



Critical Appraisal of the Medical Literature for Therapies: A Foundation for Health Care Decision-Making



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How to “Read” a Study



Delfini
Evidence- and Value-based Solutions for Health Care™
Clinical Improvement Consults, Content Development, Training & Seminars

Critical Appraisal Tutorial
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
DelfiniGram™ GET ON OUR UPDATE LIST
SHORT CRITICAL APPRAISAL TUTORIAL: EVALUATING BIASED EFFICACY RESULTS IN SUPERIORITY TRIALS
Menu.....
• Lack of Critical Appraisal May Hurt Patients
• Unreliable Science & The Distorting Effects of Bias
• Simple Steps to Critical Appraisal
• Resources
• Contact Delfini
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• Videos
• How to Read a Study Video • Video slides

At Critical Appraisal Tutorial
Read Our Blog...
Menu.....
• Use of our website implies agreement to our policies
• Agreement for references available upon request
• What's New Blog
• Seminars
• Services
• Delfini Group Publishing
• Sample Projects
• Metrics

Mike Stuart MD

Sheri Ann Strite

- Evidologists
- Medical information scientists
- Clinical improvement experts
- Medical communications specialists
- Evidence evaluators
- Teachers
- Trainers
- Authors....



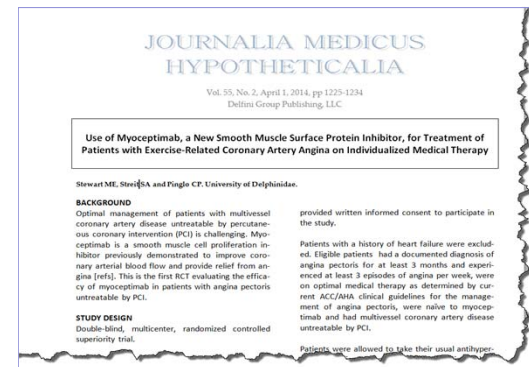
Basics For Evaluating Medical Research Studies: A Simplified Approach

And Why Your Patients Need You To Know This

Delfini Group Evidence-based Practice Series
A Short How-to Guide Book

See Books at www.delfini.org
Click on the book cover at our menu to the left...

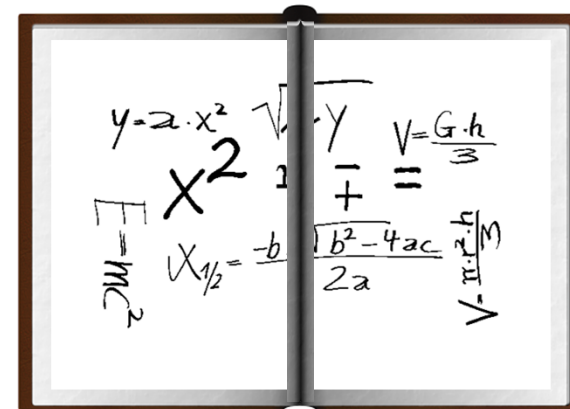
Everything Using Medical Science Should be Evaluated for **Validity** & Clinical **Usefulness**



Are the Results True?
If Yes, Are They Useful?



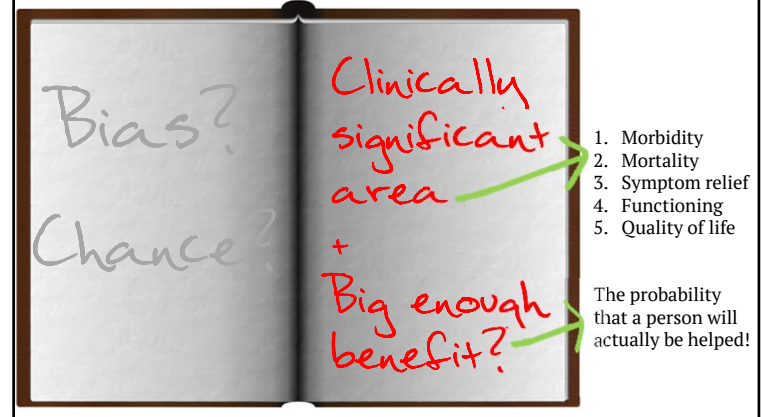
Don't I Need to Know a Lot About **Statistics!?!?!?!?**



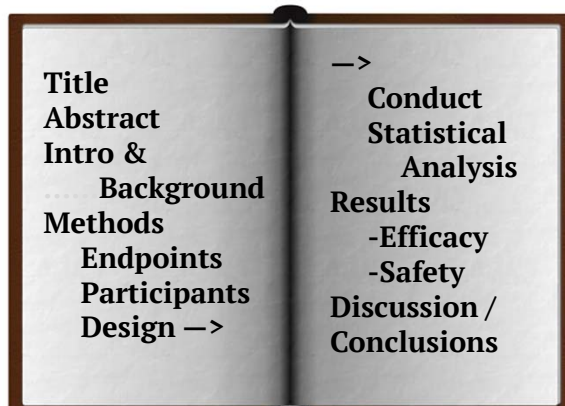
Are the Results True?
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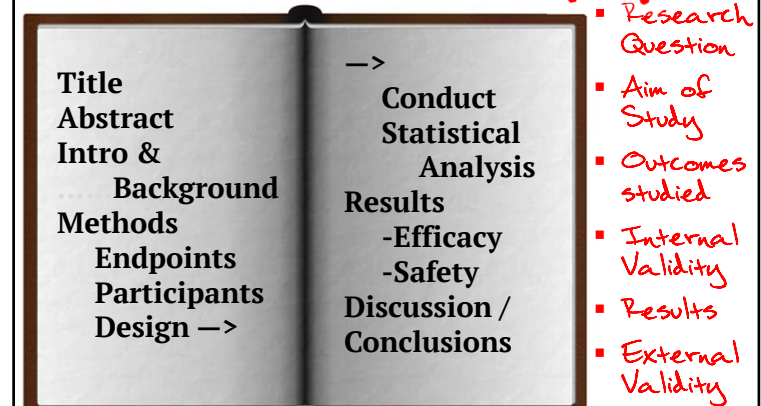
Are the Results True?
If Yes, Are They Useful?



Here Is How
Studies Come To You



Here Is What
You Do With Them



How Can I Evaluate A Medical Research Study



We Don't Really "Read" the Study



1

Get yourself some
useful + helpful
tools!

A screenshot of the Delfini website homepage. The header includes the Delfini logo and the tagline "Evidence- and Value-based Solutions for Health Care". A blue banner on the right says "Resources at www.delfini.org". The main content area is divided into sections: "Quick Picks", "Help For You", "Books", and "Workshops". Red arrows point to the "Resources" link in the "Help For You" section and the "Books" section. The "Books" section lists "Basics For Evaluating Medical Research Studies" and "Critical Appraisal of the Medical Literature for Therapies". The "Workshops" section lists "Critical Appraisal of the Medical Literature for Therapies". The right sidebar contains a "Menu" with links like "Home", "What's New", "Blog", "Services", "DelfiniGram", "Publications", "Resources", "Sample Projects", "Notices", "About Us & Our Work", "Testimonials", "Other", "Site Search", "Contact Info/Updates", and "Quick Navigator to Selected Resources".

Quick Navigator

change... real success... improved patient care... valuable..."

"...thanks for presenting this valuable information in a fun and memorable way..."

"...I thought the subject was going to be boring and not much use...I was very wrong...I cannot thank you and Sheri enough."

"I know a couple hundred people...who have got to hear your message!"

"Best one-day educational program I've experienced in 25 years!"

Delfini evidence reviews are consistently praised as useful, rigorous and transparent. Delfini average training program scores are 4.8 out of 5.0.

"... gifted facilitators and passionate educators... have rarely encountered presenters so well-prepared and well-versed in their subject matter... both are engaging, up-beat and empowering... extremely generous with their knowledge and expertise..."

See all of our **Testimonials**.

Testimonials
Other Site Search
Contact Info Updates
Quick Navigator to Selected Resources
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The Healthcare Information Problem
Tutorials
DelfiniClick™-commentaries
On the Same Page™-patient decision support
Evidence Messaging Scripts
Delfini Publications
Medical Leader Interviews
Glossary
Recommended Reading
Recommended Web Links
Delfini Critical Appraisal Filter
Get DelfiniGram™ Updates

1-Page Tools!

For Learners
www.delfini.org/Delfini_Pearls_Basics_Therapy_Superiority.pdf

The Professional Tool
www.delfini.org/Delfini_Tool_Study_Validity_Short.pdf

Delfini Evidence Tool Kit
Short Critical Appraisal Checklist: Interventions for Prevention, Screening & Therapy

Study Purpose: Study Type: Study Aim: Data: Evaluation:

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

Study Design Assessment:

- ☐ Is the design appropriate to the research question? Is the research question useful?
- ☐ For efficacy, use of experimental study design (meaning there was no choice made to determine intervention)
- ☐ Clinically significant area for study (morbidity, mortality, symptom relief, functioning and health-related quality of life) and reasonable definitions for clinical outcomes such as response, treatment success or failure

POTENTIAL EXCEPTION: ALL OR NONE RESULTS

- ☐ If composite endpoints used, reasonable contribution
- ☐ Ensure prespecified and appropriate 1) research questions, 2) populations to analyze, and 3) outcomes

Internal Validity Assessment: Can bias, confounding or chance explain the study result? See below

Selection Bias

- ☐ Groups are appropriate for study, of appropriate size, assessment and similar in prognostic variables
- ☐ 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 (allocation by minimization may be acceptable)
- ☐ Consistent of allocation strategies are employed to prevent anyone affecting assignment to study arm

Performance Bias

- ☐ Double-blinding methods employed (i.e., subject and all working with the subject or subject's data) and achieved
- ☐ Reasonable intervention and reasonable comparator used (e.g., placebo)
- ☐ 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, study duration, changes due to time etc.)

Data/Attrition Bias

- ☐ Evaluate bias in measurement activities
- ☐ Might attrition, including missing data, discontinuations or loss to follow-up, have resulted in distorted outcomes?

Assessment Bias & Chance Assessment

- ☐ Assessors are blinded
- ☐ Low likelihood of findings due to chance, false positive and false negative outcomes
- ☐ Non-significant findings are reported, but the confidence intervals include distally meaningful differences
- ☐ If variables are dichotomous, **Intention-to-Treat Analysis (ITT)** performed for efficacy (not safety) (all people are analyzed as randomized + reasonable method for imputing missing values). (May not be an issue if missing values are very few)
- ☐ If time-to-event analysis performed, appropriate, transparent and unbiased. Evaluate censoring rules.
- ☐ Analysis methods are appropriate and use of modeling only with use of reasonable assumptions
- ☐ No problems of selective reporting or selective exclusion of outcomes

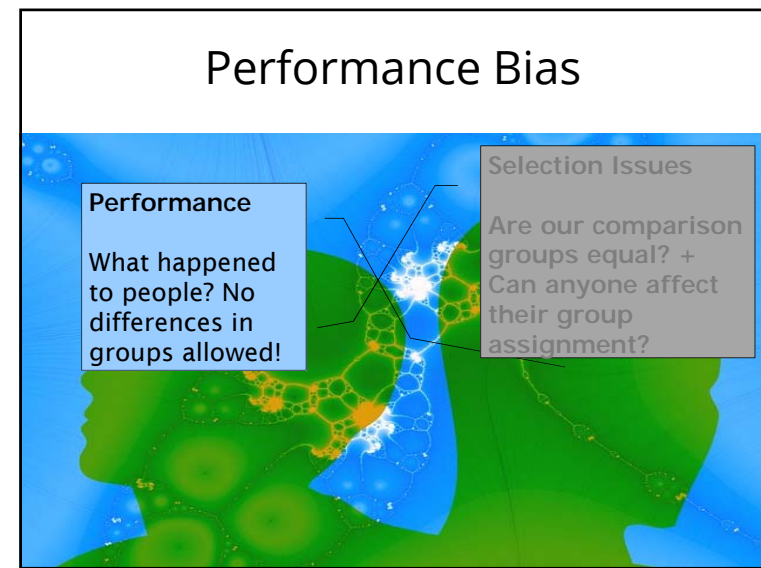
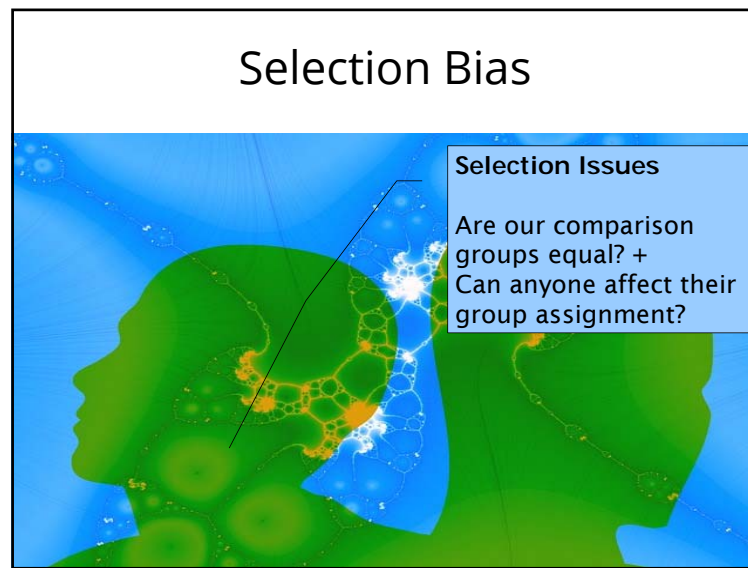
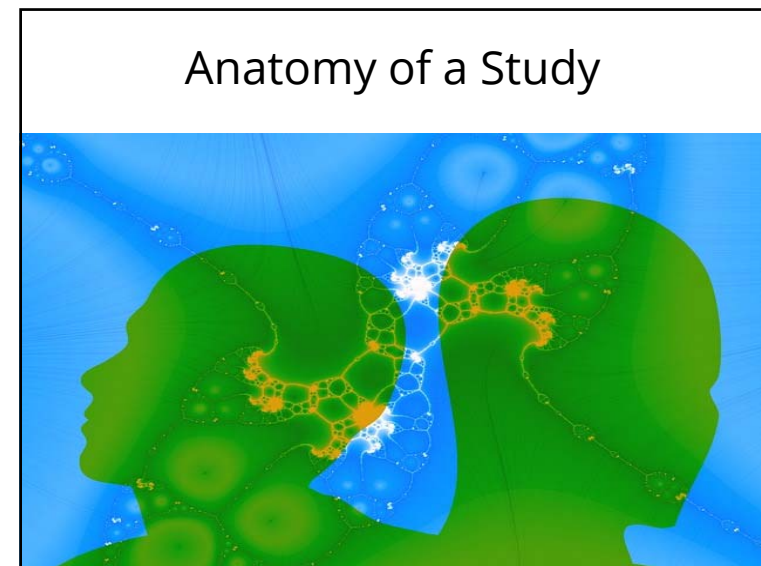
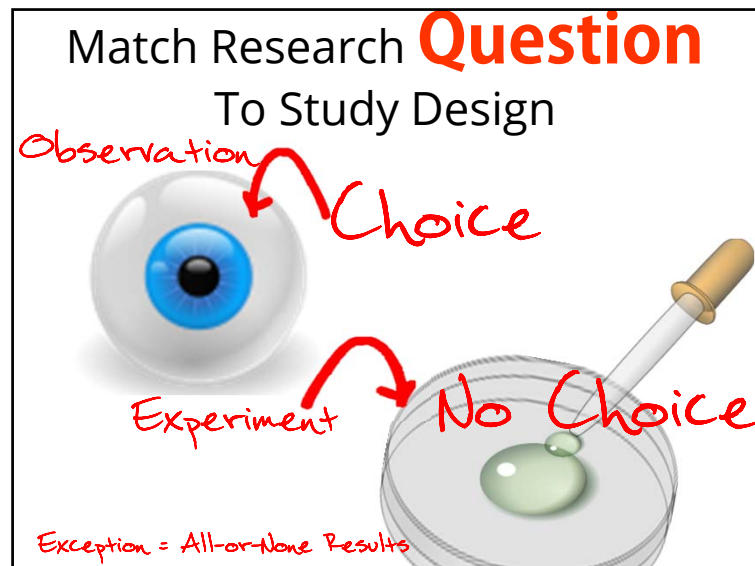
Usefulness & Other Considerations

- ☐ Does the study address a sufficient knowledge gap to justify the effort and cost of the study?

2

Familiarize yourself with what to evaluate.

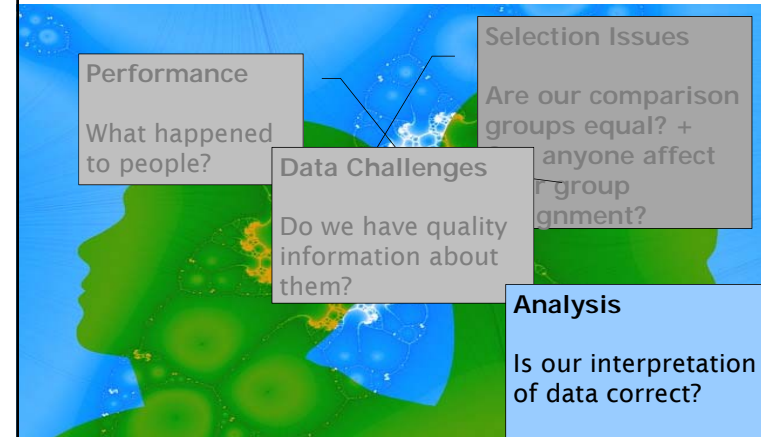
Match Research Question To Study Design



Data + Attrition Bias



Assessment Bias



[www.delfini.org/
Delfini Tool
StudyValidity
Short.pdf](http://www.delfini.org/DelfiniToolStudyValidityShort.pdf)

[www.delfini.org/
Delfini Pearls
Basics
Therapy
Superiority.pdf](http://www.delfini.org/DelfiniPearlsBasicsTherapySuperiority.pdf)

Delfini Evidence Tool Kit	
Short Critical Appraisal Checklist: Interventions for Prevention, Screening & Therapy	
Study Reference	Study Aim:
Study Type:	Evaluator:
Date:	
General: Note sponsorship, funding and affiliations, recognizing that any entity or person involved in research may have a bias.	
Study Design	<input type="checkbox"/> Is the design appropriate to the research question? Is the research question useful? <input type="checkbox"/> For efficacy, use of experimental study design (meaning there was no choice made to determine intervention) <input type="checkbox"/> Clinically significant area for study (morbidity, mortality, symptom relief, functioning and health-related quality of life) and measurable definitions for clinical outcome such as response, treatment success or failure <input type="checkbox"/> If composite endpoints used, reasonable combination <input type="checkbox"/> Ensure prespecified and appropriate 1) research questions, 2) populations to analyze, and 3) outcomes
POTENTIAL EXCEPTIONS: ALL OR NONE RESULTS	
Internal Validity Assessment: Can bias, confounding or chance explain the study results? See below	
Selection Bias	<input type="checkbox"/> Groups are appropriate for study, of appropriate size, assessment and similar in prognostic variables <input type="checkbox"/> Methods for generating the group assignment sequence are truly random, sequencing avoids potential for anyone affecting assignment (e.g. a study arm and randomization remains intact (allocation by minimization may be acceptable)) <input type="checkbox"/> Concealment of allocation strategies are employed to prevent anyone affecting assignment to a study arm
Performance Bias	<input type="checkbox"/> Double blinding methods employed (i.e., subject and all working with the subject or subject's data) and achieved <input type="checkbox"/> Reasonable intervention and reasonable comparator used (e.g., placebo) <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 experience, co-interventions, concomitant medication use, adherence, inappropriate exposure or migration, cross-over threats, protocol deviations, study duration, changes due to time etc.)
Data/Attrition Bias	<input type="checkbox"/> Evaluate bias in measurement activities <input type="checkbox"/> Might attrition, including missing data, discontinuations or loss to follow-up, have resulted in distorted outcomes? <input type="checkbox"/> Assumptions are believed <input type="checkbox"/> Low likelihood of findings due to chance, false positive and false negative outcomes <input type="checkbox"/> Non-significant findings are reported, but the confidence intervals include clinically meaningful differences <input type="checkbox"/> If variables are dichotomous, Intention-to-Treat Analysis (ITT) performed for efficacy (not safety) (all people are analyzed as randomized + reasonable method for imputing missing values). (May not be an issue if missing values are very few.) <input type="checkbox"/> If time-to-event analysis performed, appropriate, transparent and unbiased. Evaluate censoring rules. <input type="checkbox"/> Analysis methods are appropriate and use of modeling only with use of reasonable assumptions <input type="checkbox"/> No problems of selective reporting or selective exclusion of outcomes
Usefulness & Other Considerations	
Assessment	<input type="checkbox"/> Clinically significant area + sufficient baseline, prognostic and/or treatment effect data to justify or effect on outcomes

3

ABBV

Embed in your head
some little codes
+
get ready to
Roll!

aim

rand

intv

incl

excl

blind

loss

stats

res

4

Make a quick Assessment!



Is Reading This Study Worth Your Time?

1. Right study **design**???
2. If the results are reliable, are they **useful** and usable? Would they change your practice?
3. Are the results in **clinically significant** areas? If not, is there a reliable causal chain of evidence to support use of an intermediate marker?
4. Were outcomes and analyses determined in **advance**?
5. Are **definitions** of outcomes such as success/failure, improvement/no improvement, etc. reasonable?
6. Are the **confidence intervals** wholly inclusive of clinical benefit? If **non-significant**, are the confidence intervals wholly exclusive of clinical benefit?
7. Is this a **new intervention**? If yes, safety is likely to be unknown.



5

Hunt for trouble! (doing the markup)

the "hunting
for
bias + chance
dance"



JOURNALIA MEDICUS HYPOTHETICALIA

Vol. 55, No. 2, April 1, 2012, pp 1225-1234
Delfini Group Publishing, LLC

Use of Myoceptimab, a New Smooth Muscle Surface Protein Inhibitor, for Treatment of Patients with Exercise-Related Coronary Artery Angina On Individualized Medical Therapy
Pinglo Harold S, Twister Michael E and Stuart Martha E. University of Delphinidae.

BACKGROUND

Myoceptimab is a smooth muscle cell proliferation inhibitor that affects coronary arterial blood flow and provides relief from angina.

METHODS

MC
INCL We conducted a randomized, double-blind trial in 18 centers with similar populations in the US to assess the efficacy and safety of myoceptimab in patients aged 55 and older who had a history of coronary heart disease (CHD), exercise-related angina and were on optimal medical therapy as determined by their physicians for stable coronary artery disease

EXCL patients with a history of heart failure were excluded. Eligible patients experienced at least three episodes of angina per week, were on optimal medical therapy as determined by their physicians for stable coronary artery disease

of the trial regardless of their participation status.

INTV
DUR
FATE
CA
Patients were randomly assigned to receive 60 mg of myoceptimab or placebo daily for 36 months utilizing a computer-generated sequence. Allocation was concealed through use of identical, locked, metal containers maintained under the control of the Central Pharmacy Director who was not otherwise involved in the study. Assignment to study group was carried out utilizing local pharmacy personnel not aware of the study objectives and not otherwise involved in the study.

BLND
Study medications were identical in both groups in all aspects such as medication size, color, and taste. Myoceptimab and identical placebo were provided by the pharmaceutical companies without charge and were placed in identical capsules by Tech Inc., a laboratory not

To Watch Me Mark-up A Study, Follow These Instructions

- Go to www.delfini.org
- On the left, look for **FREE ONLINE TUTORIAL**



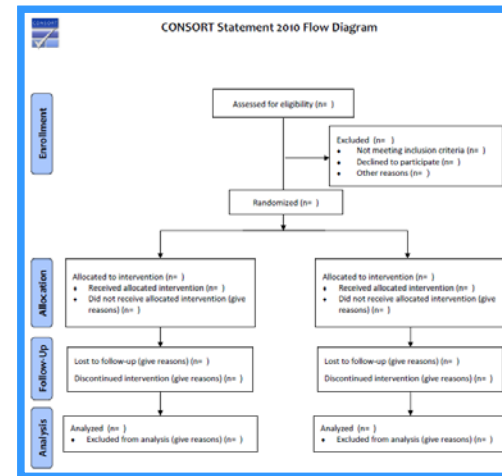
- Click + select "Videos"



Menu.....

- Lack of Critical Appraisal May Hurt Patients
- Unreliable Science & The Distorting Effects of Bias
- Simple Steps to Critical Appraisal
- Resources
- Contact Delfini
- References
- Videos

Look at Text + Tables



We Review the Checklist

Fast First Pass + Mark-up



- Fast pass is *fast!*
- Logs critical appraisal elements **in your head** as you go
- Answers to **questions might be addressed later**, so helps minimize just-in-time struggle
- Mark** negative items, questions, need for action steps along with your entries as you go
- Review your **checklist** and add **missing items as threats** or questions to the top
- Advantages
 - Helps makes it **fast to summarize** your critical appraisal
 - Makes it easy to **find elements of interest**
 - Is your **documentation**

We List Threats to Validity

Delfini Critical Appraisal Case Study

HYPOTHETICAL CASE STUDY: MYOCEPTIMAB PREVENTS CARDIOVASCULAR MORBIDITY
Critical Appraisers & Date: Sheri A. Stille & Michael E. Stuart MD, Delfini Group; April Fool's Day 2000-Any Year

PUBLISHED ABSTRACT

Background
Elevated myoreactive protein has been demonstrated to be associated with increased risk of myocardial infarction (MI). Myoceptinab is an inhibitor of myoreactive protein and has been shown to reduce myoreactive protein levels.

Methods
We conducted a randomized, double-blind trial in the Beaverton University Heart Care Center to assess the efficacy and safety of myoceptinab compared to placebo in patients with elevated myoreactive protein levels.

RESULTS
The trial was terminated early due to a high rate of adverse events in the myoceptinab group.

CONCLUSIONS
Myoceptinab is not recommended for the treatment of elevated myoreactive protein levels.

ADDITIONAL REVIEWER COMMENTS
Safety: No reported differences in safety outcomes.

CRITICAL APPRAISAL

Design

- Primary endpoint: questionable composite

Selection

- Study size: small
- Randomization: not truly randomized; patients assigned to groups by study consent date
- Concealment of allocation: no details
- Baseline characteristics: slightly higher rate of angina in the placebo group

Performance

- Blinding: insufficient details and no indication of blind assessment

Then We Grade
or Tag It With a
Rating

Usually we only appraise
until grade is determined.



Basics For Evaluating Medical Research Studies: A Simplified Approach

And Why Your Patients Need You To Know This

Delfini Group Evidence-based Practice Series
A Short How-to Guide Book

The Pharmacy & Therapeutics Committee Evidence-Based Decision-Making Handbook

Practical Guidance, Advice, Strategies, Tips and Efficiencies

Delfini Group Evidence-based Practice Series

The Medical Technology Assessment Evidence-Based Decision-Making Handbook

Practical Guidance, Advice, Strategies, Tips and Efficiencies

Delfini Group Evidence-based Practice Series

The Evidence-Based Clinical Improvement Project Process Map & Clinical Guideline Advice

Practical Guidance, Advice, Strategies, Tips and Efficiencies

Delfini Group Evidence-based Practice Series

EBM Guide For Scientists to Sales Reps Medical Evidence in the World of Payers & Health Care Systems

A Handbook For Industry to Better Understand, Communicate and Navigate These Worlds

Delfini Group Evidence-based Practice Series

What You Don't Know Can Hurt You A Guide for Patients

Help for Navigating Medical Information & Making Informed Decisions

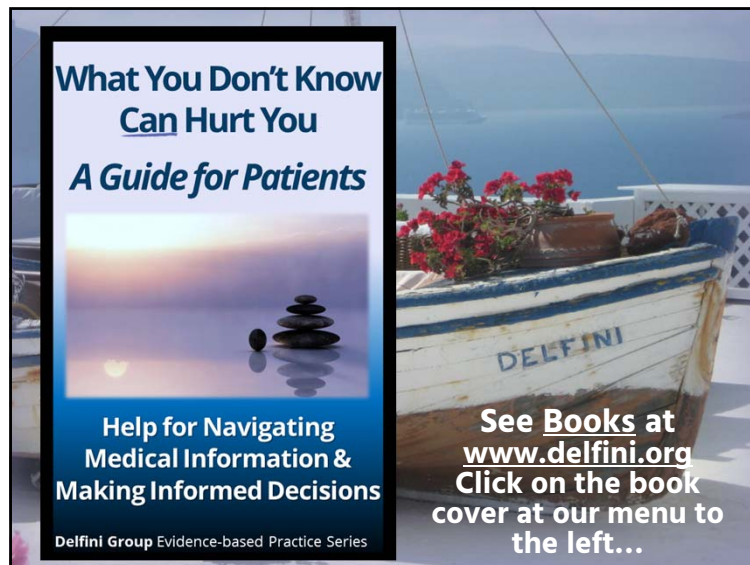
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- Includes a link to freely available patient resources
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