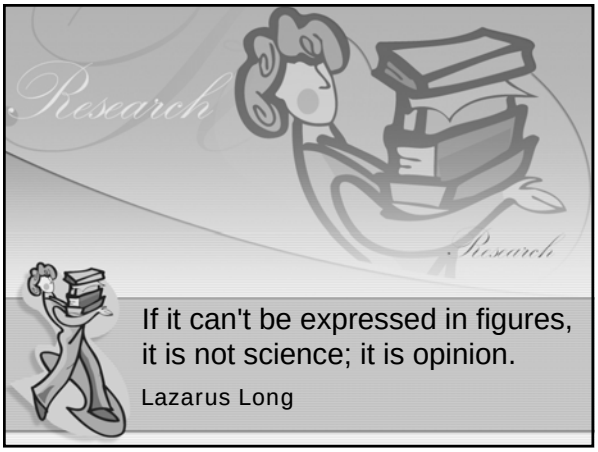
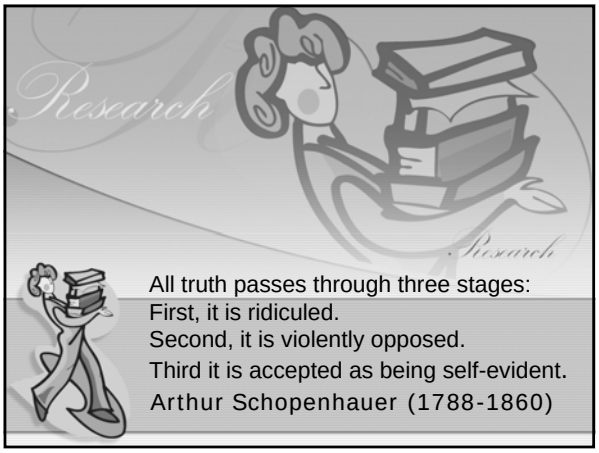
Objectives

At the conclusion of the presentation the participant will:

- Identify one source where research on a topic can be conducted.
- List two types of research presentations.
- List the key components of a research paper.
- List the key components of the methods section.
- Identify two statistical measurements which can be used to evaluate outcomes.
- Differentiate between internal and external validity.
- Differentiate between the various levels of evidence.





Goal of Presentations

- To make you comfortable
  - Knowing how to perform a research search.
  - Knowing how to read a research article from a journal.
  - In changing your practice.

How do clinicians make a decision to change practice?

- Decision-making by anecdote.
- Decision-making by press cutting.
- Decision-making by GOBSAT.
  - "Good old boys sitting around a table"
- Decision-making by cost minimization.
- Decision-making by impression. (RJZ)

How To Read a Paper: The basics of evidence-based medicine. T. Greenhalgh (2006)

Where to start?

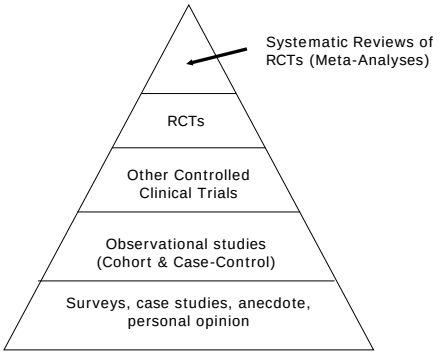
- Start with what it is that you are trying to find out?
  - My patient has colistin ordered. What is this medication and what do I need to know about it.
  - What the heck is Wegener's Granulomatosis.
  - Can you mix acetylcysteine with budesonide?

On-line Databases

- Pubmed (http://www.ncbi.nlm.nih.gov/sites/entrez)
  - Government (NIH) website.
  - Over 17 million citations.
  - Let's search…
- CINHAL (http://www.cinahl.com/)
- Cochrane Collaboration (www.cochrane.org)

- Search Engines
  - Google
- Other "sites"
  - Wikipedia
  - WebMD

Types of Research Reports



Types of Reports - Detail

- Personal Opinion
  - "I am not one of those who in expressing opinions confine themselves to facts" Mark Twain
- Anecdote
  - The telephone game
  - What about the details?
- Case Report
  - Usually a very weak form of evidence.
  - Can be illustrative.
  - Can get valuable information out quickly.
    - McBride WG. Thalidomide and congenital abnormalities. *Lancet* 1961; ii: 1358

Types of Reports- Detail

- Surveys
  - Cross-sectional surveys
    - Collection of data at a particular point in time.
    - Usually reflects opinions/attitudes based upon prior events.
    - Sample collection size is critical.
    - Example: What do RTs feel about the use of BiPAP in patients with a DNR order.
- Case-Control studies
  - Retrospective look at two groups: one group contains a disease or malady; the other does not.
  - Usually concerned with etiology of a disease (Does drinking water from this lake cause cancer?)
  - Weak evidence because of retrospective nature and possible bias in the placement into either group.

Types of Reports- Detail

- Cohort Studies
  - Study where a group of patients with a specific disease (e.g. children with asthma) are followed to see if they develop a particular disease (COPD) or other outcome (growth retardation)
  - Requires a long period of time.
  - Example: Doll R, Hill AB. Mortality in relation to smoking: ten years' observation on British doctors. *BMJ* 1964; 1 (5396): 1460-7.

Types of Reports- Detail

- Randomized Control Studies
  - Participants are randomly placed into an experimental group or a control group.
    - The premise is that because a subject has the chance of ending up in either group, any effect of treatment in the experimental group compared to the control group is due to the treatment being studied.
  - Considered the 'gold standard' for research that is concerned with determining if a therapy is better than nothing or another existing one.

Advantages of RCT

- Evaluation of a single variable in a precisely defined patient group.
- Prospective design.
- Uses hypotheticodeductive reasoning.
  - Aims to falsify its own hypothesis.
  - Prove the null-hypothesis.
- Eliminates bias by comparison of two otherwise identical groups.
- Allows later for meta-analysis.

Disadvantages of RCT

- Expensive & Time consuming
  - Performed on too few patients.
  - Performed for too short a time.
  - Performed with "support" which may introduce bias in the design.
  - Use of surrogate end-point
    - Concentration of drug in system rather than objective improvement in patient.
- Hidden bias
  - Imperfect randomization
  - Failure to randomize all eligible patients
  - Failure to disclose who was eliminated and why
  - Failure to blind assessors to randomization status of participants.

Types of RCTs

- Parallel group comparison
  - Each group receives a different treatment with both groups entered at the same time.
- Paired (or matched) comparison
  - Participants receiving different treatments are matched to balance potential confounding variables such as age or sex.
- Within-participant comparison
  - Participants are assessed before and after an intervention.
  - Example: Pre- and post-test
- Blinded study
  - Single Blind: Participants did not know which treatment they were receiving.
  - Double Blind: Neither did the investigators

Types of RCTs (Cont.)

- Crossover
  - Each participant receives both the intervention and control treatment. There should be a period of washout where no treatment occurs.
- Placebo controlled
  - Control participants receive a placebo which has similar characteristics to the item being tested.
- Factorial design
  - Investigation of the effects of more than one variable (independent) on a given outcome.
  - Example is Placebo, Drug A, Drug B, Drug A+B

Format of a Research Report

- Abstract
  - Brief synopsis of the IMRD.
- I – Introduction
  - Why was this study conducted.
- M – Methods
  - How was it done and how were the results analyzed.
- R – Results
  - What was found.
- D - Discussion
  - What did the authors think the results meant.

Introduction

- Sets the stage for why the study is important.
- Provides background information and other pertinent research on the topic.
- May include the philosophical approach to what is being studied.

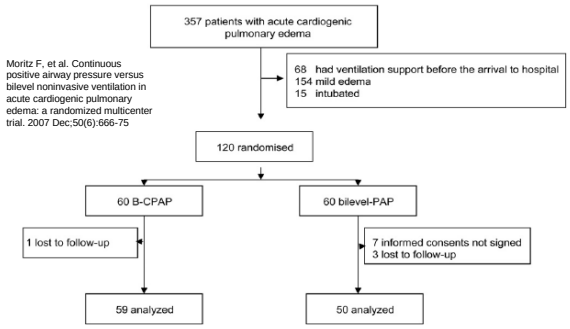
Methods

- THE MOST CRITICAL SECTION
  - And the one that is skipped by most readers!
- If an article is to be rejected, it should be done based upon the Methods section.
  - "Bad science is bad science regardless of whether the study addressed an import clinical issue, whether the results are 'statistically significant', whether the things changed in the direction you would have liked them to and whether, if true, the findings promise immeasurable benefits for patients or savings for the health system" (Greenhalgh, p.41)
- Describes what was done and how.
  - Must have sufficient detail.
  - Must allow replication.
- Is what was done what was said?
  - Reality is reproducible!

Methods (cont.)

- Subjects
  - Who (what) was studied?
  - How were they recruited?
  - Who was included/excluded?
  - Was the testing environment "real"?
- Procedure
  - Detailed explanation of how measurements were made and how subjects were tested.
  - Was the study blinded?
  - Was the study qualitative or quantitative?
  - Was the study controlled?
    - How was randomization done.
    - If a group comparison, were there differences in the group?
- Measurements/Calculations
  - What was being measured (dependent) and what was being manipulated (independent)?
  - How was it measured (and is that method appropriate)?
  - Were there other confounding variables?

Example of Participant Flow Chart



Moritz F, et al. Continuous positive airway pressure versus bilevel noninvasive ventilation in acute cardiogenic pulmonary edema: a randomized multicenter trial. 2007 Dec;50(6):666-75

Figure 3. Flow of participants through each study stage.

Examples of Problems in Methods Section

What the authors said	What they should have said	An example of
We measured how doctors treat low back pain	We measured what doctors say they do when faced with a patient with low back pain.	Assumption that what doctors say they do reflects what they actually do.
We compared a nicotine-replacement patch with placebo.	Participants in the intervention group were asked to apply a patch containing 15 mg nicotine twice daily; those in the control group received identical-looking patches.	Failure to state dose of drug or nature of placebo.
We randomized patients to either "individual care plan" or "usual care"	The intervention group were offered an individual care plan consisting of…; control patients were offered…	Failure to give sufficient information about intervention.
To assess the value of an educational leaflet, we gave the intervention group a leaflet and a helpline number. Control group received neither.	If the study is purely to assess the value of the leaflet, both groups should have got the helpline number.	Failure to treat groups equally apart from the specific intervention being tested.

Statistical Analysis

- What test was done?
  - If no statistical testing was done, seriously question the study.
- What level of significance was used?
  - $p<0.05$ means that there is a 95% certainty that the results obtained could not have been due to chance.
- What is the sample size?
  - Is the size large enough?
  - If the sample size is small, a higher level of significance must be used ($p<0.01$)

More Statistical Stuff

- What type of data is reported?
  - Nominal: Scale of measurement based upon categories: e.g. Colors of shirts
  - Ordinal: Rank of items. Something is "greater than" something else, but tells nothing about how much.
  - Interval: There is a measurable difference between two values, but there is no absolute zero. (e.g. Fahrenheit scale)
  - Ratio: There is a measurable difference between two values AND there is an absolute zero
    - 3 hours is not only greater than 1 hour, it is also two hours greater and it is three times greater.

Results

- Provides the results of the experimental group.
- If tables are available, take a look at them BEFORE reading the section and try and explain what you find. Then go back and read the text and see if that is what the author intended.

Chronic Obstructive Pulmonary Disease and Weaning of Difficult-to-Wean Patients from Mechanical Ventilation: Randomized Prospective Study

Table 3. Effects of T-tube and pressure support ventilation method for weaning difficult-to-wean patients with chronic obstructive pulmonary disease from mechanical ventilation on weaning outcomes

Weaning outcomes	No. (%) of patients		
	T-tube (n = 31)	PSV* (n = 32)	*P*
MV weaning duration (median, IQR, hours)	63 (51-69)	43 (35-49)	<0.001†
MV total duration (median, IQR, hours)	187 (143-222)	163 (113-203)	<0.001†
Time spent in ICU (median, IQR, hours)	241 (211-268)	210 (186-241)	<0.001†
Successful extubation	17 (56.0)	23 (72.0)	<0.001‡
Need for reintubation§	8 (24.0)	6 (16.0)	–
ICU mortality rate§	4 (12.0)	2 (8.0)	–

*Abbreviations: MV – mechanical ventilation, PSV – pressure support ventilation, IQR – interquartile range, ICU – intensive care unit.
†Mann-Whitney test.
‡χ^2 test.
§Not analyzed due to small number of patients.

Croat Med J. 2007;48:51-8

The outcome of weaning from MV was assessed on the basis of duration of weaning, total MV duration, time the patient spent in ICU, number of successfully vs unsuccessfully extubated patients, number of patients requiring reintubation, and ICU mortality rate. Median weaning time from MV and median MV duration were both significantly longer in T-tube group than in PSV group (Table 3). Weaning time accounted for 43% of the total MV duration in T-tube group and for 36% in PSV group. Patients in T-tube group also spent significantly more time in ICU than did the patients in PSV group. Extubation was successful in 17 patients in T-tube and in 23 patients in PSV group, while it was unsuccessful in 14 patients in T-tube and in 9 patients in PSV group (Table 3). Eight patients in T-tube and 6 in PSV group needed reintubation. Four patients in T-tube group and 2 in PSV group died. Two patients in each group died of septic shock, one patient in T-tube group died of peritonitis and one of coagulopathy.

Table 3. Effects of T-tube and pressure support ventilation method for weaning difficult-to-wean patients with chronic obstructive pulmonary disease from mechanical ventilation on weaning outcomes

Weaning outcomes	No. (%) of patients		
	T-tube (n = 31)	PSV* (n = 32)	*P*
MV weaning duration (median, IQR, hours)	63 (51-69)	43 (35-49)	<0.001†
MV total duration (median, IQR, hours)	187 (143-222)	163 (113-203)	<0.001†
Time spent in ICU (median, IQR, hours)	241 (211-268)	210 (186-241)	<0.001†
Successful extubation	17 (56.0)	23 (72.0)	<0.001‡
Need for reintubation§	8 (24.0)	6 (16.0)	–
ICU mortality rate§	4 (12.0)	2 (8.0)	–

*Abbreviations: MV – mechanical ventilation, PSV – pressure support ventilation, IQR – interquartile range, ICU – intensive care unit.
†Mann-Whitney test.
‡χ^2 test.
§Not analyzed due to small number of patients.

Probabilities vs. Natural Frequencies

The probability that a woman aged 40 to 50 participating in a mammography screening program has breast cancer is 0.8 percent. If a woman has breast cancer, the probability is 90 percent that she will have a positive mammogram. If a woman does not have breast cancer, the probability is 7 percent that she will have a positive mammogram. Imagine a woman having a positive mammogram. What is the probability that she actually has breast cancer?

Eight out of every 1,000 women have breast cancer. Of these eight women who have breast cancer, 7 will have a positive mammogram. Of the remaining 992 women who don't have breast cancer, some 70 will still have a positive mammogram. Imagine a sample of women who have a positive mammograms in screening. How many of these women actually have breast cancer?

7 of 77 women who test positive actually have breast cancer. 7/77 = 9%

Test Outcomes

SENSITIVITY: Correctly identifies the positive case.

SPECIFICITY: Correctly identifies the negative case.

TEST RESULT	DISEASE	
	YES	NO
POSITIVE	(a) Sensitivity	(b) False Positive
NEGATIVE	(c) False Negative	(d) Specificity

Test Outcomes - Example

Fecal Occult Blood Result	Patients with Bowel Disease		203 patients are screened. 200 are negative; 3 are positive.
	YES	NO	
POSITIVE	True Positive = 2	False Positive =18	Positive Predictive Value = 2/(2+18)=**10%**
NEGATIVE	False Negative = 1	True Negative = 182	Negative Predictive Value = 182/(1+182)=**99.5%**
	Sensitivity = 2/(2+1) = **66.7%**	Specificity = 182/(18+182) = **91%**	**A negative test is pretty conclusive, a positive one is not.**

Risk Reporting

- Out of 1,000 people who took a drug over a 5-year period, 32 died. Over the same period, of 1,000 people who did not take the drug (but instead a placebo), 41 died. What is the reduction in risk of dying from taking the drug?
- **Relative Risk**: 9(41-32)/41 = 22%
- **Absolute Risk**: 9 less per 1,000, or 0.9%
- **Number Needed to Treat**: 9 lives saved per 1,000 people, or 1 live saved for every 111 treated.

ARDSnet

- Number of patients in "low-tidal volume" group: 432.
- Number of patients in "traditional tidal-volume" group: 429
- Percent of deaths in "low-tidal volume" group: 31% (133 deaths).
- Percent of deaths in "traditional tidal-volume" group: 39.8% (171 deaths).
- The relative risk reduction was expressed as a **22%** reduction in deaths by using the low-tidal volume approach (171-133/171).
- The number of deaths decreased from 171 in placebo (conventional) to 133 with experimental group; a reduction of 38 deaths for roughly 430 patients, or an absolute risk reduction of around **8.8%**.
- The number needed to treat (i.e. the number of people who must participate in the treatment to save one life) is 38 in 430 or 1 in 11.3. This means that for every 11 people treated with a low-tidal volume approach, one additional life will be saved.

Discussion

- Summarizes the main findings of the study.
- Should list the implications of what the findings mean.
- Should put the results in some sort of context.
  - Is the results novel?
  - Are they consistent with what we already know?
  - Are they controversial?
- Are there limitations to the study
  - ALL studies have flaws!
- Where do we go from here?

The change of practice

- Adoption of new technology/practice is slower in medicine than pretty much anywhere else!
- Requires an open mind and a recognized need for the change.
- Provision of base information may be the first step.

Enlightenment is man's emergence from his self-imposed nonage. Nonage is the inability to use one's own understanding without another's guidance. This nonage is self-imposed if its cause lies not in lack of understanding but in indecision and lack of courage to use one's own mind without another's guidance. Dare to know!
Immanuel Kant - 1784

Research Assignment

- Copy of article due to me by March 3.
- Completion of Article Review Sheet (see last page of handout)
- Short summary of findings in your own words.
  - A grade of zero will be given for plagiarism.
- Presentation of findings orally to class.
  - Minimum time – 3 minutes
  - Maximum time – 7 minutes
- Sign-up sheet for presentation day is available.

EXAMPLE

- **Article**
  - **Title of article**: Cannabis use and risk of lung cancer – control study.
  - **Journal**: European Respiratory Journal
  - **Citation**:
    - Year: 2008
    - Volume:31
    - Issue:2
    - Page(s): 280-286

- **Where was article found?** daily.headlines@medpagetoday.com]
- **Why was study done?** The aim of the study was to determine the risk of lung cancer associated with cannabis smoking.
- **Who is the study about?** Patients with confirmed lung cancer aged ≤ 55 years at the time of diagnosis, identified from hospital databases and the New Zealand Cancer Registry between January 2001 and July 2005.
  - **How were patients recruited?** The patients were not recruited per se; rather this is a retrospective study where medical records were reviewed and patients were contacted and asked to participate.
  - Control subjects were randomly selected from the electoral roll and frequency matched in 5-year age groups and district health boards.
  - **How many participants were included in the study?** 102 eligible cases were identified and contacted to participate, of which 79 (77%) agreed to participate. 493 controls were contacted and 324 (66%) agreed to participate.

- **Were any participants excluded from the study?** Yes. Subjects were excluded in the initial screening of lung cancer cases if the cancer was a metastasis from a distant primary site other than the lung, or a histological diagnosis of carcinoid or melanoma.
- **Was the testing situation "real life"?** This was a survey of a population that has a high incidence of marijuana use, the marijuana is rarely mixed with tobacco, New Zealand has one of the highest rates of lung cancer worldwide, and the Maori population that is indigenous to the country has the highest incidence of any ethnic group.

- **Was the design sensible?** Yes.
- **Was the study qualitative or quantitative?** Quantitative.
- **Variables:**
  - **Dependent**: The amount of cannabis smoking that individuals in both groups performed.
  - **Independent**: This was a case-control study. No experimental manipulation was done.
  - **Confounding**: Adjustments for age, joint-years of cannabis smoking and pack-years of cigarette smoking were made.

- **Was the study controlled?** Yes. There were actually 4 times as many subjects in the control group as in the case group.
  - **Was the randomization process described and if so was it adequate**? The case group was not randomized; all participants who were in the case group that agreed to participate were included. No reference is made as to why the 23 non-participants did not want to participated. The control group was randomly selected from a large pool and by region. No mention of the randomization process is present.

- **If it was a group comparison, were there any characteristics that were not equal?** Both groups were stratified based upon age quartiles (e.g. 35-39, 40-44, etc.) and were similar. Similarly, the pack-years of cigarette smoking and cannabis smoking were stratified and compared, as was the age of onset of cannabis use.
- **Was the assessment of outcome "blind"?** This was not an experimental design, so therefore it isn't relative.

- **Results**
  - **Were charts/tables provided?** Yes. There were three tables: A frequency distribution of cases and controls for selected variables; A summary of tobacco use, cannabis use, and alcohol consumption and the risk of lung cancer; and a comparison of cannabis use and tobacco use, as continuous variables (as opposed to the stratified variable in the other charts) and the risk of lung cancer.
  - **Were you able to interpret the results from the table?** Yes.

- **Statistics**
  - **What type of data is reported?** Some nominal (ever/never), some ratio (years smoked)
  - **What statistical test was done?** As this is not an experimental design, a comparison of relative risks was done using linear regression models. They did mention using the "Akaike's Information Criteria" "to assess the linearity of dose-response relationship of the risk of lung cancer after fitting parameters as continuous or categorical variables".
  - **What level of significance was used?** Not applicable.

- **Is there any reference to any of the following, and if so, what was the finding?**
  - **Relative Risk Reduction**: The relative risk for developing lung cancer was compared between those who admitted to smoking cannabis with those who did not.
- **Conclusion**: "This population-based, case-control study provides evidence of a relationship between smoking cannabis and lung cancer in young adults. For each joint-year of cannabis exposure the risk of lung cancer was estimated to increase by 8%.
- **Limitations:** The authors acknowledge the method of surveying, the populations involved, and the nature of the study are limiting factors and the data should be interpreted accordingly.

Case Study Presentation

- 5 minute summary of case.
- Who, what, when, why, how.
- How could this change practice?