

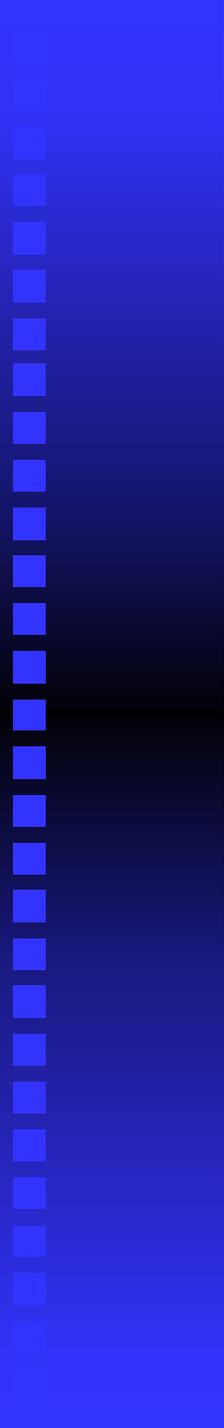
2nd Annual Summer Institute
on
Randomized Clinical Trials

Airlie Conference Center

Warrenton, Virginia

July 28-August 9, 2002

Peter G. Kaufmann, Ph.D.



Why am I here?



“You must always be students,
learning and unlearning ‘till your
life’s end”

Joseph Lister

Purpose 1

- To promote advances in knowledge through randomized clinical trials involving behavioral interventions.
 - ◆ RCTs are the gold standard.
 - ◆ Deceptively simple – difficult to carry out well, avoiding bias.

Avoiding bias

- Elements of clinical trials:
 - ◆ Appropriate design.
 - ◆ Meticulous conduct.
 - ◆ Correct statistical analysis.
 - ◆ Correct interpretation and reporting of results.

Purpose 2

- To increase the number of RCTs
 - ◆ RCTs - rarely ideal
 - ◆ Generalizability
 - ◆ Subgroups
 - ◆ Dosing
 - ◆ Timing of treatment
 - ◆ Stage of illness
 - ◆ Replication: Meta-analyses

Purpose 3

- To promote Evidence-Based Medicine

Evidence-Based Medicine

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

David L. Sackett

BMJ, 1996

What are “decisions about...care”

- Diagnosis
- Prognostic markers
- Clinically relevant research
- Clinical experience
- Patient's preferences

What is
“best evidence” ?

- Randomized Clinical Trials

Best evidence – Case 1

- 1824: France imports 33 million leeches.com to suck up 85,000 l of blood.
- 1835: Pierre Louis observes how cure rates vary with delay: leeches of no value.
- 1837: France imports 7,000 leeches.com.

Best evidence – Case 2

- 1953: Batterzatti introduces internal mammary artery ligation surgery for angina.
- 1957: Prestigious medical journal (Reader's Digest) publishes article praising IML.
- 1958 Diamond; 1959 Cobb: publish RCTs showing IML to have no benefit..

IML RCTs

■ Diamond, 1958:
10 of 13 improve
with IML surgery

■ Cobb, 1959:
3 of 8 improve
with IML surgery

IML RCTs

■ Diamond, 1958:
10 of 13 improve
with IML surgery

5 of 5 improve
with sham
surgery

■ Cobb, 1959:
3 of 8 improve
with IML surgery

4 of 9 improve
with sham
surgery

Best Theory – Case 3

- Ventricular Premature Complexes (VPCs) predispose to v. arrhythmias, sudden death.
- Long-acting antiarrhythmic drugs protect against VPCs;
- 1985: 3,000-patient post-marketing database.
- Cardiac Arrhythmia Suppression Trial (CAST).

Best theory – Case 3

- Cardiac Arrhythmia Suppression Trial (CAST); 1989.
- n = 2309.
- Post-myocardial infarction, 6 PVCs/hr.
- Encainide, Flecainide, Moricizine.
- 10 months follow-up.
- Outcome: RR of death 3.6 in favor of placebo for deaths and non-fatal events.

“A remedy which is known to work, though nobody knows why, is preferable to a remedy which has the support of theory without confirmation in practice.”

Richard Asher
Lancet, 1961

Best (observational) evidence – Case 4

- Women's Health Initiative (WHI).
- RCT of Estrogen + Progestin HRT for post-menopausal women.
- $n = 16,608$.
- Expected benefits, based on observational data, for non-fatal MI and CHD death.
- 5.2 years of follow-up.

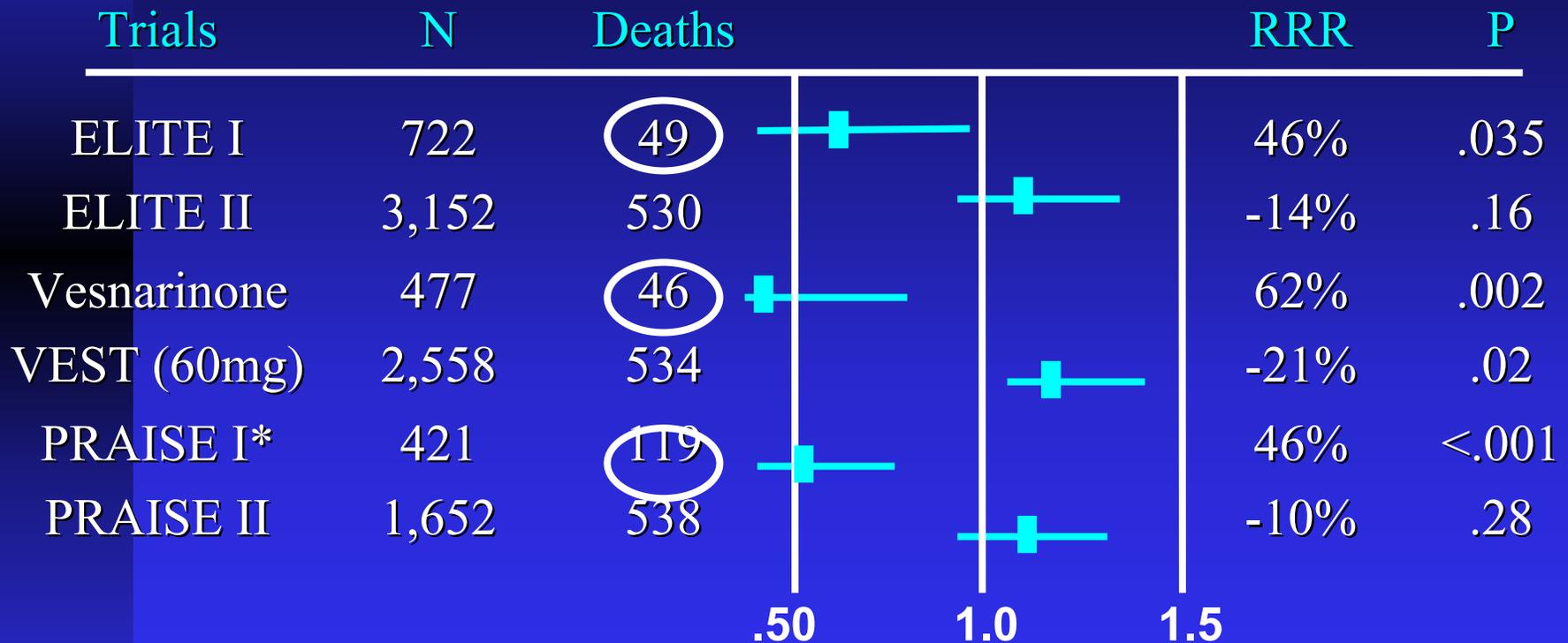
Best (observational) evidence – Case 4

- Women's Health Initiative (WHI)
 - Hazard Ratios, selected outcomes:
 - CHD: 1.29 (1.02-1.63)
 - Breast cancer: 1.26 (1.00-1.59)
 - Stroke: 1.41 (1.07-1.85)
 - Pulmonary embolism: 2.13 (1.39-3.25)
- JAMA, July 17, 2002

Best (close to home) evidence – Case 5

- ENRICHD - 2002
- Treating Depression and Perceived Low Social Support.....

Small Trials in Cardiology are Unreliable



* (non-ischemic only)

Our own myths ?

- Eye Movement Desensitization Training.
- Relaxation Training.
- Thought Field Therapy.

James Herbert et al.
Clin Psych Rev, 2000.

What is “best evidence” ?

RCT

How sick should the the study participants be?

How should the outcomes be ascertained?

How powerful should the intervention be?

How many patients should be enrolled?

How certain will the conclusions be?

“Counting (the outcome of treatment) requires more labor and time than the most distinguished members of our profession can dedicate to it”

Pierre Louis

“Heaven is other people...”

Jean-Paul Sartre
1905-1980

“Heaven is (other) people...

...collaborating in clinical trials.”

Jean-Paul Sartre

1905-1980

Don't go it alone!