劑（ H2 blocker-cimetidine ），可以減少再出血率。
- 建議（2）：使用omeprazole infusion for 3 days, followed by oral omeprazole, 20 mg/day 時，daily infusion dose ， either 80 or 200 mg 效果無顯著差異。

How can I apply the results to patient care?

- Comparison between your patient and patients in available studies
  - Patient
  - Intervention
  - Comparison
  - Outcome
- Will the reproducibility of the study result and its interpretation be satisfactory in my clinical setting?
- Are the results applicable to the patient in my practice?
- Will the results change my management strategy?
- Will patients be better off as a result of the study?

Dr. Chen's examples

- 51-year-old Chinese man, lone atrial fibrillation, ask for warfarin dosage adjustment
  - Dosage of Anticoagulants for Chronic Atrial Fibrillation in Chinese Adults
- 70-year-old woman undergoes a health examination, which shows bacteriuria. She does not have dysuria, urinary frequency or other discomfort
  - 老年女性發生無症狀之尿菌症(asymptomatic bacteria)時是否需要抗生素的治療?
- 66-year-old man with dyspnea
  - BNP as diagnosis for CHF vs. COPD

Clinical Scenario

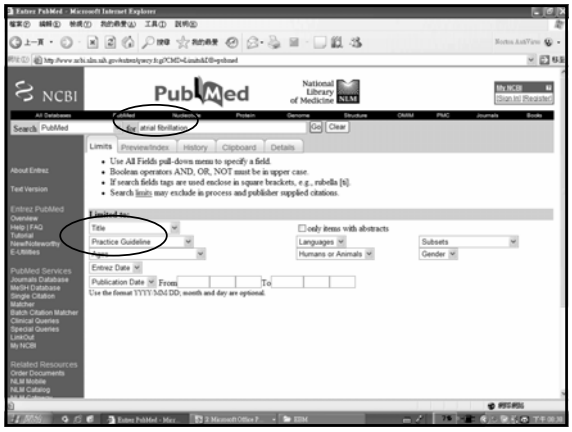
- A 51-year-old Chinese gentleman comes to your clinics because of chronic atrial fibrillation
- He has no other medical disorders
- What is the optimal dose of warfarin for prophylaxis for embolic stroke?

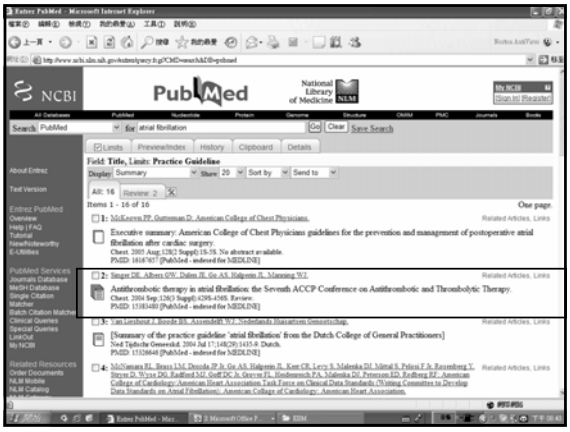
PICO

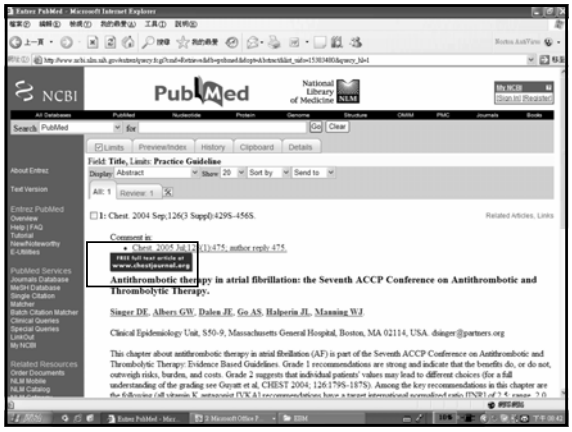
- Patient
  - 51 y/o male, chronic atrial fibrillation
- Intervention
  - warfarin with INR 2.0-3.0
- Comparison intervention
  - Warfarin with INR < 2.0 or > 3.0
- Outcome
  - Embolic stroke, bleeding
  - Morbidity, mortality

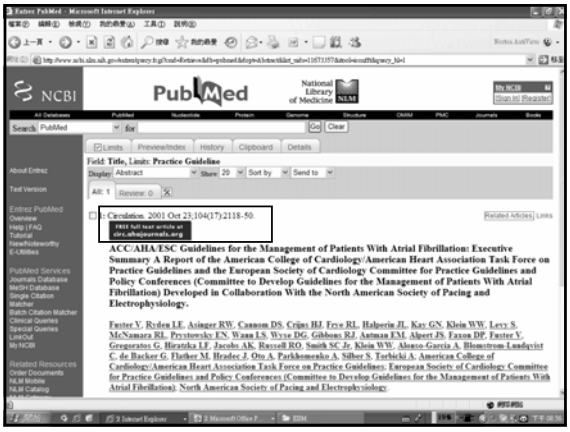
Source of Evidence

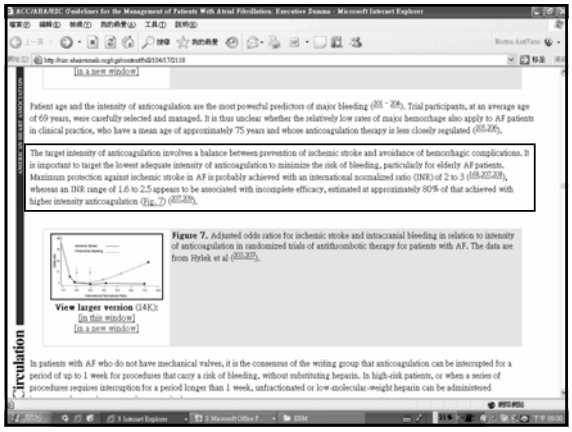
- Primary database
  - PubMed, Medline
- Secondary database
  - Cochrane Database of Systematic Review
  - UpToDate





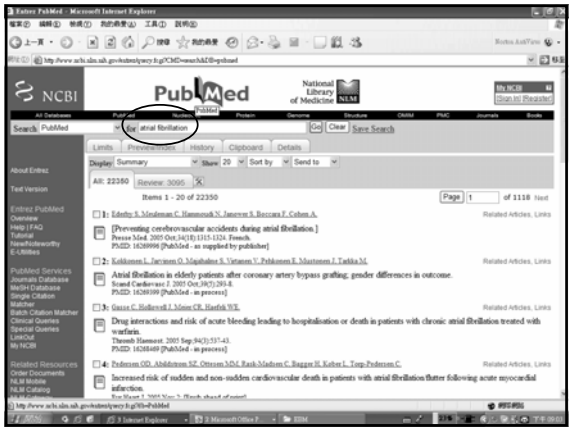


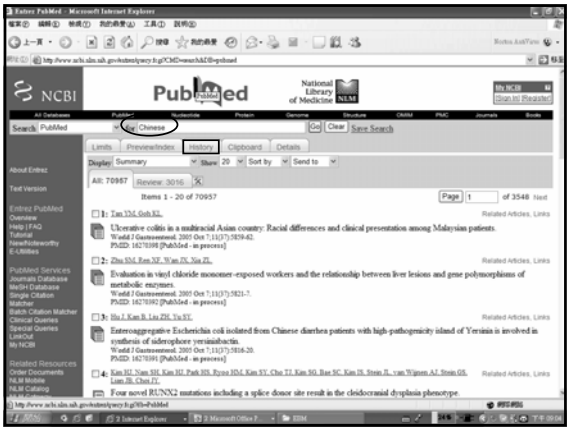


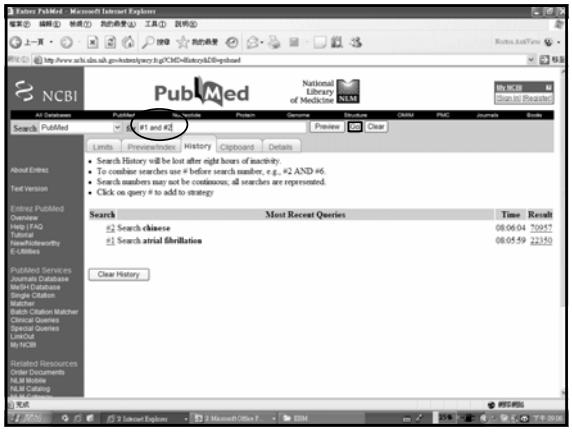


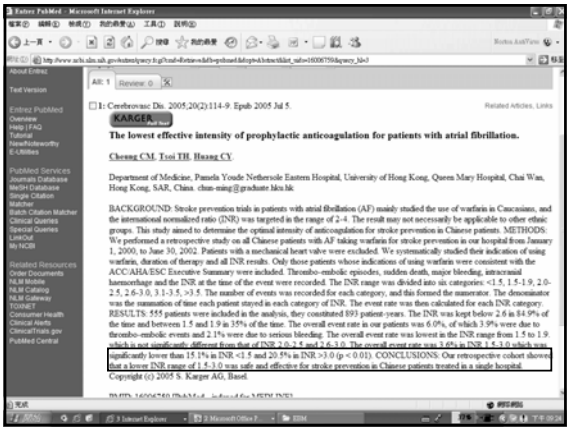
External Validity

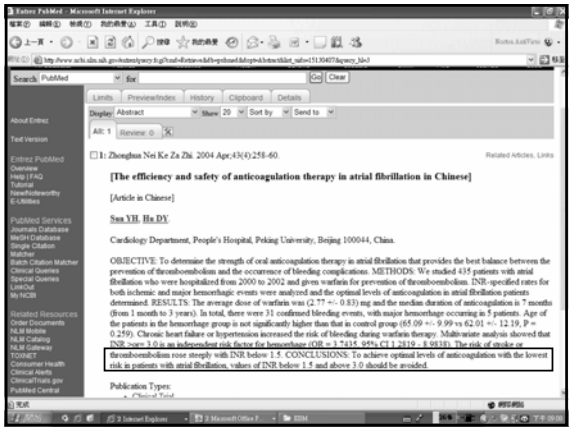
- Can the recommendations be applied to this patient?











Summary

- The optimal dose of warfarin for chronic atrial fibrillation in Chinese population may be lower than that in white population

Clinical Scenario

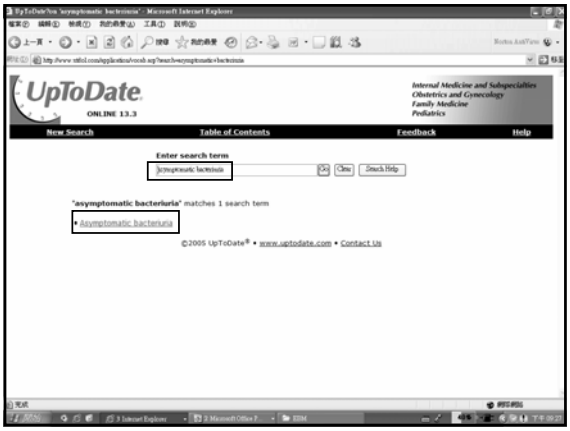
- A 70-year-old healthy woman has a health examination and is diagnosed to have asymptomatic bacteriuria
- Reside in the community
- Question: Is antibiotic treatment needed for this patient?

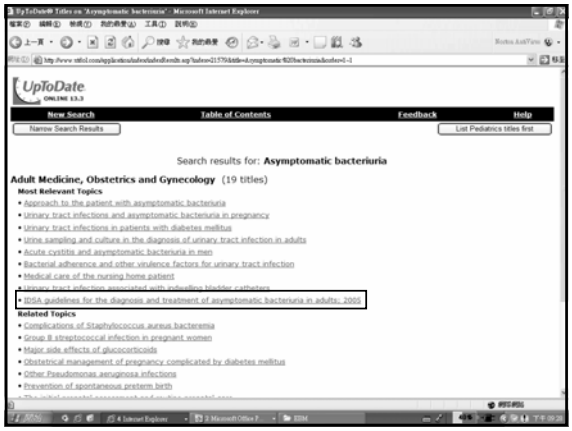
PICO

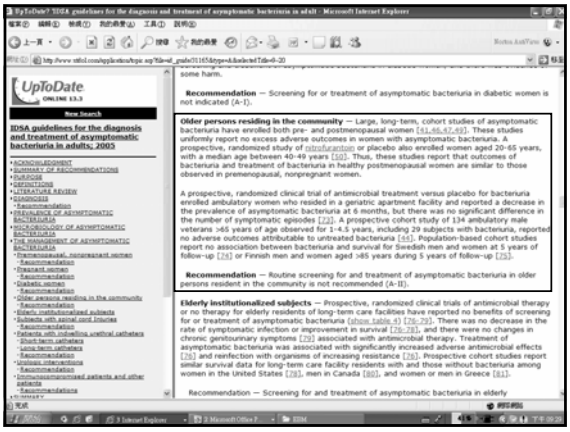
- Patient:
  - 70 y/o female, asymptomatic bacteriuria
- Intervention
  - Antibiotic treatment
- Comparison intervention
  - No antibiotics
- Outcome
  - Prevalence of asymptomatic and symptomatic bacteriuria
  - Mortality

Source of Evidence

- Primary database
  - PubMed
- Secondary database
  - UpToDate







Summary

- Treatment of asymptomatic bacteriuria in older persons residing in the community is not recommended

Clinical Scenario

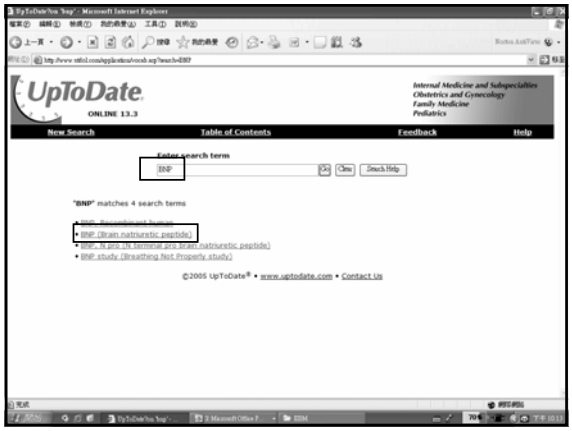
- A 64-year-old man presents to the ER with acute dyspnea
- He has a history of DM, HTN, CHF and COPD
- Medications:
  - glipizide 5 mg once daily
  - enalapril 5 mg twice daily
  - furosemide 40 mg once daily
  - ipratropium/albutamol 2 puffs twice daily

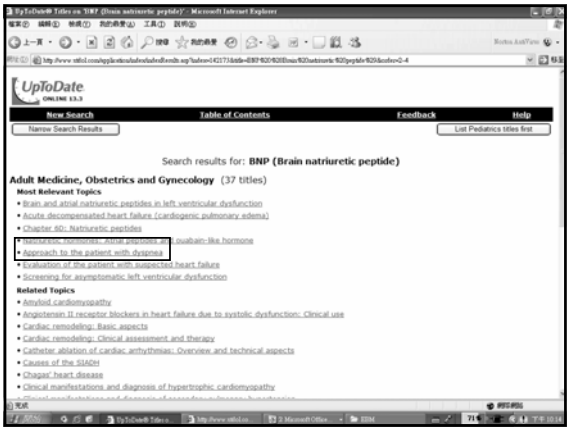
PICO

- Patient
  - 66 y/o male, acute dyspnea due to CHF and/or COPD
- Intervention
  - Brain Natriuretic Peptide (BNP) test
- Comparison intervention
  - Symptoms/signs
  - Echocardiography
- Outcome
  - Diagnosis of CHF vs. COPD

Source of Evidence

- Primary database
  - PubMed, Medline
- Secondary database
  - Cochrane Database of Systematic Review
  - UpToDate

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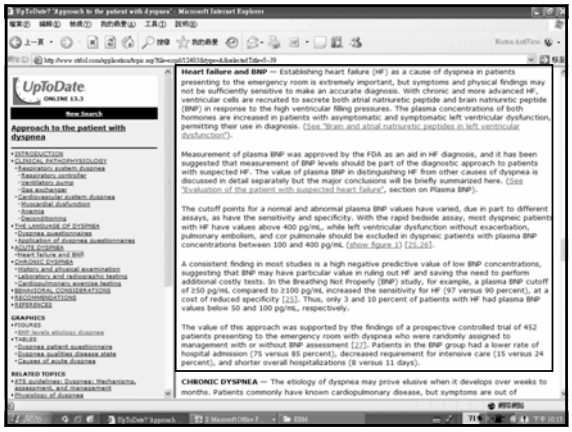
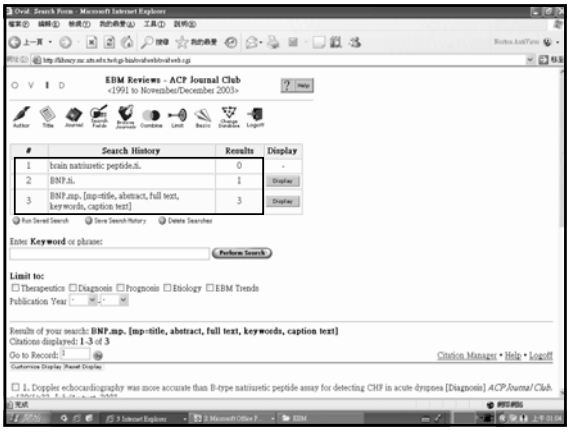
Adult Medicine, Obstetrics and Gynecology (37 titles)
Most Relevant Topics
Related Topics


UpToDate
Approach to the patient with dyspnea
Heart failure and BNP — Establishing heart failure (HF) as a cause of dyspnea in patients presenting to the emergency room is extremely important, but symptoms and physical findings may not be sufficiently sensitive to make an accurate diagnosis.
CHRONIC DYSPNEA — The etiology of dyspnea may prove elusive when it develops over weeks to months.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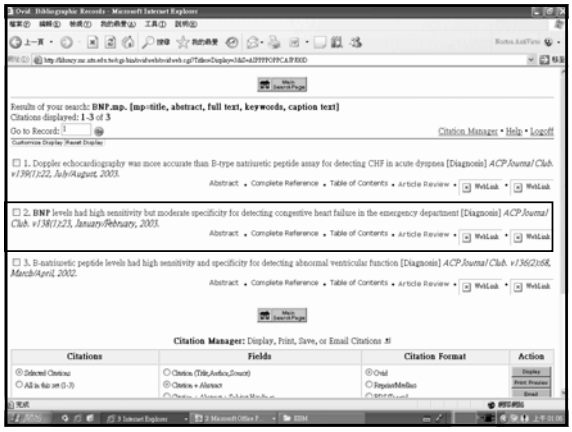
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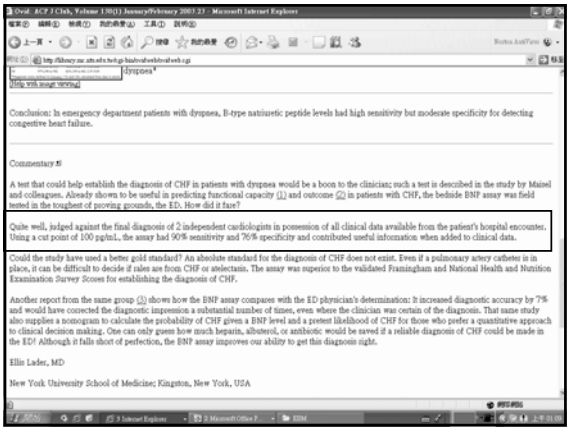
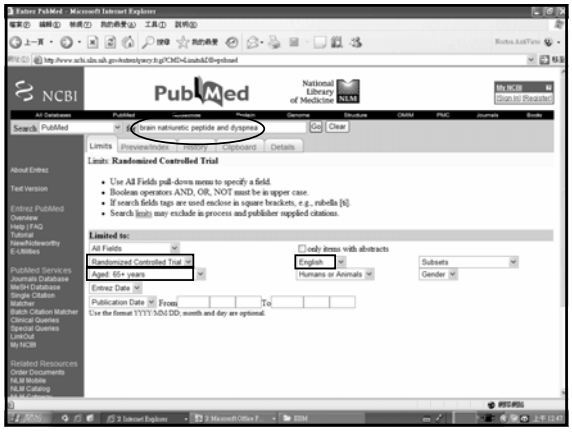

dyspnea
Conclusion: In emergency department patients with dyspnea, B-type natriuretic peptide levels had high sensitivity but moderate specificity for detecting congestive heart failure.
Commentary
Ellis Lader, MD
New York University School of Medicine; Kingston, New York, USA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brain natriuretic peptide and dyspnea
Limits: Randomized Controlled Trial
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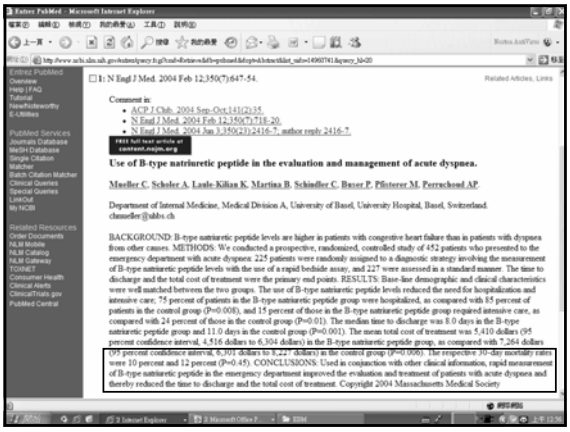
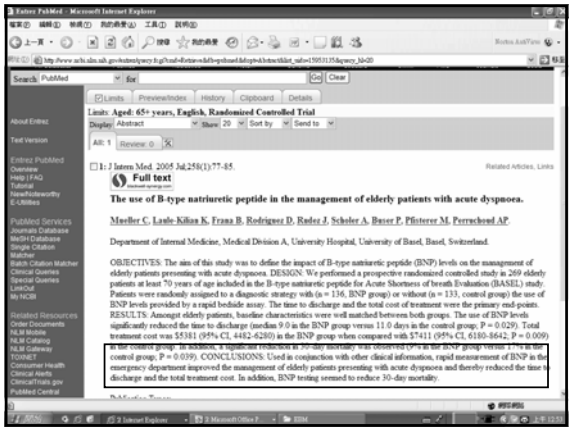
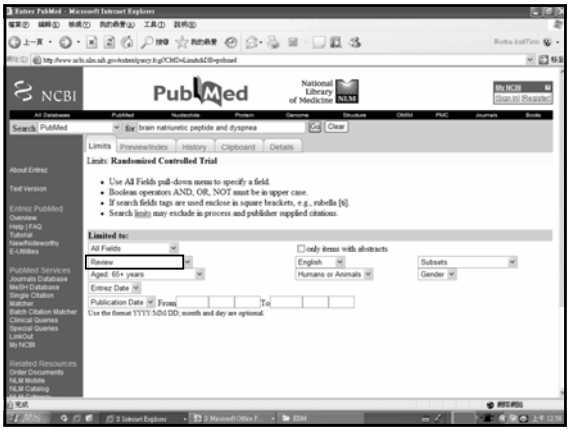
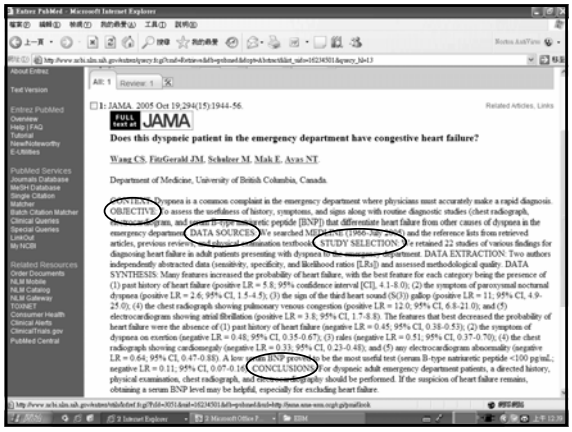
Randomized Controlled Trial
Aged: 65+ years









Summary

- B-natriuretic peptide is helpful in detecting heart failure among patients with acute dyspnea
- Cutoff level: 100 pg/mL

Evaluating the data

- Methodology
  - Study design, study subjects, intervention, measurement, bias, error,
- Critical appraisal of the literature

Techniques in reviewing the original data

- Study design
  - Randomized controlled clinical trial design
  - Observational
    - Cohort
    - Case-control
    - Cross-sectional
    - Case report
  - Meta-analysis, systematic review ?

How to critically review an empirical study

- Empirical study: actual observation or measurement in a population, study design
- Compared with:
  - Theoretical, review article, development of new measurement, case report
- Abstract & Objective, Materials and methods, Results, Discussion

Validity of measurement in research

- Measurement methods
- Validity of causal studies
  - Comparability between exposed and reference groups
  - Sampling procedures
- Validity of descriptive studies
  - Representativeness of the sample
  - Non-respondents

Examination of the results and discussion

- Is there any new finding in this study, and has the study achieved its goal?
- If I carry out a similar study, how shall I modify the study design and data analysis?
- Practice makes perfect
- How to write up a paper based on an empirical study

Special issues in EBM articles

- Randomized clinical trial
- Diagnosis
- Meta-analysis
- Etiology
- prognosis

Appraisal therapy articles: randomized controlled trial

- Is the study valid?
  - Was there a clearly defined research question?
  - Was the assignment of patients to treatments randomized and was the randomization list concealed?

Appraisal therapy articles: randomized controlled trial

- Randomization
- Double-blinding
- Placebo-control, active-control
- “Intention to treat” principle
- Relative risk, hazard risk, risk difference
- Number needed to treat (NNT)
- Subgroup analysis

Appraising diagnosis articles

- Is the study valid?
  - Was there a clearly defined question?
  - Was the “gold” or reference standard available?
  - Was the test evaluated on an appropriate spectrum of patients?
  - Was the reference standard applied to all patients?
- Are the results important?
  - What is mean by test accuracy?

Appraising diagnosis articles

- Sensitivity
- Specificity
- Positive predictive value
- Negative predictive value
- Likelihood ratio

Appraising systematic reviews

- Is the systematic review valid?
  - Is high-quality studies?
  - Does the method section adequately describe?
  - Are the studies consistent, both clinically and statistically?
- Are the results important?

Appraising systematic reviews <u>Meta-analysis</u>

- Systematic review, synthetic analysis
- Effect sizes
- Heterogeneity
- Fixed effects vs. random effects model
- Forest plot
- Publication bias

Appraising articles on etiology

- Is the study valid?
  - Clearly defined research question
  - Clearly defined, similar groups of patients
  - Exposure and clinical outcomes measured the same ways in both groups
  - Follow-up complete and long enough
  - Suggestive causative link
- Are the valid results from this study important?

Appraising prognosis studies

- Is the sample representative?
  - At a common point in their illness
  - Account for other important factors
  - The setting representativeness
- Was the follow-up enough for the clinical outcome?
- Was follow-up complete?
- Where outcomes measured “blind”?
- Are the results important?

Applying the evidence

- Are your patients similar to those of the study?
- How much of the study effect can you expect for your patient or problem?
  - Therapy, diagnostic tests
- Is the intervention realistic in your setting?
- Does the comparison intervention reflect your current practice?
- Was alternatives are available?
- Are the outcomes appropriate to your patient?

Suggested points to GP:

- Specify problems, build up PICO
- Primary or secondary sources first
- Strategy for data searching
- Critical appraisal of data
- Apply back to your patient’s problems