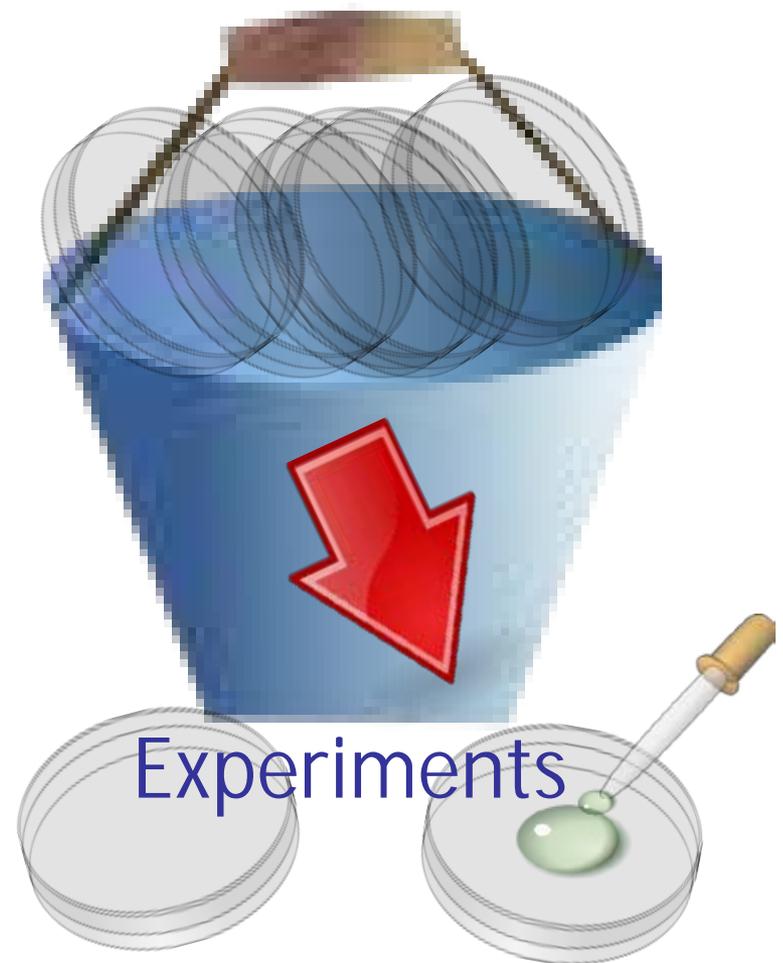


# Study Types: There Are Two Big Buckets



Observations



Experiments

# Randomization...



- Randomized controlled trials (RCTs) utilize randomization in an attempt to create equal groups by distributing prognostic variables across groups
- Eliminates choice
  - Choice often results in confounding
    - Does taking vitamin pills reduce coronary heart disease; or,
    - Are people who take vitamins likely to engage in other healthy behaviors that reduce CHD (aka “the healthy-user effect)?
- Note: “Minimization” is not random, but may be other acceptable method

# Observations versus RCTs



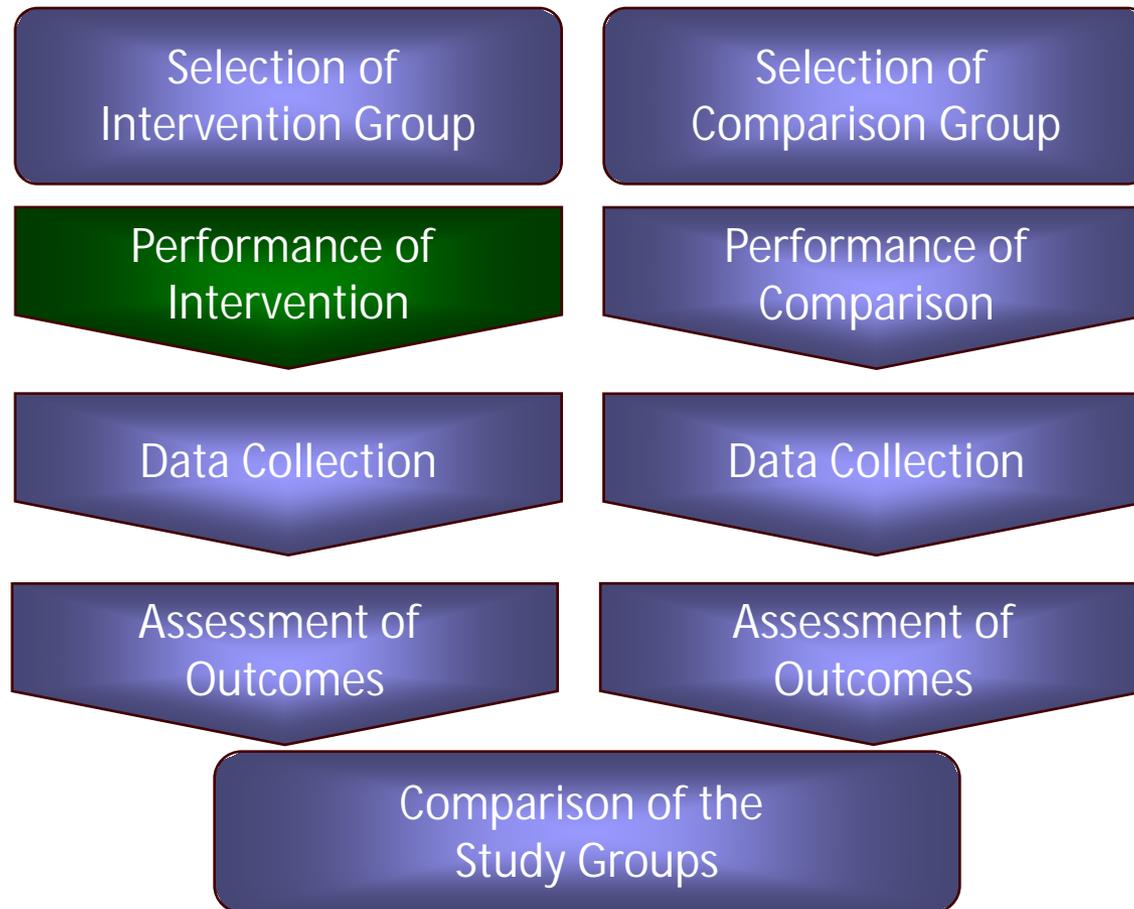
+/-	Study O: Two concurrent groups for study	+/-	Study R: Two concurrent groups for study
	Varying baseline profile		Baseline similar
	Adjusted baseline characteristics		Not adjusted
	Patients' doctors choose intervention		Computer generated random number table determines intervention
	Everyone knows who gets which treatment		No one knows who gets which treatment
	No formal treatment protocol		Formal treatment protocol
	Varying meds use, measurement methods, duration		Med use controlled, uniform measurement methods, duration

# Positive Predictive Values of Various Study Types

Well-done RCT	0.85
Meta-analysis of well-done RCTs	0.85
Meta-analysis of small, inconclusive RCTs	0.41
Well-done epidemiological (observational) study	0.20
Epidemiologic study with threats to validity	0.12
Discovery-oriented exploratory research	0.0010

Ioannidis JPA. Why Most Published Research Findings are False. PLoS Med 2005; 2(8):696-701

# The 4 Stages of Clinical Trial



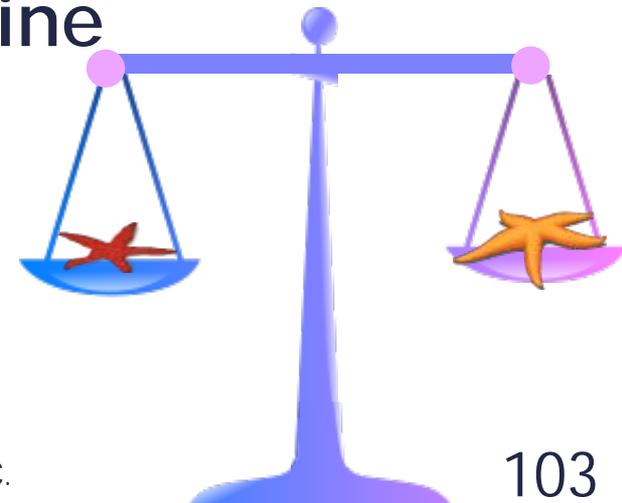
# Who Do You Get & How Do You Get Them Into Their Groups?



Photo by by Pentadact

# Generation of the Sequence For Study Assignment

- Random allocation of study subjects to their groups (minimization may be acceptable) is optimal
- A sequence for assignment is generated
- Random sequencing is optimal
  - Avoids predictability: A A A B A C C B A C
  - Balanced distribution of prognostic variables—“gestalt” via baseline characteristics



# Reporting Example

## Randomization: Generation of Sequence

### IN REALITY

- Randomization was conscientiously and successfully performed.

#### Uncertain Risk of Bias

- No mention  
except in title

#### Acceptable

- A computer-generated list of random numbers was used to allocate patients to groups.
- 

# Blinding the Allocation = “Concealment of Allocation”

- Concealment of the randomization sequence...





# Selection Biases:



## Concealment of Allocation

- Adequate methods for blinding the allocation of subjects to their groups (aka “concealment of allocation”) so that no one can affect assignment to a group
  - + Call-in center, sealed containers ≠ issues with envelopes



VERSUS



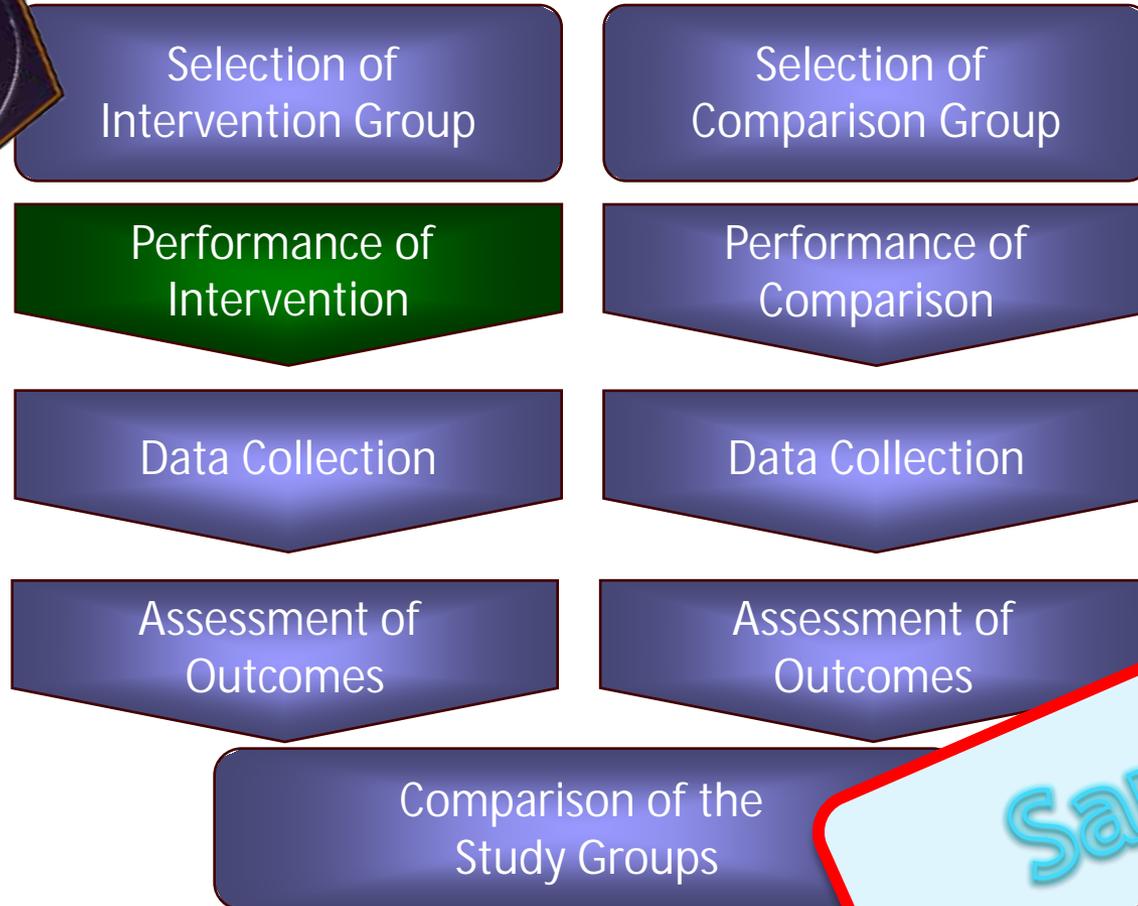
# Can Someone Unblind it?



# Performance Bias Examples

- Execution
- Exposure (e.g., adherence)
- Co-interventions

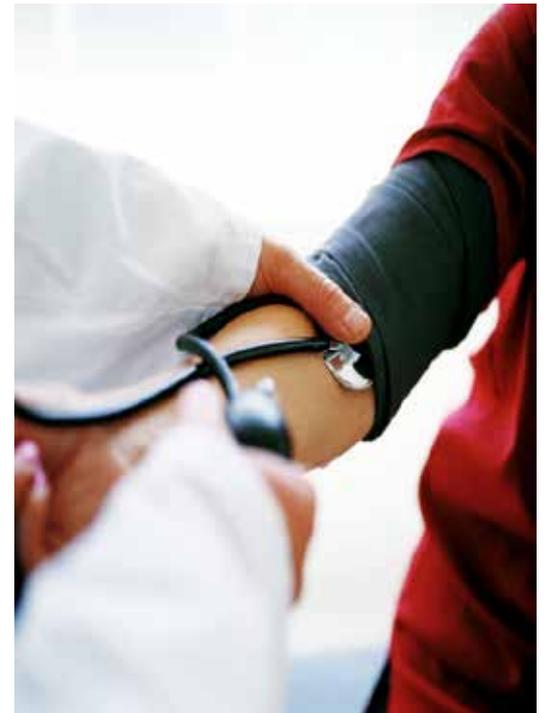
# Except For What Is Being Studied, Any Difference Is A Bias



Same

# Data Collection Biases

- Are measurement methods valid?
  - What information is collected?
  - How is it collected?
  - Is it likely to be accurate?
- “Validated” may not really be valid. You may need to critically appraise the validation study
  - Face Validity: Does it make sense?
  - Content Validity: Does it include all the right stuff?
  - Construct Validity: Is it accurate and dependable?
- Are groups treated the same?
- Might missing data affect the study results è



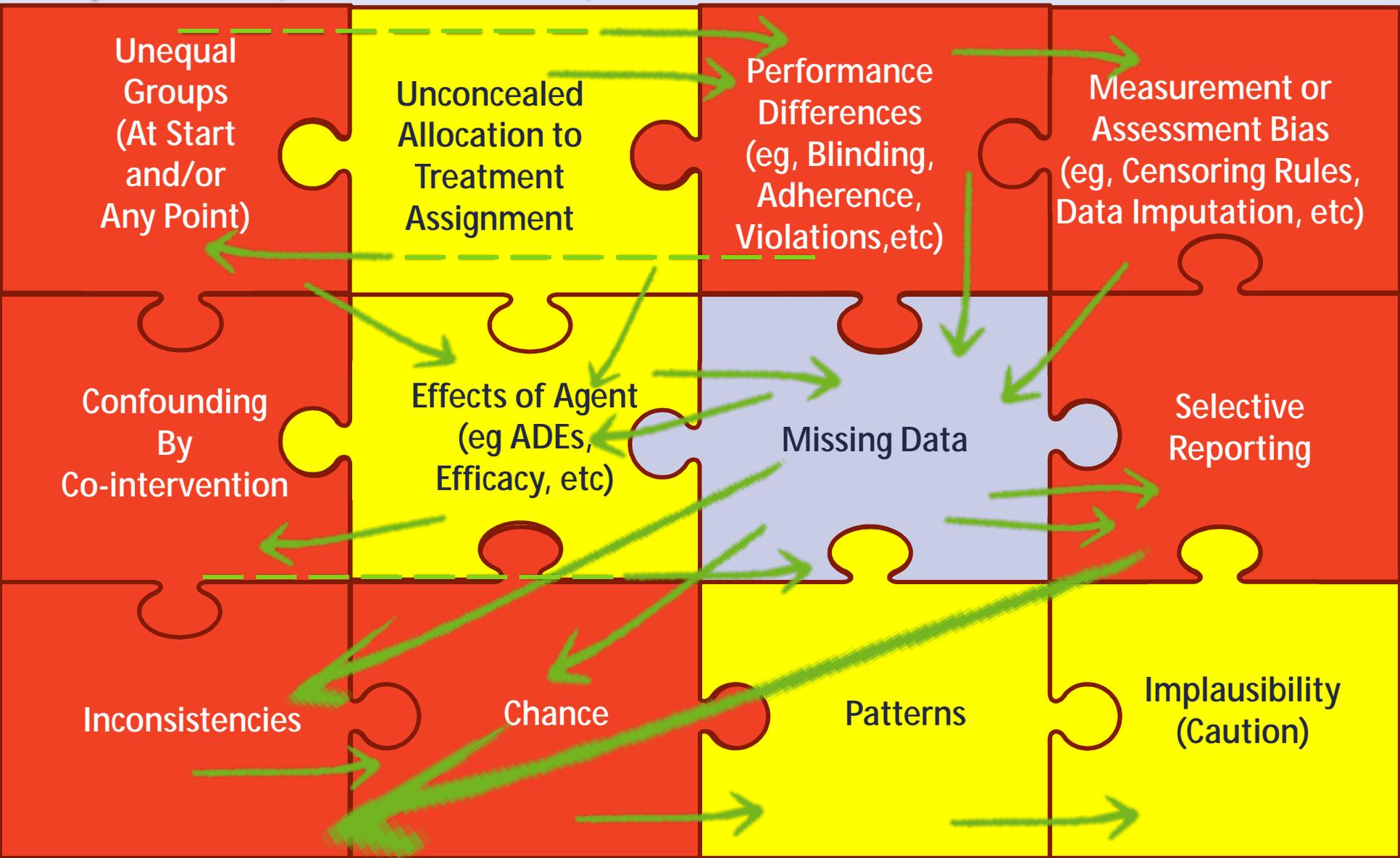
# Attrition Bias

- Given that attrition has occurred, are the study results likely to be true?
  - No clear answers for evaluating and impact
- Look at the contextual elements of the study and reasons for discontinuation and loss
  - Look for clues
  - Loss that is not differential overall, may still result in difference in prognostic variables between groups
  - Might groups be treated differently





# Detective Work: “What Could Possibly Explain (or Refute) the Outcomes?”



# Example: Blinding

- If blinding is not successful, patients may selectively be removed from the study, discontinue the study or be influenced to discontinue
- Balance in numbers attriting might not expose this

*Of course my patient isn't doing well on placebo! I need to get him off this study now...*



# Assessment Bias Examples

- Not blinded
- Invalid assumptions for modeling
- Problems with analysis methods, etc.



# Review 1-Pager Critical Appraisal Essentials



# Meaningful Clinical Benefits Defined

A Quick Tour



# If True, Are The Results Useful?

Meaningful clinical benefit means benefit to patients in 5 areas—

1. Morbidity
2. Mortality
3. Symptom relief
4. Emotional, mental or physical functioning
5. Health-related quality of life

+

**Size of the outcomes**

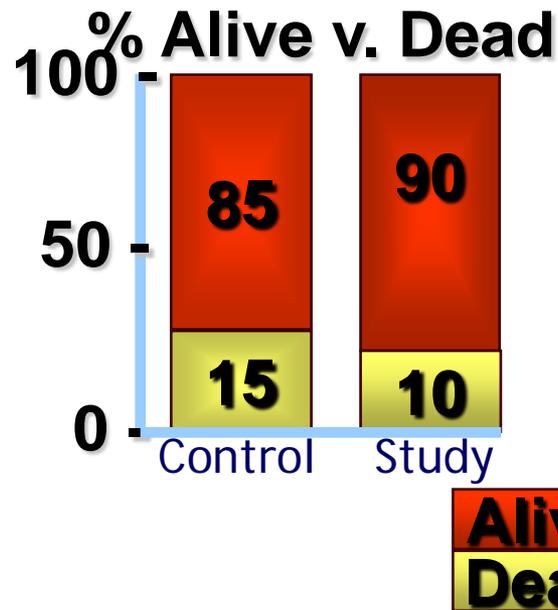


# Let's Talk Group Differences

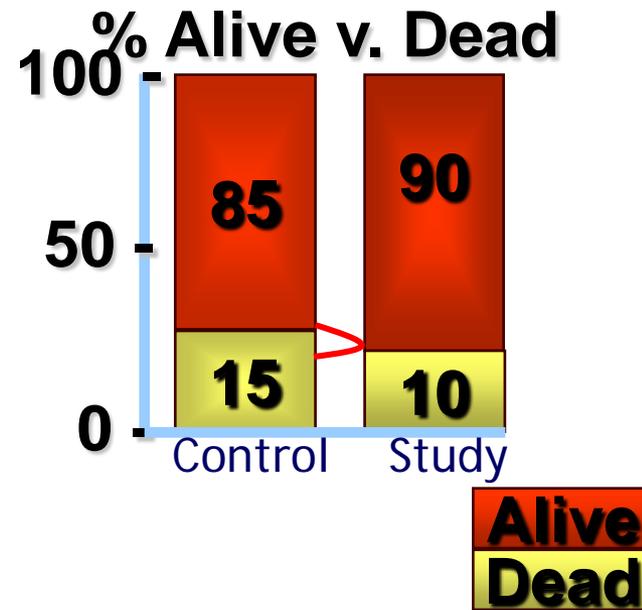
You read in the newspaper that global improvement scores were 30% higher in people with fibromyalgia who exercised compared to patients who did not exercise. What should your first question be, looking strictly at this statement (e.g, besides questioning if the study is valid or other issue not directly stated above)?

# Absolute versus Relative Measures

- Absolute



- Relative



- Actual difference =  
"Absolute Risk Reduction" ARR
- $15\% - 10\% = 5\%$

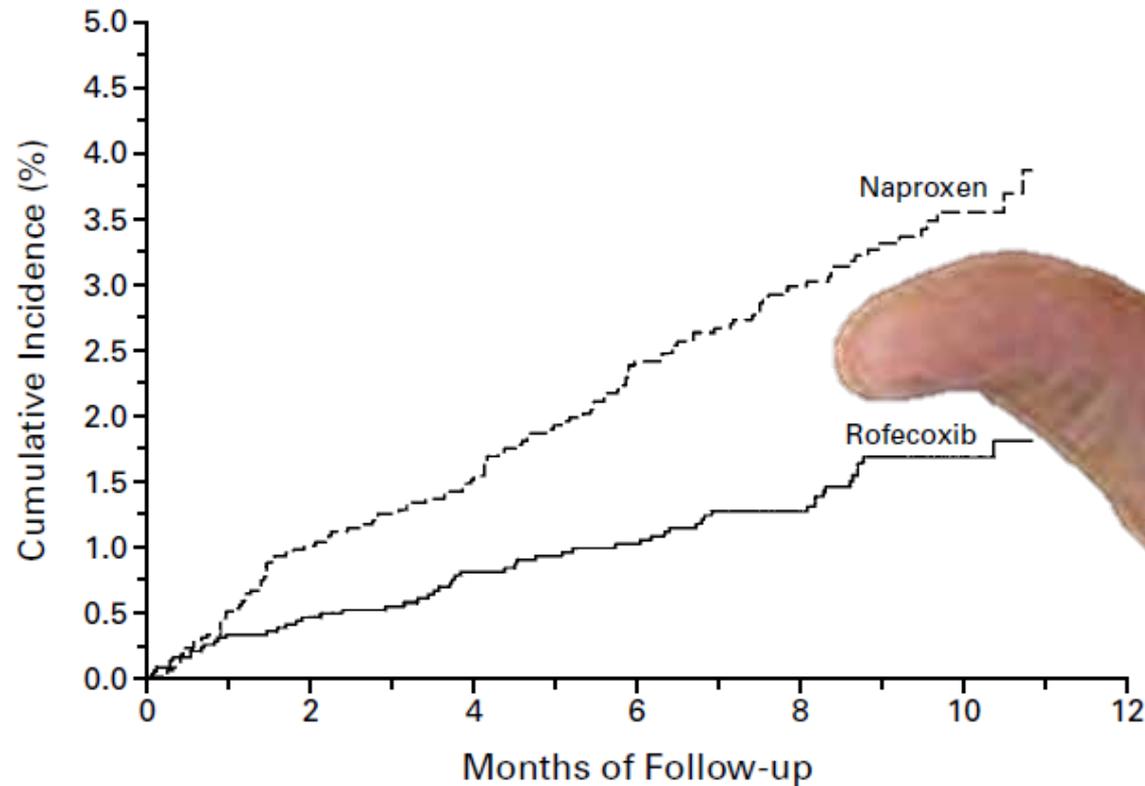
- Relative difference =  
"Relative Risk Reduction" RRR
- 10 is 1/3<sup>rd</sup> smaller than 15 = 33%
- $(15\% - 10\%) / 15\% = 33\%$

# Let's Make a Deal!!!



Kuala Lumpur Malaysia: jubei kibagami from Kuala Lumpur, Malaysia

# There is a Kaplan Meier Curve



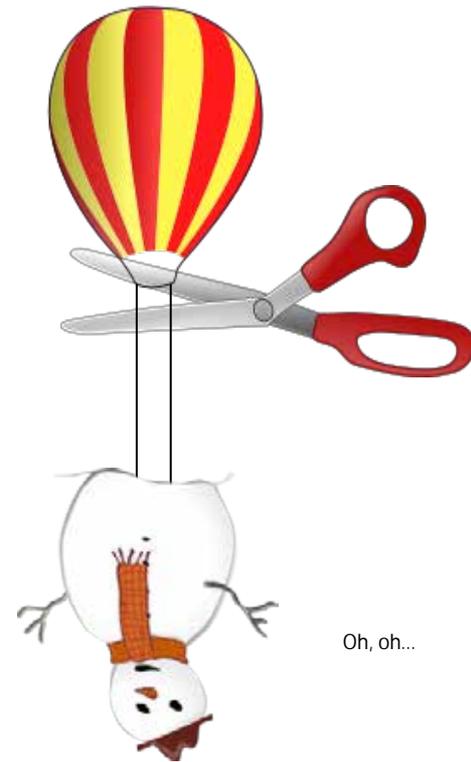
No. AT RISK

Rofecoxib	4047	3641	3402	3180	2806	1073	533
Naproxen	4029	3644	3389	3163	2796	1071	513

**Figure 1.** Cumulative Incidence of the Primary End Point of a Confirmed Upper Gastrointestinal Event among All Randomized Patients.

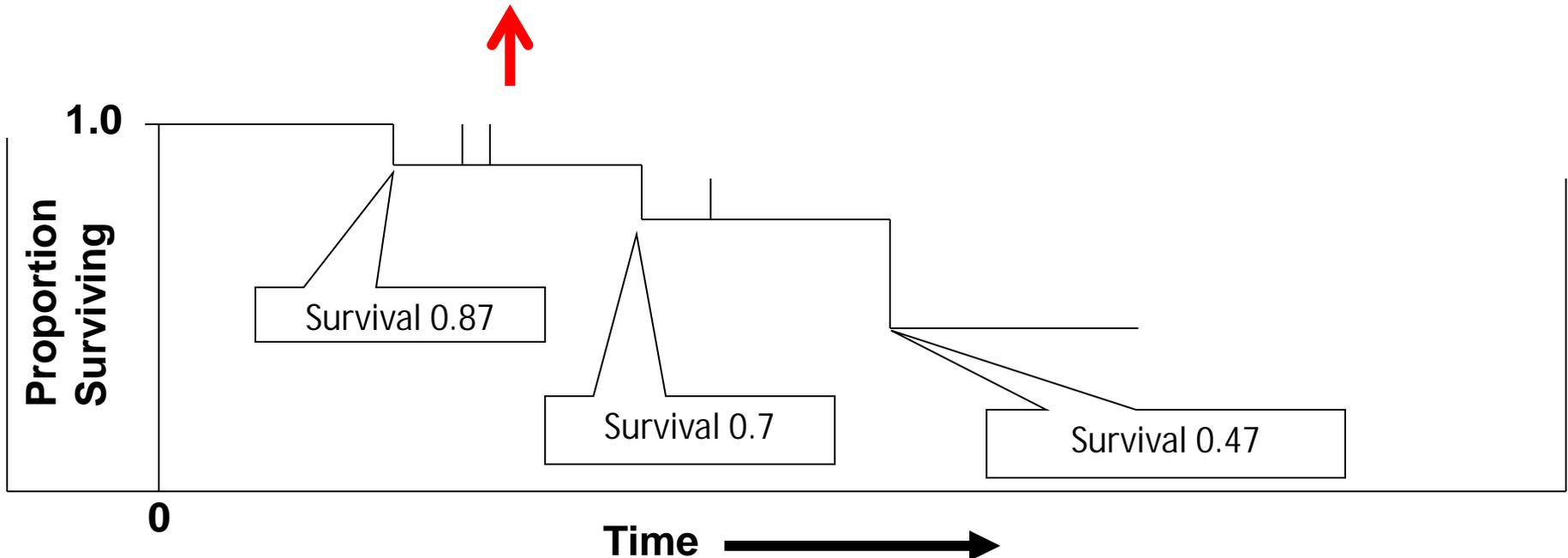
# Censoring

- Censoring is the practice of removing the patient from the curve at a specific point in time
- Examples of censoring
  - Late-entry patients who don't experience the event (administrative censoring)
  - Other reasons determined by the investigators and called "censoring rules" (non-administrative censoring such as lost to follow-up or dying before a non-mortality outcome of interest is reached)
- Censored patients are **assumed**, on average, to have the same risk for the event as non-censored patients



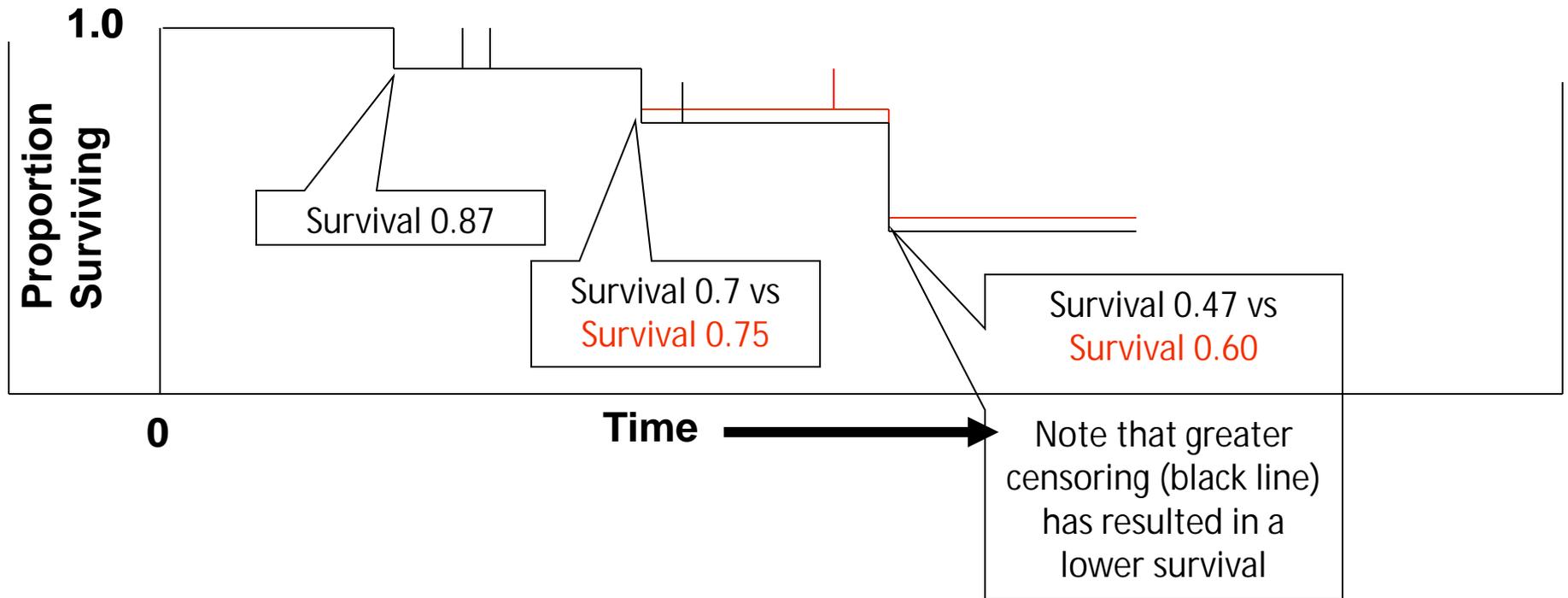
# Kaplan Meier Curve

Time Interval	# Subjects Start	Censored	# Died (or other event)	Subjects in Denom	Subjects Surviving Interval	Cumulative Survival
0-1	8	0	1	8	$7/8=0.87$	0.87
1-2	7	2	1	5	$4/5=0.8$	$0.87*0.8=0.7$
2-3	4	1	1	3	$2/3=0.67$	$0.7*.67 =.47$



# Censoring Changes the Curve

## Comparing the previous two KM Curves



# Safety

- Hard to assess
- Observational data, chance and wording
- Safety population not the same as efficacy
- Selective reporting potential
- Duration issues
- **BEWARE OF NON-SIGNIFICANT FINDINGS!**





# Power Is About People

- In shorthand, people talk about studies being “powered”
- What that means is that you need a sufficient number of people to capture events—this is dependent upon the frequency of events in the population
- If you reach statistical significance, **by definition**, you *had enough people*
- If you **did not** reach statistical significance, you have a question è



# Is It True There Is No Difference?

- Power is about the number of people needed to show a statistically significant difference if there is one
- Scenario: Drug A will harm 1 out of 100 people, but we only studied use of it in 40 people—we missed the one who would have had the outcome

- Drug A



- Placebo



- Conclusion: “There was no difference in safety between the groups.”
- Wrong: The study was insufficiently powered for safety

# Using CIs to Establish Meaningful Clinical Outcomes

- For statistically significant results, is the confidence interval wholly within your judgment for meaningful clinical benefit?
  - Example: You decide you want to see at least a 1 percent reduction in mortality - this is a judgment
  - ARR 2, 95% CI (1,3) meets your requirement for meaningful clinical benefit and, therefore, these results can be considered conclusive (given a 5% margin for the play of chance)

# Adverse Events and CIs

- Authors of RCTs may mislead readers when reporting adverse events, (eg, “Adverse effects were similar in both groups”)
- Example: Lassen et al. PMID: 12049858
  - Authors report, “The 2 groups did not differ in clinically relevant bleeding.”
  - Actual rates for major bleeding: 47/ 1140 (4.1%) fondaparinux vs 32/ 1133 (2.8%) enoxaparin,  $p=0.11$
  - But CIs provide more information: ARI, (95% CI) = 1.3, (-0.21 to 2.8) and since the true difference could be as great as 2.8% (ie, clinically relevant) the authors’ conclusion is misleading
  - Lack of statistically significant difference may be due to Type II error (meaning a power issue or not enough people to show a statistically significant difference if there is one)
  - In this case a systematic review reported a statistically significant increased bleeding rate with fondaparinux vs enoxaprin 96/3616 (2.7%) vs 63/3621 (1.7%), OR (95% CI) 1.54 (1.11 to 2.16), Bounemeux PMID: 14615118

# Cochrane Handbook

## 9.7 Common errors in reaching conclusions

A common mistake when there is inconclusive evidence is to confuse 'no evidence of an effect' with 'evidence of no effect'. When there is inconclusive evidence, it is wrong to claim that it shows that an intervention has 'no effect' or is 'no different' from the control intervention. It is safer to report the data, with a confidence interval, as being compatible with either a reduction or an increase in the outcome. When there is a 'positive' but statistically non-significant trend authors commonly describe this as 'promising', whereas a 'negative' effect of the same magnitude is not commonly described as a 'warning sign'. Authors should be careful not to do this.



# Objective 1

- Define evidence-based medicine from a science-based perspective.

# Objective 2

- Describe the importance of an evidence-based approach for quality patient care.



# Speciality Societies



# Clinical Practice Guidelines: Quality

- Only as good as the evidence used
  - Most not “evidence-based” (even when so labeled)
    - Beware the “evidence-sprinkled”
- Rarely assess impacts of practice change
- Many outdated
- Bias can stem from who developed and why
  - Even best can have bias where evidence not strong or lacking
- May include recommendations without clarity about strength of the evidence vs clinical judgment

# IOM on Trustworthiness of Guidelines

114 randomly chosen guidelines using the IOM standards and found poor adherence [Kung]

- The overall median number of IOM standards satisfied was only 8 of 18 (44.4%)
- Few guidelines groups included information scientists, and even fewer included patients or patient representatives
- Subspecialty societies tended to satisfy fewer methodological standards
- This study shows that there has been no change in guideline quality over the past decade and a half

Kung J, Miller RR, Mackowiak PA. Failure of Clinical Practice Guidelines to Meet Institute of Medicine Standards: Two More Decades of Little, If Any, Progress. Arch Intern Med. 2012 Oct 22;172(16):1211-6. doi: 10.1001/2013.jamainternmed.56. [Epub ahead of print] PubMed PMID: 23089902.

Brito JP et al. Systematic reviews supporting practice guideline recommendations lack protection against bias. *J Clin Epidemiol.* 2013 Jun;66(6):633-8. PubMed PMID: 23510557.

- Systematic review of all diabetes RCTs cited in The Endocrine Society's Clinical Practice Guidelines published between 2006 and January 2012.
- Risk of bias (low, unclear or high) was assessed in 142 trials using the Cochrane Risk of Bias Tool
- Overall, 69 trials (49%) had at least one domain of six with high risk of bias.
- Inadequate reporting frequently hampered the risk of bias assessment: the methods for developing allocation sequence was unclear in 82 trials (58%) and allocation concealment was unclear in 78 trials (55%)
- The authors conclude that these trials have serious limitations that put the findings in question and therefore inhibit evidence-based quality improvement (QI).

# Secondary Studies & Other Secondary Sources



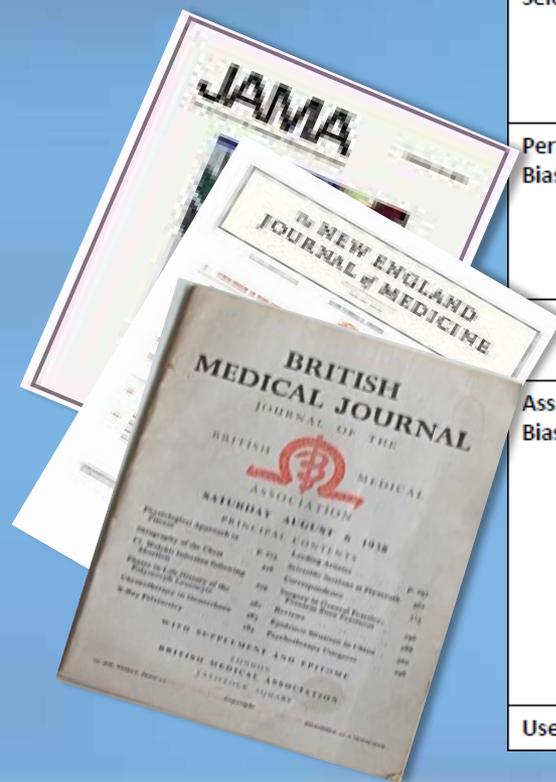


# Our Short List

Information	Content Provider	Comments
Other Sources	ACP Journal Club	Selected studies with commentaries (many without critical appraisal)
Systematic Reviews	Agency for Healthcare Research and Quality (AHRQ)	Evidence-based Practice Center reports and other EB information
Other Sources	Bandolier	Eclectic EBM site for reviews, editorials, NNT info, etc.
Systematic Reviews	Canadian Agency for Drugs & Technology in Health (CADTH)	Evidence-based technology and drug class assessments
Systematic Reviews	Cochrane Collaboration (subscription)	Database of Systematic Reviews (RCTs)
Systematic Reviews	Database of Abstracts of Reviews of Effects (DARE)	Review of Systematic Reviews
Other Sources	Dynamed <sup>®</sup>	Frequently updated source of graded studies; useful first pass
Other Sources	FDA	For new drugs and devices or if you want information regarding pivotal trials
Other Sources	Google and GoogleHealth	Good for definitions, background reading
Other Sources	Informed Health Online	Information for patients from Cochrane
Other Sources	MEDLINEplus	Information for patients from NLM about medications, conditions
Other Sources	MedScape	Sometimes a means for getting full text of articles
Systematic Reviews	Oregon Health Resources Commission	Evidence-based drug reviews freely available
Other Sources	Pubcrawler	"It goes to the library. You to go to the pub." Free service to scan NLM daily by topic
Primary Studies, Secondary Studies, Secondary Sources, Other Information	PubMed	Database of Systematic Reviews, RCTs, observational studies, guidelines, pharmacoeconomics
Other Sources	TRIP Database (Turning Research Into Practice)	For evidence reviews and guidelines.
Systematic Reviews	United States Preventive Services Taskforce (USPSTF)	Evidence-based review of clinical preventive services
Other Sources	UpToDate <sup>®</sup>	Popular site for clinicians. Contains up-to-date but not critically-appraised information about what can be used, but may result in overuse. Good for background reading.
Other Sources	WONCA	Primary care alerts (need to appraise studies)

# The Critical Appraisal Core Competencies

Study Design Assessment	<ul style="list-style-type: none"> <li><input type="checkbox"/> Is the design appropriate to the research question? Is the research question useful?</li> <li><input type="checkbox"/> For efficacy, use of experimental study design (meaning there was no choice made to determine intervention)</li> <li><input type="checkbox"/> Clinically significant area for study (morbidity, mortality, symptom relief, functioning and health-related quality of life) and reasonable definitions for clinical outcome such as response, treatment success or failure</li> <li><input type="checkbox"/> If composite endpoints used, reasonable combination used — and used for safety if used for efficacy</li> </ul>
Internal Validity Assessment	<ul style="list-style-type: none"> <li><input type="checkbox"/> Can bias, confounding or chance explain the study results?</li> <li><input type="checkbox"/> Ensure prespecified and appropriate 1) research questions, 2) populations to analyze, and 3) outcomes</li> </ul>
Selection Bias	<ul style="list-style-type: none"> <li><input type="checkbox"/> Groups are appropriate for study, of appropriate size, concurrent and similar in prognostic variables</li> <li><input type="checkbox"/> Methods for generating the group assignment sequence are truly random, sequencing avoids potential for anyone affecting assignment to a study arm and randomization remains intact</li> <li><input type="checkbox"/> Concealment of allocation strategies are employed to prevent anyone affecting assignment to a study arm</li> </ul>
Performance Bias	<ul style="list-style-type: none"> <li><input type="checkbox"/> Double-blinding methods employed (i.e., subject and all working with the subject or subject's data) and achieved</li> <li><input type="checkbox"/> Reasonable intervention and reasonable comparator used (e.g., placebo)</li> <li><input type="checkbox"/> No bias or difference, except for what is under study, between groups during course of study (e.g., intervention design and execution, care experiences, co-interventions, concomitant medication use, adherence, inappropriate exposure or migration, cross-over threats, protocol deviations, measurement methods, study duration, changes due to time etc.)</li> </ul>
Attrition Bias	<ul style="list-style-type: none"> <li><input type="checkbox"/> Might attrition, including missing data, discontinuations or loss to follow-up, have resulted in distorted outcomes?</li> </ul>
Assessment Bias	<ul style="list-style-type: none"> <li><input type="checkbox"/> Assessors are blinded</li> <li><input type="checkbox"/> Low likelihood of findings due to chance, false positive and false negative outcomes</li> <li><input type="checkbox"/> Non-significant findings are reported, but the confidence intervals include clinically meaningful differences</li> <li><input type="checkbox"/> Intention-to-Treat Analysis (ITT) performed for efficacy (not safety) (all people are analyzed as randomized + reasonable method for imputing missing values which puts the intervention through a challenging trial or reasonable sensitivity analysis) or missing values are very small.</li> <li><input type="checkbox"/> If time-to-event analysis performed, appropriate, transparent and unbiased.</li> <li><input type="checkbox"/> Analysis methods are appropriate and use of modeling only with use of reasonable assumptions</li> <li><input type="checkbox"/> No problems of selective reporting</li> </ul>
Usefulness	<ul style="list-style-type: none"> <li><input type="checkbox"/> Clinically significant area + sufficient benefit size = meaningful clinical benefit (consider efficacy vs effectiveness)</li> </ul>



# Appraisal of Secondary Studies: SR Tool

## Delfini Evidence Tool Kit

### Study Validity & Evidence Usability: Tool and Primer for Secondary Studies (Including Systematic Reviews & Meta-analyses)

Study Reference:

Study Type:                      Study Aim:

Date:                                      Evaluator:

General: Note sponsorship, funding and affiliations, recognizing that any entity or person involved in research may have a bias.

#### Systematic Review Study Details

PICOTS (population, intervention, comparator, outcomes, timing, setting):

Number of studies included / Number of subjects included:

Reported Results	3. <b>Commentaries:</b> Documentation of any flaws or pertinent information found in study "commentaries" in PubMed.					
Primary outcome measure	<b>Your Assessment:</b>					
Secondary outcome measure	4. <b>Research Question:</b> Clearly stated and meaningful questions to the literature? For example, can you tell from the questions they pose to the literature that they will be capturing the right information for population, condition, intervention or exposure and outcome.					
Authors' conclusions:	<b>Your Assessment:</b>					
1. <b>Best Sources:</b>	<table border="1"> <tr> <td><b>Poor Quality Answer:</b> We retrieved all studies dealing with pimecrolimus therapy for atopic dermatitis in the last 5 years.</td> <td><b>Good Quality Answer:</b> We utilized a two part question to the medical literature including the condition and the intervention. In PubMed the search terms were: atopic dermatitis, pimecrolimus OR Elidel OR SDZ ASM 981.</td> </tr> <tr> <td colspan="2">(Having many questions or many outcomes assessed is a red flag.)</td> </tr> </table>		<b>Poor Quality Answer:</b> We retrieved all studies dealing with pimecrolimus therapy for atopic dermatitis in the last 5 years.	<b>Good Quality Answer:</b> We utilized a two part question to the medical literature including the condition and the intervention. In PubMed the search terms were: atopic dermatitis, pimecrolimus OR Elidel OR SDZ ASM 981.	(Having many questions or many outcomes assessed is a red flag.)	
<b>Poor Quality Answer:</b> We retrieved all studies dealing with pimecrolimus therapy for atopic dermatitis in the last 5 years.			<b>Good Quality Answer:</b> We utilized a two part question to the medical literature including the condition and the intervention. In PubMed the search terms were: atopic dermatitis, pimecrolimus OR Elidel OR SDZ ASM 981.			
(Having many questions or many outcomes assessed is a red flag.)						
<ul style="list-style-type: none"> <li>▪ If from a "best source" <ul style="list-style-type: none"> <li>○ We still need to search</li> <li>○ Ensure the search is comprehensive</li> </ul> </li> </ul>						
<b>Your Assessment:</b>						
2. <b>DARE Review:</b> Is there an abstract and DARE says use with "confidence" conclusions about efficacy.	5. <b>Clinical Significance of Question:</b> Does the research question address morbidity, mortality, symptom relief, emotional and/or physical functioning or health-related quality of life?					
	<b>Your Assessment:</b>					

# Appraisal Tool For Secondary Sources: QI Project Appraisal Tool

## Secondary Source Appraisal Tool (e.g., Clinical Guidelines, Performance Measures, etc.)

**Study Reference:**

**Study Type:**

**Study Aim:**

**Date:**

**Evaluator:**

**General:** Note sponsorship, funding and affiliations, recognizing that any entity or person involved in research may have a bias.

**Purpose:** Why are you considering using this QI content or content assessment article (e.g., gap in practice as determined by comparing current care with optimal care as defined by the best available evidence, practice variation, current performance that differs from a benchmark, clinical uncertainty, cost containment, etc. – are you attempting to solve a “fixable” problem).

CONSIDERATIONS	CONCERNS			SIDEBAR
	None	Minor	Major	
<b>Before You Start—Preliminary Evaluations</b>				
a) If this is an evaluation of a performance measure –  <b>Apply the Delfini Performance Measure Evaluation Tool, then continue with other questions in this tool.</b>				<i>Caution that many performance measures are highly flawed.</i>
b) If you are using a study about cost or cost effectiveness –  <b>Apply the Delfini Health Care Economic Study Evaluation Tool, then continue with other questions in this tool.</b>  <b>Pay close attention to issues of validity and usefulness, as many studies don't truly evaluate</b>				<i>Caution that many cost-effectiveness analysis studies are highly flawed. Frequently, your own “back of the envelope” assessment may be more effective</i>



# Requirements for An Evidence-based Approach

# The Evidence-based Organization

- Closes gaps in quality, satisfaction & cost
- Keys
  - Leadership
  - Evidence-based approach
    - Work components (resources, structures, methods, processes, tools)
    - Staff roles and skills to support and realize quality outcomes
    - Culture
  - Effective implementation
    - Evidence is global; implementation is local



# Health Care Quality System Assessment Tool

## Evidence- & Value-based Health Care Quality System Assessment Tool

Health Care System:

Evaluator:

Date:

### Background

There is a great deal of poor quality research and misleading information even in the highest quality medical journals. Health care organizations rarely recognize this and/or rarely have systems in place and staff with skills to do needed evaluations of scientific evidence. Health care should be provided by organizations that both understand the need for evaluating science, know how to do so and provide resources for doing this work.

Individual circumstances apply. Your actual findings need to take account of the whole or other factors which may serve as reasonable substitutions.

### Evaluation Tool

Part I. Scientific Evaluation Capabilities	Desired Outcome	Problem	General Advice
<p><b>1. Organizational Understanding</b> Can the organizational or quality improvement leadership articulate a true understanding of the need for a rigorous and systematic evaluation of the quality of scientific evidence before applying it?</p> <p><b>Note:</b> Leadership is vitally important to help create an evidence- and value-based system. Many leaders may be able to sound like they understand, but not actually have a true understanding.</p>	Yes:	No:	Red flag
<p><b>2. Systematic Processes for Evaluating Health Care Technologies</b> Does the organization have a system in operation for routine rigorous and systematic evaluation of new drugs, devices and procedures through rigorous and systematic evaluation of scientific quality?</p>	Yes:	No:	<p>Fails assessment</p> <p>Reminder of potential savings estimated at 15 to 30% of drugs</p>

# Part I. Scientific Evaluation Capabilities

- Organizational Understanding
- Systematic Processes for Evaluating Health Care Technologies
- Understanding of Study Types
- Performance of Rigorous Critical Appraisal
- Critical Appraisal of Clinical Recommendation Content
- Critical Appraisal Core Competencies

# Part II. Application of Valid Science

7. Clinical Improvement Implementation Skills
8. Health Care Staff Access to Quality Information
9. Consumer Access to Quality Information
10. Performance Measures & Quality Indicators (caution)

# Part III. Organizational Commitment

11. Mission Statement Reflects Priorities

12. Leadership Support

13. Aligned incentives

———

Key Points:

- Systems and structures need to be put in place and supported
- All health care decision-makers need to be trained in critical appraisal
- Expectations must be set
- Attention must be active and continuous

# Our 10 Phases of Evidence- & Value-based Clinical Improvement

## The Evidence-based Organization

1. Organizational Readiness
2. Clinical Improvement Project & Team Selection
3. Project Outline
4. Evidence Review
5. Clinical Content Development
6. Impact Assessment
7. Communication Tools Development
8. Implementation: Create, Support and Sustain Change
9. Measure and Report
10. Update and Improve

# What Staffers & Teams Need

## Foster A Culture of Attention to Evidence

- Foster A Culture of Attention to Evidence
- Support “Attention to Evidence”
- Be Realistic About The Evidence

# What Staffers & Teams Need Foster A Culture of Attention to Evidence

Leaders who understand “evidence-based stewardship” are able to...

- Convey the importance of solid evidence approaches to provide best patient care
- Ensure that the appropriate use of evidence is part of the culture
- Implement the 10 phases of evidence-based clinical quality improvement

# What Staffers & Teams Need Support “Attention to Evidence”

Leaders who understand —

- The importance of solid evidence approaches to provide best patient care
- The 10 phases of evidence-based clinical quality improvement
- The need to emphasize the appropriate use of evidence as part of the culture
- The need for resources
- That the work is labor-intensive
- The need for solid structures, methods processes and tools
- The need for roles and skills
  - Is it true, is it useful, is it usable?

# What Staffers & Teams Need Be Realistic About The Evidence

Leaders who understand —

- The importance of solid evidence approaches to provide best patient care
- The 10 phases of evidence-based clinical quality improvement
- The need to emphasize the appropriate use of evidence as part of the culture
- The need for resources
- That the work is labor-intensive
- The need for solid structures, methods processes and tools
- The need for roles and skills
  - Is it true, is it useful, is it usable?
- The need to encourage staff to speak up!
- That there is not perfection in this work—it is a process of discovery and much judgment is involved



# Evidence-based Health Care Quality Improvement Project & Clinical Practice Guideline—Kaiser Permanente Hawaii: Venous Thromboembolism (VTE) Prevention Project

The EBM Information Quest: Is it true? Is it useful? Is it usable?

Delfini Co-founders: Michael E Stuart MD, President & Medical Director . Sheri Ann Strite, Principal & Managing Partner

## Quick Picks



[Why Critical Appraisal Matters](#)



[Services](#)



[Seminars](#)



## Page Menu.....

Venous Thromboembolism Guideline Materials are posted with permission from Kaiser Permanente Hawaii and Delfini Group. Selected components of guideline documentation are available from Delfini upon request.

- [VTE/DVT Prophylaxis for Total Knee/Hip Surgery Guideline Recommendations](#)
- [VTE/DVT Prophylaxis for Total Knee/Hip Surgery -](#)

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## Kaiser Permanente Hawaii (KPHI): Prevention of Venous Thromboembolism (VTE) in Total Hip and Total Knee Replacement



Mission: Help advance evidence- and value-based medicine in an organization that has already proved a demonstrated commitment to evidence- and value-based care by dedicating resources to EBM training and support and that now seeks to progress to an even higher level in skill, depth, application and cultural transformation.

## At VTE Project



## Read Our Blog...

## Menu.....

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- Home
- What's New
- Blog
- Seminars
- Services
- Resources
- Sample Projects
- Notices
- About Us & Our Work

# Culture



## Variations in...

- Work components (resources, structures, methods, processes, tools)
- Staff roles and skills to support and realize quality outcomes

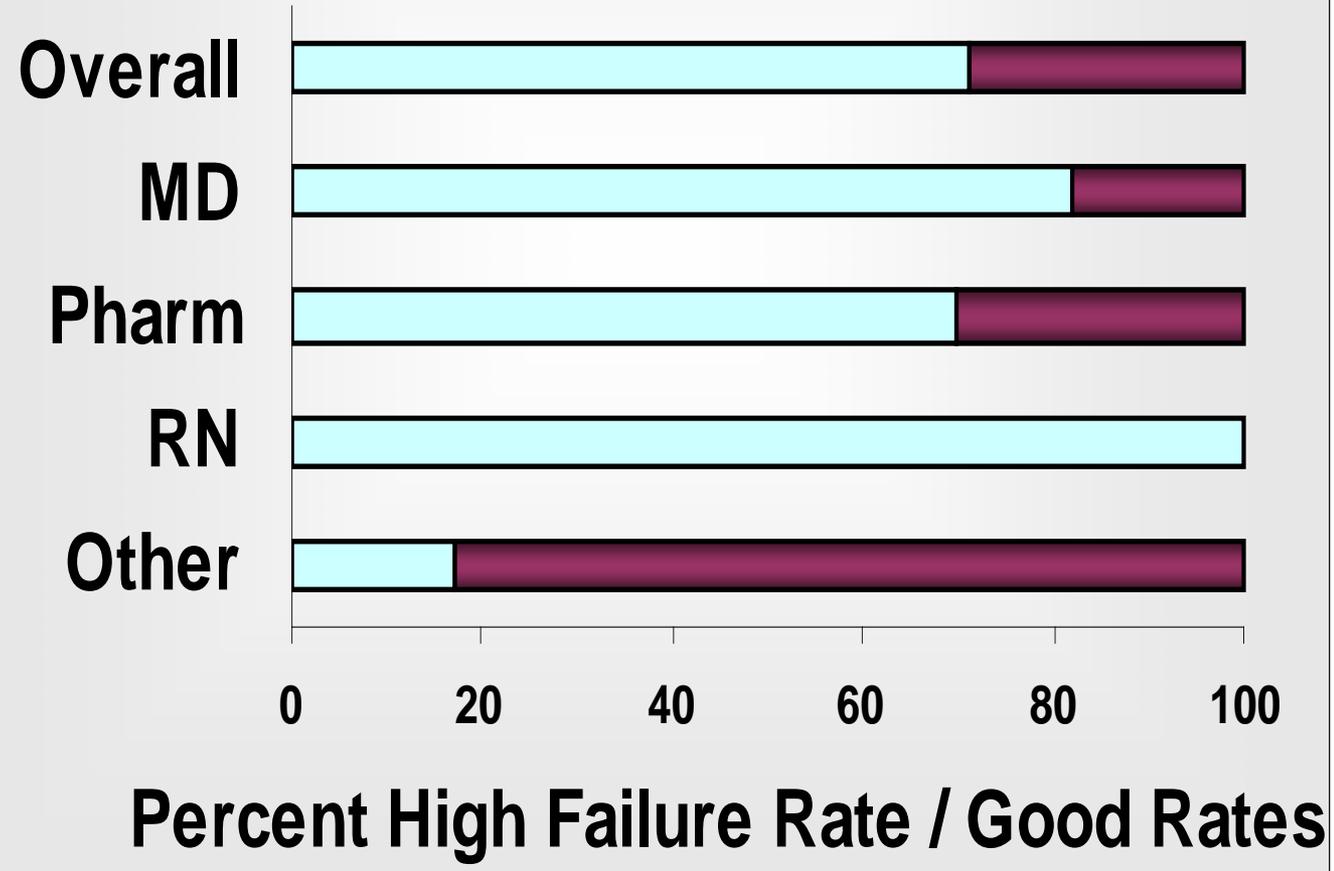
# INDIVIDUALS! FIND THEM!

Give them—

- Roles
- Resources
- Ways to engage others in projects
- Ensure they have needed EBM skills especially basic skills in critical appraisal



# Confidence Evaluating Med Lit Inconsistent with Scores



What I Think I Know Is *Not* Consistent With What I *Do* Know

# Clinical Improvement Project & Team Selection

- Stakeholders identified
- Multifaceted leadership
  - Structural & practical (from “leadership”)
  - Evidence-based experts
  - Stake-holder leadership
  - Subject matter leaders (clinical, pharmacy, nursing, patient-perspective)

# EB Clinical QI Teams

- Team members represent stakeholders
  - Around 10 members
  - Ideally respected by others, good communicators, motivated and enthusiastic, and are hard workers willing to do any task
- Ensure the team knows how to do the following—
  - Systematic search of the medical literature
  - Critical appraisal
  - Synthesize evidence
  - Create clinical recommendations
  - Create decision-support and information aids
- Teams require effective leadership and support

# EB Team Decision-making

- Separation of a determination about the evidence from other considerations (triangulations)
- Neutralize the decision-making
- Guidance è

# For Committee Deliberations

- Delfini  
EBM Committee  
Deliberations Tool

**Delfini Group™, LLC**  
*Evidence- & Value-based Solutions For Health Care*  
*Clinical Improvement Consults, Content, Seminars, Training & Tools*

**Tool for Committees & Working Groups**

## *EBM Committees:*

*Pharmacy & Therapeutics or  
Medical Technology Assessment  
Committee Deliberation Criteria*

**Delfini Group™, LLC**

<b>Michael Stuart, MD</b> President	<b>Our Mission—</b> To assist medical leaders, clinicians and other health care professionals by—
<b>Stuart Stone, Principal &amp; Managing Partner</b> www.delfini.org	<ul style="list-style-type: none"><li>• Bringing science into medical practice in an easy-to-understand way.</li><li>• Using simplified methods to help navigate the complexities of such areas as evidence-based medicine and other topics.</li><li>• Building competence and confidence in improving medical care through our well received consultations, educational programs and tools.</li><li>• Providing inspiration to others to improve medical care and help bring about needed change.</li></ul>

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# Committee Deliberations

- New agent delivers improved outcomes
- New agent less costly with similar outcomes
- Other considerations

# Framework for Critical Appraisal and Decision-Making

- q Appropriate design, acceptable methods, clinically meaningful results?
  - q Is the information true?
  - q Is the information useful?
  - q Is the information useable?

# Framework for Critical Appraisal and Decision-Making

Appropriate design, acceptable methods, clinically meaningful results?

## Key Question(s)

- q Population
- q Intervention
- q Comparison
- q Outcomes
- q Timing
- q Setting

## Design

- q Observation
- q Experiment

## Methods

- q Population
- q Selection Bias
  - q Generation Sequence
  - q Concealment Allocation
  - q Baseline Characteristics
- q Performance Bias
  - q Blinding
  - q Similar treatments & care experience both arms
- q Attrition Bias
  - q How much, when, why, how missing data managed
- q Assessment Bias
  - q Blinding
  - q Time to event issues

## Results

- q Efficacy and Safety
- q Mortality, morbidity, symptom relief, QOL, functioning
- q Size of benefits?
- q Confidence intervals?

## Overall

- q Anything else that may explain or distort results

# Framework: Triangulations

- Science
- Patient perspective
  - Benefits
  - Harms
  - Risks
  - Costs
  - Uncertainties
  - Alternatives
  - Applicability
  - Satisfaction,
  - Clinical considerations (eg tolerability, ease of use, dependency or abuse potential)
  - Unmet needs
  - Special populations
- Clinician perspective
- Other decision considerations
  - Accreditation issues
  - Community standards
  - Cost
  - Ethical considerations
  - Liability and risk management issues
  - Marketing
  - Media or press issues
  - Medical community impacts
  - Medical-legal
  - Public relations
  - Purchasing issues
  - Regulatory
  - Research realities (eg, no evidence will be able to answer clinical questions, etc.)
  - Utilization and capacity issues
  - Overall impact on the health care organization
  - Other

# Committee Deliberations

## Sufficient Evidence of Effectiveness

Is there sufficient evidence to conclude that the intervention or technology is effective?

- The scientific weight of the evidence, resulting from valid, clinically useful studies, must be sufficient for determining health care outcomes (Grade A, Grade B or Grade B-U as described in Delfini Grading Tool).

No  
 Yes  
 ?

## Sufficient Evidence of Safety

Is there sufficient evidence to conclude that the intervention or technology is safe?

- For safety, Grade B or Grade B-U evidence may not be available (e.g., studies frequently are underpowered for harms, outcomes are not prespecified and harms are frequently noted from case reports); therefore, Grade U evidence described in Delfini Grading Tool may be used.

No  
 Yes  
 ?

# Considerations Suggesting Efficacy

- All or none (e.g., ~80% RRR)
  - Dramatic change following application of the intervention or technology that is unlikely to be due to confounding (ie, close to all-or-none results—example: before treatment all died and following treatment, high survival rate).
- **Observational public health interventions** may at times “behave” more like experiments. For example choice is often not involved and the number of people experiencing the intervention is frequently so great that there is a wide distribution of prognostic variables (ie, a high likelihood that all prognostic variables are represented in the “treated” pool) and co-interventions in the treated group, reducing the likelihood that a confounder is the explanation for the outcome

# Considerations Suggesting Efficacy

- There is extremely low likelihood of improvement without some intervention; and,
  - Outcomes of interest are highly likely to be attributable to the intervention
    - (eg, a **single intervention or technology** was utilized and the likelihood of patients utilizing co-interventions is low or co-interventions were equivalent in compared groups [note: equivalence should take into account considerations such as administration, duration, dosing, etc.]);
    - **And convincing sustained improvement** is documented following use of the intervention or technology.

# Other Evidentiary Considerations

1. Intervention or technology is considered to be safe or has low likelihood of harm or the adverse effects are acceptable. The intervention or technology is unlikely to result in other unacceptable untoward effects or unacceptable unintended consequences and is of acceptable cost (e.g., dietary change).  
 Meets criteria
2. No other effective treatments or technologies exist, and adverse clinical outcomes are likely if the condition is not treated.  Meets criteria
3. Other related interventions or technologies already in use also have insufficient evidence, and there may be advantages for intervention or technology over alternatives. Caution is urged if assuming “class effect.” The criteria for concluding the existence of “class effect” are controversial.  
 Meets criteria
4. Well-designed studies are unlikely (e.g., condition or disease is rare, topic does not lend itself to valid study design or execution and adverse clinical outcomes are likely if the condition is not treated.)  Meets criteria
5. There is sufficient evidence of effectiveness and safety in other populations to suggest net clinical benefit in this population.  Meets criteria

# Our 10 Phases of Evidence- & Value-based Clinical Improvement

## The Evidence-based Organization

1. Organizational Readiness
2. Clinical Improvement Project & Team Selection
3. Project Outline
4. Evidence Review
5. Clinical Content Development
6. Impact Assessment
7. Communication Tools Development
8. Implementation: Create, Support and Sustain Change
9. Measure and Report
10. Update and Improve



# Objective 3

- Identify at least three factors needed for an evidence-based approach.

# What Patients Need for Patient-Centered Decision-making

# What we all want from our health care...

1. That we don't die prematurely (mortality).
2. That we don't suffer from conditions or diseases that we can avoid (morbidity).
3. That our health issues do not detract from our quality of life (health-related quality of life).
4. That we do not experience unpleasant symptoms from our health issues (symptom relief).
5. That health issues do not interfere with our daily activities (emotional, physical and mental functioning).

Health care professionals refer to these five items as "health care outcomes."

# The 8 Key Questions

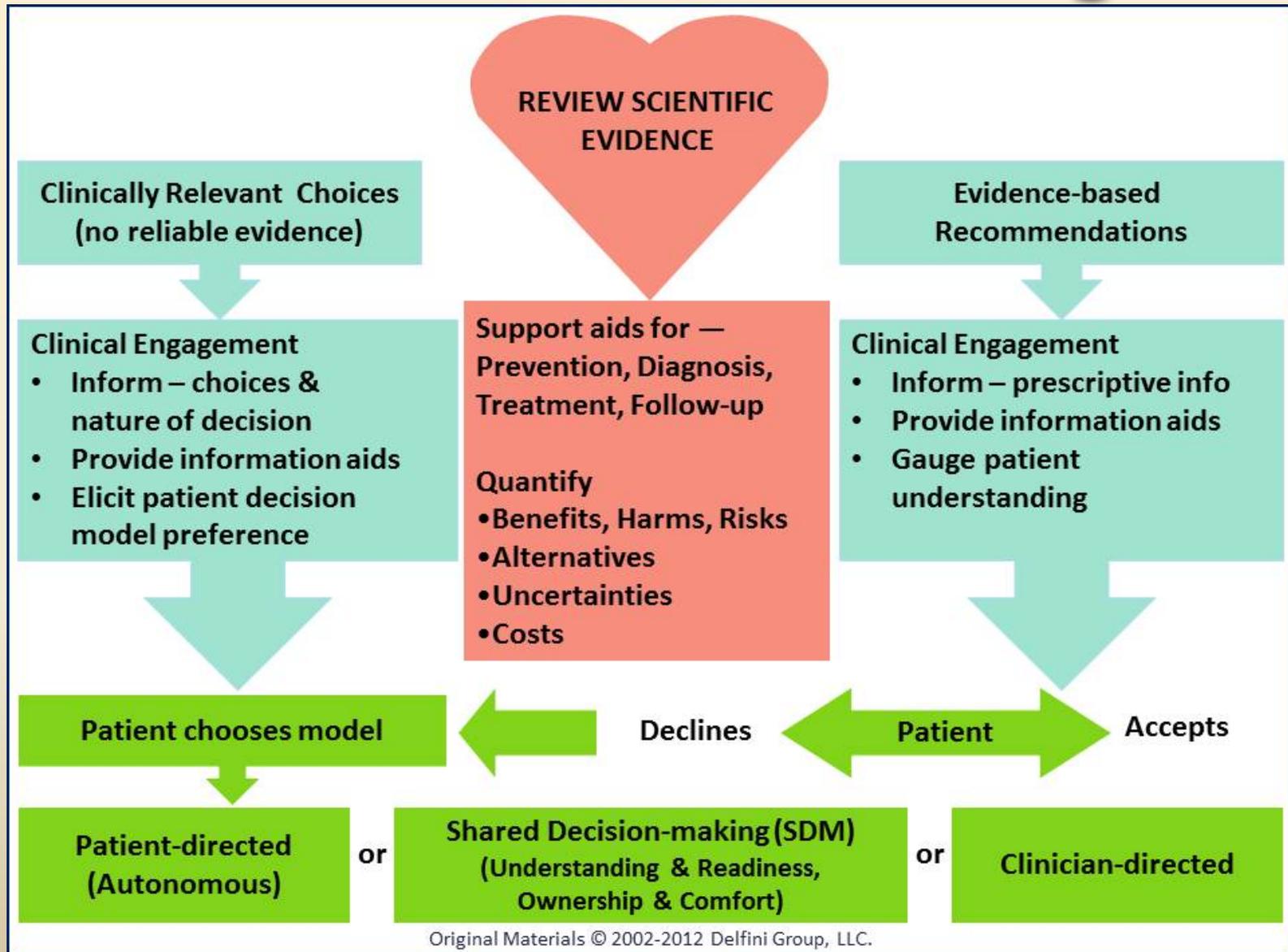
## Patients Want Answered

1. What do I have or what might I get?
2. Why do I have it?
3. How did I get it?
4. What might it do to me?
5. What is known and unknown about it?
6. What choices do I have?
  - How will each choice affect me, e.g., what is the likelihood of benefit and harm and the quality of the evidence for each choice?
  - What are the costs?
7. What is your advice?
8. What details do I need to know to get it done?

# Patients Deserve...

1. To be treated respectfully.
2. Useful information that will help them make a good decision about whether or not to buy a service (or submit their life or a loved one's life to it).
3. To be listened to.
4. To be able to decide how they want to make their decisions.
5. Comfort in and the ability to question services.
6. Comfort in and the ability to reject services.
7. Good customer service.
8. To receive the right care.
9. Attention to their requirements: **individual health care problems and needs, wants, individual circumstances, values and preferences**

# Our Patient Decision-Making Model



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# GLIDE MODEL

[http://www.delfini.org/Delfini\\_Tool\\_PatientEncounterMap.pdf](http://www.delfini.org/Delfini_Tool_PatientEncounterMap.pdf)

## Delfini Clinical Tool

### Patient Information & Engagement Tool: GLIDE & the Patient Encounter Map

*Engagement Tips: G-L-I-D-E through the patient encounter*

- Attend to non-verbal cues you send, use positive talk, avoid negative talk, adopt non-judgmental attitude throughout

<p><i>Greet</i></p>	<p><i>“Good to see you!”</i></p> <ul style="list-style-type: none"> <li>Prepare to give patient full attention and apply positive-talk principles</li> <li>Friendly greeting &amp; personal opening</li> <li>Shake hands</li> </ul>				
<p><i>Listen</i></p>	<p><i>“You have my complete attention. Tell me why you’re here today.”</i></p> <ul style="list-style-type: none"> <li>Listen to the patient’s story</li> <li>Do not interrupt</li> <li>Ask open-ended questions</li> <li>Keep patient-centered</li> <li>Ensure the patient has truly finished: “Anything else?”</li> <li>Demonstrate empathy-- understanding of patient’s needs, problems, feelings, views</li> </ul>	<p><i>Emotions?</i></p> <ul style="list-style-type: none"> <li>~ Acknowledge the emotion (upset, stressed, sad, afraid)</li> <li>~ Support the patient (“I will help you through this.”)</li> </ul>			
<p><i>Inquire &amp; Exchange Information</i></p>		<p><i>Determine &amp; Decide</i></p>		<p><i>Effectively End</i></p>	

# Ph messaging scripts

- [http://www.delfini.org/page\\_SamePage\\_RxMessagingScripts.htm](http://www.delfini.org/page_SamePage_RxMessagingScripts.htm)

## Sample: Blood Pressure Treatment (Personalized Example)

*Delfini* Rx Messaging Scripts™

This patient is a good candidate for...

### Blood Pressure Treatment

This 70 year old patient has a BP of 195/90. With this blood pressure, he has a 28% mortality risk over the next 5 years. The best available valid and useful evidence indicates that if 25 people with systolic hypertension, who are similar in age, are treated for their elevated blood pressure for 5 years, during that time period, as compared to placebo—

1 person may avoid death due to cardiovascular disease

24 people will not receive a mortality benefit from blood pressure treatment, but may avoid a cardiovascular event.



# Objective 4

- List at least four elements of patient-centered decision-making from the viewpoint of the patient

# Objective 4

- List at least four elements of patient-centered decision-making from the viewpoint of the patient
- **Information based on high quality evidence, quantified information on probability of benefits, harms, alternatives, impacts including costs.**

# What Policy Makers Need for An Evidence-based Approach

# Delfini's Advice:

## Understand At A Minimum—

- Why Evidence-based Medicine and Critical Appraisal Are So Important for Patient Care
- Critical Appraisal Sampler
- Requirements for an Evidence-based Approach
- What Patients Need for Patient-centered Decision-making
- General understanding of EBM Concepts

# Information & Decision Support

## “Semaphore” Example

Criteria, Considerations, Comparisons & Examples to Inform Decisions & Judgments	Questions: What is the level of confidence that...	Outcome	Level of Confidence
Likelihood of Outcomes (See above for considerations for Clinical Significance)	1. these outcomes will be achieved, realized or experienced?	Increased detection of breast cancer	HIGH
		Decreased need for other tests	LOW
		Changes in treatment plans (e.g., wider excisions, more mastectomies, unnecessary mastectomies)	HIGH
		Decreased re-excision rates	LOW
		Decreased recurrence rates	LOW
		Decreased mortality	LOW
Size of the Outcomes	2. the estimate is likely to be correct?	2-5 additional cancers detected/100 MRIs, but with uncertain benefit in mortality, potential for risk and increase in cost	HIGH
Size of the Outcomes	3. the estimate is likely to be correct?	Up to 11 additional benign biopsies/100 MRIs	MEDIUM
Safety	4. the estimate is correct?	No increase in meaningful adverse psychological outcomes	MEDIUM
		No increase in adverse outcomes from radiation	HIGH
Cost	5. the estimate is correct?	Increased cost of technology: MRI 10 times the cost of mammography	HIGH
QALY: Evidence Quality for Mortality and Methods Overall [Possibly reasonable QALY judgment: + <\$50K, ? \$50-150k, — >\$150k]	6. the estimate is correct?	Cost per QALYs saved: ~\$30,000 to ~\$310,000 depending upon risk and assumptions	LOW
Alternatives Available	7. the information about alternatives is correct?	Mammography: lower sensitivity, but fewer false positive biopsies	HIGH

# Our Goals for Today

- Why Evidence-based Medicine and Critical Appraisal Are So Important for Patient Care
- Critical Appraisal Sampler
- Requirements for an Evidence-based Approach
- What Patients Need for Patient-centered Decision-making
- What Policy Makers Need for an Evidence-based Approach