Sample Size Issues and Determination in Maternal and Child Health

Ruben Smith, PhD., MS.
Adriana Perez, PhD., MS.
Juan Acuña, M.D., MS.
Brian Morrow, MA.

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Instructors

Ruben Smith, PhD, MS.
Applied Sciences Branch. Division of Reproductive Health. Centers for Disease Control and Prevention
Atlanta, GA 30341

Adriana Perez, MS., PhD
The University of Louisville
School of Public Health. Department of Bioinformatics & Biostatistics
Louisville, KY 40292

Juan M. Acuña, M.D., MS.
Maternal and Child Health Epidemiologist and CDC MCH EPI Team Leader
Applied Sciences Branch. Division of Reproductive Health
Atlanta, GA 30341

Brian Morrow, MA.
Applied Sciences Branch . Division of Reproductive Health . Centers for Disease Control and Prevention
Atlanta, GA 30341

Timeline and logistics

Day 1:

- 1:00-3:00 Session I
- 3:00-3:15 Break
- 3:15-5:00 Session II

Day 2:

- 8:30-10:00 Session III
- 10:00-10:15 Break
- 10:15-12:15 Session IV
- 12:15- 1:30 Lunch
- 1:30- 4:00 Session V

Outline

1. **Sample Size – Basic Issues** (Juan Acuña)
2. **Sampling foundations** (Brian Morrow)
3. **Sample size determination: Introduction** (Ruben Smith)
4. **Sample size determination: Confidence interval approach** (Ruben Smith)
5. **Sample size determination: Test of significance approach** (Adriana Perez)
6. **Sample size for sample surveys** (Ruben Smith)

Sample Size – Basic Issues

Juan Acuña, MD, MSc

Pre-conference Training Workshop

13th Maternal and Child Health Epidemiology Conference, December 10-11, 2007 -Atlanta, GA

The findings and conclusions in this presentation have not been formally disseminated by the Centers for Disease Control and Prevention and should not be construed to represent any agency determination or policy

Centers for Disease Control and Prevention
National Center for Chronic Disease Prevention and Health Promotion

Presentation Outline

- Introduction
- Basic epidemiologic issues
- Basics of sample size
  - Statistical errors
  - Alpha, beta
  - Small, large samples
- Epidemiological consequences of sample size

Introduction

- Sampling ≠ sample size
  - Goal is to maximize value of research
  - Value is measured in resources
  - Maximize efficiency of research processes

OPEN ACCESS Freely available online

PLoS one

A Randomized Controlled Pilot Trial of Azithromycin or Artesunate Added to Sulfadoxine-Pyrimethamine as Treatment for Malaria in Pregnant Women

Linda Kalilani[1]*, Innocent Mofolo[2], Marjorie Chaponda[2], Stephen J. Rogerson[3], Alisa P. Alker[1], Jesse J. Kwiek[1], Steven R. Meshnick[1]

1 Department of Epidemiology, University of North Carolina, Chapel Hill, North Carolina, United States of America, 2 College of Medicine, University of Malawi, Blantyre, Malawi, 3 University of Melbourne, Parkville, Australia

Purposes of Sampling

- Improve efficiency of research processes
- Assure adequacy of the research process
- Address methodological adequacy to respond to research questions
- Address the consequences related to testing (i.e. interventions) in more or less of needed subjects

Purpose of Sample Size Calculation

- Address planning adequacy
- Economic reasons (what if each record for a birth weight study would cost $1?)
- Decrease potentially harmful exposures within research settings
- Address ethical concerns
- Assure the adequacy of the conclusions from the perspective of the hipothesis

Approaches to sample size calculation

- Specify the desired measure to be addressed by the study (for example the with of a confidence interval)
- Bayesian approach (based on conditional functions such as precision and cost)
- Defining the power to test an hypothesis

Power Approach

- Specify a hypothesis test on a parameter of importance for the research
- Specify the level of alpha
- Specify an effect size (or an alternative value for the parameter in step 1)
- Obtain evidence of certainty (or guidance, at least) on the effect size
- Specify a target value of the power when the parameter to be tested equals the final parameter (effect size =0)

Economic Consequences of Preterm Birth

- Hospital charges for premature infants[1] totaled $18.1 billion in 2003.
- Premature infants accounted for half of the hospital charges for all infants ($36.7 billion).
- The average charge for the most severe stays[2] was $77,000 compared to $1,700 for an uncomplicated newborn stay.

[1]Includes any diagnosis of prematurity/low birthweight
[2]Defined as having a principal diagnosis of prematurity
Source: Agency for Healthcare Research and Quality, 2003 Nationwide Inpatient Sample.
Prepared by March of Dimes Perinatal Data Center, 2006.

US National Standard Birth Certificate

U.S. STANDARD CERTIFICATE OF LIVE BIRTH

LOCAL FILE NO.

BIRTH NUMBER:

CHILD

1. CHILD'S NAME (First, Middle, Last, Suffix)
2. TIME OF BIRTH (24 hr)
3. SEX
4. DATE OF BIRTH (Mo/Day/Yr)
5. FACILITY NAME (if not institution, give street and number)
6. CITY, TOWN, OR LOCATION OF BIRTH
7. COUNTY OF BIRTH

MOTHER

8a. MOTHER'S CURRENT LEGAL NAME (First, Middle, Last, Suffix)
8b. DATE OF BIRTH (Mo/Day/Yr)
8c. MOTHER'S NAME PRIOR TO FIRST MARRIAGE (First, Middle, Last, Suffix)
8d. BIRTHPLACE (State, Territory, or Foreign Country)
9a. RESIDENCE OF MOTHER-STATE
9b. COUNTY
9c. CITY, TOWN, OR LOCATION
9d. STREET AND NUMBER
9e. APT. NO.
9f. ZIP CODE
9g. INSIDE CITY LIMITS? ☐ Yes ☐ No

FATHER

10a. FATHER'S CURRENT LEGAL NAME (First, Middle, Last, Suffix)
10b. DATE OF BIRTH (Mo/Day/Yr)
10c. BIRTHPLACE (State, Territory, or Foreign Country)

CERTIFIER

11. CERTIFIER'S NAME: _____
TITLE: ☐ MD ☐ DO ☐ HOSPITAL ADMIN. ☐ CNM/CM ☐ OTHER MIDWIFE
☐ OTHER (Specify)_____
12. DATE CERTIFIED ____/____/_____ MM DD YYYY
13. DATE FILED BY REGISTRAR ____/____/_____ MM DD YYYY

INFORMATION FOR ADMINISTRATIVE USE

MOTHER

14. MOTHER'S MAILING ADDRESS: 9 Same as residence, or: State: City, Town, or Location:
Street & Number: Apartment No.: Zip Code:
15. MOTHER MARRIED? (At birth, conception, or any time between) ☐ Yes ☐ No
IF NO, HAS PATERNITY ACKNOWLEDGEMENT BEEN SIGNED IN THE HOSPITAL? ☐ Yes ☐ No
16. SOCIAL SECURITY NUMBER REQUESTED FOR CHILD? ☐ Yes ☐ No
17. FACILITY ID. (NPI)
18. MOTHER'S SOCIAL SECURITY NUMBER:
19. FATHER'S SOCIAL SECURITY NUMBER:

INFORMATION FOR MEDICAL AND HEALTH PURPOSES ONLY

MOTHER

20. MOTHER'S EDUCATION (Check the box that best describes the highest degree or level of school completed at the time of delivery)
- ☐ 8th grade or less
- ☐ 9th - 12th grade, no diploma
- ☐ High school graduate or GED completed
- ☐ Some college credit but no degree
- ☐ Associate degree (e.g., AA, AS)
- ☐ Bachelor's degree (e.g., BA, AB, BS)
- ☐ Master's degree (e.g., MA, MS, MEng, MEd, MSW, MBA)
- ☐ Doctorate (e.g., PhD, EdD) or Professional degree (e.g., MD, DDS, DVM, LLB, JD)

21. MOTHER OF HISPANIC ORIGIN? (Check the box that best describes whether the mother is Spanish/Hispanic/Latina. Check the "No" box if mother is not Spanish/Hispanic/Latina)
- ☐ No, not Spanish/Hispanic/Latina
- ☐ Yes, Mexican, Mexican American, Chicana
- ☐ Yes, Puerto Rican
- ☐ Yes, Cuban
- ☐ Yes, other Spanish/Hispanic/Latina

(Specify)_____

22. MOTHER'S RACE (Check one or more races to indicate what the mother considers herself to be)
- ☐ White
- ☐ Black or African American
- ☐ American Indian or Alaska Native (Name of the enrolled or principal tribe)_____
- ☐ Asian Indian
- ☐ Chinese
- ☐ Filipino
- ☐ Japanese
- ☐ Korean
- ☐ Vietnamese
- ☐ Other Asian (Specify)_____
- ☐ Native Hawaiian
- ☐ Guamanian or Chamorro
- ☐ Samoan
- ☐ Other Pacific Islander (Specify)_____
- ☐ Other (Specify)_____

FATHER

23. FATHER'S EDUCATION (Check the box that best describes the highest degree or level of school completed at the time of delivery)
- ☐ 8th grade or less
- ☐ 9th - 12th grade, no diploma
- ☐ High school graduate or GED completed
- ☐ Some college credit but no degree
- ☐ Associate degree (e.g., AA, AS)
- ☐ Bachelor's degree (e.g., BA, AB, BS)
- ☐ Master's degree (e.g., MA, MS, MEng, MEd, MSW, MBA)
- ☐ Doctorate (e.g., PhD, EdD) or Professional degree (e.g., MD, DDS, DVM, LLB, JD)

24. FATHER OF HISPANIC ORIGIN? (Check the box that best describes whether the father is Spanish/Hispanic/Latino. Check the "No" box if father is not Spanish/Hispanic/Latino)
- ☐ No, not Spanish/Hispanic/Latino
- ☐ Yes, Mexican, Mexican American, Chicano
- ☐ Yes, Puerto Rican
- ☐ Yes, Cuban
- ☐ Yes, other Spanish/Hispanic/Latino

(Specify)_____

25. FATHER'S RACE (Check one or more races to indicate what the father considers himself to be)
- ☐ White
- ☐ Black or African American
- ☐ American Indian or Alaska Native (Name of the enrolled or principal tribe)_____
- ☐ Asian Indian
- ☐ Chinese
- ☐ Filipino
- ☐ Japanese
- ☐ Korean
- ☐ Vietnamese
- ☐ Other Asian (Specify)_____
- ☐ Native Hawaiian
- ☐ Guamanian or Chamorro
- ☐ Samoan
- ☐ Other Pacific Islander (Specify)_____
- ☐ Other (Specify)_____

Mother's Name _____

Mother's Medical Record No. _____

26. PLACE WHERE BIRTH OCCURRED (Check one)
- ☐ Hospital
- ☐ Freestanding birthing center
- ☐ Home Birth: Planned to deliver at home? 9 Yes 9 No
- ☐ Clinic/Doctor's office
- ☐ Other (Specify)_____

27. ATTENDANT'S NAME, TITLE, AND NPI
NAME: _____ NPI:_____
TITLE: ☐ MD ☐ DO ☐ CNM/CM ☐ OTHER MIDWIFE
☐ OTHER (Specify)_____

28. MOTHER TRANSFERRED FOR MATERNAL MEDICAL OR FETAL INDICATIONS FOR DELIVERY? ☐ Yes ☐ No
IF YES, ENTER NAME OF FACILITY MOTHER TRANSFERRED FROM:
_____

Gestational diabetes, other diabetes, or both, as reported on hospital discharge vs. birth/fetal death certificates, MA residents, CY 1998-2004

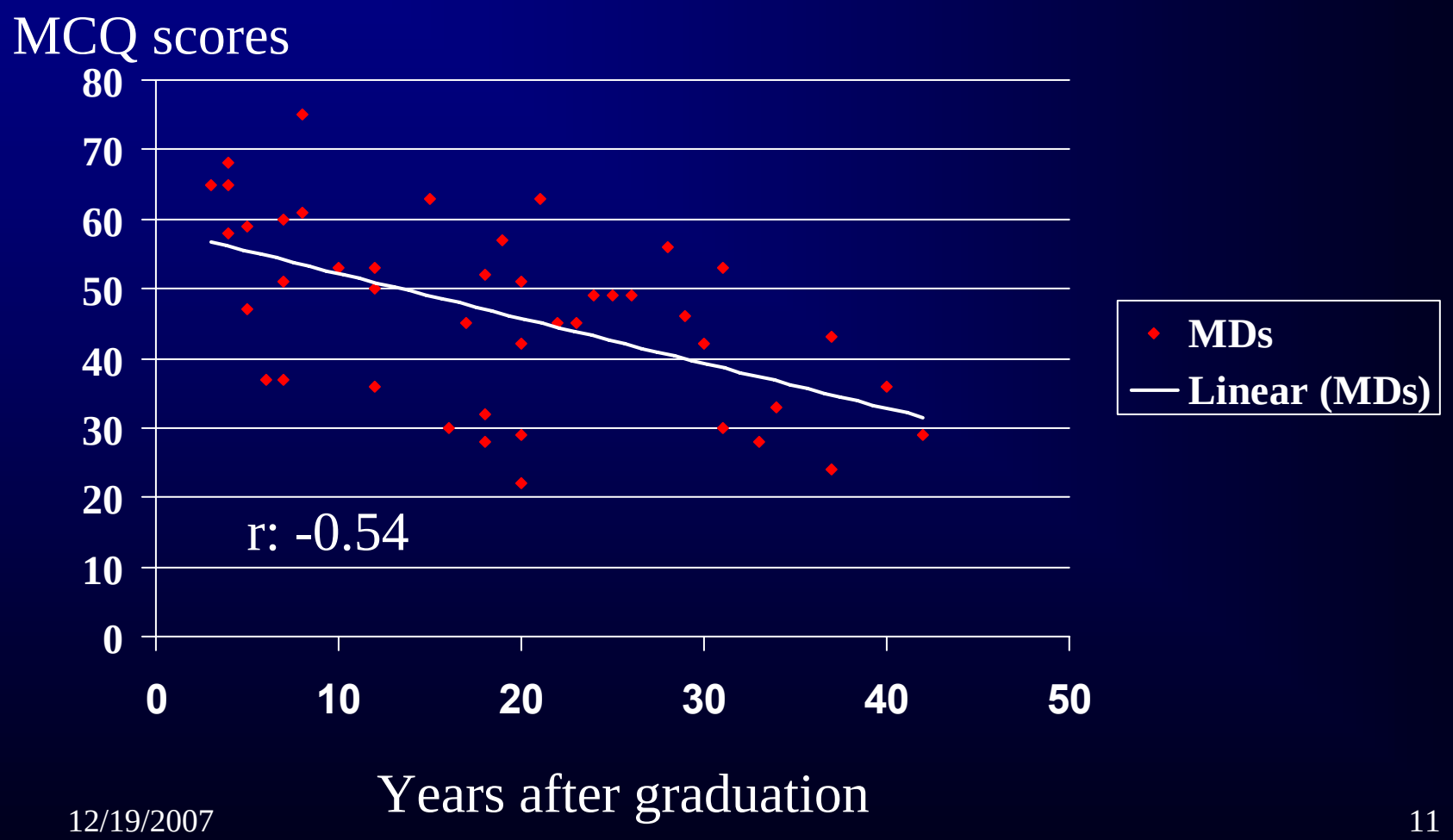
Birth/Fetal Death Cert	Hospital Discharge Data				Total
	No Diabetes	Gest. Diabetes	Other Diabetes	Both (Gest and Others)	
No Diabetes	521,738	6,763	411	50	528,962
Gest. Diabetes	3,345	12,713	329	85	16,472
Other Diabetes	1,098	461	1441	15	3,015
Both (Gest. and other)	354	871	95	32	1,352
Total	526,535	20,808	2,276	182	549,801

Gest Only: 22,821 Other: 5,249 Total: 28,070

Source: PELL

Small Sample Example

Ramsey PG, et al: Changes over time in the knowledge base of practicing internists. JAMA 1991;255:501-4



Elements in Sample Size

- Hypothesis
- Hypothesis testing:
  - Type I error
  - Type II error
- Level of alpha: usually 5% (0.05)
- Power level: (1-ß) usually 80% (0.8)
- Effect size:
  - Point estimator, boundaries, variance

Hypothesis

- Research question
- Null hypothesis (or hypothesis of no difference, no association)
- Needs to be tested
- The whole idea is to “reject” the hypothesis
- If it cannot be rejected, the alternative hypothesis is not true

Example hypothesis test *:

The average height of foreign people in the US is 175cms

- Let us assume that in reality our sample mean is 180cms and the population standard deviation (sd) is 5cms (known).
- We can then form a test statistic as follows:

$$Z = \frac{\bar{X} - 175}{\sigma / \sqrt{n}} = \frac{5}{5 / \sqrt{n}} \sim N(0,1)$$

for small *n* and unknown sd we should use a student-t distribution

- For a 1-sided Z test we wish $Z = \sqrt{n} > 1.645$ and so we need our sample to be of size 3 to reject H_0, using a student-t distribution increases this to 5. (Here $\alpha = 0.05$)
- However if the sample mean had been only 176cms then we would need $n > (1.645*5)^2 = 68$ foreigners to reject H_0

* Modified from Brown W.

Power calculations

- This concept is somehow backwards as we cannot get from a given sample mean to choosing a sample size!
- What we do instead is use different terminology and assume we know everything
- We will choose an 'effect size', γ which will represent a guess at the increase in the sample mean for foreigners.
- There is an (approximate) formula that links four quantities, size (α), power (1-β), effect size (γ) and sample size (*n)*

$$\frac{\gamma}{SE(\gamma)} \approx z_{1-\alpha} + z_{1-\beta}$$

Here SS is sum of cases H_0 true and H_0 false.

- SE of γ is a function of *n* and σ the population sd which is assumed known.
- Real question? what sample size is required given α,1-β and γ?

Foreigners' height example

Here we have looked at two examples with effect sizes 5 and 1 respectively. Assume σ takes the value 5 and so let us suppose we take a sample of size 25 foreigners.

$$\frac{\gamma}{SE(\gamma)} \approx z_{1-\alpha} + z_{1-\beta}$$

Case 1: $5/(5/\sqrt{25})=1.645+z_{1-\beta}, z_{1-\beta}=3.355$

$\beta=0.9996$

a sample of 25 foreigners from a population with mean 180cms would almost always result in rejecting H_0,

Case 2: $1/(5/\sqrt{25})=1.645+z_{1-\beta}, z_{1-\beta}=-0.645$

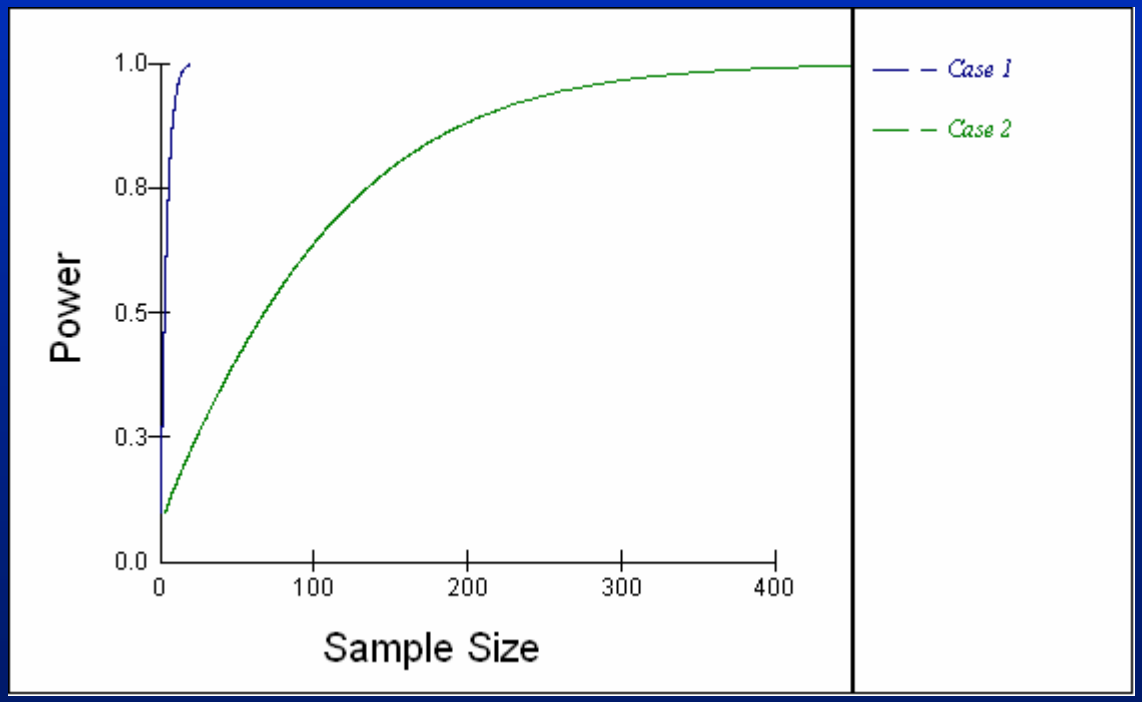
$\beta=0.25946$

if the population mean is 176cms then only 26% of such samples would be rejected.

We can plot curves of how power increases with sample size as shown in the next slide.

Power curve for foreigners' example*

Here we see the two power curves for the two scenarios:



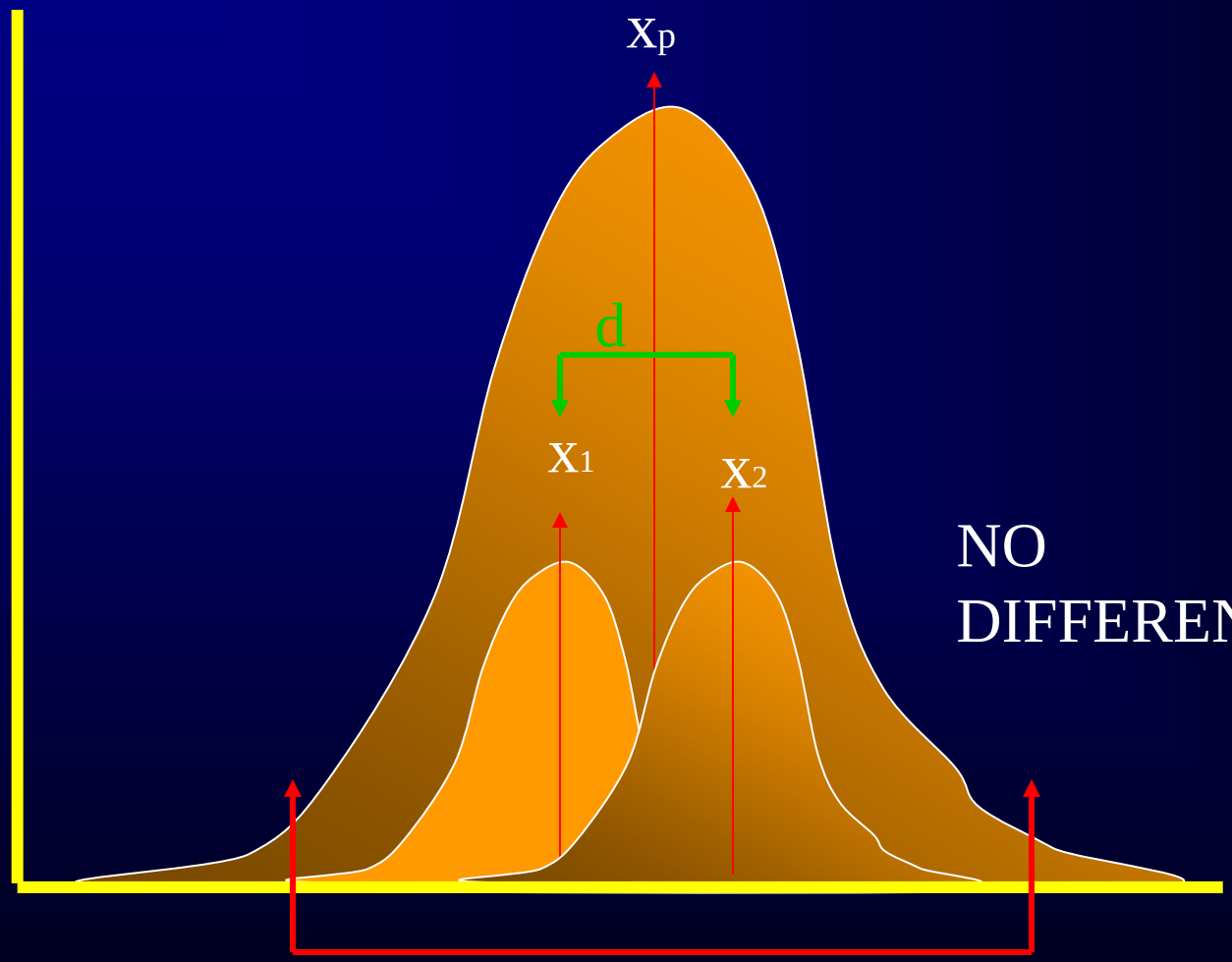
* Modified from Brown W.

Hypothesis Testing

H_0	Study Decision: accept	Study Decision: reject
true	Correct	Error (Type I)
false	Error (type II)	Correct

Bonus: Type III error: the right answer to the wrong question

Statistical difference:

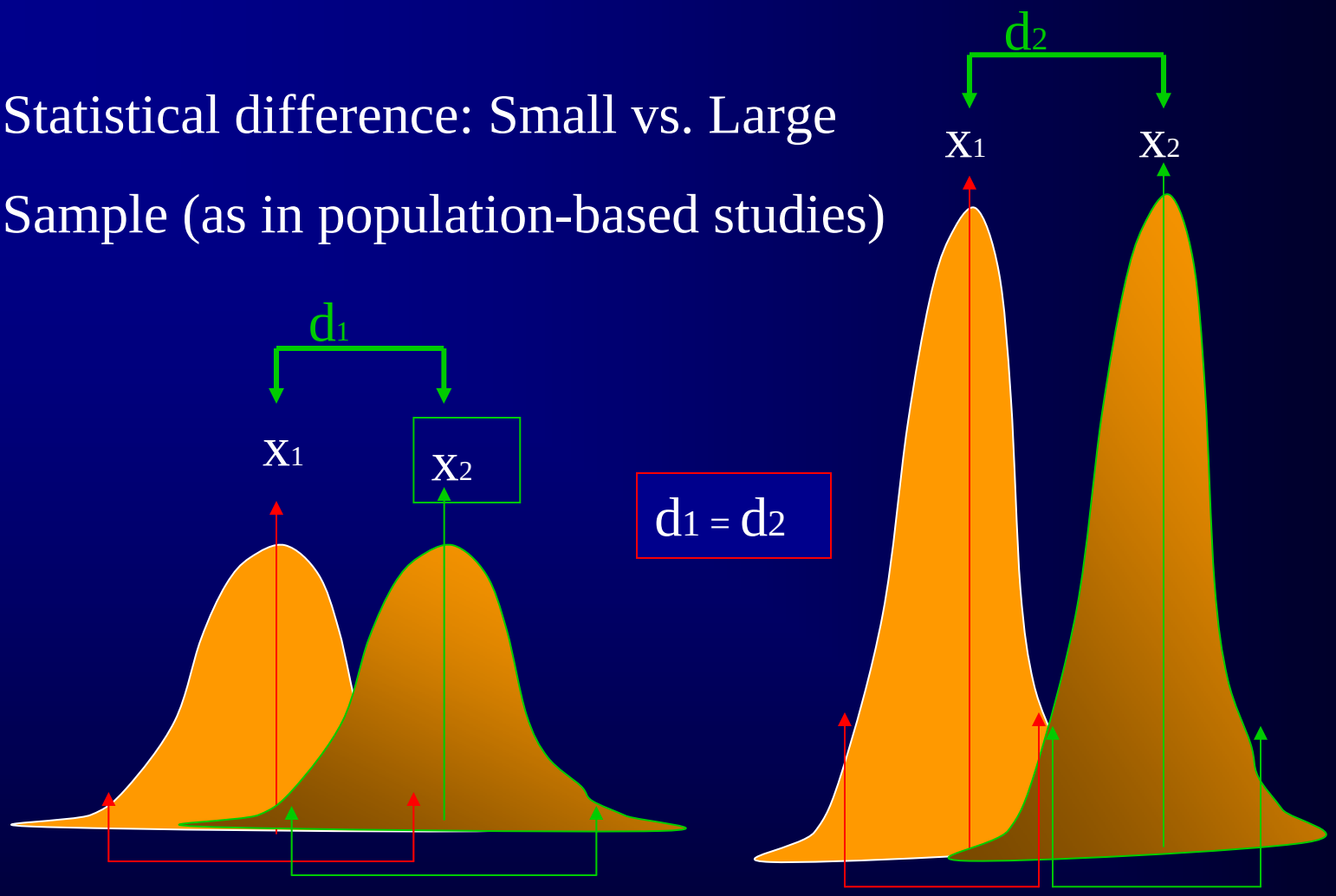


NO DIFFERENCE

In order to understand…

- Differences between large samples and small samples
  - In large samples, statistical significance is assured many times, even when clinical significance is not reached
  - In small samples, statistical significance might not be reached even in the presence of clinical interest

Statistical difference: Small vs. Large Sample (as in population-based studies)



NOT DIFFERENT

DIFFERENT !

Take home message: beware of studies with statistical significance and huge samples, that don't make much sense (from the clinical perspective)

Effect Size

- It is probably the most important single element in sample size calculation
- It is hypothesis-dependent
- Needs a known baseline
- Needs a final estimate
- Most likely, to be determined by a content expert without statistical/epidemiological background

Example: clinical trial

BMC Pregnancy and Childbirth

BioMed Central

Study protocol

Open Access

Birth after caesarean study – planned vaginal birth or planned elective repeat caesarean for women at term with a single previous caesarean birth: protocol for a patient preference study and randomised trial

Jodie M Dodd*[1], Caroline A Crowther[1], Janet E Hiller[2], Ross R Haslam[3] and Jeffrey S Robinson[1]

- Sample: 2314 women
- Alpha: 0.5 Power: 0.8
- Effect size: adverse neonatal outcome from 1.6% to 3.6%

Conclusions

- Good sample size determinations do not equal adequate sampling
  - Data-based validation of parameters
  - Team: statistical-epidemiological-content
- Despite simple formulas (few elements involved), a highly technical part of study design

Contact Information

Juan Acuña

Medical Epidemiologist

Maternal and Child Health Epidemiology Program

National Center for Chronic Disease Prevention and Health Promotion (NCCDPHP)

Centers for Disease Control and Prevention

770-488-5133

jacuna@cdc.gov