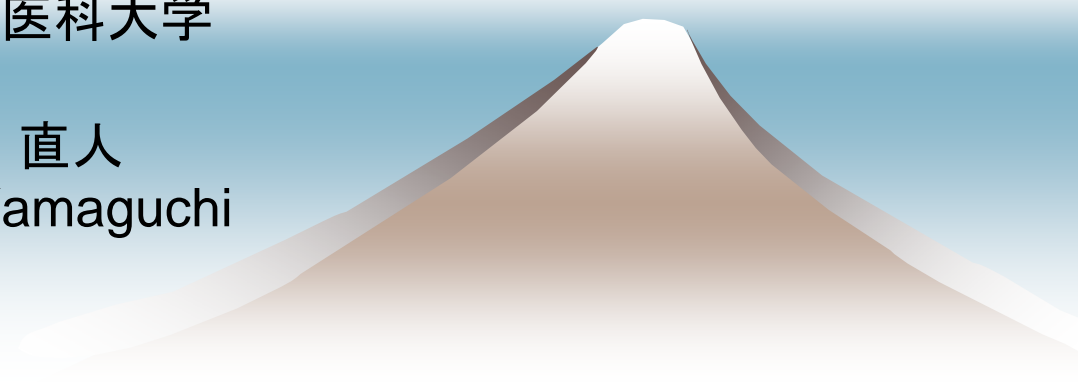


日本の診療ガイドラインの作成と活用の現状

Development and Implementation of  
Clinical Practice Guidelines  
in Japan

(財)日本医療機能評価機構  
東京女子医科大学

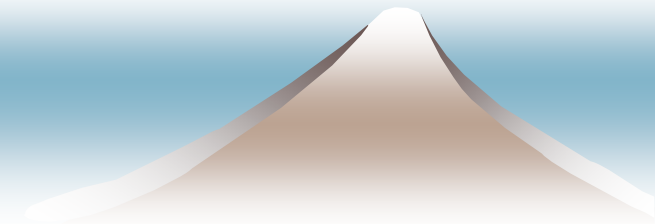
山口 直人  
Naohito Yamaguchi



# MHLW Initiative

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- ◆ Ministry of Health, Labor and Welfare (MHLW) took the initiative to implement the evidence-based medicine in Japan
  - Primarily aiming at quality assurance
  - But also, economical incentive working



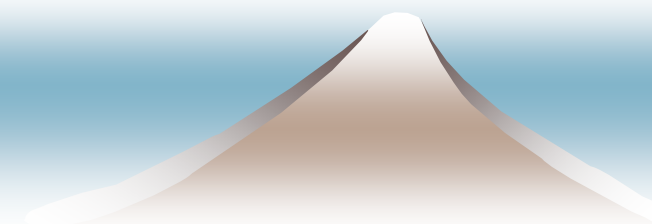
# MHLW Initiative 2

---

- ◆ MHLW started supporting the development of clinical practice guidelines (CPG) in 1999.
  - To implement EBM in Japan
  - 23 diseases were selected primarily based on disease burden (but also with some political pressures)

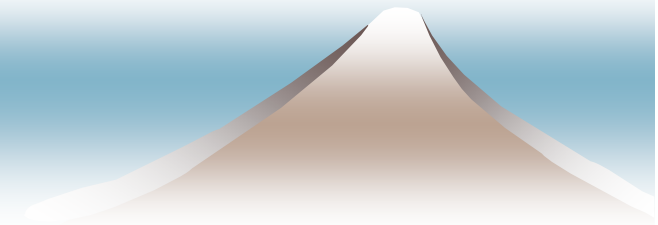
# Selected diseases

- ◆ Acute myocardial infarction
- ◆ Hypertension
- ◆ Allergic rhinitis
- ◆ Bronchial asthma
- ◆ Cataract
- ◆ Diabetes mellitus
- ◆ Alzheimer disease
- ◆ Brain infarction
- ◆ Brain hemorrhage
- ◆ Subarachnoid hemorrhage
- ◆ Gastric ulcer
- ◆ Acute pancreatitis
- ◆ Acute cholecystitis
- ◆ Rheumatoid arthritis
- ◆ Fracture of the femur
- ◆ Lumbar disc hernia
- ◆ Low back pain
- ◆ Benign prostate hypertrophy
- ◆ Incontinence
- ◆ Urinary stone
- ◆ Gastric cancer
- ◆ Liver cancer
- ◆ Lung cancer
- ◆ Breast cancer
- ◆ Prostate cancer



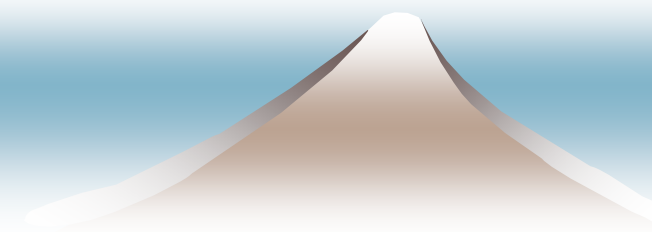
# Implementation of CPG

- ◆ Japan Council for Quality Health Care (JCQHC) launched in 2002 a medical information service to disseminate CPG in Japan.
- ◆ Financial support by MHLW
- ◆ Internet-based distribution of CPG and related information



# Minds

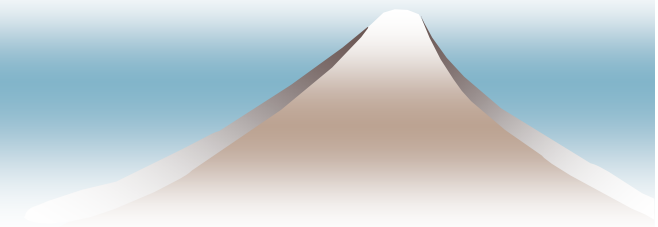
Medical Information Network Distribution Service



# MINDS takes into consideration:

---

- ◆ Stands neutral, avoiding influence of government and providers
- ◆ Based on sound evidence
- ◆ Supports both healthcare professionals and patients
- ◆ Provides information useful for practice
- ◆ Provides up-to-date information
- ◆ Appreciates feedback from users

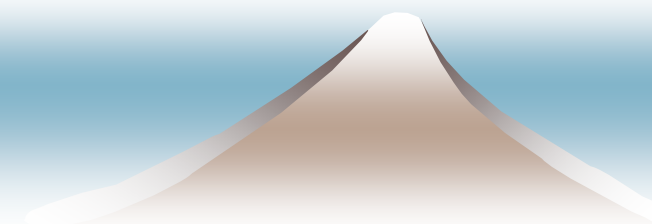


# CPG on MINDS

- ◆ Gastric ulcer ◎
- ◆ Acute myocardial infarction ◎
- ◆ Subarachnoid hemorrhage ◎
- ◆ Bronchial asthma ◎
- ◆ cataract ◎
- ◆ Acute pancreatitis ○
- ◆ Diabetes mellitus ○
- ◆ Lung cancer ○
- ◆ Brain infarct ○
- ◆ Brain hemorrhage ○

◎ For healthcare professionals and for patients

○ For health care professionals





# Top page to login (registered member users and guest users)

**Minds**  
Medical Information Network Distribution Service

医療情報サービス  
厚生労働科学研究費補助金により試験公開中

- ▶ Mindsについて
- ▶ Mindsの使い方
- ▶ 情報提供者について

「診療ガイドライン」  
をご覧になるには  
この下のボタンをクリック!!

**Mindsユーザー**  
の方はこちら **START▶**

**ゲスト**  
の方はこちら **START▶**

[Mindsユーザーになるには▶▶](#)

Mindsは**無料**で  
ご利用になれます。  
登録すると**メリット**があります。

**診療ガイドライン**

- ▶ [診療ガイドライン・各種医療情報はこちら](#)

**お知らせ**

- ▶ [『胃潰瘍』『急性心筋梗塞』の“一般向け”診療ガイドラインを公開しました](#)
- ▶ [『クモ膜下出血』の“一般向け”診療ガイドラインを公開しました](#)
- ▶ [「医療提供者向け情報START」ボタンをクリックしてもページが表示されない場合について](#)

[お知らせの一覧を全て表示▶▶](#)

**利用条件**

Mindsをご利用になる際には、下記の利用条件についてご確認ください。

- ▶ [個人情報の取り扱い](#)
- ▶ [プライバシーポリシー](#)
- ▶ [サービス利用規約](#)
- ▶ [免責条項](#)

[ヘルプ](#) ▶ [お問い合わせ](#)

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# Visual interface to help patients find easily what they want to look at

The screenshot shows the 'Minds' website interface. At the top, there is a navigation bar with links for 'ヘルプ', 'サイトマップ', and 'トップページ'. A user login area shows 'yamaguchiさん' and a 'ログアウト' button. Below the navigation bar, a '疾患選択' (Disease Selection) section is active. It contains the text '対象とする疾患を選択してください。' (Please select the disease you are interested in.) and a link '過去のガイドラインを選択する' (Select past guidelines). A central human silhouette is surrounded by two columns of organ system categories, each with a right-pointing arrow:

- Left column: 脳神経, 眼・耳鼻咽喉, 呼吸器, 循環器, 乳腺・婦人科, 消化器・肝胆膵, 泌尿器
- Right column: 内分泌, 運動器, 全身性, がん, その他

At the bottom of the page, there is a footer with links for '個人情報の取り扱い', 'プライバシーポリシー', 'サービス利用規約', '免責条項', and 'お問い合わせ'. Below these links is the logo for the Japan Council for Quality Health Care and the text '財団法人日本医療機能評価機構 copyright 2005 Japan Council for Quality Health Care. All Rights Reserved.'

# Database selection

Medical Information Network Distribution Service

ヘルプ サイトマップ トップページ

yamaguchiさん 登録変更 ログアウト

疾患切替 クモ膜下出血

データベース切替 データベースを選択してください

参照 検索

データベース切替:どの画面からでも上記プルダウンから他のデータベースを選択して、切替えることができます。  
詳しくは、[Mindsツアー](#)をご覧ください。

医療提供者向け情報

診療ガイドライン

- ▶ 「科学的根拠に基づくクモ膜下出血診療ガイドラインの策定に関する研究」平成13年度研究報告書/ガイドライン(用文献(2001年まで)簡易版抄録を掲載)

[厚生科学研究作成班編/医療提供者向け](#)

Minds PLUS+

- ▶ Mindsオリジナルコンテンツ「Mindsアブストラクト」を掲載

[MindsPLUS/医療提供者向け](#)

一般向け情報

診療ガイドライン

- ▶ 「科学的根拠に基づくクモ膜下出血診療ガイドラインの策定に関する研究」平成13年度研究報告書

[厚生科学研究作成班編/一般向け](#)

データベースの説明

Mindsでは、上記のように最大4つ(医療提供者向け情報「診療ガイドライン」「MindsPLUS」/ 一般向け情報「診療ガイドライン」「MindsPLUS」)にカテゴリ分けされたそれぞれの情報を、データベースとしています。\*疾患により、カテゴリー、データベースの数が異なる場合があります。

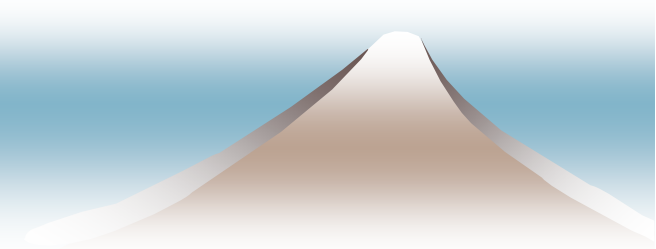
[ページの先頭へ戻る](#)

個人情報の取り扱い | プライバシーポリシー | サービス利用規約 | 免責事項 | お問い合わせ

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# MINDS Contents

- ◆ For healthcare professionals
  - CPG
  - MINDS PLUS (contents provided by MINDS)
    - MINDS Abstract (of latest RCTs)
    - Cochrane CDSR Abstracts translated into Japanese
    - CPG reviews (of oversea CPGs)
    - Topics
- ◆ For patients/public
  - CPG
  - MINDS PLUS
    - What's in CPG for healthcare professionals
    - Medical terminology glossaries



# Reading CPG

The screenshot shows the Minds website interface. At the top left is the logo "Minds" with the tagline "Medical Information Network Distribution Service". To the right are navigation buttons for "投稿" (投稿: 診療質問, ケースレポート), user information for "yamaguchiさん" (登録変更, ログアウト), and a dropdown menu for "疾患切替" (胃潰瘍). Below this is a search bar and a "データベース切替" menu (厚生科学研究作成班編/医療向け). The left sidebar contains a tree view of the site's structure, with "2 出血性潰瘍診療指針" selected. The main content area has tabs for "ガイドライン" and "引用文献". The title is "2 出血性潰瘍診療指針". Below the title is a sub-section "2 内科的治療". Underneath is a list item "[1 ガイドラインによる診療指針]" followed by a text box containing the following text: "出血性胃潰瘍に対する治療は、出血部が明らかな場合は内視鏡的止血法をまず行い、絶食下に胃酸分泌抑制薬の経静脈的投与を行う。出血部が同定できない時は胃酸分泌抑制薬を第一選択とする。絶食期間は基本的に3日とし、止血確認後にH. pylori感染陽性例には除菌治療も考慮する。しかし、プロトンポンプ阻害薬投与時はH. pylori感染診断には適していないので、投与中止後に診断を行う。". Below this is another list item "[2 フローチャート]" followed by a flowchart. The flowchart consists of three boxes: "内視鏡的止血治療" (Endoscopic hemostatic treatment) -> "絶食 (3日間、グレードB) 補液 胃酸分泌抑制薬 (グレードB) (経静脈的) ●プロトンポンプ阻害薬 ●H<sub>2</sub>受容体拮抗薬" (Fasting (3 days, Grade B) Fluids PPI (Grade B) (intravenous) ●PPI ●H<sub>2</sub>RA) -> "H. pylori除菌 (グレードB)" (H. pylori eradication (Grade B)).

個人情報の取り扱い | プライバシーポリシー | サービス利用規約 | 免責条項 | お問い合わせ

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# List of references cited in CPG

Minds 医療情報サービス  
Medical Information Network Distribution Service

ヘルプ yamaguchiさん 登録変更 ログアウト

投稿: 診療質問 ケースレポート

疾患切替 胃潰瘍

データベース切替 厚生科学研究作成班編/医療向け

参照 検索

診療ガイドライン-解説-

- 1 フローチャート解説
- 2 出血性潰瘍診療指
  - 2-1 内視鏡的治
  - 2-2 内科的治療
- 3 *H. pylori* 除菌治療
- 4 非除菌治療
- 5 維持治療
- 6 NSAID潰瘍
- 7 メタアナリシス
- 8 医療経済的評価
- 参考文献
- 診療ガイドラインの作成と

ガイドライン 引用文献

18件中1~10件表示 次△

一括	著者	タイトル(原タイトル)/研究デザイン/出典	発行年
<input type="checkbox"/>	Wong SKH/Yu LM/Lam YH/et al.	<a href="#">Prediction of therapeutic failure after adrenaline injection plus heater probe treatment in patients with bleeding peptic ulcer</a> // Gut50巻 Page322-5	2002
<input type="checkbox"/>	Gisbert JP/Gonzalez L/Calvet X/et al.	<a href="#">Proton pump inhibitors versus H2-antagonists: a meta-analysis of their efficacy in treating bleeding peptic ulcer</a> // Aliment Pharmacol Ther15巻 Page917-26	2001
<input type="checkbox"/>	Sharma VK/Sahal AV/Corder FA/et al.	<a href="#">Helicobacter pylori eradication is superior to ulcer healing with or without maintenance therapy to prevent further ulcer hemorrhage</a> // Aliment Pharmacol Ther15巻 Page1939-47	2001
<input type="checkbox"/>	Lai KC/Hui WM/Wong WM/et al.	<a href="#">Treatment of Helicobacter pylori in patients with duodenal ulcer hemorrhage-a long-term randomized, controlled study</a> // Am J Gastroenterol95巻 Page2225-32	2000
<input type="checkbox"/>	Lau JYW/Sung JJY/Lee KKC/et al.	<a href="#">Effect of intravenous omeprazole on recurrent bleeding after endoscopic treatment of bleeding peptic ulcers</a> // N Engl J Med343巻 Page310-6	2000
<input type="checkbox"/>	Lin HJ/Lo WC/Lee FY/et al.	<a href="#">A prospective randomized comparative trial showing that omeprazole prevents rebleeding in patients with bleeding peptic ulcer after successful endoscopic therapy</a> // Arch Intern Med158巻 Page54-8	1998
<input type="checkbox"/>	de Ledinghen V/Beau P/Mannant PR/et al.	<a href="#">When should patients with bleeding peptic ulcer resume oral intake? A randomized controlled study</a> // Gastroenterol Clin Biol22巻 Page282-5	1998
<input type="checkbox"/>	Riemann JF/Schilling D/Schauwecker P/et al.	<a href="#">Cure with omeprazole plus amoxicillin versus long-term ranitidine therapy in Helicobacter pylori-associated peptic ulcer bleeding</a> // Gastrointest Endosc46巻 Page299-304	1997
<input type="checkbox"/>	Sung JJY/Leung WK/Suen R/et al.	<a href="#">One-week antibiotics versus maintenance acid suppression therapy for Helicobacter pylori-associated peptic ulcer bleeding</a> // Dig Dis Sci42巻 Page2524-8	1997
<input type="checkbox"/>	Hsu PI/Lai KH/Lin XZ/et al.	<a href="#">When to discharge patients with bleeding peptic ulcers: a prospective study of residual risk of recurrent bleeding</a> // Gastrointest Endosc44巻 Page382-7	1996

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- 診療ガイドライン
- 1 フローチャート
- 2 出血性潰瘍
  - 2-1 内視鏡
  - 2-2 内科的
- 3 *H. pylori* 除菌
- 4 非除菌治療
- 5 維持治療
- 6 NSAID潰瘍
- 7 メタアナリシス
- 8 医療経済的
- 参考文献
- 診療ガイドライン

有用と考えられる。しかしながら、科学的根拠となる無作為比較試験の成績は、欧米を中心とした海外のものが主であり、また、十二指腸潰瘍による上部消化管出血として検討されたものが多く、出血性胃潰瘍として検討されたものは少ない(図3)。

### 【3 ステートメント】

- [1] 出血性胃潰瘍の再出血予防には胃酸分泌抑制薬が有効である。グレードB レベルI
- [2] 出血性胃潰瘍の再出血予防にはH<sub>2</sub>受容体拮抗薬が有効である。グレードB、レベルI
- [3] 出血性胃潰瘍の再出血予防にはH<sub>2</sub>受容体拮抗薬が有効である。グレードB、レベルI

### 【4 ステートメント】

(1)出血性胃潰瘍の

1)H<sub>2</sub>受容体拮抗薬が出血性胃潰瘍の

を認めないとする無作為試験のメタ

潰瘍の再出血率が血予防にはH<sub>2</sub>受容

- 診療ガイドライン
- 1 フローチャート
- 2 出血性潰瘍
  - 2-1 内視鏡
  - 2-2 内科的
- 3 *H. pylori* 除菌
- 4 非除菌治療
- 5 維持治療
- 6 NSAID潰瘍
- 7 メタアナリシス
- 8 医療経済的
- 参考文献
- 診療ガイドライン

#### ガイドライン 引用文献

MindsID [Society of Gastroenterology and Hepatology](#)

#### Cimetidine and tranexamic acid in the treatment of acute upper-gastrointestinal-tract bleeding

著者: Barer D/Ogilvie A/Henry D/et al.  
出典: N Engl J Med/308巻, 1571-5頁/発行年: 1983年

PMID: [6343868](#) [PubMedヘルプ](#)

#### 研究デザイン

Evidence level : II

#### 対象者

775例(胃潰瘍186例)。

#### 介入(要因曝露)

上部消化管出血に対するトラネキサム酸、シメチジンの効果。

#### エンドポイント(アウトカム)

主要トラネキサム酸、シメチジン投与群にて、死亡率の低下を認めた。再出血率、死亡率に差はなかった。

# Viewing PubMed contents

The screenshot shows the Minds Medical Information Network Distribution Service interface. At the top, there is a navigation bar with the Minds logo and the text "医療情報サービス Medical Information Network Distribution Service". To the right, there are buttons for "投稿" (Submission) with sub-buttons for "診療質問" (Clinical Question) and "ケースレポート" (Case Report), and a user profile for "yamaguchiさん" with "登録変更" (Change Registration) and "ログアウト" (Logout) buttons. Below this, there are dropdown menus for "疾患切替" (Disease Switch) set to "胃潰瘍" (Gastric Ulcer) and "データベース切替" (Database Switch) set to "厚生科学研究作成班編/医療向け" (Ministry of Health Research and Development/For Medical Use).

The main content area features a search bar with "PubMed" selected and a "Search" button. Below the search bar, there is a list of search results. The first result is from "N Engl J Med. 1983 Jun 30;308(26):1571-5." with a "Search" button. The article title is "Cimetidine and tranexamic acid in the treatment of acute upper-gastrointestinal-tract bleeding." The authors listed are Barer D, Ogilvie A, Henry D, Dronfield M, Coggon D, French S, Ellis S, Atkinson M, and Langman M.

The abstract text reads: "We studied the effects of tranexamic acid (an antifibrinolytic agent) and cimetidine on acute upper-gastrointestinal-tract bleeding in a double-blind randomized placebo-controlled trial in 775 patients with hematemesis or melena or both. Mortality was significantly reduced in patients receiving either tranexamic acid (mortality, 6.3 per cent) or cimetidine (7.7 per cent), as compared with patients receiving placebo (13.5 per cent) (P = 0.0092 for tranexamic acid vs. placebo, P = 0.045 for cimetidine vs. placebo). Ninety-nine patients were withdrawn before the code was broken, mainly because their primary illness was considered not to be due to acute upper-gastrointestinal-tract bleeding. Mortality among those withdrawn was high (22 per cent), and their exclusion reduced death rates to 4 per cent in those given tranexamic acid, 8 per cent in those given cimetidine, and 11 per cent in those given placebo (P = 0.0072 for tranexamic acid vs. placebo, P greater than 0.50 for cimetidine vs. placebo). The reduced mortality associated with tranexamic acid was detectable at both participating hospitals and in most of the main subgroups of patients classified according to site of bleeding. However, treatment with this agent was not associated with any decrease in the rate of rebleeding or the need for operation."

Below the abstract, there is a section for "Publication Types:" with a bulleted list: "Clinical Trial" and "Randomized Controlled Trial". The PMID is listed as "PMID: 6343868 [PubMed - indexed for MEDLINE]".

On the right side of the article, there is a "Pubmedヘリンク" (PubMed Link) button and a "Related Articles, Books, LinkOut" section. The text "acute upper-" is visible at the top of this section, and "た。再出血率、死亡率に差" is visible at the bottom.

At the bottom of the page, there is a "Help" link and a copyright notice: "copyright 2005, Japan Council for Quality Health Care. All Rights Reserved."



# **Evidence Based Medicine and Policy in the United States**

**Harold C. Sox, MD, MACP**

**Editor**

**Annals of Internal Medicine**

# My experience

- **ACP Clinical Efficacy Assessment Subcommittee (1988-91)**
- **US Preventive Services Task Force (1990-1996)**
- **Medicare Coverage Advisory Committee (1999-2003)**
- **Several Institute of Medicine Committees**

**Evidence-based medicine is the conscientious, explicit, and judicious use of current best evidence in making decisions about the care of patients.**

**Sackett et al. BMJ. 1996;312:71-72.**

# POLICY DEFINED

**Policy: something you do every time**

# Types of policy

- **Clinical policy: a routine practice**
  - e.g. mammography in women aged 50-69 years
  - **Example:** US Preventive Services Task Force
- **Administrative policy**
  - e.g. Medicare covers PET scanning for staging lung cancer
  - **Example:** Medicare Coverage Advisory Committee

# EBM and policy



- **Policy-makers use EBM**
  - Guidelines: USPSTF
  - Coverage policy:
    - Center for Medicare Services
    - Blue Cross-Blue Shield

# EBM and policy



- **Physicians use evidence-based policies**
  - Example: practice guidelines from the US Preventive Services Task Force

# EBM and policy



- **Searching for best evidence takes time; doctors are busy.**
- **Arguably most EBM occurs when**
  - physicians follow evidence-based practice guidelines
  - Physicians have to follow evidence-based policies (such as coverage policy)



**How is clinical policy made  
in the U.S. ?**

**The body of evidence**



**Systematic review**



**Policy**

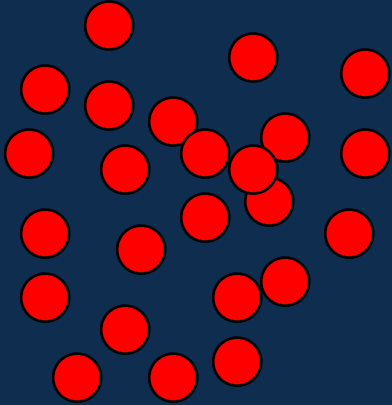
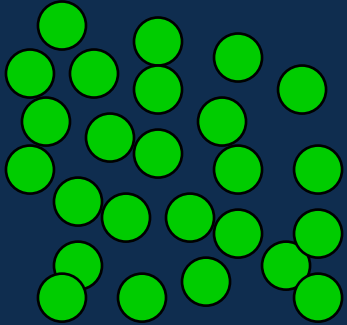
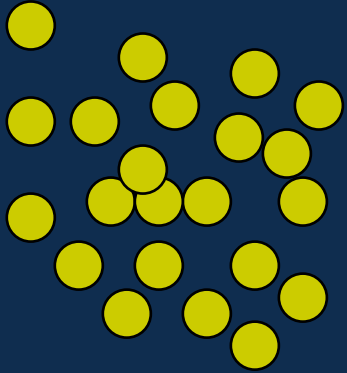
- Practice guidelines
- Performance measures
- Insurance coverage

**AHRQ  
Evidence-  
Based  
Practice  
Centers**

- **USPSTF**
- ACP
- NIH
- BC
- **CMS**
- **IOM**

**Where does a body of evidence  
come from?**

- = Positive trial
- = Negative trial
- = inconclusive trial

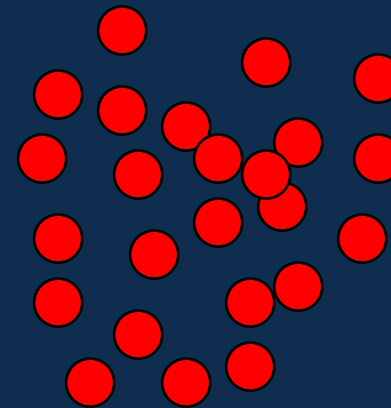
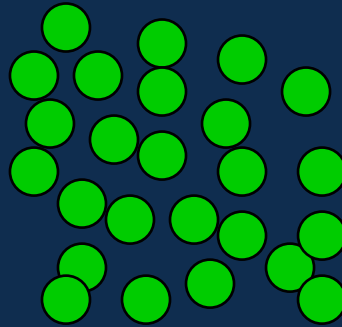
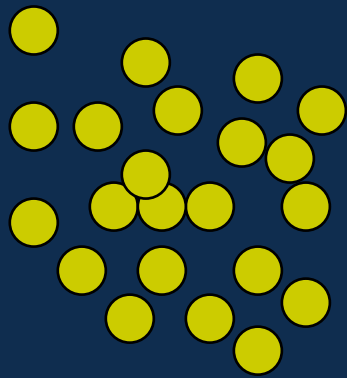


**The body of evidence**



?

- = Positive trial
- = Negative trial
- = inconclusive trial



**The body of evidence**



**Clinical policy**

# Summary of evidence: how to do it

# A systematic review

- **Characteristics of a systematic review**
  - Exhaustive search for research reports
  - Identify reports that meet inclusion criteria
  - Extract data → evidence table
  - Evaluate quality of each included study
  - Test for homogeneity of results
    - **Homogeneous: OK to combine studies**
    - **Heterogeneous: not OK to combine studies**
  - Report results (Forest plot)

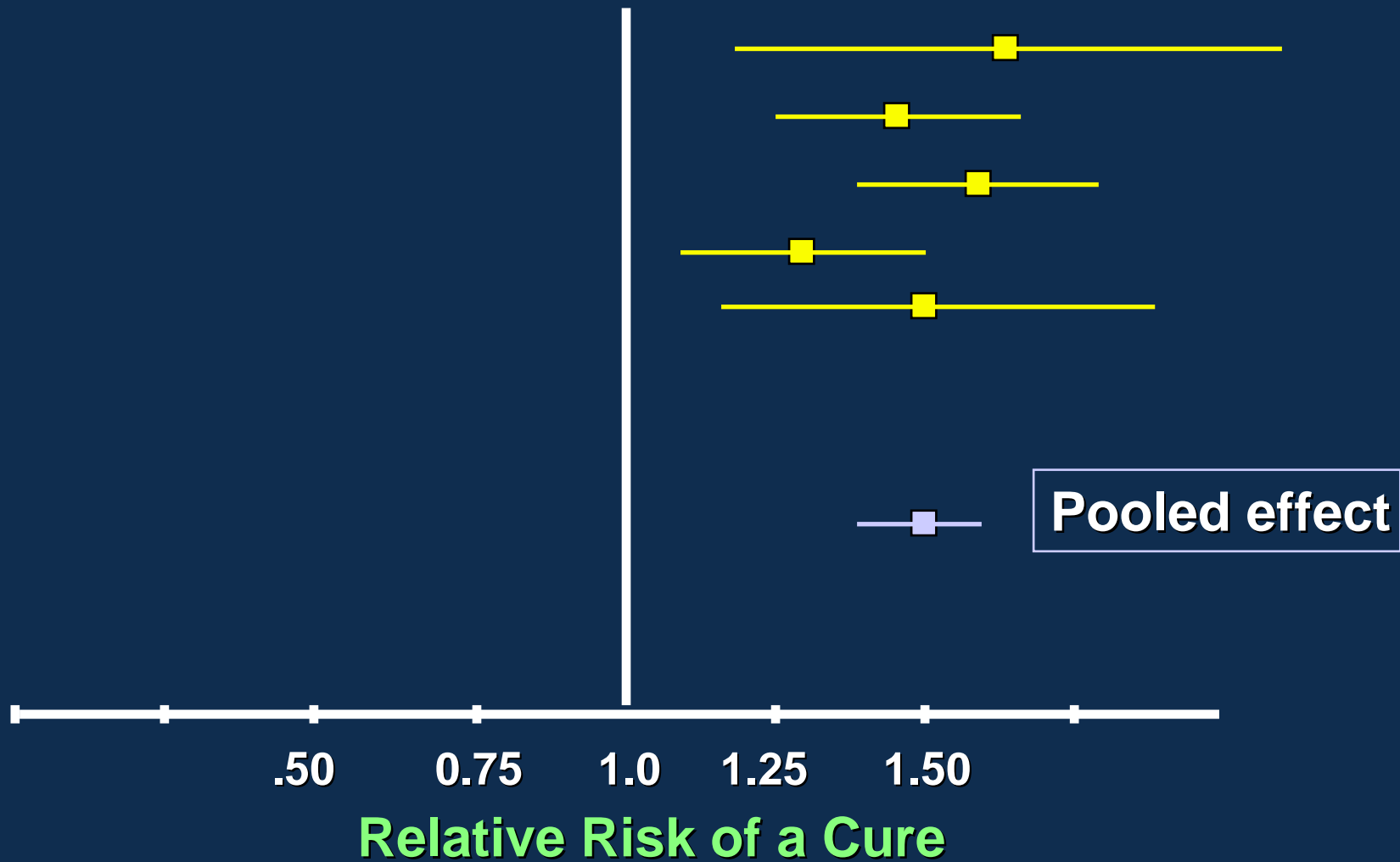
# An evidence table

	<b>Study population</b>	<b>No. of patients</b>	<b>Inter-vention</b>	<b>Primary outcome</b>
<b>Study 1</b>				
<b>Study 2</b>				
<b>Study 3</b>				
<b>Study 4</b>				



# A Forest plot

Published studies



# The US Preventive Services Task Force

# History of USPSTF

- **1976 - Canadian Task Force on PHE**
- **1984 - USPSTF established by PHS**
- **1989 - *Guide to Clinical Preventive Services***
- **1996 - 2<sup>nd</sup> Edition of *Guide* (over 200 interventions, 70 conditions)**
- **2001 - 3<sup>rd</sup> USPSTF begins release of recommendations**
  - To be published on the web and in journals (e.g. *Annals of Internal Medicine*)

Courtesy of the USPSFT (reformatted)

# USPSTF Composition

- **Government support, but independent**
- **Experts in primary care, prevention, research**
- **Family medicine, internal medicine, pediatrics, obstetrics/gynecology, nursing, preventive medicine**
- **Scientific support from one EPC**
- **Officials from medical societies and Federal agencies attend meetings**

Courtesy of the USPSTF (reformatted)

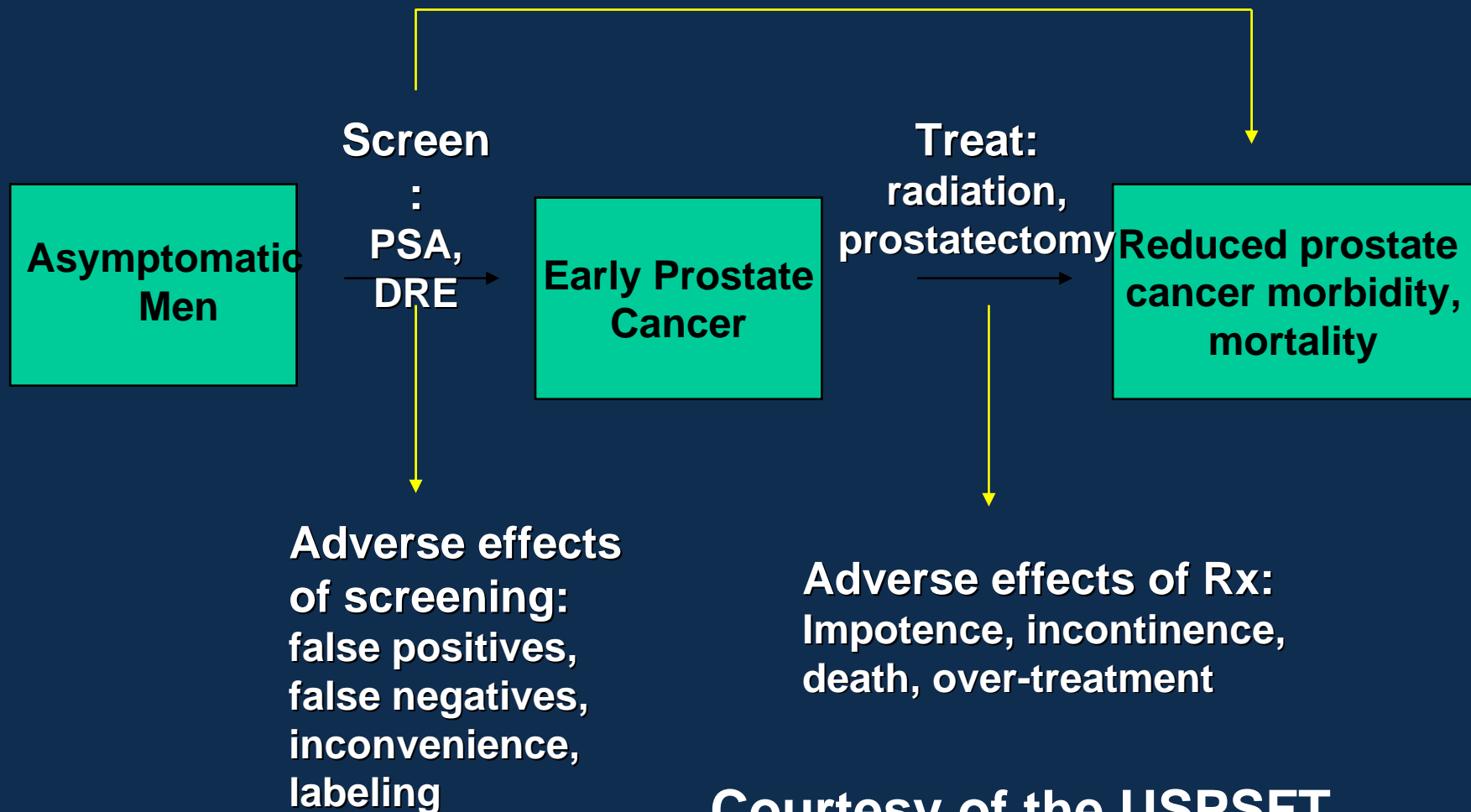
# USPSTF Methodology

- **Define outcomes of interest**
- **Create analytic framework**
  - Defines key questions to answer
- **Systematic review for each key question**
- **Evaluate quality of individual studies**
  - base conclusions on best studies
- **Consider balance of benefits and harms**

Courtesy of the USPSFT (revised)

# Analytic Framework

## Example: Prostate Cancer



Courtesy of the USPSFT

# Wording of Recommendations

## A - Strongly recommend

good evidence, benefits substantially outweigh harms

## B - Recommend

at least fair evidence, benefits outweigh harms

## C - USPSTF makes no recommendation

fair to good evidence, benefits and harms closely balanced

## D - Recommend against routine use

ineffective or harms outweigh potential benefits

Courtesy of the USPSFT (reformatted)

# **I - Insufficient Evidence to Recommend For or Against**

- **Lack of evidence on clinical outcomes**
- **Poor quality of existing studies**
- **Good quality studies with conflicting results**

**Confidence interval on effect size includes clinically important benefits and harms**



## **USPSTF example:**

- **Chemoprophylaxis of breast cancer**
- **Illustrates variability of the balance of harms and benefits**

# Chemoprophylaxis of breast cancer

- **Estrogens are an important risk factor for breast cancer**
  - Early menarche, late menopause
  - Older at first pregnancy, few or no pregnancies
  - Post-menopausal estrogen for >5 years increases risk 1.4x

# Chemoprophylaxis of breast cancer

- **Anti-estrogens reduce breast cancer**
- **Tamoxifen**
  - estrogen-like effect on uterus
  - Anti-estrogen effect on breast
- **Adjuvant treatment of breast CA with tamoxifen -->**
  - half the risk of breast CA in the contra-lateral breast
- **Reduces risk of DCIS --> invasive CA**

# Randomized trials of anti-estrogens

			Breast cancers /1000 woman yrs		
Study (n)	Drug	Breast CA type	Placebo	Active	P value
BCPT (13,175)	T	Invasive	6.8	3.4	<.00001
MORE (7705)	R	Invasive	4.3	1.5	<.001
UK (2471)	T	All	5.0	4.7	.8
Italian (5408)	T	All	2.3	2.1	.64

# Adverse events in the Breast Cancer Prevention Trial

Adverse Event	Cumulative rate / 1000 women		Relative risk (95% CI)
	Placebo	Active	
Endometrial CA	0.91	2.30	2.53 (1.35-4.97)
Stroke	0.92	1.45	1.59 (.93-2.77)
Pulmonary embolism	0.23	0.69	3.0 (1.15-9.27)
DVT	0.84	1.34	1.60 (.91-2.86)

# Balance of harms and benefits

- **Harms**

- Relatively small in number but serious
- Affect all patients

- **Benefits**

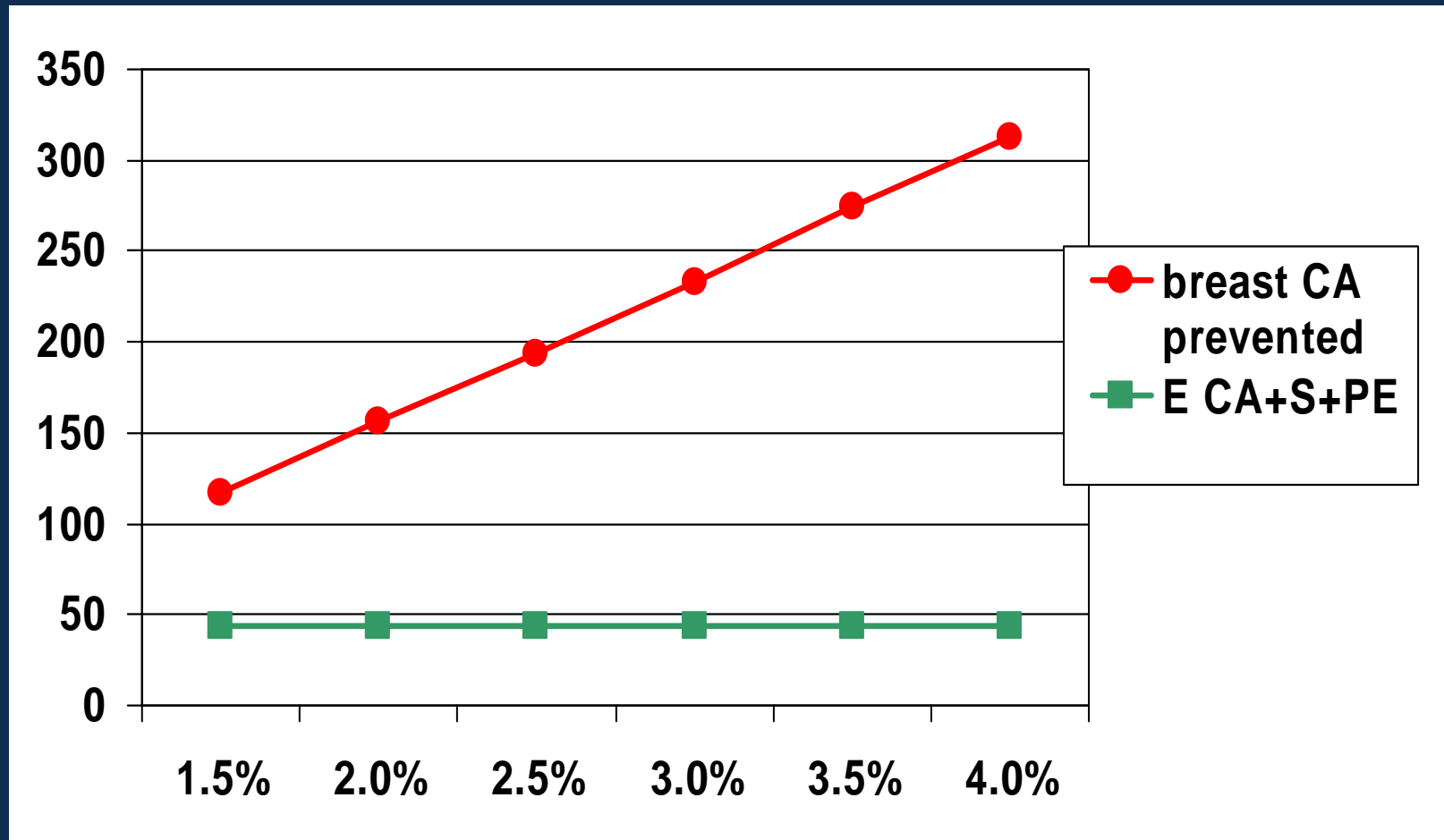
- Substantial absolute reduction in risk of breast CA
- Affect only patients destined to get breast CA

- **Balance of harms and benefits**

- Shifts toward net benefit as risk of breast CA increases
- Shifts toward net harm as risk of adverse effects increases

# Effect of chemoprophylaxis: age 40-49

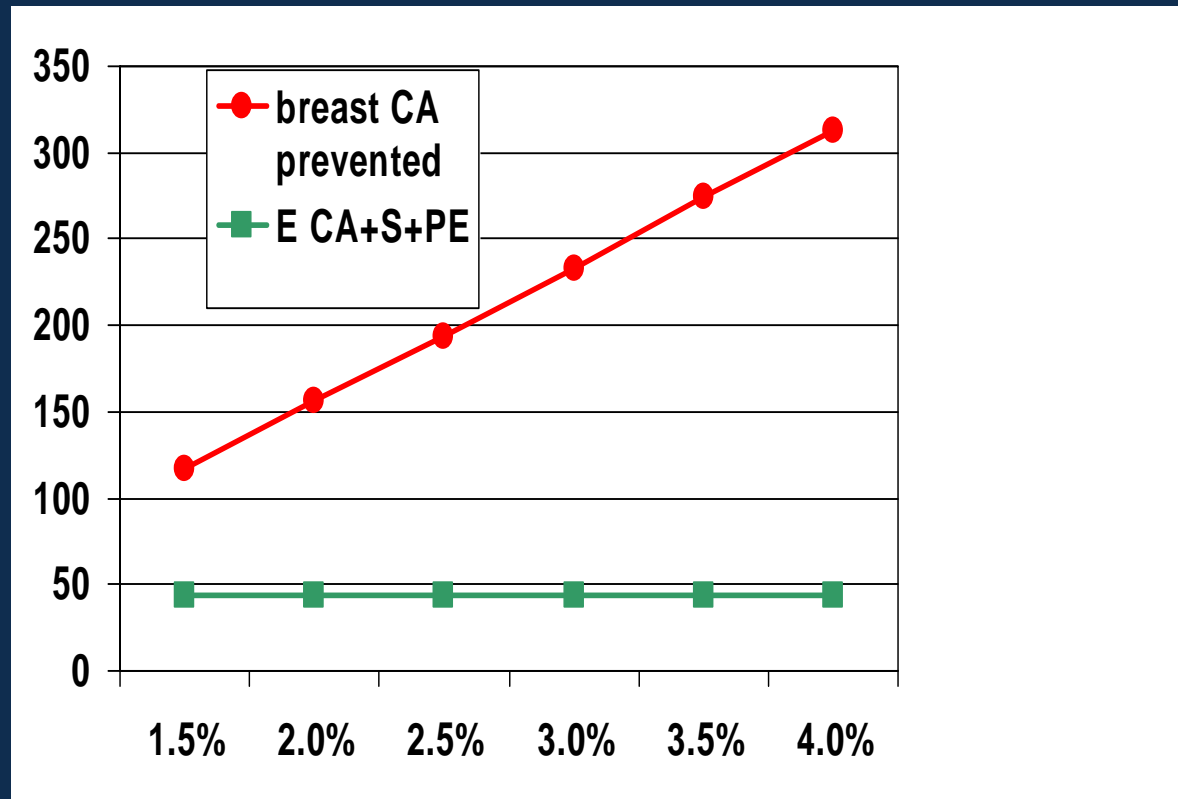
Events per 10,000 women treated



Estimated 5-year risk of invasive breast CA

Modified from Gail et al. JNCI Monographs. No. 25,1999.

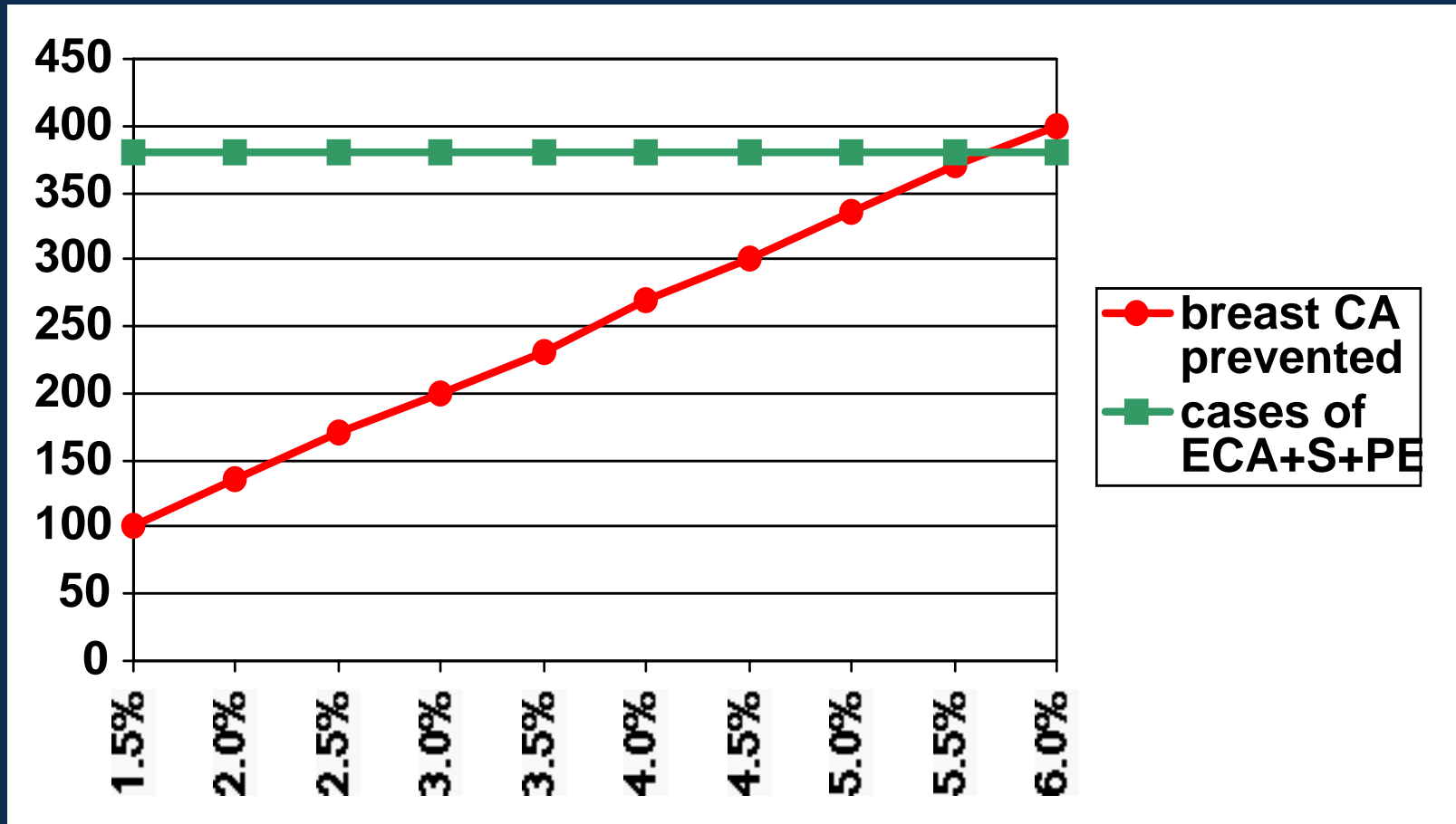
# Should we recommend routine chemoprophylaxis for women aged 40-49 years?





# Effect of chemoprophylaxis: age 60-69

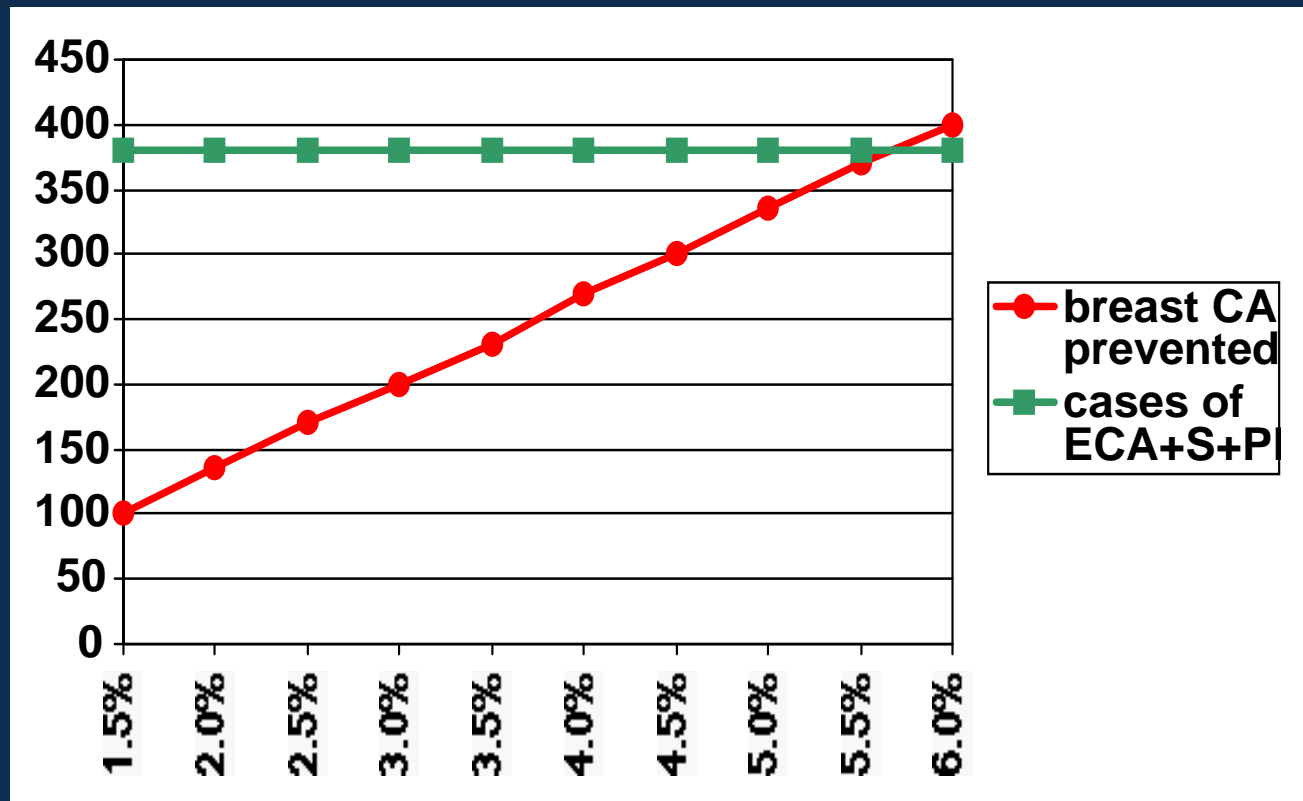
Events per 10,000 women treated



Estimated 5-year risk of invasive breast CA

Modified from Gail et al. JNCI Monographs. No. 25,1999.

# Should we recommend against chemoprophylaxis for all women aged 60-69 years?



# 5- year benefits and harms of tamoxifen in 1000 65 year old women

	- FHx	+FHx
5-year risk	1.5%	3.2%
Invasive breast CA	7-8 avoided	16 avoided
Non-invasive breast CA	2-3 avoided	4-5 avoided
Hip fracture	5 avoided	5 avoided
Endometrial CA	21 caused	21 caused
Stroke, PE, DVT	21 caused	21 caused

**USPSTF Evidence Report, 2001**

# What to recommend?

- **One size does not fit all!**
- **Possible recommendation:**
  - The evidence that prophylaxis works is good
  - Assess risk of breast CA in everyone
  - Explain harms and benefits; show risk +/- prophylaxis
  - Elicit patient's feelings about possible outcomes
    - **Breast cancer**
    - **Adverse events**

# Summary: US Preventive Services Task Force

- **Analytic framework to define key questions**
- **Systematic review of evidence**
- **Graded recommendations**
- **Balance of harms and benefits**
- **Highly respected and influential**
  - Coverage policy
  - Performance measures for health plan accreditation



# EBM and Administrative Policy

- **Medicare Coverage Advisory Committee**
- **Use of principles of EBM to advise Medicare in forming coverage policy**
  - Blue Cross-Blue Shield has a similar system

# The federal government and new health technology

- **The Food and Drug Administration (FDA)**
- **The Center for Medicare Services (CMS)**
- **The Agency for Health Research and Quality (AHRQ)**



# The Agency for Health Research and Quality

- Provides systematic evidence reviews for policy-makers
- Evidence-based Practice Centers (~12)
  - Contract with end-users
  - Customers
    - US Task Force
    - CMS
    - Private sector (e.g. ACP-ASIM)

# The federal government and new technology: the FDA

- **FDA has two main divisions**
  - Drugs
  - Devices
- **Close relationship with industry**
- **Controls market entry**
  - FDA approval required to market product

# Center for Medicare Services

- **CMS purchases medical services**
  - Nation's largest purchaser
  - Effectively controls market entry
- **CMS is concerned with value**
  - Effectiveness relative to existing technology
  - Costs and cost-effectiveness aren't explicitly a concern of CMS

# Coverage policy

- Will CMS pay a hospital for doing a CT scan on a patient?
- Only if CMS makes a coverage policy decision to pay for the CT scan
  - A coverage policy determines payment everywhere in USA

# CMS coverage decision

1. **FDA approval is required**
2. **Decide if CMS already covers item**
3. **Make coverage decision**
  - o (~40 per year)
4. **Assign a billing code**
5. **Decide payment rate**

## CMS pricing policy

- **The Medicare budget is basically a zero-sum game**
  - ICD coverage (\$multi-billion) will result in lower payment for other services/DRGs
- **CMS does not use cost-effectiveness in making coverage decision**
  - “Too slippery in practice, too definition-dependent”
  - Use resource use/consumption to determine price

# FDA and CMS Advisory groups

- **Valuable but**
  - ...resource-intensive
  - Add time to the decision process
- **They use them sparingly**
  - Perhaps 15% of 40 CMS coverage decisions per year use panel advice
  - FDA uses advisory panels mostly for advice on conceptual issues
- **Most approvals are done by staff**

# MCAC history

- **Medicare Coverage Advisory Committee**
- **Established in 1999 by US Congress**



# Medicare Coverage Advisory Committee: Charter

- **Function:**

- “Review and evaluate medical literature on the effectiveness of medical services that are covered by Medicare or are eligible for coverage by Medicare.”
- “Provide technical advice to assist HCFA in determining reasonable and necessary applications of medical services.”

# MCAC history

- **Established in 1999**
- **Published its policies in February 2000.**
  - “Interim Recommendations for Evaluating Effectiveness”
  - Resistance from industry → acceptance
- **The PET scan case (November 2000)**
  - Guidelines for evaluating diagnostic tests

# Factors influencing MCAC evaluation

- **Validity of the evidence**
  - Several concordant RCTs is ideal
  - Observational studies → selection bias and confounders
- **Applicability of the evidence to Medicare patients**
- **Magnitude of the effect**
  - relative to already covered options
- **Diagnostic tests: different model needed**

## Adequacy of the evidence

- **All well-designed observational studies must have a control group**
  - When a panel decides that observational evidence is adequate, it must explain why bias is unlikely
- **A body of evidence consisting solely of studies with no controls is never adequate.**
  - Industry did not like this rule

# What categories of topics are best addressed by MCAC?

- **Advise the coverage group when:**
  - The evidence is complex
  - The topic is controversial
  - The nature of the problem requires a new approach to evaluating the evidence (e.g., Dx tests)

# Process of formulating questions for MCAC to answer

**Choose topic**



**Formulate analytic  
framework**



**Post analytic framework  
on MCAC website for comment**



**Contract with EPC to  
research key questions**

## How should MCAC arrive at recommendations?

- **Use the analytic framework**
- **Evaluate the evidence for each link**
- **The strength of the recommendation is proportional to the strength of evidence at each link**
  - **Missing link → weak recommendation**

# Evaluating diagnostic tests

- **Measures of test performance**
  - Sensitivity, specificity, likelihood ratios
- **These measures do not necessarily imply health effects**
  - Need to measure consequences of test results
- **PET scanning in cancer: a political challenge**
  - → a method for using test performance measures to estimate health effects



**Evaluate studies of  
test performance**



**Test sensitivity and  
specificity**



**Calculate post-test  
probability**



**Does test result  
change probability  
enough to change  
management?**

## ***Example: PET scanning to detect scar recurrence of colon cancer***

- **Is an indurated area near the original incision**
  - scar tissue?
  - a local recurrence of cancer?

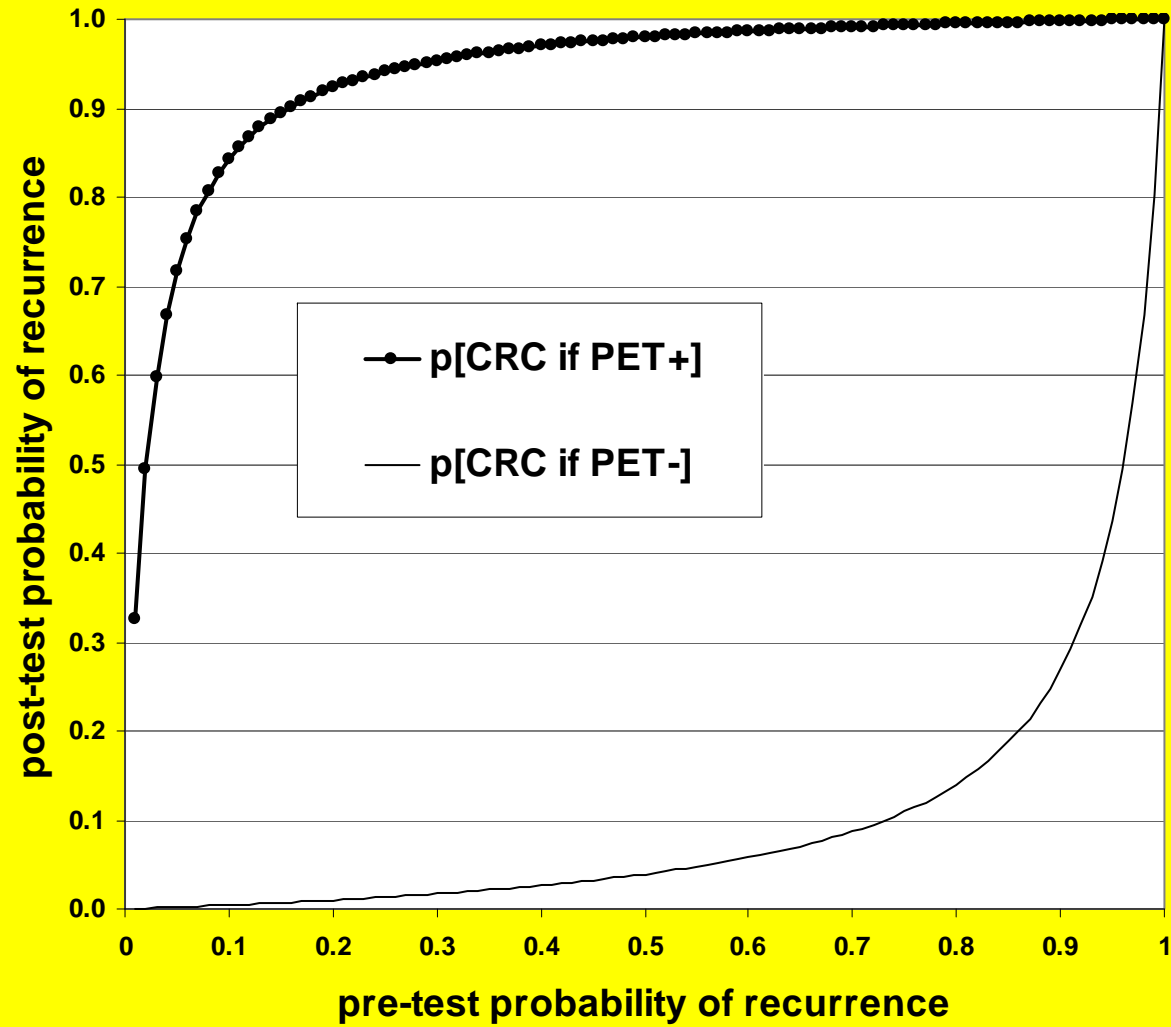
# Studies of PET for local recurrence

- **Study quality:**
  - 5/6 were of patients with suspected local recurrence
  - 0/6 had blinded reading of PET scan
  - 4/6 were prospective
- **Did PET identify CT- patients with recurrence ?**
  - PET had higher sens/spec than CT in 4/4 head to head comparisons of PET and CT
  - 0/6 studies evaluated PET's ability to detect recurrence in CT- patients

# The effect of PET on management

- **Does a negative PET scan lower the probability of recurrence enough to alter the decision to biopsy the mass?**
  - Pre-test probability of recurrence = 0.69
  - Sensitivity of PET = 0.96
  - Specificity of PET = 0.98
- **Use Bayes' theorem to calculate post-test probability of recurrence**

### Post-test probability of recurrent CRC after PET scan of peri-operative scar





# The Institute of Medicine

- **Founded in 1970**
- **Part of the National Academies of the USA (NAS, NAE, and IOM)**
  - founded by President Abraham Lincoln
- **Functions**
  - Election to membership is an honor
  - Advise the government on difficult policy issues

## An IOM study

- **Study sponsor (e.g., US Congress) states tasks of study (the charge)**
- **Convene committee of experts**
- **Do systematic review for each task**
- **Write a report**
  - Describe problem and evidence
  - Make recommendations
  - Explain recommendations
- **Another expert panel reviews report**



# IOM Review process

- **Draft report sent to panel of 12 to 15 reviewers**
- **Monitor and Coordinator of review read reviews and summarize key problems.**
- **Committee changes report to respond to key problems**
- **Monitor and Coordinator evaluate response**
  - Their approval is necessary to release the report

# Review process

- **Assures that the report meets good scientific standards**
  - **Committee can't ignore reasonable criticism**

# Conclusions

- **The principles of EBM**
  - Formulate the question as an hypothesis
  - Search the literature
  - Evaluate the studies
  - Base your conclusions on the best studies
- **apply to health policymaking in the USA**
  - Clinical policy: practice guidelines
  - Administrative policy: coverage decisions

# Timeline of change in the U.S.

<b>1968</b>	<b>RWJ Foundation Clinical Scholars</b>
<b>1980</b>	<b>ACP starts CEA Program</b>
<b>1984</b>	<b>USPSTF begins</b>
<b>1980's</b>	<b>Blue Cross starts tech eval program</b>
<b>1999</b>	<b>CMS starts MCAC → evidence rules</b>
<b>2000</b>	<b>IOM report: 100,000 deaths from errors</b>
<b>2000</b>	<b>AHRQ gets money; starts EPC program</b>
<b>2005</b>	<b>Pay for Performance</b>

# Key causes of change to EBM-based policy in U.S.

- **The capacity to do systematic reviews:**
  - Many physicians who are skilled in critical appraisal of research.
  - Government support to do systematic reviews.
- **Many influential “clients” for practice guidelines.**
  - Insurers, payers, large practices, accreditation organizations
- **National concern about quality of care.**
  - 50,000 to 100,000 deaths per year from errors

**The body of evidence**



**Systematic review**



**Policy**

- Practice guidelines
- Performance measures
- Insurance coverage

**AHRQ  
Evidence-  
Based  
Practice  
Centers**

- **USPSTF**
- ACP
- NIH
- BC
- **CMS**
- **IOM**



# Medicare Coverage Advisory Committee: Charter

- **Function:**

- Review and evaluate medical literature on the effectiveness of medical services that are covered by Medicare or are eligible for coverage by Medicare.
- Provide technical advice to assist CMS in determining reasonable and necessary applications of medical services.



# Interim Recommendations for Evaluating Effectiveness

- **Suggestions about how to evaluate evidence**
  - Adequacy of the evidence
  - Magnitude of benefit
- **Specific procedures for panels to use**

# Evaluation of the evidence

- **Adequacy of evidence**
  - Is the evidence adequate to draw conclusions about effectiveness in routine use in Medicare beneficiaries?
    - **Validity**
    - **General applicability to the population of interest**

# Adequacy of the evidence

- **Bias**

- Does a study systematically over- or underestimate the effect of the intervention because of possible bias in assigning patients to intervention and control groups?

# Adequacy of the evidence

- **Observational studies**
  - Observe patient care in groups whose members are selected or self-select for an intervention
  - Are effects due to the intervention or to other factors that lead to selection to receive the intervention?
  - It is difficult to be confident that biased assembly of intervention and control groups is not responsible for effects.

# Adequacy of the evidence

- **Random allocation of subjects**
  - Eliminates systemic selection bias
  - Random assignment means that intervention and control groups are alike with respect to all variables, measured and unmeasured, except the intervention itself
  - Any observed difference in health outcomes is due to the intervention

# External validity

- **The panels must answer these questions:**
  - Do the results apply to Medicare patients?
  - Do the results apply to the usual practice setting?

## **Size of the health effect**

- **Evidence from well-designed studies must establish how the effectiveness of the new intervention compares to the effectiveness of established interventions**

## Decision on PET

- **A negative PET scan lowers the probability of scar recurrence from 0.69 to 0.08**
- **You would biopsy if  $p[\text{recurrence}]$  was 0.69**
  - Would you biopsy if  $p[\text{recurrence}]$  was 0.08? Or would you observe the patient?
- **The panel was divided on whether to to biopsy.**
  - Therefore, PET could change management
  - the panel advised CMS that PET was useful in managing suspected scar recurrence.



# Categories of effect size

- **Breakthrough technology**
- **More effective**
- **As effective but with advantages**
- **As effective with no advantages**
- **Less effective but with advantages**
- **Less effective with no advantages**
- **Not effective**

# Specific procedures for panels to use

- **Structure of evidence provided to panels**
  - the evidence report: a critical evaluation of published evidence
- **Panel member involvement**
  - Help frame the questions the panel must answer
  - Several members should participate in developing evidence report
  - Several other members should be primary reviewers of the evidence report

# Specific procedures for panels to use

- **Expert review of evidence reports**
- **A panel must explain its conclusions in writing**
  - Will make the process more explicit and accountable
  - Reports will serve as a body of “case law”

What should drive the decision  
when the evidence is incomplete?

**The physician's values?**

**The patient's values?**