

**Statistical Challenges in Medical Research:
What Consumers Need to Know**

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The Clinical Trial

Backbone of Medical Progress
Cancer Survival Rates
Synthetic Estrogen
Vaccines – Smallpox, Diphtheria Tb
Debilitating Diseases – Rheumatoid Arthritis, MS
Can End Up With Erroneous Findings

(2)

Researcher Mistakes

Wrong Doses, Measurements, Length
Inappropriate Analyses
Economic, Political, Religious Ideology
Media - Distorted Public Perception

(3)

Most Findings Are False
J. Ioannidis

Statistical - N, Effect Size, P, No. Tests
Other - Outcome, Design, Conflict Interest
Medical Community Response
5 Supportive Replies
1 Criticism - Over-estimate (math model flaw)
100 K Downloads "Cult Classic"

(4)

Seven Deadly Flaws

1. The Unknown Population
2. The Imperfect Sample
3. Inequality Among Treatment Groups
4. Uncontrolled Experimental Setting
5. Breakdown of Blinding
6. Impractical Results
7. Insufficient Sample Size

(5)

1. Unknown Population

- The Research Paradigm
 - Define the population
 - Draw a Representative Sample
 - Do a Research Study
 - Infer Sample Results to Population
- The Research Reality
 - Population not Identifiable
 - Start by Selecting Investigators
 - Are Study Population and Target Population Alike?

(6)

2. Imperfect Population

- Volunteers Only
- Non-Volunteers - A Different Type
- Example from Clinical Pharmacology Trial
 - More Psychiatric Illness
 - More with Other Medical Conditions
- Ok if No Effect on Outcomes

(7)

3. Unequal Treatment Groups

Baseline Equivalence Required

Use Randomization

Large Sample = Protection

Baseline Differences – Neutralized

Unaware of Factors

Human Genome

• (8)

4. Uncontrolled Experimental Setting

Ideal - Only Treatments Vary

Physical Science Controls Factors

Biological Science Example – Diuretics

Clinical Trial - Uncontrollable Environment

(9)

5. Breakdown of Blinding

Blinding Not Always Feasible

Patient Recognition (e.g. Dry Mouth)

Investigator Recognition (e.g. Flushing)

Example - Psychotropic Drug Study

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6. Impractical Result

Research Setting – Optimized

MD Setting – “Real World”

Bypass Surgery Example

(11)

7. Insufficient Sample Size

Determined by Formula

Know Mean, Variation

Test Many Variables

N is too small, N is too Large

The Rare Deadly Side Effect

N > 5K, Length > 5 Years

289 Paired Mega Trials

Inconsistent Result – 27%

(12)

Conclusion

Small Probability for Single Flaw

Escape All Flaws = Luck

Researcher Appreciation

 Their Fortitude, Perseverance, Diligence

 Bit of Divine Intervention

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