

# 근거중심의학

Evidence-Based Medicine

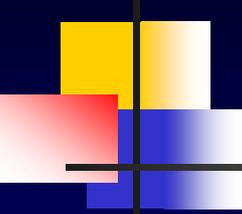
2010. 4

안형식

# 근거중심의학 발전과정

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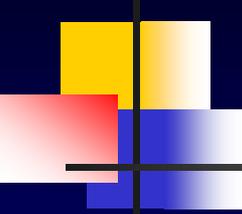
- McMaster 의과대학 임상역학, PBL  
논문 비평 (critical appraisal) 로 시작
- Sackett, Haynes 등이 기여



# 발전과정

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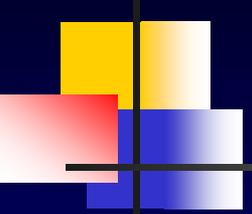
- 1980년대초에 Canadian Medical Association Journal 시리즈;
- 비판적 문헌 평가와 근거의 강도에 (A,B,C,D,E.) 의해 분류하는 방법 전개.



# 발전과정

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- 1980년대 말 ~ 1990년대 초 : JAMA 문헌이 비판적인 평가법의 일련의 시리즈를 연재, 출간
- ‘비판적 평가’의 개념
  - 환자의 최적진료를 위해 비판적 평가로부터 나온 정보를 사용
  - EBM으로 발전



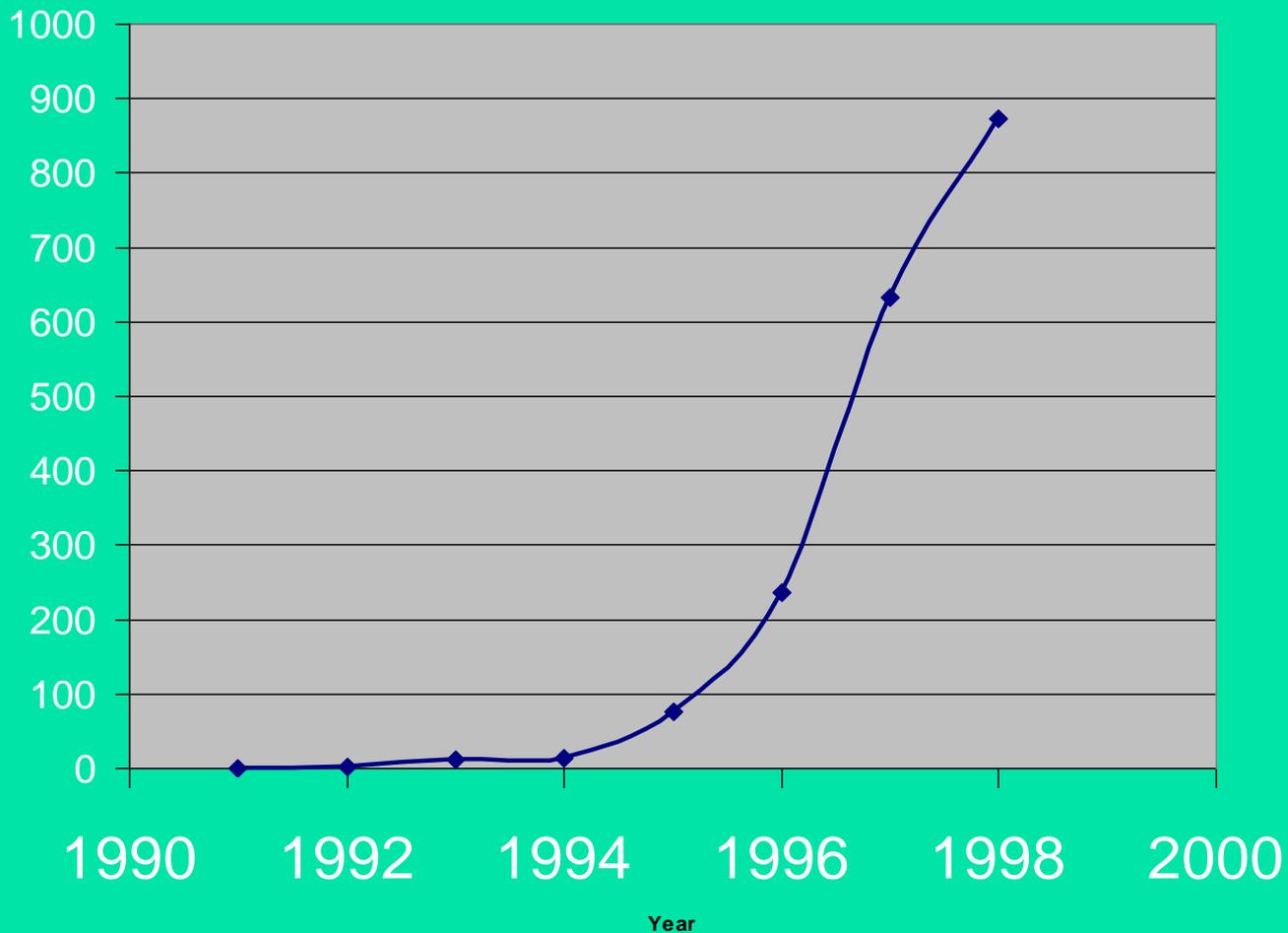
# 발전과정

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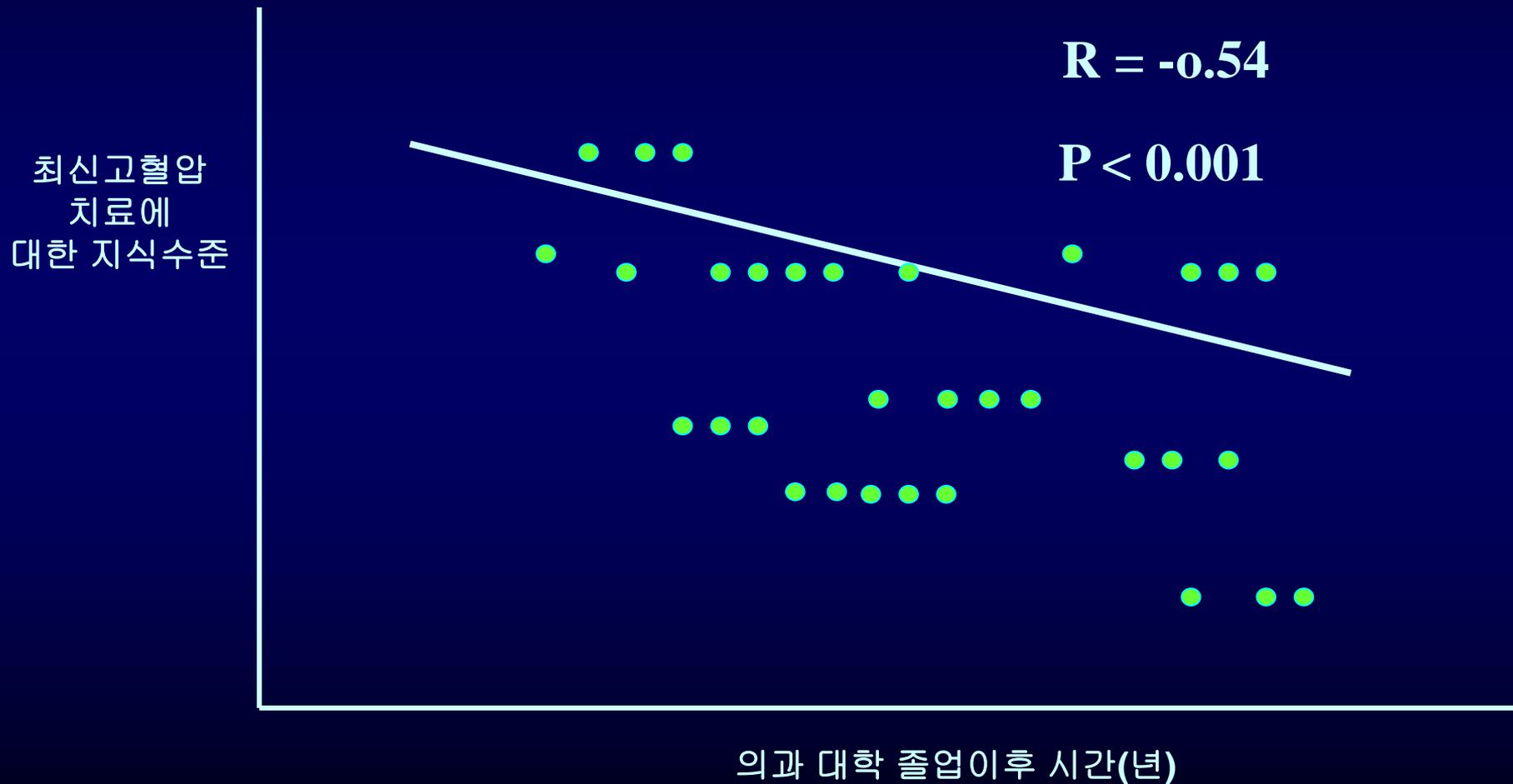
- 영국 NHS 등에서 의료체계 발전의 주요목표와 방법으로 채택
- Evidence-based health care, nursing, mental health, clinical practice

# EBM 문헌의 증가

EBM 문헌수



# 의과대학 졸업년도와 의학지식수준



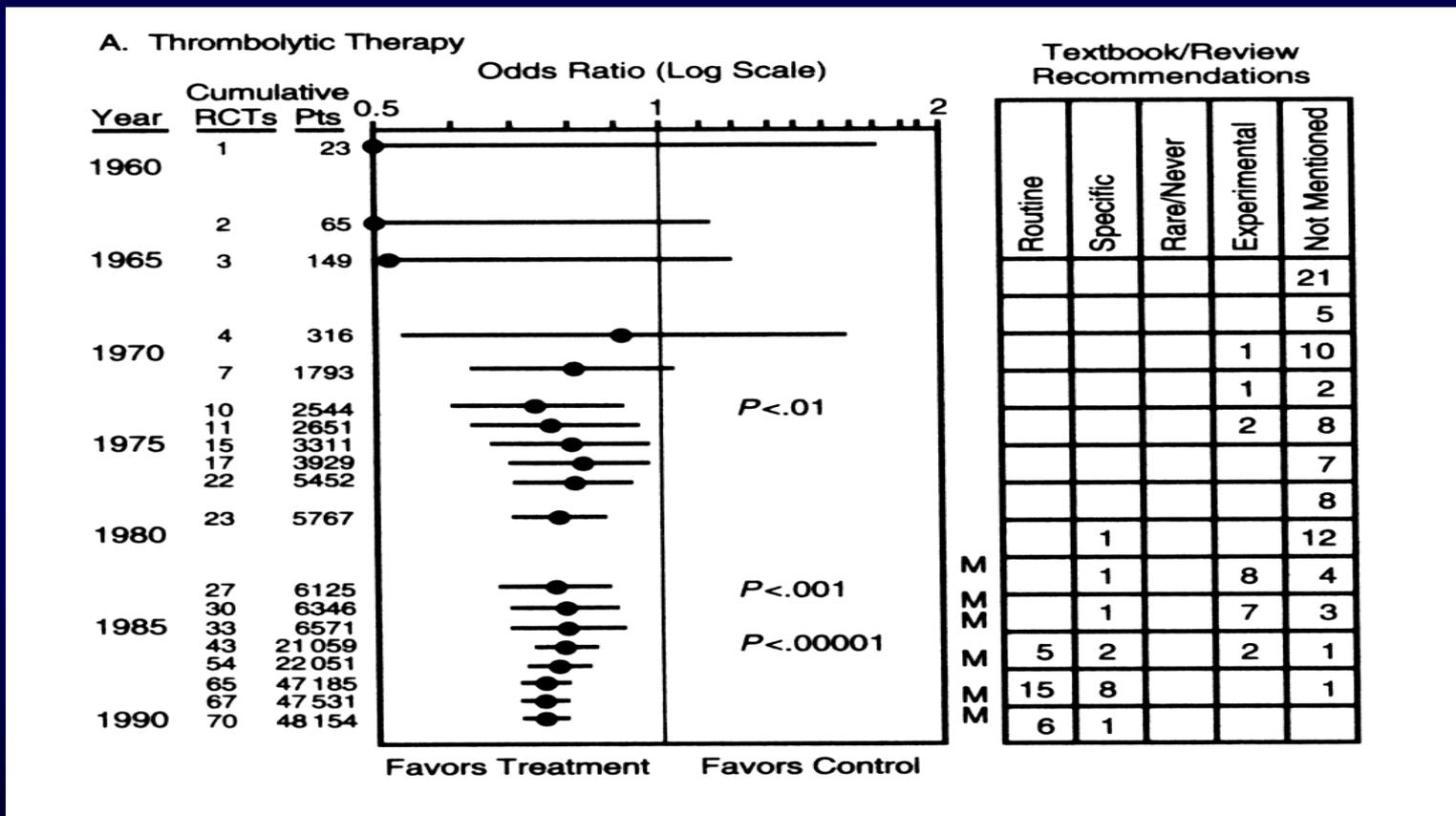
# 의사의 의학지식 습득

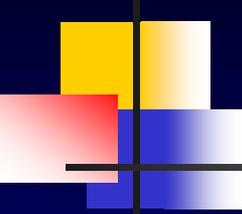
- 제약회사 판촉
- 약품광고
- 연수교육
- 동료조언
- 교과서
- 문헌의 참조
  - 많은 시간, 노력 기억 소요

# Publication to Implementation

Antman EM, Lau J, Kupelnick B, Mosteller F, and Chalmers TC.

JAMA, 268:240-8, 1992

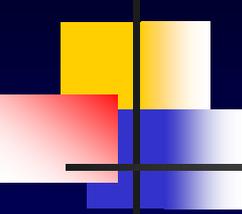




## 논문 출판후 진료적용까지의 시간

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- thrombolytic therapy : 13년
- 태아 폐성숙 촉진을 위한 코티코스테로이드 적용 : 10년



# 의사에 대한 최신 정보제공

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- CME
- 진료지침
- 전문저널

# 근거중심의학 ; 정의

- 가장 좋은 최신의 근거를  
(current best evidence)
- 공정하고, 명백하고 현명하게 사용하여  
(conscientious, explicit and judicious use)
- 개개의 환자에 대한 의사결정을 하는 것  
(in making decision about care of individual patients)

# EBM의 세가지 접근

- 의사 스스로 근거중심의학의 방법론 습득
- 검토된 근거 중심의 이차 문헌 생성
- 근거중심의 체계적 분석과 진료지침

# 문헌평가 – EBM 방법론

- 문헌 및 정보에 대한 접근과 자료의 수집
- 의학 문헌에 대한 평가 기술
- 임상 의사결정 (clinical decision making)

# 의학 출판 현황

## ■ 국제 의학 출판

연간 발행되는 도서량

의학학술지 : 20,000 종

신간의학도서 : 17,000 권

Medline 등재 학술지

학술자수 : 4000 종

참고문헌 : 600 만개

연간 등재 논문수 : 400,000 개

## ■ 국내 의학 출판

학술지수 : 200 개

연간 발행 논문수 : 15,000 개

# 문헌 검색의 고려조건

## ■ be sensitive

- use multiple sources and try to find all the available literature

## ■ minimise bias

- don't limit your search by language, year, publication status

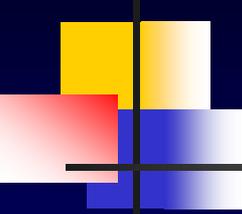
## ■ be efficient

- start where you expect highest yield, keep your search within reason

sensitivity



efficiency

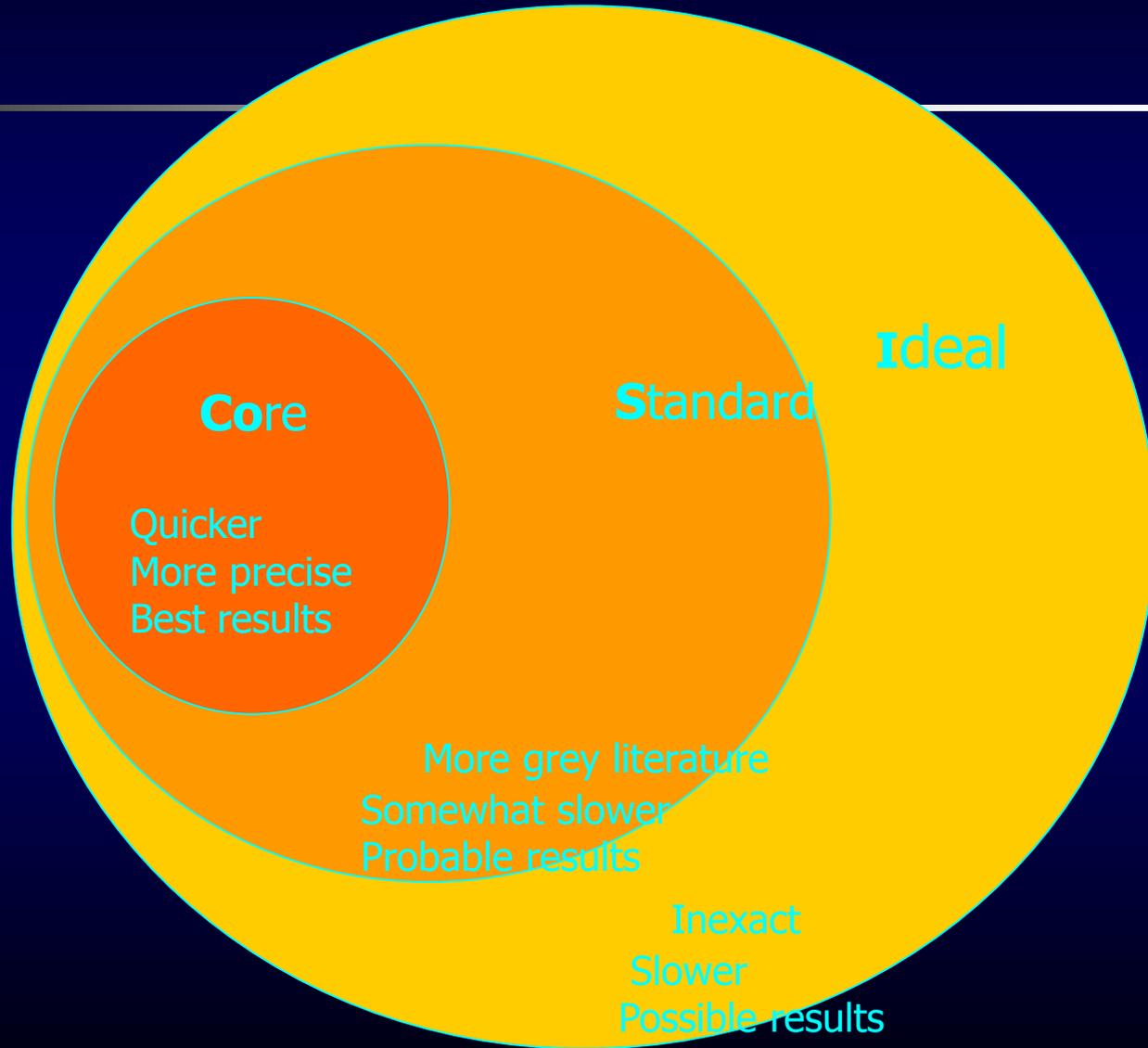


# 문헌평가의 유용성

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$$\text{유용성} = \frac{\text{타당도} \times \text{관련성}}{\text{작업량}}$$

# The COSI model



# 문헌검색 데이터베이스

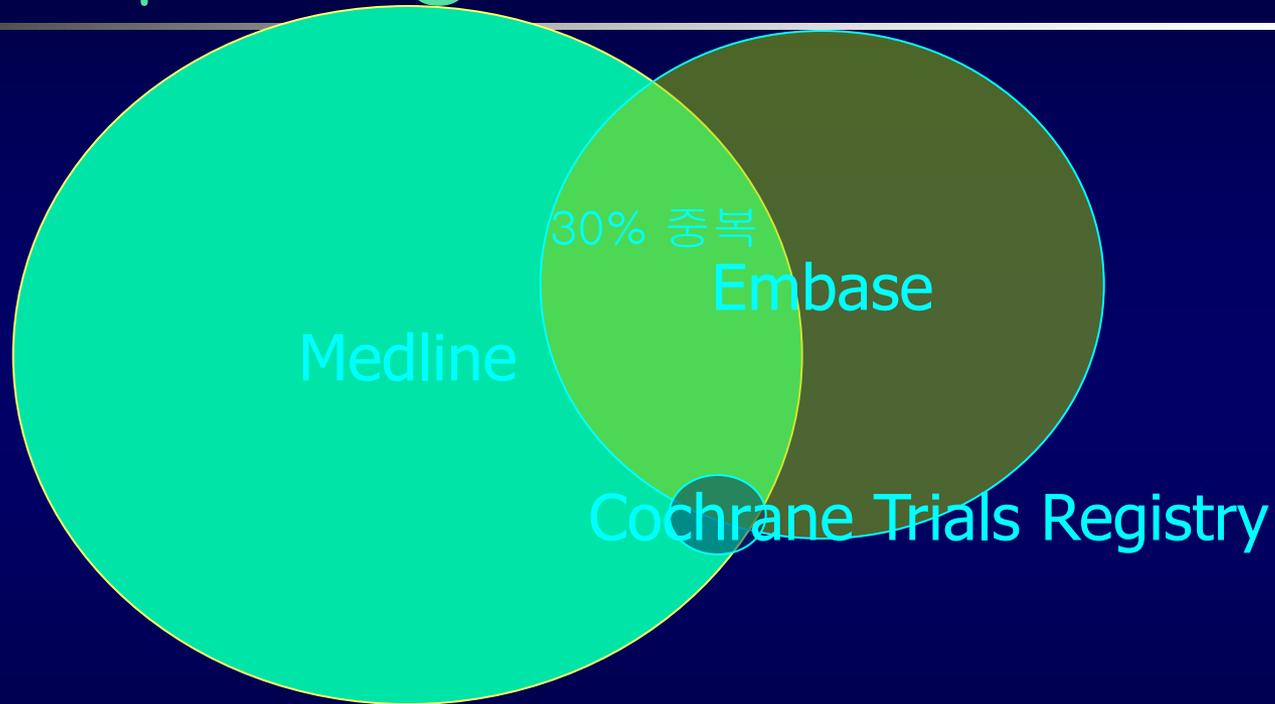


CENTRAL (*The Cochrane Library – includes Specialized Registers*)

- MEDLINE
- EMBASE
- 국내데이터베이스(KMBase, KOREAMED)
- and possibly...
  - regional databases (AMI, LILACS)
  - subject-specific databases (CINAHL, PsycInfo)
  - search engines (Google, TRIP)
  - references and citations of included studies (Web of Science)
  - handsearching
  - trials registers (clinicaltrials.gov)

# Where to look for studies

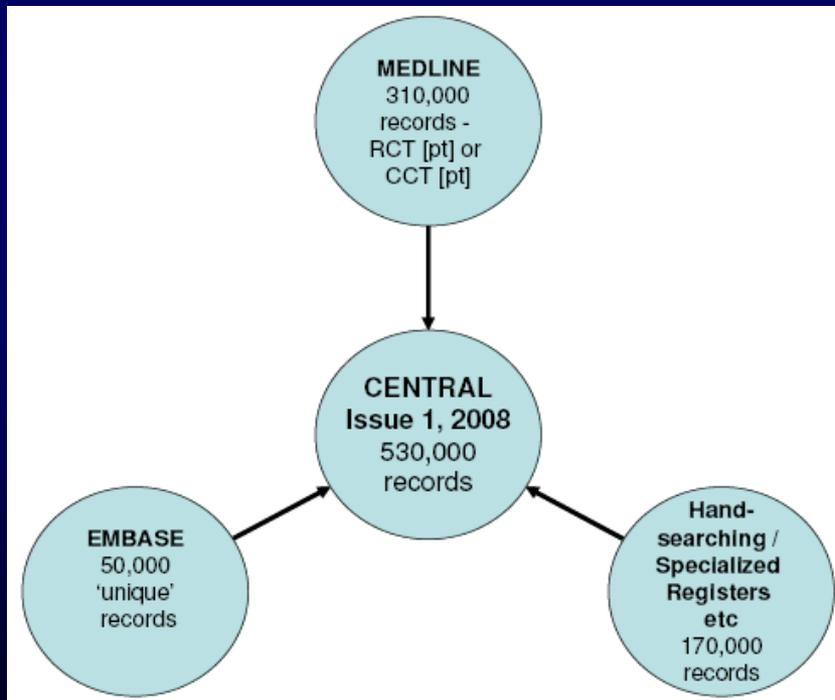
## Comparing Databases



Medline = Pubmed, Webspirs, OVID, ...

# CENTRAL in *The Cochrane Library*

Most comprehensive source of reports of controlled trials (530,000 as of Issue 1, 2008)



Wiley InterScience home

Home | About Cochrane | Access to Cochrane | For Authors | Help | Save Titles to My Profile

## The Cochrane Library

Evidence for healthcare decision-making

BROWSE  
 Cochrane Reviews: [By Topic](#) | [New Reviews](#) | [Updated Reviews](#) | [A-Z](#) | [By Review Group](#)  
 Other Resources: [Other Reviews](#) | [Clinical Trials](#) | [Methods Studies](#) | [Technology Assessments](#) | [Economic Evaluations](#) | [More Info](#)

SEARCH  
 Enter search term [Title, Abstract, Full Text] | [Advanced Search](#) | [MeSH Search](#) | [Search](#)

**Product Descriptions**

The Cochrane Library is a collection of databases that contain high-quality, independent evidence to inform healthcare decision-making. Cochrane reviews represent the highest level of evidence on which to base clinical treatment decisions. In addition to Cochrane reviews, The Cochrane Library provides other sources of reliable information: other systematic review abstracts, technology assessments, economic evaluations, and individual clinical trials – all the current evidence in one single environment.

**Record Counts**

Database	Total Records
<a href="#">Cochrane Database of Systematic Reviews (CDSP, Cochrane Reviews) *</a>	5171
<a href="#">Database of Abstracts of Reviews of Effects (DARE, Other Reviews)</a>	7048
<a href="#">Cochrane Central Register of Controlled Trials (CENTRAL, Clinical Trials)</a>	
<a href="#">Cochrane Methodology Register (CMR, Methods Studies)</a>	
<a href="#">Health Technology Assessment Database (HTA, Technology Assessments)</a>	
<a href="#">NHS Economic Evaluation Database (NHS-EEED, Economic Evaluations)</a>	
<a href="#">About The Cochrane Collaboration (About Cochrane Groups) †</a>	

\* Comprises 3385 complete reviews and 1786 protocols, of which 86 are new reviews, 66 updated reviews includes 13 complete reviews and 10 protocols transferred from the Cochrane Database of Methodology  
 † The Cochrane Collaboration: 1, Cochrane Review Groups (CRGs): 51, Fields: 15, Methods Groups: 12, C

	Total Records
	5171
	7048
	527,885
	18,181
	7177
	22,978
	92

# 타당성 - 문헌 평가

- 타당도 ; 연구 결과는 사실과 가까운가?
- 체계적 오류(systematic bias)는 없는가?

치료	진단	고찰
<i>RCT?</i> 추적관찰?	맹검 비교?	방법론?

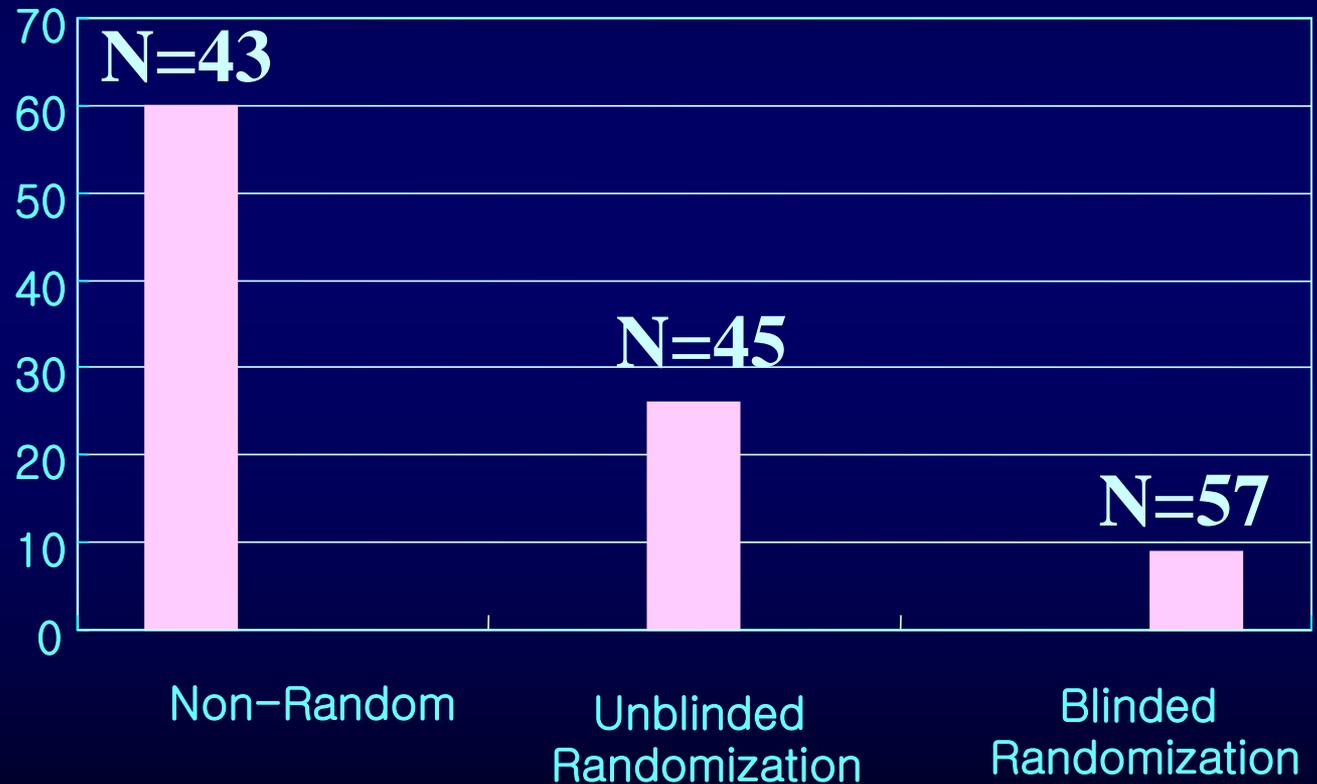
# 근거의 수준 평가

수준	내용
1	여러가지의 잘 설계된 무작위 임상시험의 결과에 대한 하나 이상의 체계적인 고찰에서 얻어진 강력한 근거
2	하나 이상의 적절하게 설계된 무작위 임상시험의 결과에서 얻어진 강력한 근거
3	잘 설계된 무작위 할당이 없는 임상시험, 단일군의 사전-사후 연구, 코호트 연구, 시계열 혹은 짝지은 환자 대조군 연구에서 얻어진 근거
4	하나이상의 대상군이나 연구단위에서 시행된 잘 설계된 비 실험적 연구에서 얻어진 근거
5	임상적 근거에 기초한 존경받는 권위자의 의견, 기술적 연구 혹은 전문가 위원회의 보고

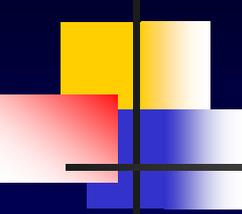
# 임상시험 설계:

## 급성심근경색증 환자의 치료

Case-Fatality  
Rate의 차이



Chalmers, et al. N Engl J Med 1983; 309:1358-61



# 관련성 – POEM

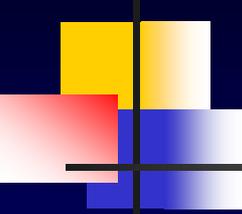
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- Patient-Oriented (환자지향)
- Evidence (근거)
- That Matters (문제 )

: 환자의 건강과 직접적 관계?

맞다면 진료의 내용을 바꾸어야 함

→ 직접적 연관



## 관련성 : 근거의 유형

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- POE (Patient Oriented Evidence) : 환자 지향 근거  
: 사망률, 이환율, 삶의 질
- DOE (Disease Oriented Evidence) : 질병 지향 근거  
: 병리생리학, 약리학, 병인학

# DOES 와 POEMs의 비교

예	질병지향 근거 (DOE)	환자지향 근거 (POEM)	설명
항부정맥 치료	항부정맥약X는 PVC를 줄임	항부정맥약X는 사망률을 증가시킴	POEM 결과와 DOE의 결과 상반적임.
항고혈압 치료	항고혈압제가 혈압을 낮춤	항고혈압제가 사망을 낮춤	POEM 결과와 DOE의 결과 일치
전립선암 선별진단	PSA가 전립선암을 초기에 발견함	PSA가 전립선암에 대한 사망률을 줄이는지 높이는지 알 수 없음	DOE가 알려져 있다해도 중요한 POEM은 현재 알 수 없음

# EBM 이차문헌 (Pre-Digested Evidence)

- ACP Journal Club
- Evidence-based Medicine
- 기타

# ACP Journal Club

Linking Research to Practice in Internal Medicine

March/April 1997

Volume 126 • Number 2

Vol. 2 No. 5 pp. 129-160

SEPTEMBER/OCTOBER 1997

Published  
Bimonthly  
by the  
American College  
of Physicians

## ■ THERAPEUTICS

Lowering LDL cholesterol levels reduced fatal coronary events in patients with acute MI and average cholesterol levels	29
Amlodipine did not increase morbidity or mortality rates in severe heart failure	30
Meta-analysis: Mortality is reduced when fibrinolytic therapy is started soon after the onset of MI symptoms	31
Hirudin was no more effective than unfractionated heparin for acute MI	32
Hirudin reduced death or MI more than heparin at 48 hours but not at 30 days	33
Meta-analysis: $\beta$ -blockers improve function in dilated cardiomyopathy	34
Meta-analysis: Thrombolytic therapy increases the risk for early death and intracranial hemorrhage after acute ischemic stroke	35
Meta-analysis: Misoprostol reduces NSAID-induced gastrointestinal mucosal injury	36
Meta-analysis: Pentoxifylline improves walking in intermittent claudication	37
Meta-analysis: Respiratory rehabilitation relieves dyspnea in COPD	38
Review: Antitoxins are ineffective for acute bronchitis	39
Implantable insulin pump improved quality of life in NIDDM	40
Valaciclovir accelerated healing in recurrent herpes genitalis	41
Subcutaneous tunneling reduced catheter-related sepsis in critically ill patients	42

## ■ DIAGNOSIS

D-dimer levels detected DVT in patients hospitalized for stroke rehabilitation	43
CSF proteins 130 and 131 were specific for diagnosing Creutzfeldt-Jakob disease	44
Brain protein 14-3-3 was a sensitive test for Creutzfeldt-Jakob disease	45
Meta-analysis: Glycosylated hemoglobin levels are useful for diagnosing diabetes	46

## ■ PROGNOSIS

Ischemic stroke with accompanying atrial fibrillation was associated with reduced survival and functional status	47
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## ■ ETIOLOGY

LDL particle size was smaller in CAD, but other lipid parameters were stronger predictors of CAD	48
Triglyceride level but not LDL particle size was an independent risk factor for MI in men	49
Low cholesterol levels were associated with suicide in men	50

## ■ ECONOMICS

Low-molecular-weight heparin was cost-effective for perioperative prevention of DVT	51
Cost-effectiveness of pravastatin in the secondary prevention of CAD in men varied with the risk profile of the patient	52
Intensive therapy extended life and was cost-effective for IDDM	53

Other Articles Noted	54
Glossary	56
Contents	A-7
Purpose and Procedure	A-13
Editorial: Transferring evidence from research into practice: 3. Developing evidence-based clinical policy	A-14

ACP/J 126(Nº 2)29-56(1997)US ISSN 1056-8751

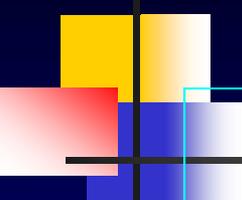
# Evidence-Based Medicine



American College  
of Physicians

BMJ  
Publishing  
Group

# ACP Journal Club



Journals	No.	No. of issue	No. of Articles abstracted	Issue per article
Core	9	272	139	2
Others	17	188	39	5
The rest	21	199	0	$\infty$

NEJM, Ann Intern Med, JAMA, Arch Intern Med, Circulation, Lancet, Am J Med, BM J, J Intern Med

# 체계적 분석 (systematic review)

MI 환자에게 Beta blocker를 투여하여 심부전을 예방할 수 있는가?

- 1981년도 문헌 검색

# 개별 임상시험 결론

The mortality and hospital readmission rates were not significantly different in the two groups.

Reynolds and Whitlock

Until the results of further trials are reported long-term beta-adrenoceptor blockade is recommended after uncomplicated anterior myocardial infarction.

Multicentre International Study

The trial was designed a 50% reduction in mortality and this was not shown. The nonfatal reinfarction rate was similar in both groups.

Baber et al

We conclude that long-term treatment with timolol in patients surviving acute myocardial infarction reduces mortality and the rate of reinfarction.

The Norwegian Multicentre Study Group

# 종설 (Review) 결론

It seems *perfectly reasonable to treat patients* who have survived an infarction with timolol.

European Heart Journal (1981)

We still *have no clear evidence* that beta-blockers improve long-term survival after infarction despite almost 20 years of clinical trials.

BMJ (1981)

# 서술형 고찰 (narrative review)

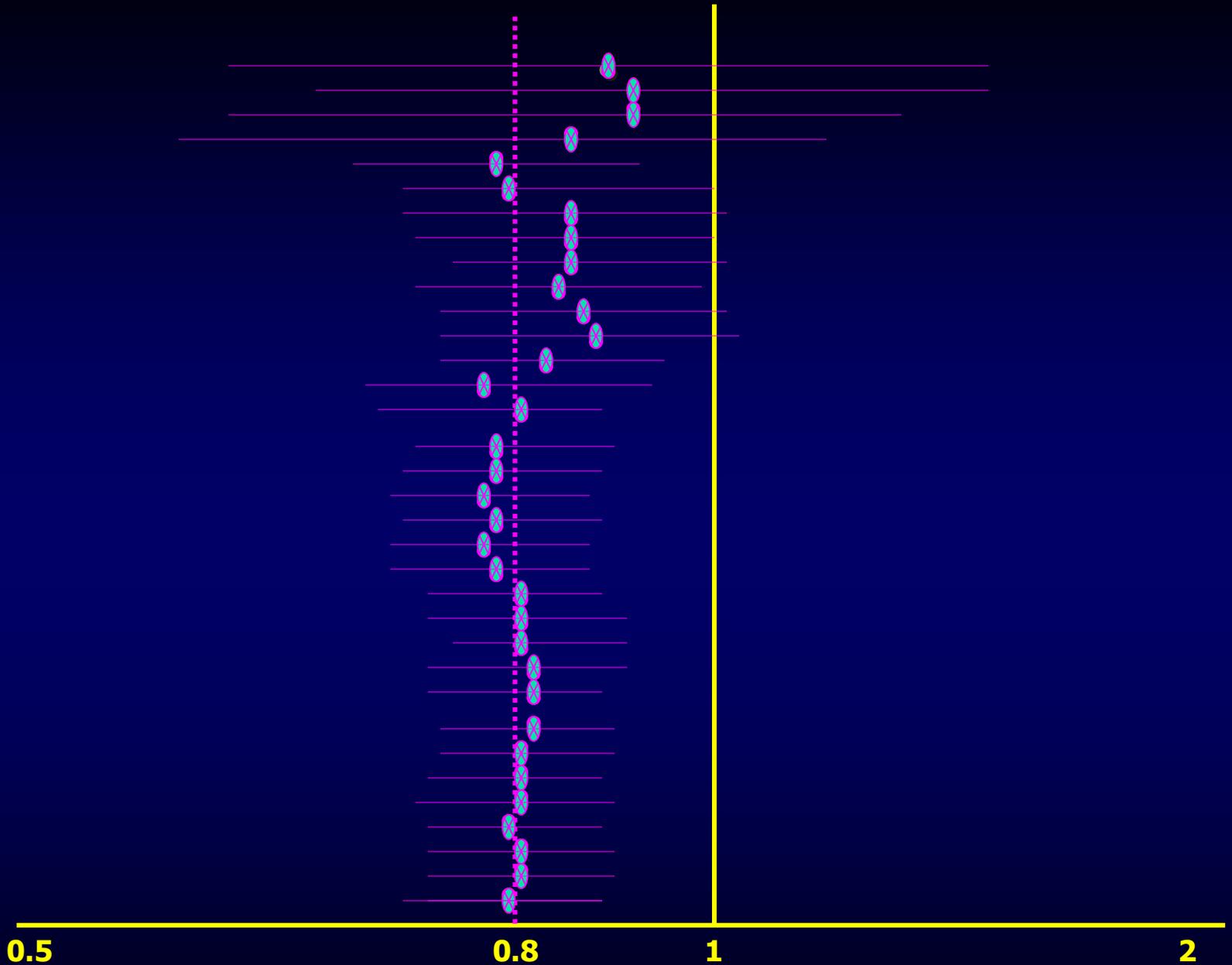
- 문헌 수집과정이 주관적
  - (49/50 가 수집과정 기술안됨 Murrow)
- 체계적 문헌평가 과정 없음
- 문헌의 숫자계산; 표본수, 효과크기, 연구설계 등이 반영안됨
- *저자의 주관적 판단 - 오류의 가능성*

# 체계적 분석 (systematic review)

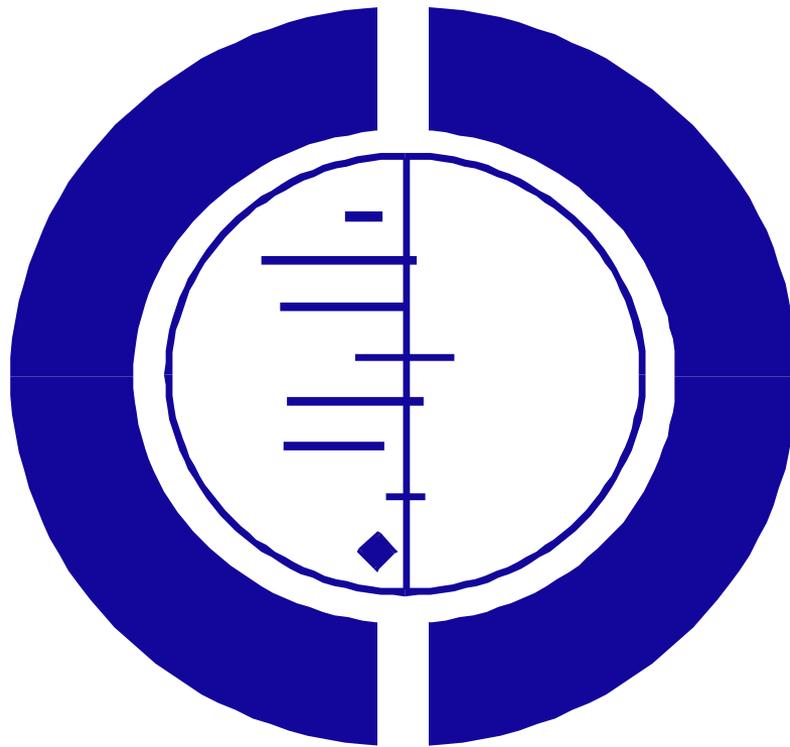
- 체계적인 문헌 수집
- 엄격한 문헌 평가 방법론
- 대개 메타분석 시행
  - 종합 추정치 (pooled estimate) 제시

year

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메타분석 결과



**Cochrane Systematic Reviews (1022; another 500 in preparation)**  
**Database of Abstracts of Reviews of Effectiveness (1895)**  
**Registry of Randomised Controlled Trials (218,355)**

# Cochrane Library

- The Cochrane Database of Systematic Reviews (CDSR)
- The York Database of Abstracts of Reviews of Effectiveness (DARE)
- The Cochrane Controlled Trials Register (CCTR)
- The Cochrane Reviews Methodology Database (CRMD)

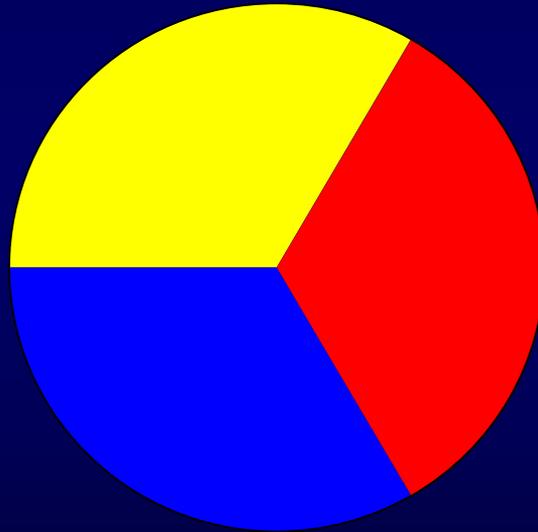
# 체계적 분석과 근거중심 진료 지침

- 근거중심 지침(Evidence-based Guideline)
- 명시적 지침(Explicit Guideline)
- 공식적, 비공식적 합의

• EBM 에 대한 논란

# 환자 개인에 대한 의사결정

과학적 근거



환자의  
상황

취향  
가치  
권리

- 임상경험이 무시된 진료:

*evidence-tyrannized medicine*

과학적 연구결과가 무시된 진료

*eminence-based, eloquence-based,  
confidence-based, providence-based  
.....medicine*

# 사회적 관점과 개인적 관점 (가상적 사례)

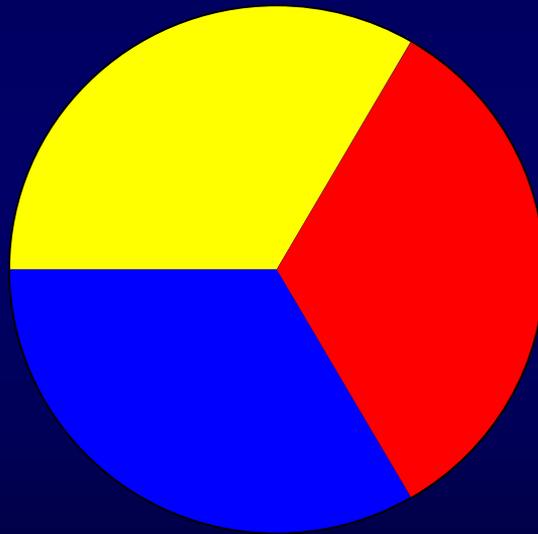
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치료법	A	B
생존년수	5년	10년
비용	1500만원	7000만원
추가 5년 생존을 위한 비용		5500만원
추가비용에 따른 생존연장 연수	18.3년	5년

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# 사회적 관점과 EBM

과학적 근거 : 효과



자원 제약

효율

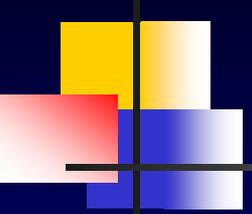
가치  
형평

# 의료체계와 EBM

- 의료서비스의 과학성  
의사개인의 노력, 체계적 지원 불비
- 행위별 수가제, 의료보험 심사제도.....  
과학적 근거에 입각한 의사결정의 어려움

# EBM 수행을 위한 방안

- 의학 정보에 대한 접근도 향상  
연구정보의 보완 활용도 제고
- 근거중심의학 지원 자원  
EBM center, Cochrane network
- 지침 개발 보급 활용, 유인책
- 의학교육



# 우리나라의 임상연구

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- 양; 국내 의학 출판  
학술지수 : 200 개  
연간 발행 논문수 : 15,000 개
- 임상연구의 질
- 무작위 임상시험?

# 의학교육

## 의학 전문가의 내적 동기와 **EBM**