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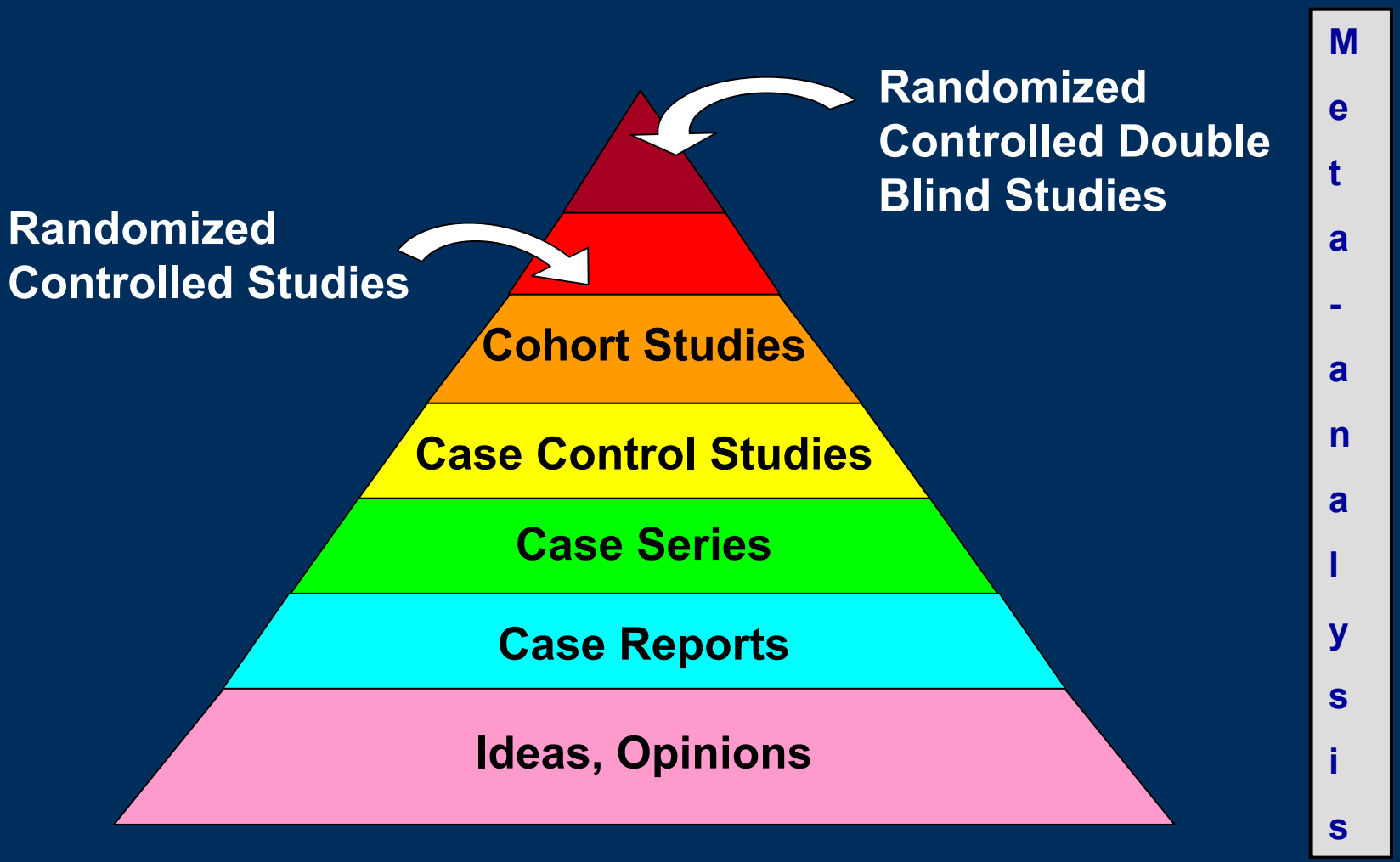
Disclaimer

Levels of Decision Making

Level I: "Would you have this done for yourself or for someone else in your immediate family?" Influenced by one's personal experience with the disease and capacity to deal with risk.

Level II: Physician making a recommendation for his/her patients. Also influenced by prior experience, but the strength of the scientific evidence may play a greater role.

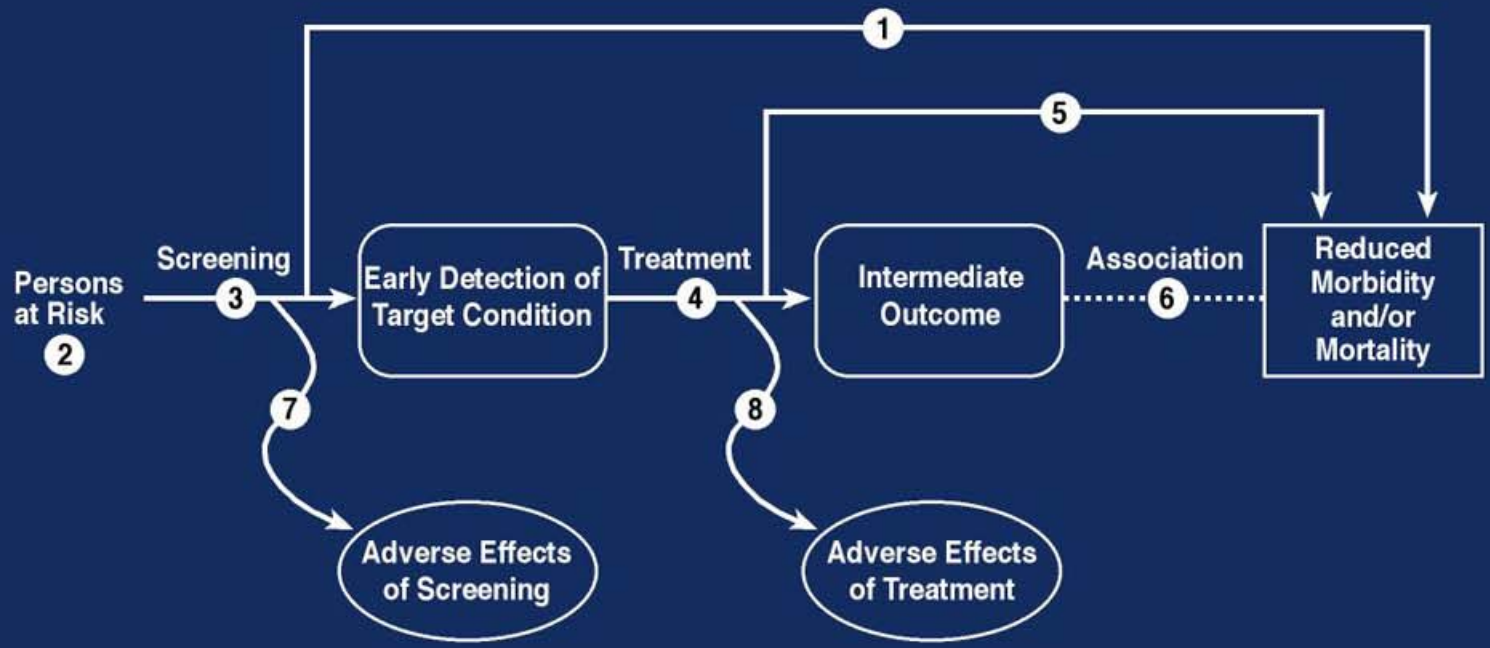
Level III: Across-the-board recommendations for a population. Must be based even more on rigorous assessment of the scientific evidence.


Randomized Controlled Double Blind Studies
Randomized Controlled Studies
Cohort Studies
Case Control Studies
Case Series
Case Reports
Ideas, Opinions
Meta-analysis

"Propositions arrived at purely by logical means are completely empty as regards reality. Because Galileo saw this, and particularly because he drummed it into the scientific world, he is the father of modern physics - indeed of modern science altogether."

Albert Einstein

Analytic Framework (Causal Pathway) for Screening Tests:
U.S. Preventive Services Task Force



R. Harris, Am. J. Prev. Med 2001

Prevention Levels of Evidence

1. Evidence obtained from at least one randomized controlled trial
2. Evidence obtained from controlled trials without randomization
3. Evidence obtained from cohort or case-control analytic studies
4. Evidence obtained from multiple-time series with or without intervention
5. Ecologic (descriptive) studies (e.g., international patterns studies, migration studies)
6. Opinions of respected authorities

Prevention Endpoints

A. Cancer Mortality

B. Cancer Incidence

C. Generally accepted intermediate endpoint (e.g., large adenomatous polyps)

Screening Levels of Evidence

1. Evidence obtained from at least one randomized controlled trial
2. Evidence obtained from controlled trials without randomization
3. Evidence obtained from cohort or case-control analytic studies
4. Evidence obtained from multiple-time series with or without intervention
5. Opinions of respected authorities

Treatment Levels of Evidence

1. Randomized controlled clinical trial(s)
    i. Double-blinded
    ii. Nonblinded
2. Nonrandomized controlled clinical trial(s)
    (e.g., allocation by birth date, chart number, etc.)
3. Case series
    i. Population-based consecutive cases
    ii. Consecutive cases (not population-based)
    iii. Nonconsecutive cases

Treatment End Points

A. Total mortality

B. Cause-specific mortality

C. Carefully assessed quality of life

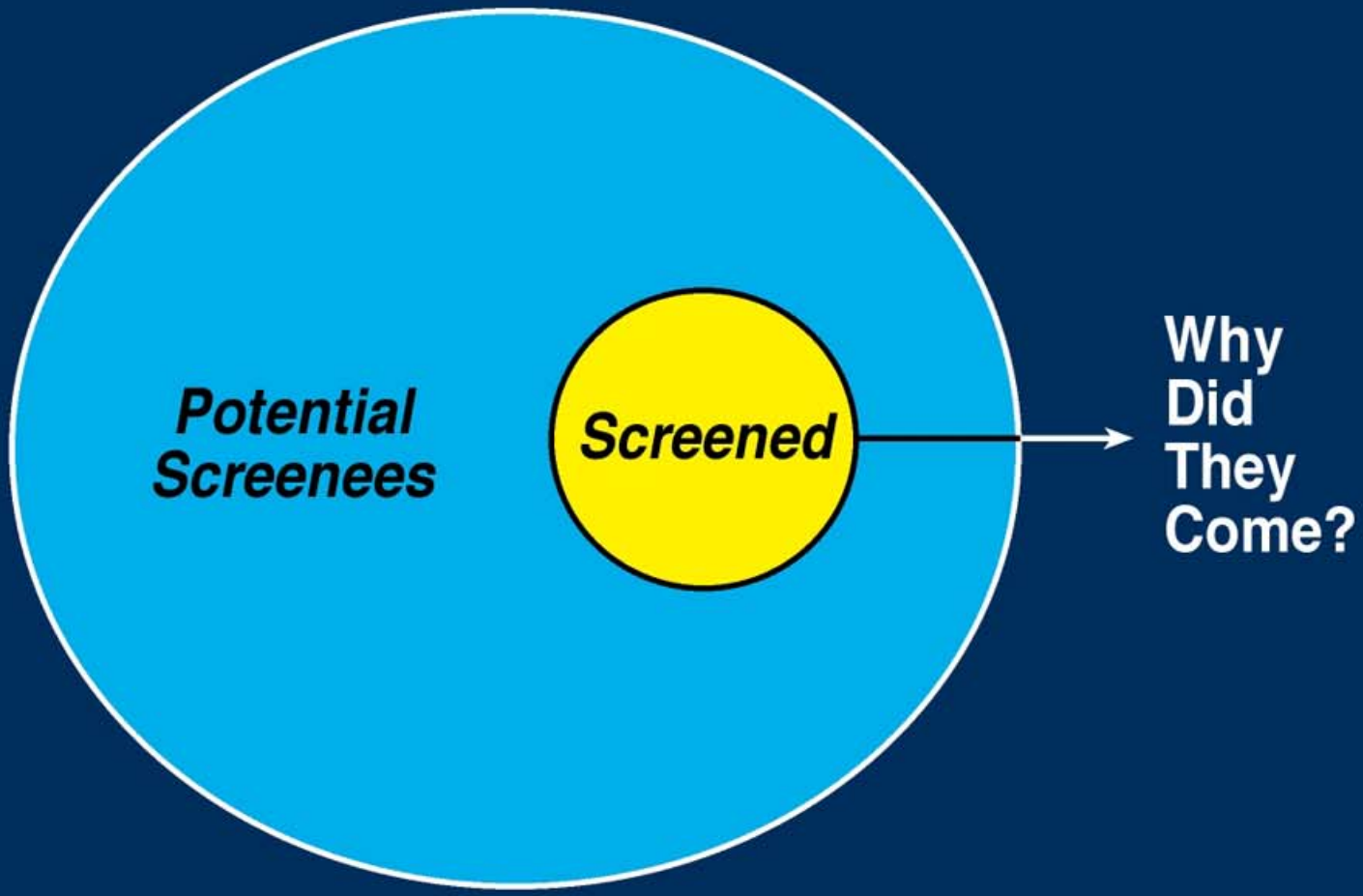
D. Indirect surrogates

   i. Disease-free survival

   ii. Progression-free survival

   iii. Tumor response rate

Selection Bias



Selection Bias in an Ovarian Cancer Screening Program

Design: 5,479 women screened with transabdominal U/S annually x3

Cancer Type	Deaths Expected	Deaths Reported	% Standardized Mortality Rate
Breast	70	71	101%
Ovarian	25	22	90% (ns)
Colorectal	32	19	59%
Stomach	11	4	45%
Lung	59	20	34%
Cervical	9	2	23%
Other	106	82	77%
Total	**312**	**220**	**71%**

(Crayford et al., *Lancet*, 2000)

Relationship of Placebo Adherence to Mortality

5-Year Mortality in Patients Given Clofibrate or Placebo

Adherence	Clofibrate (N=1065)	Placebo (N=2695)
<80%	24.6%	28.2%
	p=.0001	$p=4.7\times10^{-16}$
≥80%	15.0%	15.1%
Total	**18.2%**	**19.4%** (pNS)

Coronary Drug Project Research Group, *NEJM*, 1980

"There is simply no serious scientific alternative to the generation of large-scale randomized evidence."

R. Peto et al.,
J Clin Epidemiol 1995;48:23-40

The Hippocratic Injunction

It is worse for a physician to make a patient worse off than it is not to benefit a patient.


OK, stranger... What's the circumference of the Earth?.. Who wrote "The Odyssey" and "The Iliad?"... What's the average rainfall of the Amazon Basin?
HOTEL
Bart, you fool! You can't shoot first and ask questions later!