"TOOL-KIT FOR PRACTICING OH PHYSICIANS"

Working towards a healthier India

Dr. SANJAY P. ZODPEY, MD, PhD

Director, Indian Institute of Public Health, New Delhi
Director, Public Health Education,
Public Health Foundation of India, New Delhi

February 03, 2010

APPRECIATION & CORRECT INTERPRETATION OF COMMON STATISTICAL TERMS

Working towards a healthier India

Dr. SANJAY P. ZODPEY, MD, PhD

Director, Indian Institute of Public Health, New Delhi
Director, Public Health Education,
Public Health Foundation of India, New Delhi

February 03, 2010

SCOPE

- Key terms (statistical / epidemiological)

ERRORS

1. Random Errors
2. Systematic Errors (Bias)

RANDOM ERROR

- Describes the role of chance, particularly when the effects of explanatory or predictive factors have already been taken into account.

SYSTEMATIC ERROR (BIAS)

- Describes deviations that are not a consequence of chance alone,
- Several factors (e.g. patient selection effects) might contribute to it,
- Can usually be removed or reduced by good design and conduct of the experiment.

BIASES IN MEDICAL RESEARCH

- *"On being asked to talk on the principles of research, my first thought was to arise after the chairman's introduction, to say, 'Be careful', and to sit down……*

Cornfield J. Principles of Research. 1959

BIAS - DEFINITION

- Bias is defined as ‘any effect at any stage of investigation or inference tending to produce results that depart systematically (i.e. one-sidedly) from the true values. *(Last JM. A dictionary of Epidemiology, Oxford University Press; 1983)*

- *Bias is systematic deviation from truth (Validity)*

VALIDITY

- Validity = Accuracy
- The degree to which the variable actually represents what it is suppose to represent.
- Validity is the extent to which the results are free from bias
- A function of systematic error or bias.

- Bias may affect - Internal & External Validity.

INTERNAL VALIDITY

- It's capacity to yield sound conclusions with respect to the study population
- Concern: Are the results correct for the subjects in the study?

EXTERNAL VALIDITY

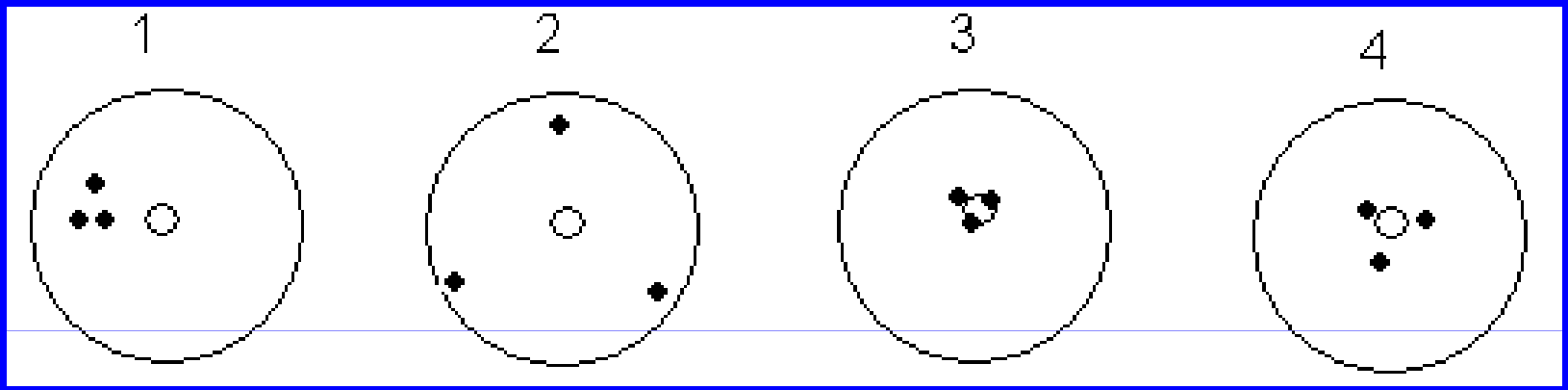
- The ability to make valid generalizations to a broader reference population.
- Concern: To which population are the results of the study applicable or generalizable?

PRECISION (RELIABILITY)

- The degree to which variable has the same value when measured several times.

- A measure of consistency
- Simply refers to the width of CI
- A function of random error

ACCURACY AND PRECISION



1	2	3	4
NOT ACCURATE	NOT ACCURATE	ACCURATE	ACCURATE
PRECISE	NOT PRECISE	PRECISE	NOT PRECISE

STUDY VARIABLES

- Dependent / independent
- Discrete / continuous
- Quantitative / qualitative

NULL HYPOTHESIS (H_0)

- A hypothesis of no difference among groups (or no association between the predictor and outcome variables) that needs to be tested.

ALTERNATIVE HYPOTHESIS (H_a)

- A hypothesis that in some sense contradicts the null hypothesis.
- There is a difference among the groups (or there exists an association between the predictor and outcome variable).
- H_a cannot be tested directly, it is accepted by exclusion if the test of significance rejects H_0.

A ONE-TAILED (ONE-SIDED) HYPOTHESIS

- Specifies the difference (or effect or association) in one direction only.
- Patients with pancreatic cancer will have a higher rate of coffee drinking than control patients.
- *A one-tailed approach leads to a smaller sample size.*

A TWO-TAILED (TWO-SIDED) HYPOTHESIS

- Specifies the difference (or effect or association) in either direction.

- Patients with pancreatic cancer will have a different rate of coffee drinking - either higher or lower - than control patients.

TYPE I (α) ERROR

- Occurs if an investigator rejects a null hypothesis that is actually true in the population.
- It is the error of falsely stating that two drug effects are significantly different when they are actually equivalent.
- The probability of making α error is called as level of significance.

TYPE II (β) ERROR

- Occurs if the investigator fails to reject a null hypothesis that is actually false in the population.
- It is the error of falsely stating that two drug effects are equivalent when they are actually different.

Truth in the population versus the results in the sample: The four possibilities.

		Truth in the Population	
		Difference/ Association	No Difference/ No Association
		+	-
Study Results	+	Correct (1-β)	α
	-	β	Correct

POWER (1-β)

- Probability that the test will correctly identify a significant difference / effect / association in the sample, should one exist in the population.

EFFECT SIZE

- The term refers to the magnitude of effect under alternative hypothesis.
- Effect size should represent the smallest difference but that would be of clinical or biological significance.

SAMPLE SIZE AND EFFECT SIZE

POWER=80%, TWO-TAILED α = 5%

Effect Size (2 Sample Proportions)	n per group
30% Vs 40% (i.e. small effect size)	356
30% Vs 50% (i.e. intermediate effect size)	93
30% Vs 60% (i.e.large effect size)	47

APPROACHES: STATISTICAL INFERENCE

- Estimation
  (Confidence Interval Approach)

- Hypothesis Testing
  (Test of Significance Approach)

ESTIMATION (CI APPROACH)

- To determine the true treatment effect, we calculate the CI for our point estimate
- CI is a range of values within the “true” treatment effect is believed to be found, with a given level of confidence
- 95% CI is a range of values within which the “true” treatment effect will lie 95% of the time

ESTIMATION (CI APPROACH)

Interpretation: Odds Ratio (OR)

1.9 (1.3 - 2.4), 1.3 (0.9 - 1.6)

0.6 (0.2 - 0.9), 0.8 (0.3 - 1.1)

HYPOTHESIS TESTING

- We want to compare the outcomes in two treatment arms (A and B)
- Testing two hypothesis

  H_0: A = B (Null hypothesis – no difference)

  H_1: A ≠ B
- Calculate test statistic based on the assumption that H_0 is true (i.e. there is no real difference)
- Test will give us a p value
- Smaller the p value, we reject H_0

HYPOTHESIS TESTING

- Smaller the p value, we reject H_0
- If $p < 0.05$ – the trial gives statistically significant evidence that there is a difference
- If $p \geq 0.05$ – Non significant – No difference

IS THIS THE CURRENT STATE OF STATISTICS NOW?

Statistics can never ***PROVE*** anything beyond ***any*** doubt, just beyond ***reasonable*** doubt!

How good is the intervention?

Love to have one sentence with one figure to answer this question…….

But,

One figure is not enough to tell the whole story about many things…….

To describe the results of a treatment study……

Use – Relative and Absolute Measures

- Risk Difference (Absolute measure)
- Risk Ratio (Relative Risk)
- Odds Ratio
- Rate Ratio

Each one gives a different perspective
Each one appeals to different constituencies

EXAMPLE

Whether treatment, with dexamethasone saves more lives in patients with acute bacterial meningitis?

RCT: 400 patients (all receive antibiotics)

Group A: 200 receive the dexamethasone in addition
Group B: 200 receive placebo in addition

Group A: 40 patients die
Group B: 50 patients die

EXAMPLE: Results of a hypothetical study

Study Results							
Treatment		**Death**		**Total**			
		Yes +	**No -**				
Group A	**Yes +**	40 a	160 b	200			
Group B	**No -**	50 c	150 d	200			

EXAMPLE: Results of a hypothetical study

Study Results					**If there was no effect (benefit) with the treatment**		
Treatment		**Death**		**Total**	**Death**		**Total**
		Yes +	**No -**		**Yes +**	**No -**	
Group A	**Yes +**	40 a	160 b	200	50	150	200
Group B	**No -**	50 c	150 d	200	50	150	200

EXAMPLE: Results in percent terms

Study Results					If there was no effect (benefit) with the treatment		
Treatment		Death		Total	Death		Total
		Yes +	No -		Yes +	No -	
Group A	Yes +	20%	80%	100%	25%	75%	100%
Group B	No -	25%	75%	100%	25%	75%	100%

Risk Difference (Absolute Risk Reduction)

- The percent or proportion of death = ‘risk’ or ‘probability’ of death
- The risk of death in treatment group (R_t) = 40/200 = 1/5 = 0.2 = 20%
- The risk of death in control group (R_c) = 50/200 = 1/4 = 0.25 = 25%
- The risk in control group = ‘Baseline Risk’ and ‘Control Event Rate’

Risk Difference (Absolute Risk Reduction)

- Difference in the risk (Risk Difference) = 20% - 25% = - 5%
- The treatment makes a difference (reduction) of - 5% in risk
- Risk Difference = Absolute Risk Difference
- '-' Minus sign: Decrease in risk with the treatment

Risk Difference (Absolute Risk Reduction)

- If there were no effect of the treatment, the risk in the treatment group would also be 25% and
- RD or ARR = Zero (25%-25%)

- One measure of 'effect of treatment' is RD (ARR)
- Simply, the difference in the risk between treatment and control group ($R_t - R_c$)

Risk Ratio (Relative Risk)

- Ratio of two risks = Risk Ratio (RR)
- Convention:

  Risk in the treatment group – numerator

  Risk in the control group – denominator
- RR = Risk in the treatment group / Risk in the control group = (R_t / R_c)
- Risk Ratio = Relative Risk

Risk Ratio (Relative Risk)

- What proportion (or fraction) or percent of baseline risk remains in the treatment group
- Remember: Baseline Risk = Risk in the control group
- ‘Risk Remaining’ – fits well with the abbreviation RR
- RR = 20%/25% = 0.2/0.25 = 0.8 (80%)

Risk Ratio (Relative Risk)

- If the treatment were totally ineffective, then
- The risk in the treatment group = The risk in the control group, i.e. 25%
- In absence of effect: RR = (25%/25%) = 1 (means risk remains 100%)
- In our example, the risk is reduced
- It does not remain 100%
- It becomes 80% relative to the baseline risk
- Relative Risk is 80%

Relative Risk Reduction (RRR)

- Relative Risk is 80%
- In relative terms: The reduction is 20% or
- Relative Risk Reduction (RRR) = (100 - 80)% = 20%
- RRR = 100 – RR (in percent), 1 – RR (in decimals)

- ARR – absolute measure
- RRR – relative measure

ARR and RRR

- ARR: How much difference the treatment makes in actual (absolute) terms,
- RRR: How much reduction of risk the treatment makes in relative terms (relative to the baseline risk which is taken as 100%)

NNT – Number Needed to Treat

- ‘NNT’ can be find out from ‘Risk Difference’
- A RD of -5% means 5 fewer (minus) deaths per 100 patients treated
- In other words: For avoiding 5 deaths we need to treat 100 patients
- For one death to be avoided, the NNT is 100/5 = 20
- Relationship: 5% in fraction terms is 5/100, whereas the NNT is 100/5

NNT – Number Needed to Treat

Estimation of NNT:

If you like decimals you can do it in two steps:

1. Find out the RD or ARR (say 0.05)
2. Take its inverse, i.e., 1/RD or 1/ARR

What you get is – NNT

NNT – Number Needed to Harm

- Sometimes, treatments are harmful.
- They increase the risk.
- What we will get – NNT to cause one extra death or harm
- We can find out –

  NNT to prevent one adverse outcome or

  NNT to cause one extra harm (side effect or adverse effect)
- The latter – NNH (Number Needed to Harm)

To recapitulate…..

Four Measures of Treatment Effect:

1. RD (ARR) = - 5% or – 0.05;
2. NNT = 20
3. RR = 80% or 0.8
4. RRR = 20% or 0.2

Adequate for communication among clinicians and are enough to deal with most situations

To recapitulate…..

- But sometimes, like in case-control studies, none of these measures apply
- The measure, which applies here, is based on odds
- Unlike all earlier measures, which are based on probabilities or risks

Odds Ratio

- The odds of England Team winning the cricket match is 1:4
- If there is one chance of winning, there are four chances of losing
- There is a one in five (20%) chance of winning and a four in five (80%) chance of losing
- Odds of 1:4 – 20% probability of winning and 80% probability of losing

Odds Ratio

- Odds looks at both sides of the coin – win vs. lose, death vs. survival, improvement vs. deterioration
- Odds of 1:4 = ¼ (o.25 or 25%)
- 25% odds of winning means a 20% probability of winning
- Need not bother about this relationship

Odds Ratio

Example:

- 20% of the patients in the treatment group died
- Means – 80% survived in the treatment group
- What are the odds of death in the treatment group?

Odds Ratio

Remember:

- For odds we will have to have the chance (probability) of death in the numerator, that is 20%
- And the chance of survival in the denominator, that is 80%
- So, the odds will be 20%/80% (in decimals, 0.2/0.8) = 1/4

Odds Ratio

Now let us say:

- 25% of the patients in the control group died
- Means, 75% survived
- The odds of death in the control group = 25%/75% (or 0.25/0.75) = 1/3
- Odds Ratio = Odds of death (or any adverse event) in the T/T group / Odds of death in the placebo group

Odds Ratio

- OR = Odds of death (or any adverse event) in the T/T group / Odds of death in the placebo group
- (1/4)/(1/3) = ¾ = 0.75 (or 75%)
- One way of expressing the treatment effect is the odds ratio = 0.75 (=75%)
- OR can be interpreted as ‘Odds Remaining’
- Odds remaining is 75%
- Odds reduction is (100-75)% = 25%

Ways to Express Treatment Effects

1. Risk of death is decreased from 25% to 20%
2. RD or ARR = -5% (5/100)
3. NNT = 100/5 i.e. 20
4. RR = 0.8 or 80%
5. RRR = 20%
6. OR = 0.75 or 75%
7. Odds Reduction is 25%

"To call in the statistician
after the experiment is done
may be no more than asking him
to perform a post mortem examination:
he may be able to say what the experiment died of."

Sir RA Fisher

Indian Statistical Congress, 1938

THANKS