

Symposium 1: EBM
Diabetes Care
Prevention

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The History of Medicine

2000 B.C. - Here, eat this root.

1000 A.D. - That root is heathen. Here, say this prayer.

1850 A.D. - That prayer is superstition. Here, drink this
potion.

1940 A.D. - That potion is snake oil. Here, swallow this pill.

1985 A.D. - That pill is ineffective. Here, take this
antibiotic.

2000 A.D. - That antibiotic doesn't work anymore. Here,
eat this root.

From the Cochrane Collaboration Consumer Network Newsletter
(September, 1999, page 10)

EBM: What Is It?

"..integrating individual clinical expertise with the best external clinical evidence from systematic research."

"conscientious, explicit and judicious use of current best evidence in making decisions about the care of individual patients."

Sackett, DL. BMJ. 1996 Jan 13;312(7023):71-2

What we're going to cover

- Review selected principles of evidence-based medicine
 - Focus on diabetes care, and screening and prevention
 - Look at the measures and expressions of risk reduction

What we're going to cover

- Review major EBM resources that answer specific clinical questions:
 - Cochrane
 - DARE
 - ACP Journal Club
- Find the best evidence in MEDLINE.
- Review evidence-based tools that answer general clinical questions:
 - UpToDate
 - eMedicine
 - National Guideline Clearinghouse
- Review resources that answer drug-related questions

Case Presentation

- BG, a 51 yo mother of 3 presents to your office complaining of polyuria, polydipsia, and weight gain of 15 lbs over 3 months. Her mother had DM. The last two of her children were large for gestational age; the last pregnancy was notable for pre-eclampsia.

Questions

- *Patient care questions*
 - What is the likelihood that someone with gestational diabetes will develop established diabetes?
- *Teaching improvement questions*
 - When a patient presents to my office, what kind of teaching should my learners (students, residents) already have had?
- *Practice improvement questions*
 - Is my patient's database easily retrievable?

Case, continued

- Her past history is notable for mild diet treated hypertension. She had a TAH-BSO 5 years ago for fibroid related menorrhagia. She has a seizure disorder and takes Dilantin®.

Question

- Does Dilantin® have any impact on glucose metabolism?

Clinical Pharmacology Online
<http://cponline.hitchcock.org/>

- *Clinical Pharmacology* is a drug information application that provides peer reviewed, clinically-relevant information on drugs available in the United States, including off-label uses and dosages, herbal supplements, nutritional products, and new and investigational drugs.

Case, continued

- A quick physical examination reveals a woman appearing her age, overweight and in no evident distress.
- VS: 155/80 P 96
T 36.5C Height 5'3" Weight 165 lbs No retinopathy/neuropathy
- Initial labs demonstrate a random blood sugar of 426 mg/dL. There is an anion gap of 12 and the BUN/Cr are 25 and 1.3 mg/dL, respectively. The urine microalbumin is 100 mcg/dl. The hemoglobin A1c is 12.6%

Question

- Should protein intake be restricted in a middle-aged patient with Type 2 diabetes and microalbuminuria?

The Major EBM Resources to Answer Specific Clinical Questions

- The Cochrane Database of Systematic Reviews
 - The ACP Journal Club
 - The Database of Abstracts of Reviews of Effectiveness (DARE)
-

- MEDLINE
-

The Cochrane Database of Systematic Reviews - via Ovid

<http://www.dartmouth.edu/~biomed>

- Published by the International Cochrane Collaboration. Updated quarterly.
- Consists of detailed, structured topic reviews of hundreds of articles.
- Teams of experts complete comprehensive literature reviews, evaluate the literature, and present summaries of the findings of the best studies.

The ACP Journal Club - via Ovid
<http://www.dartmouth.edu/~biomed>

- Electronic access to articles in *The ACP Journal Club*, published bimonthly by the ACP-ASIM.
- The editors of this journal screen the top 100+ clinical journals and identify studies that are methodologically sound and clinically relevant.
- An enhanced abstract, with conclusions clearly stated, and a commentary are provided for each selected article.

Database of Abstracts of Reviews of Effectiveness (DARE) - via Ovid

<http://www.dartmouth.edu/~biomed>

- Produced by the National Health Services' Centre for Reviews and Dissemination (NHS CRD) at the University of York, England.
- Contains structured abstracts of systematic reviews from a variety of medical journals.
- Updated monthly.

EBM Reviews

- Ovid allows you to search Cochrane, ACP Journal Club, and DARE simultaneously.
- From the Ovid database list, select "EBM Reviews - full-text"

Hypothetic Examples of RR, ARR, NNT Measures in 4 Studies

<u>Group</u>	<u># Pts</u>	<u># Events</u>	<u>RR</u>	<u>ARR</u>	<u>NNT</u>
Placebo	1000	1	50%	0.05%	2000
Treated	1000	.5			
Placebo	1000	10	50%	0.5%	200
Treated	1000	5			
Placebo	1000	100	50%	5%	20
Treated	1000	50			
Placebo	1000	1000	50%	50%	2
Treated	1000	500			

Limitations of NNT

- NNT indicates frequency, not utility
- NNT is based on an outcome for a specified period, with treatment delivered in a specified way
- NNT should not be compared across conditions
- NNT assumes that a given intervention produces the same relative risk reduction exclusive of baseline risk
- Each NNT has a confidence interval

p values or confidence intervals?

- p values test the evidence against a null hypothesis (e.g., $p=0.05$ means we can be sure the hypothesis tested is likely to be true 95% of the time.)
- Confidence intervals tell us about the strength of the evidence (e.g., 95% CI is the range of values within which we are 95% sure that the true value lies.)

MEDLINE via Ovid*

<http://www.dartmouth.edu/~biomed>

- The National Library of Medicine's premier database covering the fields of medicine, nursing, dentistry, veterinary medicine, the health care system, and the preclinical sciences.
- Contains bibliographic citations and author abstracts from more than 4,600 biomedical journals published in the United States and 70 other countries.
- Over 11 million citations dating back to the mid 60s. Updated weekly on the Ovid system.

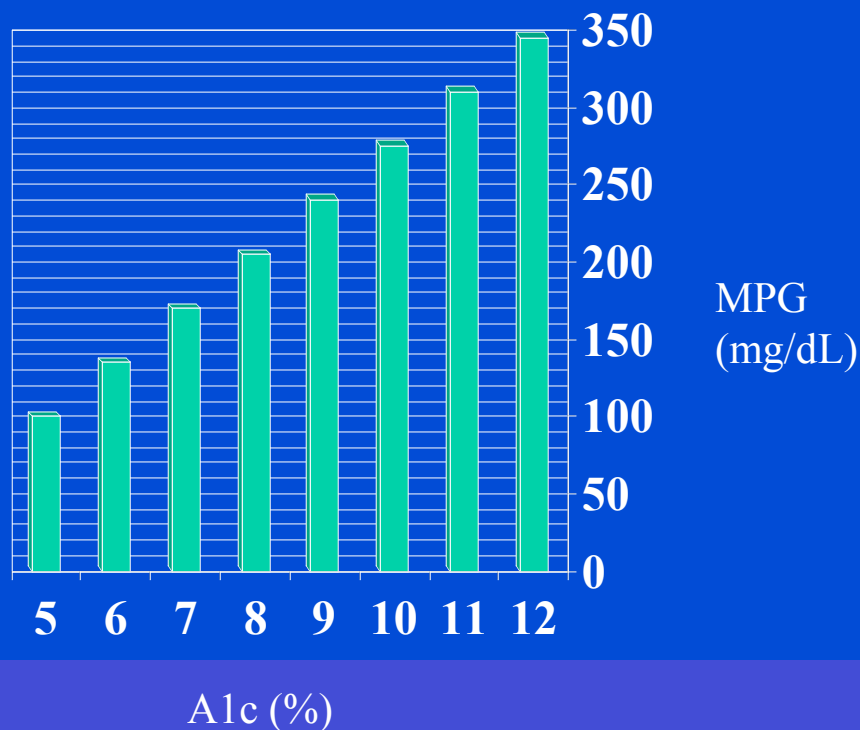
*Requires Kerberos authentication for access

Another Specific Question

- How does the *A1c* correlate with average blood sugar?

Defining the Relationship Between Plasma Glucose and HbA1c: Analysis of glucose profiles and HbA1c in the DCCT
Diabetes Care 2002;25(2):275-278

A1c vs plasma glucose



- Erythrocyte life span 120 days
- Recent (3-4 weeks) PG levels contribute more (50%) than remote (90-120 d) to A1c
- FPG tends to underestimate A1c; post-lunch PG correlates well with MPG.
- 1% change in A1c correlates with Δ MPG 35 mg/dL

Question

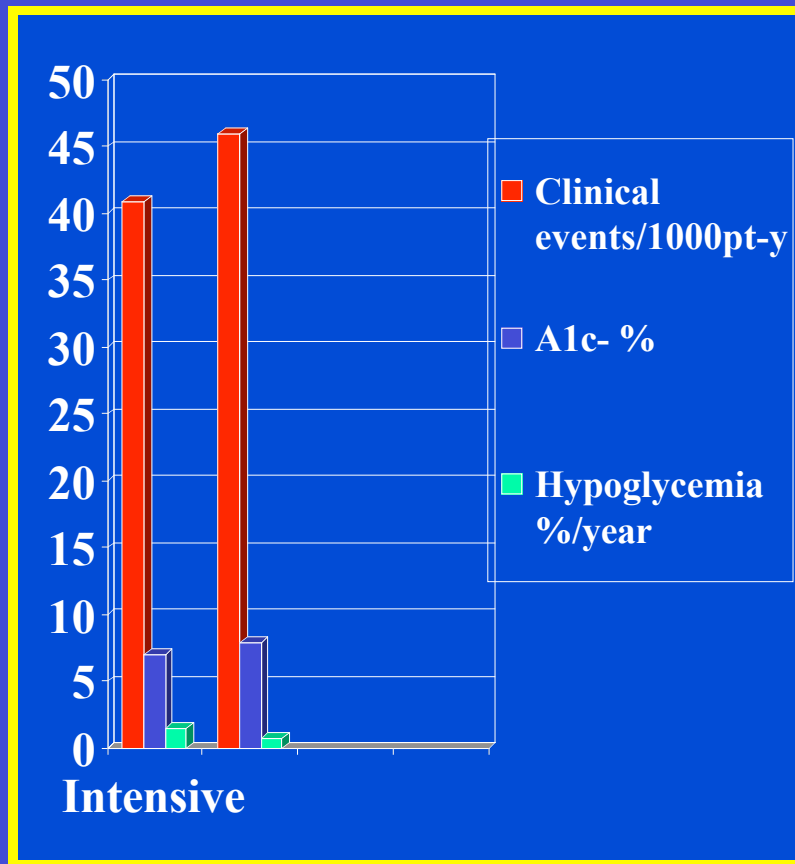
- The DCCT was a trial in type 1 diabetes. But I remember there was a UK study on A1C in type 2 diabetes; how can I find it fast?

MEDLINE via PubMed

- Free access to MEDLINE from the National Library of Medicine
- Includes links to Dartmouth's digital full-text journals, when available
 - [Note: must connect to PubMed through the Biomedical Libraries Web to access full-text]

Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS 33).

Lancet. 1998 Sep 12;352(9131):837-53.



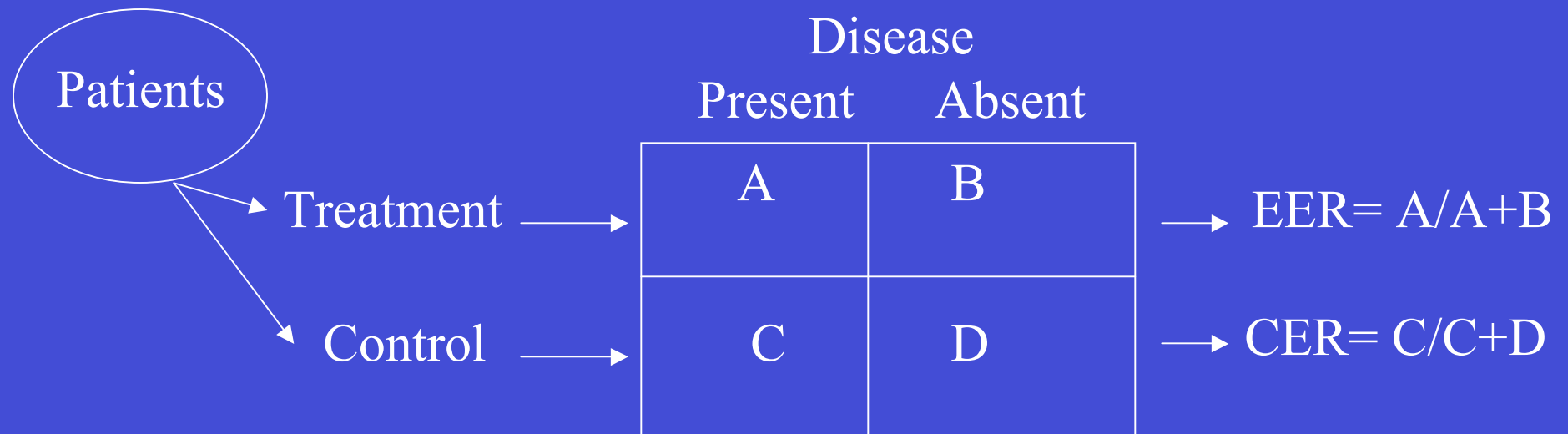
- RCT, median f/u 10 years
- 23 hospital based clinics in UK
- 3867 pts, mean age 53, 61% men, BMI 27.5, newly diagnosed after 3 mo diet therapy
- 2729 pts intensive therapy
- 1138 pts conventional dietary
- A1c 7.0% v 7.9%
- Hypoglycemia 0.7% v 1-1.8%
- Mortality- NS
- Macrovascular- NS

1% reduction in A1c subsequently associated with 35% reduction in microvascular endpoints, 18% reduction in MI, 17% reduction in all cause mortality

Randomized Controlled Trial

- The ideal population based strategy (actually, the ideal agricultural strategy)
- Tests the average efficacy of (therapeutic) interventions
- Relies on double blind methodology rather than sophisticated knowledge of clinical variables
- Biases: TNTC

The Randomized Controlled Trial



EER= experimental event rate

CER= control event rate

ARR (absolute risk reduction) = CER-EER

RRR (relative risk reduction) = ARR/CER

NNT (number needed to treat) = $1/ARR$

Case, continued

- This brief office visit has established that Ms. BG has new onset diabetes. Initial plans are formulated, including a visit to a nutritionist. A decision needs to be made concerning additional treatment. She has significant problems concerning finances. After considering the patient's clinical status, her resources and ability to return for care, an Rx for metformin is considered.

Question

- What's current information on the management of DM Type 2 with oral glycemics? If I do initiate treatment with an oral agent, which one should it be?

Evidence-based Tools to Answer General Clinical Questions

- Textbooks
- UpToDate
- eMedicine, et. al.
- National Guideline Clearinghouse

- MEDLINE

UpToDate

<http://www.dartmouth.edu/~biomed>

<http://uptodate.com>

- Topic reviews are written by recognized authorities who review the topic, synthesize the evidence, summarize key findings, and provide specific recommendations.
- Physician editors and authors review and update the content on a continuous basis; a new, peer-reviewed version is issued every four months.

eMedicine

<http://www.emedicine.com>

- Nearly 10,000 physician authors and editors contribute to the eMedicine Clinical Knowledge Base with coverage of 7,000 diseases and disorders.
- All of eMedicine's original content undergoes four levels of physician peer review plus an additional review by a PharmD.
- Contains an Image Bank of nearly 30,000 multimedia files.
- Updated daily.

Another General Question

- Is there a guideline describing the management of someone with type 2 diabetes (e.g., frequency of visits, labs, etc.)?

The National Guideline Clearinghouse

<http://www.guideline.gov>

- A comprehensive database of more than 995 evidence-based clinical practice guidelines and related documents.
- Sponsored by the *Agency for HealthCare Research and Policy* in partnership with
 - *The American Medical Association*
 - *The American Association of Health Plans*
- Updated weekly.

Back to some Previous Questions

- How can I access drug cost information quickly?
- Before I prescribe Metformin: are there any known interactions between it and Dilantin?

Handheld PDA Resources

<http://www.dartmouth.edu/~biomed/services.html/pda.resources.shtml>

Case, continued

- Ms. BG had many questions. She wanted to know what the dangers of having diabetes were, and what she could do to reduce her chances of getting them.
- She had watched her mother getting pain in her feet, and also developing problems with her vision that required laser treatment.

Question

Are there patient education materials that would help her better understand and manage her disease?

MEDLINEplus

<http://medlineplus.gov/>

- Extensive information from the National Institutes of Health and other trusted sources on over 600 diseases and conditions.
- Also includes lists of hospitals and physicians, a medical encyclopedia and a medical dictionary, health information in Spanish, extensive information on prescription and nonprescription drugs, health information from the media, and links to thousands of clinical trials.
- Updated daily.

Other consumer health resources

- <http://www.dartmouth.edu/~biomed/resources.html/conshealth.html/>

Case, continued

- Ms. BG returned 2 weeks later. She felt better and was no longer having polyuria. During the visit she stated that this was a huge wake-up call to her, and she wanted to take excellent care of herself. The nutritionist and she had worked out a good plan of diet and exercise. She wanted to address heart disease risk and cancer prevention as well.

Prevention Topics

- Breast cancer
- Colon cancer
- Prostate cancer
- Cervical cancer
- Cardiovascular
 - Cholesterol
 - Homocysteine
 - CRP

Efficacy of Mammography- Women Under 50

<u>Study</u>	<u>RR</u>	<u>ARR</u>	<u>NNS</u>
HIP	.778	.00062	1,606
Malmo	1.326	-.00005	-1,938
S2C	1.131	-.00013	-7,803
Edinburgh	.987	.00003	34,248
Stockholm	1.025	-.00003	-36,143
Canada	1.35	-.0004	-2,521
Total	1.02	-.000034	-29,565

Based on 119/79,103 deaths in control- 140/91,016 deaths in screened, 29,565 women would need to be screened to 'cause' one death.

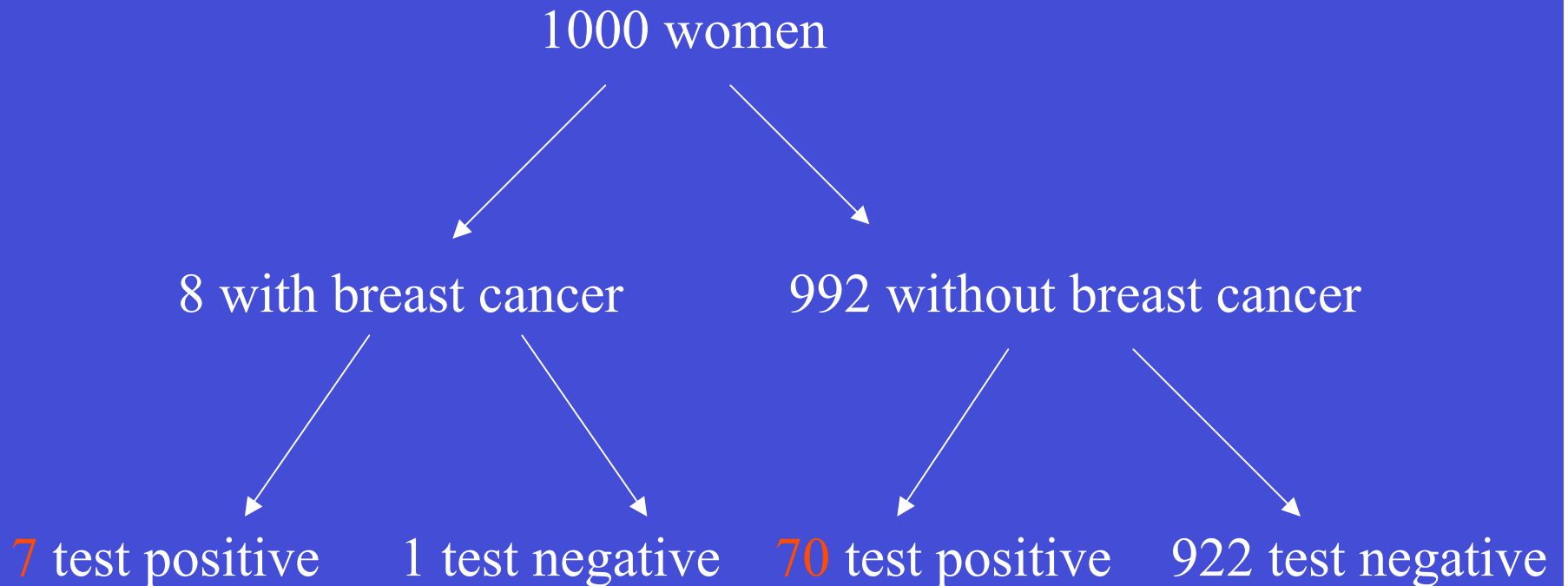
Efficacy of Mammography- Women Over 50

<u>Study</u>	<u>RR</u>	<u>AR</u>	<u>NNS</u>
HIP	.604	.00155	645
S2C	.613	.00087	1,151
Malmo	.680	.00062	1,619
Edinburgh	.810	.00075	1,335
Stockholm	.530	.00082	1,217
Canada	.974	.000052	19,069
Total	.655	.00089	1,122

Baseline risk of death from breast cancer in this age group is 0.00271.
Based in 301/116,387 deaths in control group - 247/145,711 deaths in
screened group = AR

NNS to prevent one death from breast cancer is 1122.

Breast cancer screening with mammography



Thus the probability of having cancer when the test is positive is $7/77$, or **9.1%**

WHI JAMA;2002;288:321-33
 16,608 women aged 50-79 (mean 63.3) RCT 5.2 yrs
 Event rates per patient-year

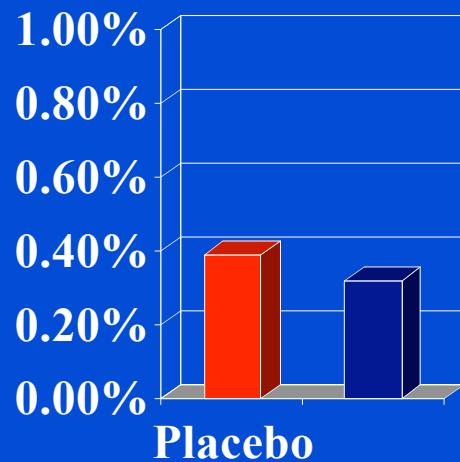
<u>Outcomes</u>	<u>HRT</u>	<u>Placebo</u>	<u>RRI(R)</u>	<u>NNH(T)</u>
CHD	0.37%	0.30%	29% (2-63)	1152 (531-16693)
VTE	0.34	0.16	111% (58-182)	565 (345-1079)
Breast Ca	0.38	0.30	26% (0-59)	1285 (567-infinity)
Hip Fx	0.10	0.15	34% (2-55)	1962 (1213-33358)
Colorectal Ca	0.10	0.16	37% (8-57)	1691 (1097-7819)

HRT use in 10,000 Women
Benefits and Harms/ Year
(from JAMA 2002;288:872-881)

Events HRT Placebo Excess (Fewer) CHD 37307 VTE 341618 Breast (

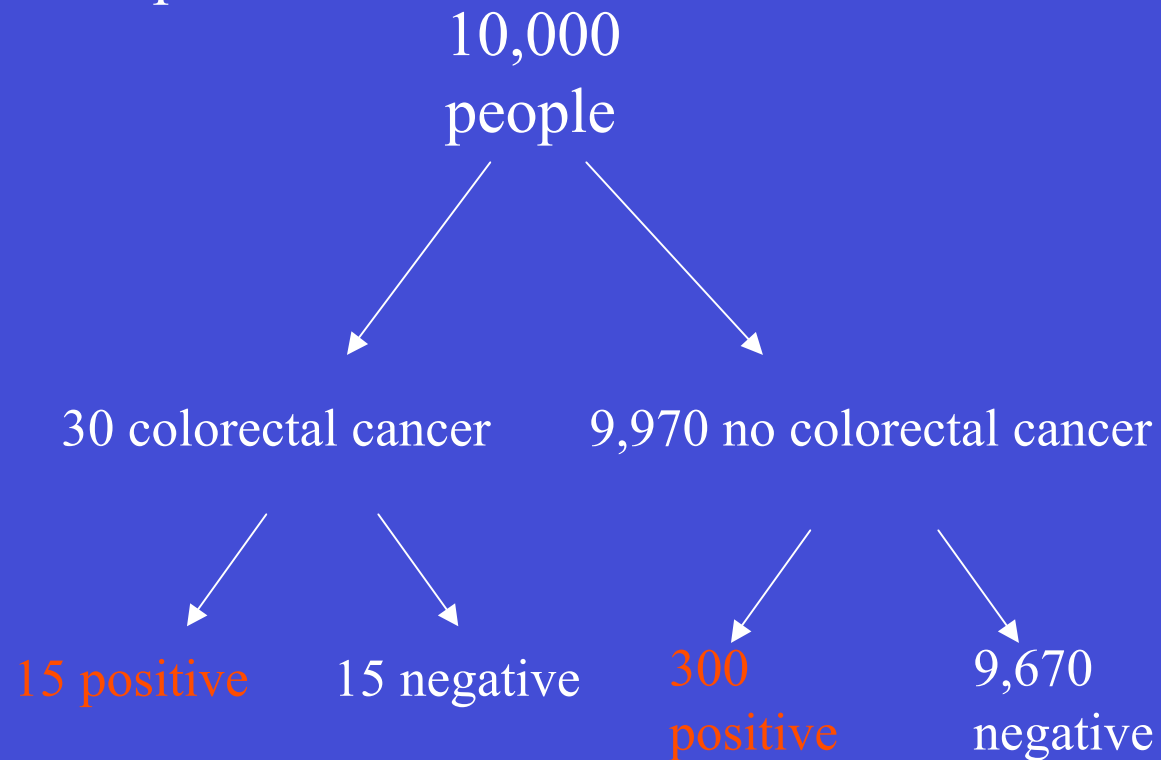
Q: Does FOBT reduce the incidence of CRC?
NEJM. 2000;343:1603-7

Incidence of CRC at 18 years



- 46,551 pts, 18 y f/u; 52% female; 91% f/u. 75% compliance
- *Incidence of cancer after 18 years*
- CER 0.39%, EER 0.32%
- NNT 1428
- ARR 0.07%
- RRR 18%

The Hemoccult problem

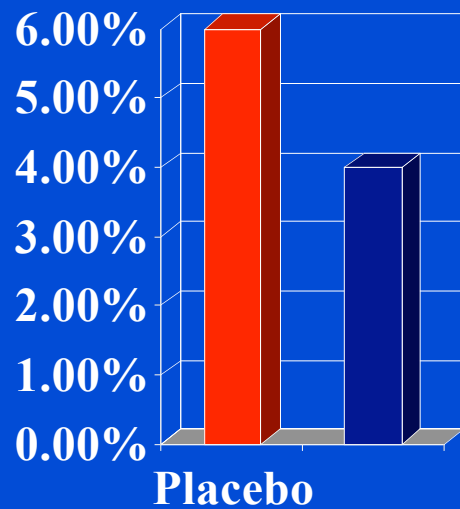


Thus the probability of having cancer when the test is positive is $15/315$, or **4.8%**

Do statins lower the risk of cardiac events (primary prevention?)

AFCAPS/TexCAPS JAMA, 1998,279:1615-22

Composite endpoint



- 6605 pts; 85% male; chol 180-264 mg/dl, HDL <45 mg/dl; f/u 5.2 yrs
- fatal/nonfatal MI, ACS, sudden death
- CER 6%, EER 4%
- NNT 50 (33-97)
- RRR 37% (21-50)

In the works....

- The *General Internal Medicine Evidence Based Resource*
 - Web access
 - PDA compatible

EBM Resources: Summary

- When you're looking for evidence on which to base specific patient care decisions, you can read and fully evaluate every article on your subject of interest.
- Or you could employ the resources that do the study reviews and filtering for you:
 - The Cochrane Database of Systematic Reviews
 - The ACP Journal Club
 - DARE

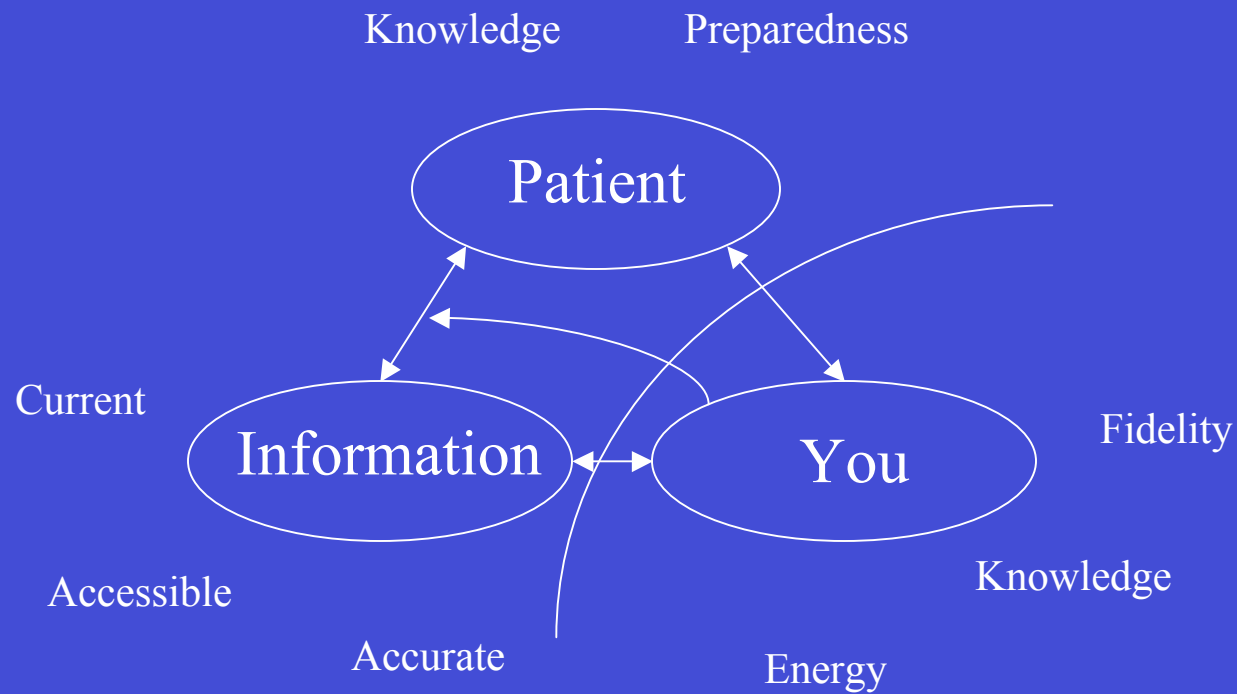
Summary, contd.

- When reviews are not available, you can craft search strategies in MEDLINE to limit your search to the evidence-producing studies.
- For overviews of broader topics, use the tools that summarize the evidence:
 - UpToDate
 - eMedicine
 - National Guideline Clearinghouse
 - et. al.

Self assessment

- What questions do I want to ask?
- Do I know how to access the resources?
- Do I know how to interpret the information?
- Can I explain the answer to a colleague or patient?
- Ask!
- Access!
- Assess!
- Apply!

The Encounter Paradigm



Thank you!

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