

**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

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## 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

(10)

## 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

(13)