Understanding Statistical Concepts in Research

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Aims

- Understand the fundamental statistical concepts associated with research
- Interpret published research
- Think more about how to design and analyse your own study, and how the design can affect the analysis and interpretation of results

No prior knowledge of statistics is assumed

Some tips for the course

- Don't think about how to calculate things by hand. You shouldn't do this. A computer can do it better (quicker and more accurately)
- It is better to spend your time on interpretation, as well as knowing which method of analysis to use (the mathematics/algebra are likely to confuse, at this level)
- Try to think that the course "is easy" and simplify each day of the course and the course itself
- This is largely done by considering the 3 main types of outcome measures; most stats analyses are built around this
- The most fundamental concepts are given on Days 1 & 2. After that you are using the same things in different ways
- We starts off with the basics, then move up to introduce advanced methods
- We will cover how to analyse and interpret data, but also how the design can affect the results and interpretation; the latter is very important,
- Most examples are on humans, but the principles covered apply to anything

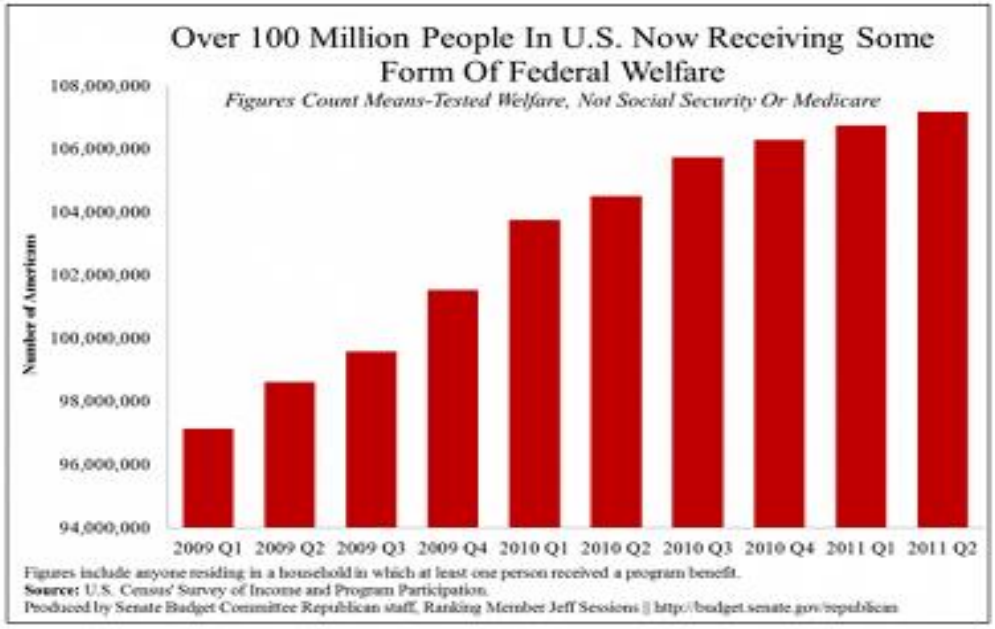
Isn’t this a striking increase?

THE BLOG

Over 100 Million Now Receiving Federal Welfare

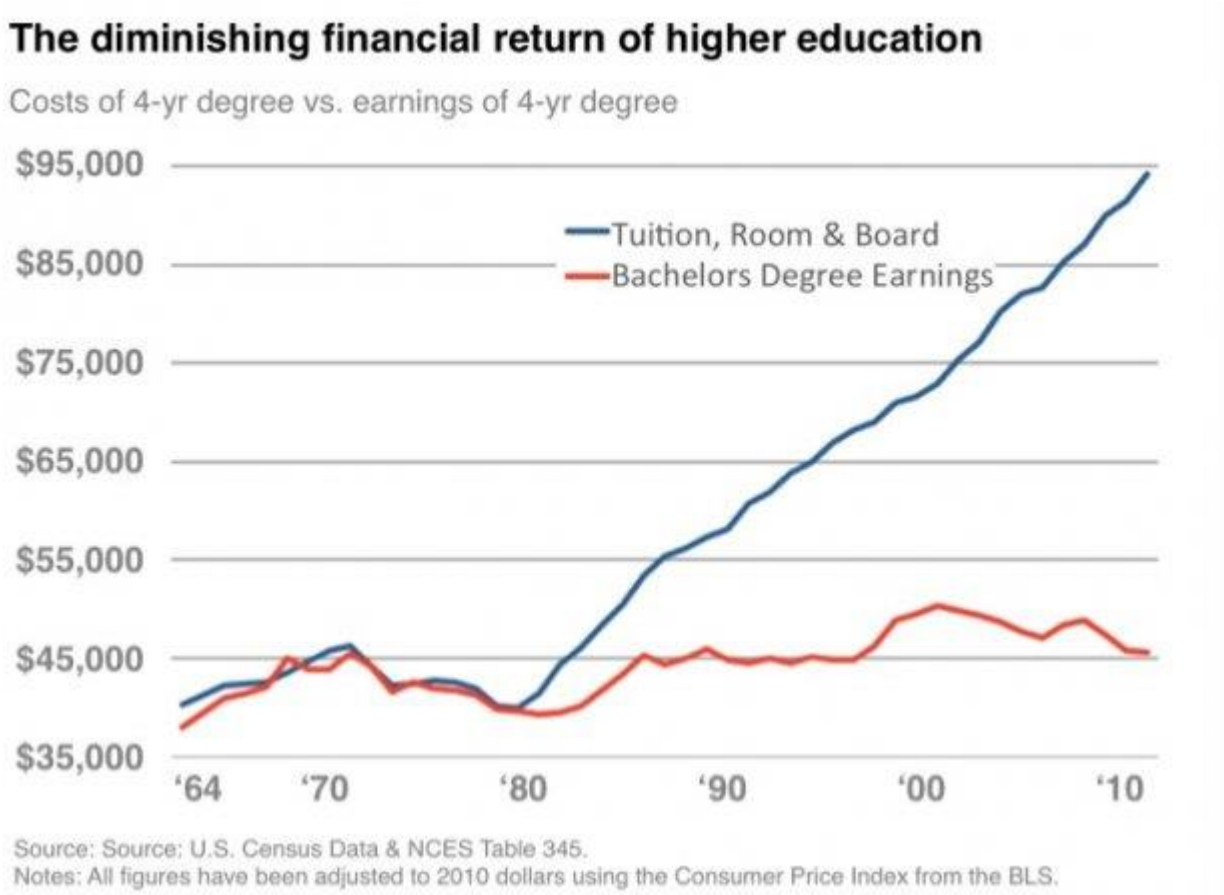
2:40 PM, AUG 8, 2012 • BY DANIEL HALPER

A new chart set to be released later today by the Republican side of the Senate Budget Committee details a startling statistic: "Over 100 Million People in U.S. Now Receiving Some Form Of Federal Welfare."



But look at the y-axis scale – only starts at 94 million

Does this look off-putting for potential students?
What is missing?



That people who don't go to university have average salary of $30k
And that over 43 year work life, the gain for graduates is $540K after subtracting cost of degree

"More than 80% of Dentists recommend Colgate"

What do you think this means?
How might you do this study?

Survey of dentists
Allow dentists to choose only 1 toothpaste or any they like?

It was actually the latter, and they chose Colgate as frequently as others!
Hence the above claim would be misleading to most people in the public

Short quiz (True or False)

1. Smoking cigarettes for several years increases the risk of getting lung cancer by about 1900%

2. Smoking cigarettes for several years increases the risk of getting lung cancer by about 20-fold

3. Drinking 2-3 glasses of wine each day reduces your chance of dying compared to not drinking alcohol at all

My Doctor said "Only 1 glass of alcohol a day". I can live with that.

In fact, defining "1 glass" is actually important!

theguardian

Friday 13 January 2012

Bacon linked to higher risk of pancreatic cancer, says report. Study claims eating two rashers or one sausage a day can increase threat of contracting disease by nearly 20%

NB: the language

Is this a small moderate, or big effect??

Daily consumption of bacon and other red meat products can raise cancer rates, according to the study.

Number of grams of processed meat per day	**Equivalent to**	**% increase in risk (from the study & media)***
50g	1 sausage, or 2 bacon rashers	19%
100g	2 sausages, or 4 rashers	38%
150g	3 sausages, or 6 rashers	57%

*compared to someone who doesn't eat any processed meats

Do the risk increases look worrying?

Put this sizzling menace into context…..

Risk of being diagnosed with pancreatic cancer is very small:
~10 per 100,000 adults each year

Number of grams of processed meat per day	**% increase in risk**	**Equivalent to number of extra cancer cases per 100,000**
50g	19%	2
100g	38%	4
150g	57%	6

- This is not saying that eating processed meats does not matter
- Rather, it is important to look at the actual impact on a person's risk
- A big % increase applied to a disorder that is very rare, has little impact
- But you can see that the middle column above looks more striking than the last column (hence gets more attention)!

Main reasons for research

- Descriptive analyses on 1 group people/things
- Looking for associations between different measurements within 1 group of people/things
- Looking at associations/differences between 2 or more groups of different people
- Establishing the cause of or risk factors for early death/disease
- Evaluating treatments for disease or methods for preventing death/disease
- Evaluating how different tissue samples respond to different stimuli in laboratory experiments
- Examining how animals react to different treatments in a laboratory experiment

"Smoking is a cause of lung cancer"

- Why is it that not all smokers develop lung cancer?
- Why do some never-smokers develop lung cancer?

Given these two observations how can we say that smoking is a cause of lung cancer?

Results from 4 surveys of voting intention just before the 2010 UK election

Tory	Labour	Difference
37%	32%	+5%
38%	28%	+10%
40%	32%	+8%
32%	40%	-8%

Research question: who will win the election and by how much?

(Analogous term in research:
Is there an effect?
How big is it)

- People, animals or objects (eg cells) naturally vary
- They have different characteristics; different habits; and react differently to the same exposure or same treatment
- Because of this **natural variation** (**variability**) we need statistics to help interpret research data
- It is often difficult to predict what will happen to a single individual
- The results of almost all clinical research applies to a **group** of people or things (not an individual)

Natural variation

- Variability is something we always need to allow for
- The less variability, the easier it is to look for associations, and therefore make clear conclusions
- Highly controlled studies (eg laboratory experiments, or some clinical trials) usually have the least variability, because the researcher has control over how the subjects/objects are selected and what is done to them

“Statins are very effective”

- What does *effective* mean? Is it:
  - A reduction in cholesterol levels?
  - the risk of having a heart attack decreases
  - the risk of dying decreases?
- Also, the word *very* is subjective; how can we quantify effectiveness?
- If statins worked in one group of people in a research study, can we be sure that it will work in another group?

Types of research studies

- Observational studies
  - Cross-sectional survey
  - Audit of data
  - Case-control studies
  - Cohort studies
- Experimental studies
  - Clinical trials
  - Laboratory experiments

Types of outcome measures

- First consider what the unit of interest is in the research study (eg person, animal, cell)
- Then what will you do to it with regards the outcome measure?
  - Count it
  - Take measurements on it
  - Measure the time taken for an event to occur (a special case of taking measurements)

Counting people (or things)

- Commonly called **binary** or **categorical** data
- You first define the characteristic of interest
- You then put people into mutually exclusive groups (categories) according to the characteristic, eg
  - dead or alive
  - disease occurrence (yes or no)
  - hair colour (black, blond, brown)
  - severity of disease (none, mild, moderate, severe)
- Each person (or thing) can only appear in one group
- The categories could have a natural ordering (disease severity) or they may not (blood group)

Taking measurements on people (or things)

- Commonly called **continuous** data
- Measurements could involve anything that has a decimal place, or a count, eg
  - age
  - blood pressure
  - weight and height
  - red blood cell count
  - number of days in hospital
- Always think of what the unit of interest is and what you are doing to it

Time-to-event data

- This is a special case of ‘taking measurements on people’, eg,
  - time from the start of the study until the person develops the disease of interest
  - time from a mouse being injected with a drug until death
- When the event has occurred, the date of the event is used in the analysis
- If the person (or object) has not had the event yet, the date last seen is used
- Must always clearly specify the start and end times

- Understanding what type of outcome measure is being used is essential for:
  - designing the study (eg method of sample size estimation)
  - analysing the data (choosing the statistical method)
  - interpreting the data (communicating the results to others)
- Using the wrong method for a particular type of endpoint will give the wrong answer
- Most statistical software packages will not tell you if you are using the correct analysis!

Objectives and outcome measures (endpoints)

- **Objectives** (or aims, purpose, hypotheses), should be a simple, easy-to-read sentence about the primary goal of the study
- **Outcome measure** is the quantitative thing used to address the objective
- Be clear about the distinction between these two

Objectives and outcome measures (endpoints)

Objectives	**Outcome measures**
To determine the effectiveness of statin therapy in people with no history of heart disease	Mean serum cholesterol level
To determine the effectiveness of statin therapy in people with a history of heart disease	The number of people (or incidence) who have a second heart attack
To evaluate blood pressure as a risk factor for stroke	Blood pressure and the incidence of those who have a first stroke
To determine whether new Drug A for asthma has a similar effect as standard therapy	The proportion of patients who suffer a severe asthma exacerbation
To show whether Test A is better than Test B in identifying pregnant women carrying a Down's syndrome fetus	The proportion of women who have a baby diagnosed with Down's syndrome
To examine the relationship between blood pressure and age	Blood pressure and age obtained for every study subject
To evaluate the effectiveness of chemotherapy in treating lung cancer	Overall survival: the time from the start of the trial until death from any cause

Objectives and outcomes

- Clinical trials often have 1-2 primary aims
- Lab experiments may have several aims/hypotheses, and so be exploratory
- Observational studies can have 1-2 aims if they have a specific purpose, otherwise they can have several aims (especially if the project is based on a completed study)

Key considerations when interpreting research

- What is the aim of the study?
  - What are the objectives?
  - What are the outcome measures?
- What are the main results?
  - Is there an effect? If so, how big is it?
- What are the implications of conducting the study on a **sample** of people/objects (**confidence intervals**)?
- Could the observed results be a **chance (ie fluke) finding** in your particular study (**p-values** or **statistical significance**)?

Key considerations when interpreting research

- How good is the evidence? Is there anything about how the study was conducted that could adversely affect the results?
  - How were people/objects selected (any **bias**)?
  - Any differences in their characteristics or how they behaved (any **confounding**)?
  - Any differences in how they were handled by the researcher (any **bias**)?
- What does the study contribute to clinical practice (**clinical importance**)?

Types of research

- For most of what we will cover, we are interested in the effect of an ‘exposure/intervention’ on an ‘outcome’
- **Exposure**: lifestyle habit, occupation, diet, intervention (eg surgery), treatment (drugs)
- **Outcome**: a disorder, early death

- To do this well, we need to compare the ‘outcome’ between the ‘exposed’ and ‘unexposed’ groups
- **Exposed**: ate lots of fruits; had surgery; given statins
- **Unexposed**: did not eat fruits; no surgery; were not given statins

Exposures

- Note that an ‘exposure’ can be anything such as:
- Personal/demographic characteristics (which we cannot change, eg age, gender, genes, biomarker, imaging marker)
- Lifestyle and occupational factors (which we can change)
- Interventions/treatments (which we can start taking)

Exposures and outcomes

Effect of the following '**exposure**'	On the following '**outcome**'
Smoking	Risk of lung cancer
Living with a smoker (among never smokers)	Lung cancer
Alcohol	Liver cirrhosis
Frequent mobile phone use	Brain cancer
Age	Heart disease
Working with asbestos	Mesothelioma
Having a BRCA1 or BRCA2 gene	Breast cancer
A new diet for overweight people	**Body weight**
Body weight (can be an outcome in other situations)	Diabetes
Family history	Alzheimer's disease
Surgery and chemotherapy (among patients with colorectal cancer)	Survival

- We also need to try and ensure that "**everything is the same**", except that one group has the exposure/intervention, and the other group does not
- If this is achieved, then any difference in **outcome** between the two groups must **only** be due to the **exposure/intervention**, not anything else
- If the groups differ with regards other factors, then we could have difficulty in attributing a difference in outcome to the exposure

- However, the only way we can 'make everything the same', is a randomised clinical trial or laboratory experiment
- In observational studies it is usually difficult to do
- The two comparison groups can be different (main reasons are **confounding** and **bias**)

Suggested books on statistics in medical research

- Medical statistics at a glance. A Petrie & C Sabin. BMJ Books, 2nd edition, 2005.
- Medical Statistics. B Kirkwood & J Sterne, Blackwells, 2nd edition, 2003.
- Statistics with confidence. D Altman et al. BMJ Books, 2nd edition, 2000 (provides some non-standard but easy to use methods)
- Nonparametric statistics for the behavioural sciences. Siegel & Castellan. McGraw-Hill 1988
- A concise guide to clinical trials. A Hackshaw. Wiley-Blackwell, 2009
- A concise guide to observational. A Hackshaw. Wiley-Blackwell, 2015