



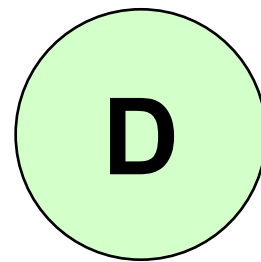
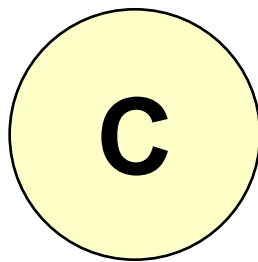
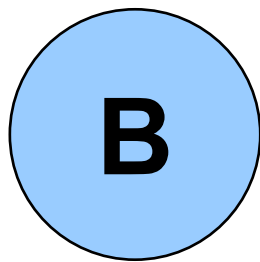
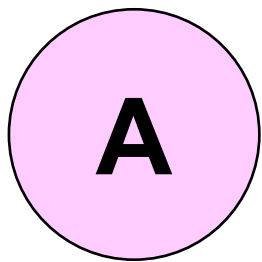
Research Integrity

or How to be a Good Scientist

Anne Segonds-Pichon, Jo Montgomery,
Sarah Inglesfield, Laura Biggins and Simon Andrews

v2024-02





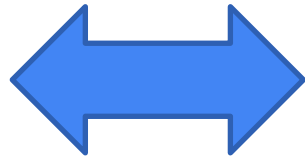


An illustration



Research Integrity

MMR = Measles, Mumps and Rubella



Autism



1998 **Link** MMR autism

Wakefield *et al.*

n=12 children

<https://pubmed.ncbi.nlm.nih.gov/9500320/>

2010

Retraction of the Wakefield *et al.* paper

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2831678/>

1999 **No link** MMR autism

Taylor *et al.*

n=498 children

<https://pubmed.ncbi.nlm.nih.gov/10376617>

2010

Andrew Wakefield found guilty of serious professional **misconduct**

<https://www.bmj.com/content/340/bmj.c593>

2001: **No link** MMR autism

Dales *et al.*

n=600-1900 children each year over 14 years

<https://pubmed.ncbi.nlm.nih.gov/11231748/>

2002-2005: **No link** MMR autism

Many more studies

<https://pubmed.ncbi.nlm.nih.gov/15366972/>

<https://pubmed.ncbi.nlm.nih.gov/15877763/>

Research Integrity



Retracted article **2010**

See the [retraction notice](#)

12 years

> [Lancet](#). 1998 Feb 28;351(9103):637-41. doi: 10.1016/s0140-6736(97)11096-0.

Ileal-lymphoid-nodular hyperplasia, non-specific colitis, and pervasive developmental disorder in children

A J Wakefield¹, S H Murch, A Anthony, J Linnell, D M Casson, M Malik, M Berelowitz, A P Dhillon, M A Thomson, P Harvey, A Valentine, S E Davies, J A Walker-Smith

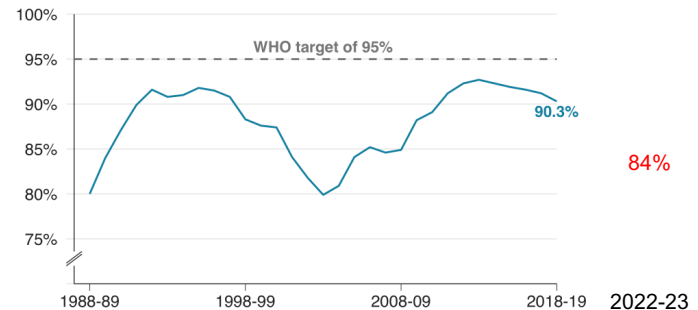
Affiliations + expand

PMID: 9500320 DOI: 10.1016/s0140-6736(97)11096-0

- Scientists and organisations across the world **spent a great deal of time and money** refuting the results of a minor paper in the *Lancet* .
- **MMR vaccination: 1995: 95%** to **2002: 81%**
- Measles outbreaks in the UK in 2008 and 2009
- **2020:** Uptake of MMR vaccine: **91%** (still below herd immunity)

MMR first dose coverage is falling in England

% of children who completed first dose of vaccine at 24 months



Source: Cover of Vaccination Evaluated Rapidly, Public Health England



Research Integrity



Rise in measles cases prompts vaccination campaign in England

UKHSA declares national incident as figures suggest more than 3.4 million children have not had MMR jab



Measles cases in the West Midlands have been at their highest level since the mid-1990s. Photograph: MedStockPhotos/Alamy

- **2016:** UK declared measles free
Now lost this status
- Increases in number of measles cases
- **2022-23: : 84% children in England**
- **(74% in London, vs 90% South West)**
- Need vaccination rate of **95%**
- **Current decline due to:**
 - Vaccine misinformation
 - Not serious?
 - Difficulty accessing appointments
 - Impact of covid pandemic

Obvious examples are obvious, but...





Outline of the course



Research Integrity

What does it mean?

Questioning

Definitions

In Practice

Ethics

Keeping Track

How can we apply it?

Publications

Misconduct

When is it tested?

Responsibility

Bottom line

Good Science





What is Research Integrity?



Research Integrity

a.k.a. Scientific Integrity

- **Scientific integrity** (From Wikipedia):
Scientific integrity deals with ‘**best practices**’ or rules of professional practice of researchers.
- Organisation for Economic Co-operation and Development (OECD) report, 2007 **replication (or reproducibility) crisis** and the **fight against scientific misconduct**.

Research Integrity

a.k.a. Scientific Integrity

- The **replication crisis** - scientific studies are **difficult or impossible to replicate** or reproduce.

Psychology:

Open Science Collaboration
(100 papers from 2012)

36% of the replications yielded significant findings vs 97% in the original studies.

Cancer Research:

Reproducibility Project: Cancer Biology
(53 papers from 2010 to 2012)

25% experiments could be reproduced.
Replication effect sizes were 85% smaller on average than the original findings.

<https://osf.io/82fth/>

<https://www.sciencenews.org/article/cancer-biology-studies-research-replication-reproducibility>

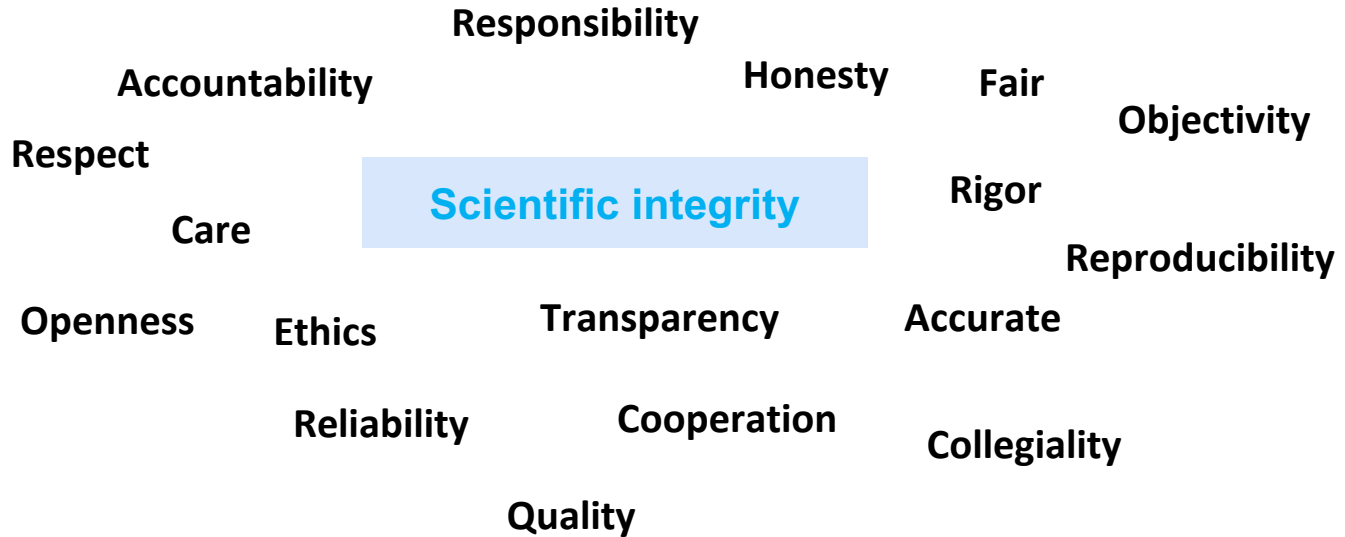
Which words are most important/synonymous with integrity?

Exercise



Research Integrity

Many words



Research Integrity

More than words

Accountability
Accurate
Care
Collegiality
Cooperation
Ethics
Fair
Honesty
Objectivity
Openness
Quality
Reliability
Reproducibility
Respect
Responsibility
Rigor
Transparency

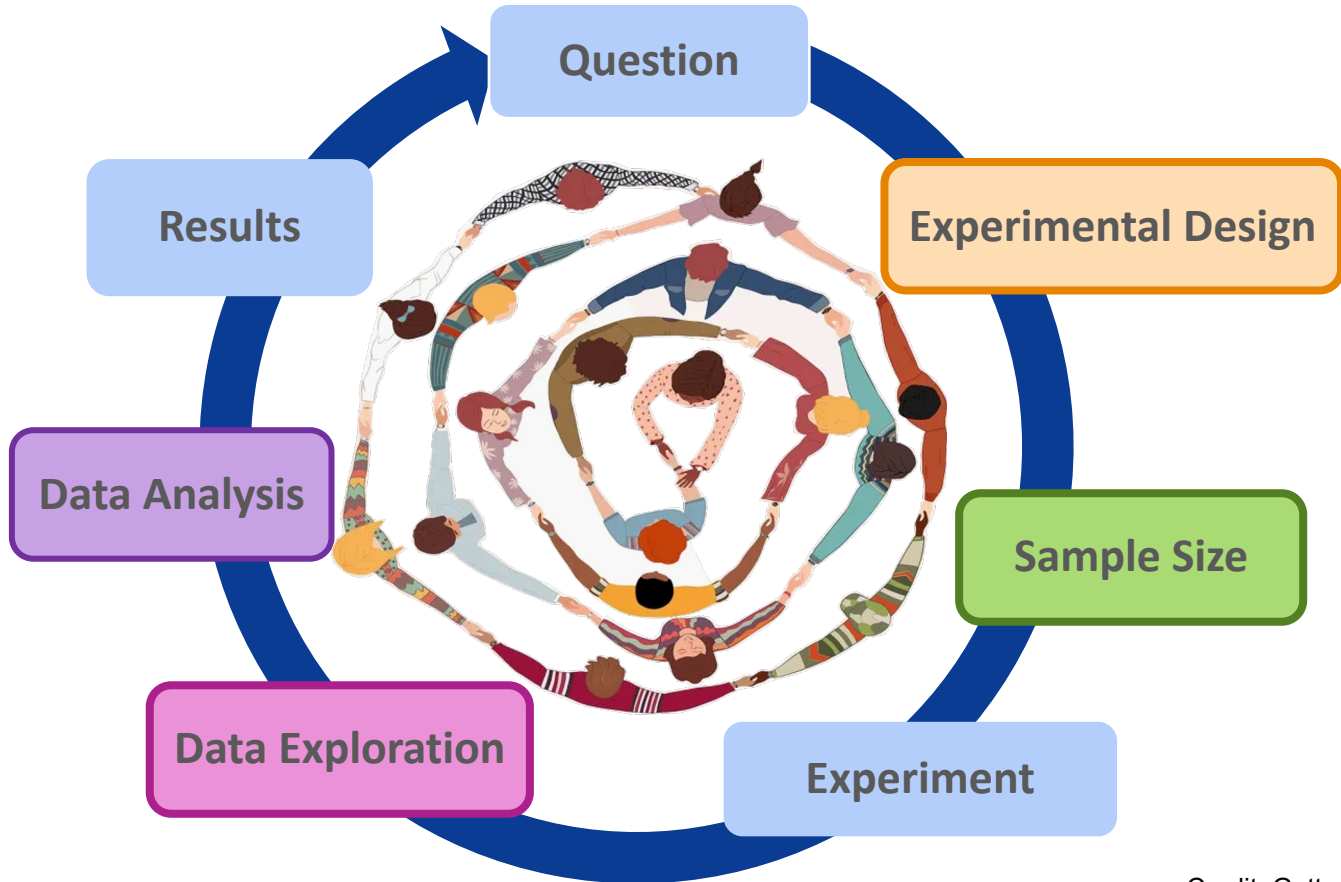
Scientific integrity



Research Integrity in practice



Research Integrity: In Practice

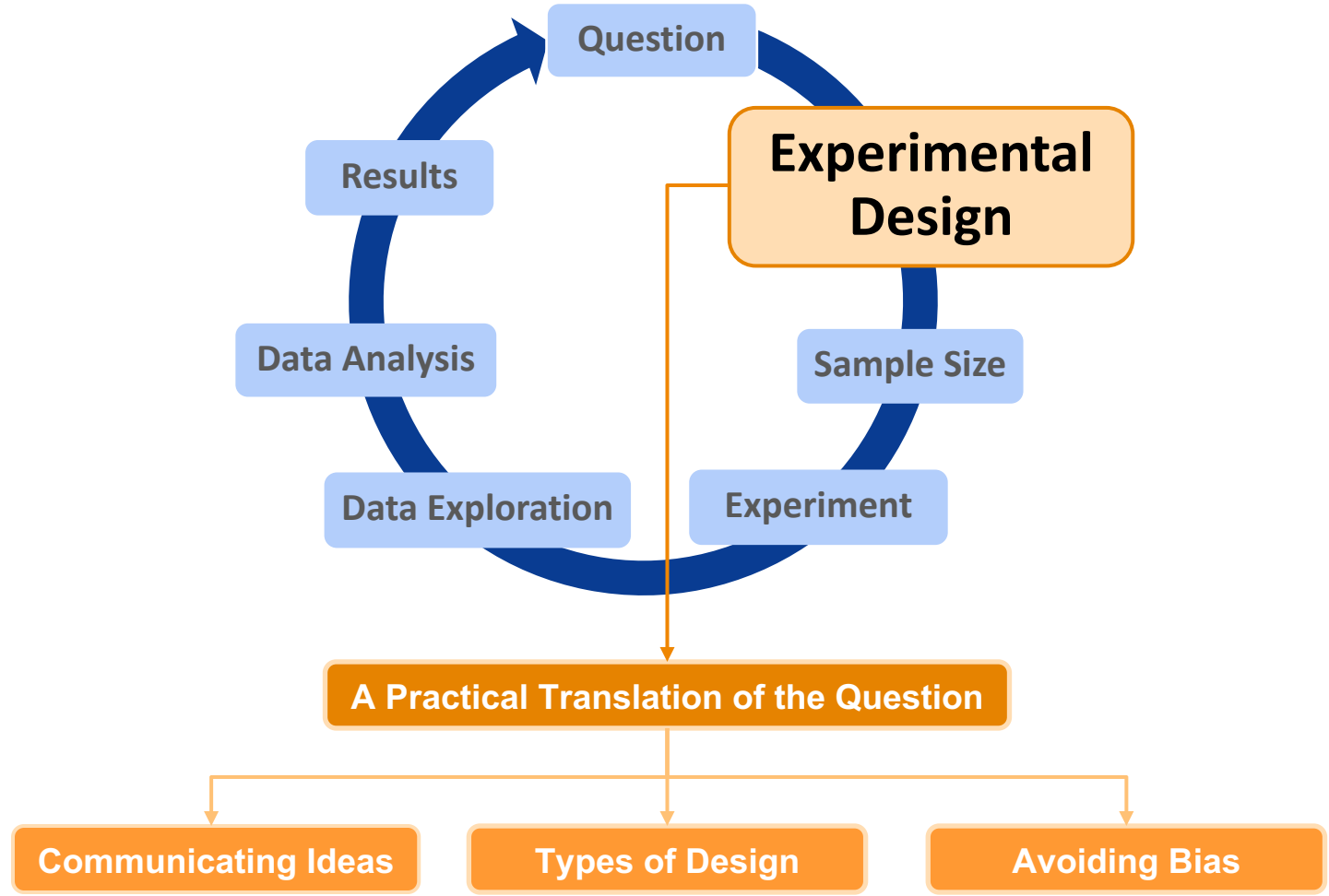


Accountability
Accurate
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Collegiality
Cooperation
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Reliability
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Respect
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Rigor
Transparency

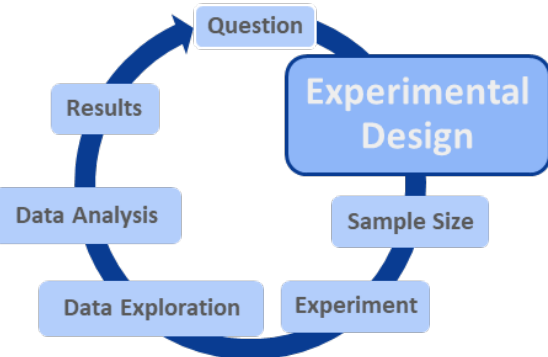
Research Integrity in practice

Experimental design

- Accountability
- Accurate
- Care
- Collegiality**
- Cooperation**
- Ethics
- Fair
- Honesty
- Objectivity**
- Openness
- Quality**
- Reliability**
- Reproducibility**
- Respect
- Responsibility
- Rigor**
- Transparency



Clear Communication

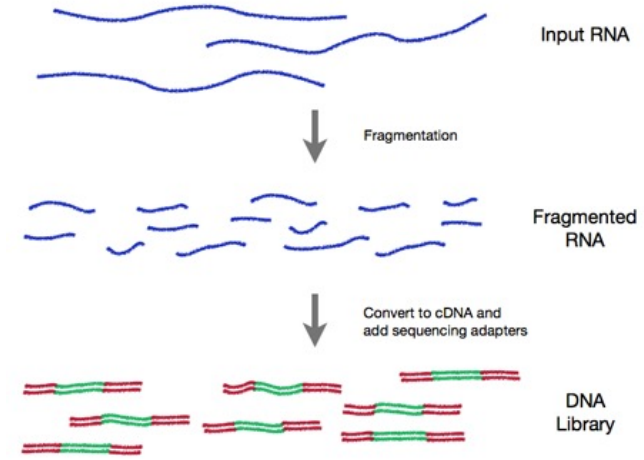


- Accountability
- Accurate
- Care
- Collegiality**
- Cooperation**
- Ethics
- Fair
- Honesty
- Objectivity
- Openness
- Quality
- Reliability
- Reproducibility
- Respect
- Responsibility
- Rigor
- Transparency



Library, Cambridge

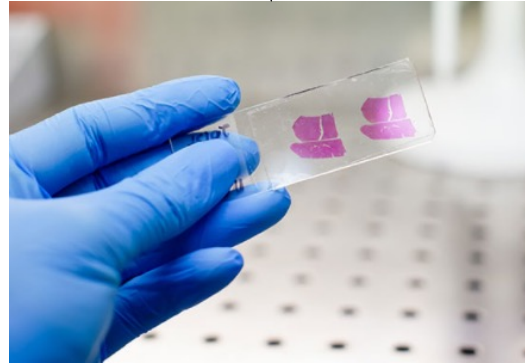
Library



RNA seq **Library**

Clear Communication

Sample

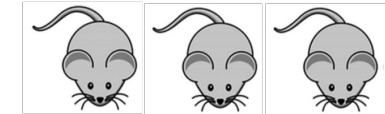


Tissue **Sample**

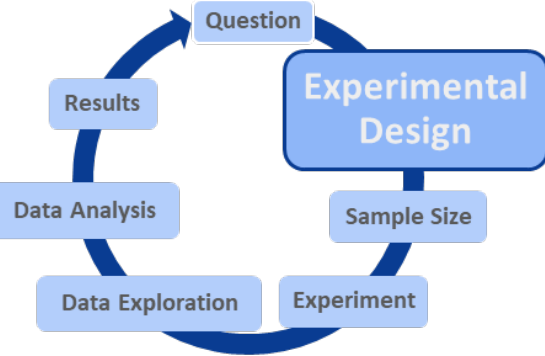
Control



Treated



Sample of mice



- Accountability
- Accurate
- Care
- Collegiality**
- Cooperation**
- Ethics
- Fair
- Honesty
- Objectivity
- Openness
- Quality
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- Respect
- Responsibility
- Rigor
- Transparency

- Different words to describe the same data/graphs
- Different traditions in different labs, areas of science

Appropriate Type of Design

Distinguish real differences from experimental artefacts...

...But experiments can be big and complicated

Seminal Wellcome Trust GWAS Study:

- 14000 cases of 7 diseases & 3000 shared controls
- Each processed at different sites and genotyped on distinct series of plates

Condition 1

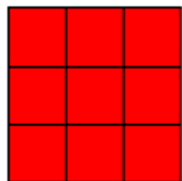


Plate 1

Condition 2

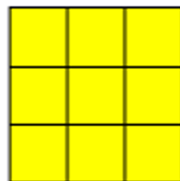


Plate 2

Condition 3 etc...

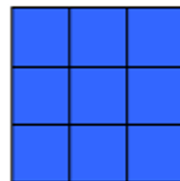
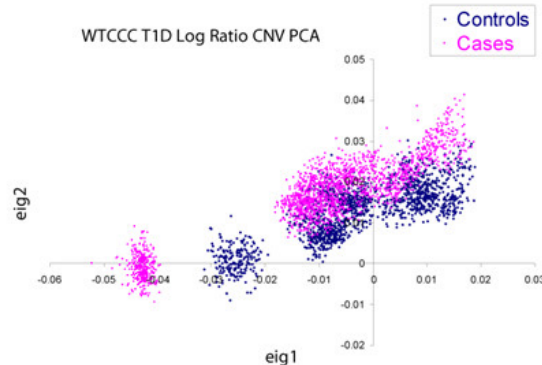


Plate 3



Differences between control and cases are confounded by plate

Question

Experimental Design

Results

Data Analysis

Sample Size

Data Exploration

Experiment

Accountability

Accurate

Care

Collegiality

Cooperation

Ethics

Fair

Honesty

Objectivity

Openness

Quality

Reliability

Reproducibility

Respect

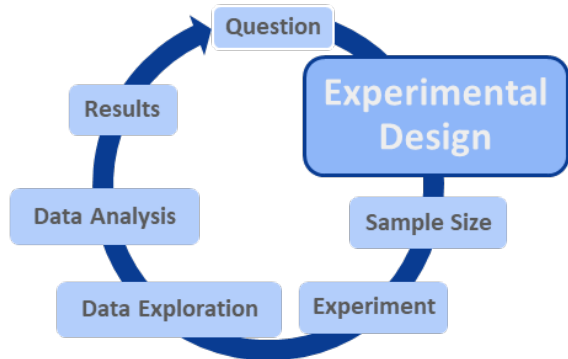
Responsibility

Rigor

Transparency

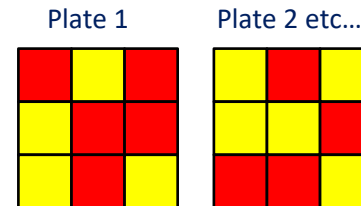


Appropriate Type of Design

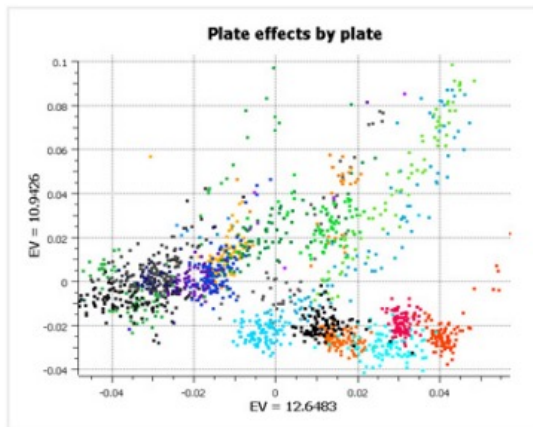


GenADA multi-site collaborative study:

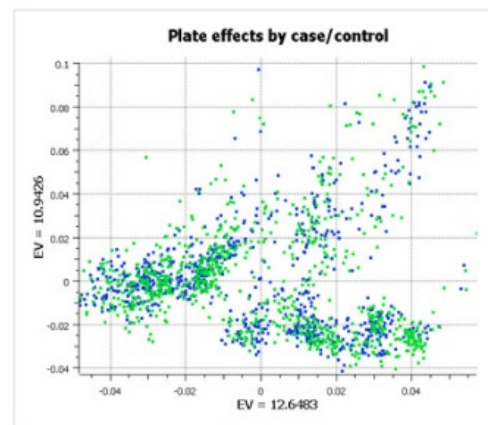
- 875 Alzheimers patients, 850 controls, 9 sites
- Randomised Block Design

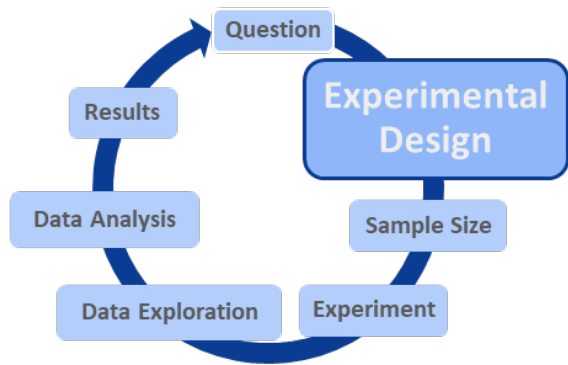


Still have differences between plates



Doesn't confound the experiment





Avoiding Bias

Humans are not always good at remaining objective...



Cognitive Bias = Pareidolia

Biases can also impact our experiments

- Accountability
- Accurate
- Care
- Collegiality
- Cooperation
- Ethics
- Fair
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- Reliability
- Reproducibility**
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Confirmation bias

Exercise



A Quick Exercise on Confirmation Bias and Hypothesis Testing

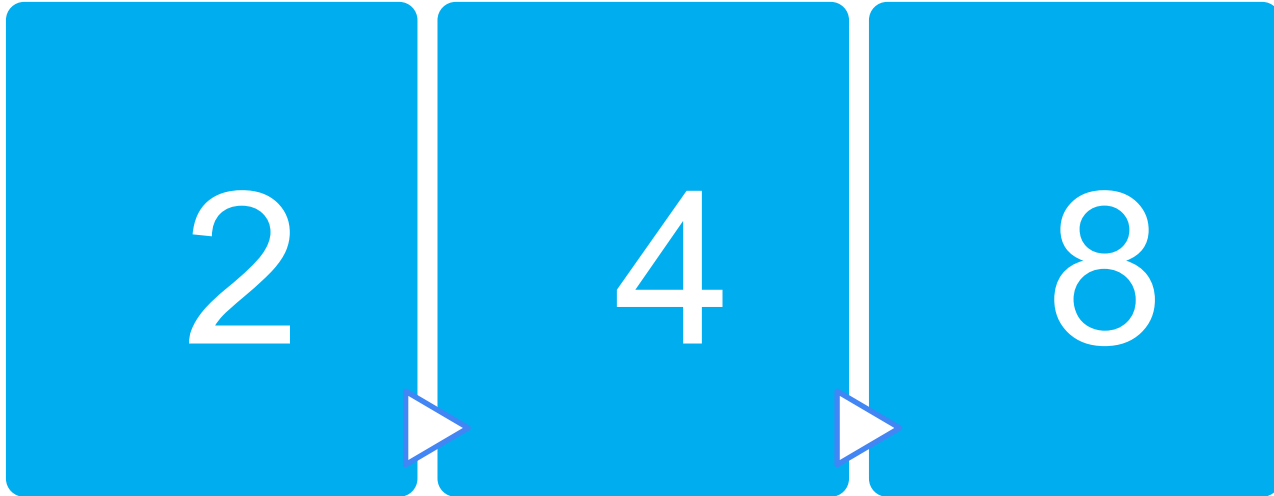
You will be presented with 3 numbers in a sequence.

You need to guess the **rule** that governs the sequence.

You can suggest any 3 numbers you like, and we will tell you whether or not your sequence follows the rule.



A Quick Exercise on Confirmation Bias and Hypothesis Testing

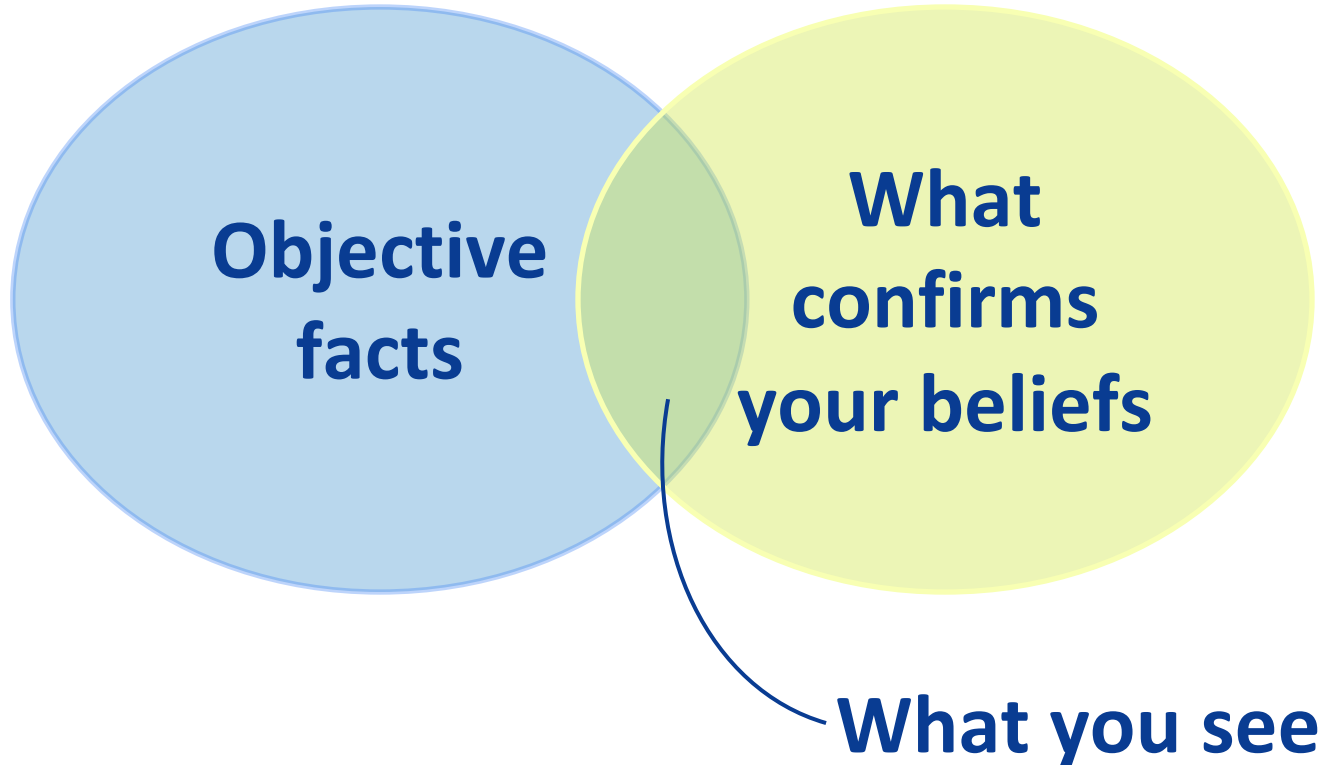


A Quick Exercise on Confirmation Bias and Hypothesis Testing

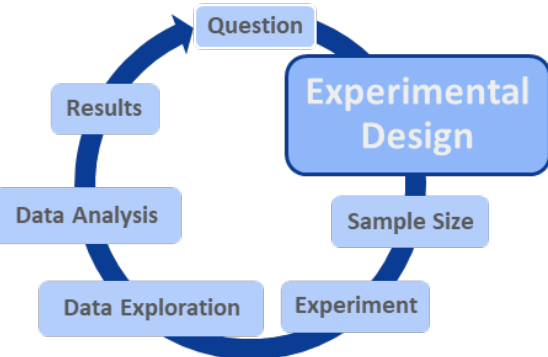
What's the rule?



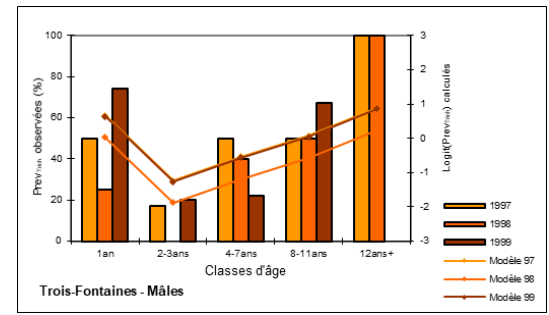
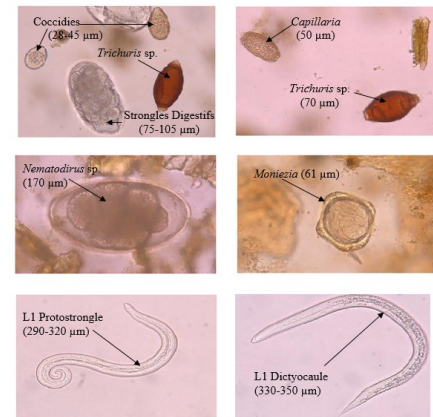
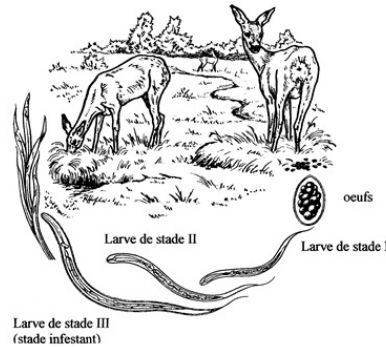
Confirmation bias



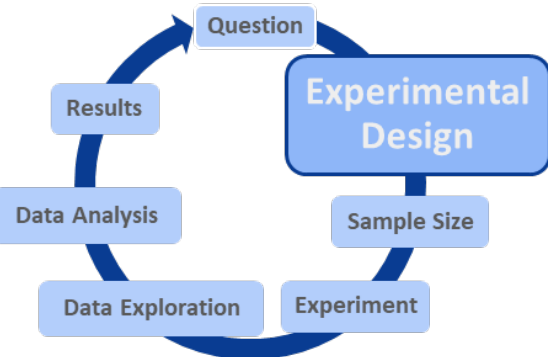
Experimenter Bias



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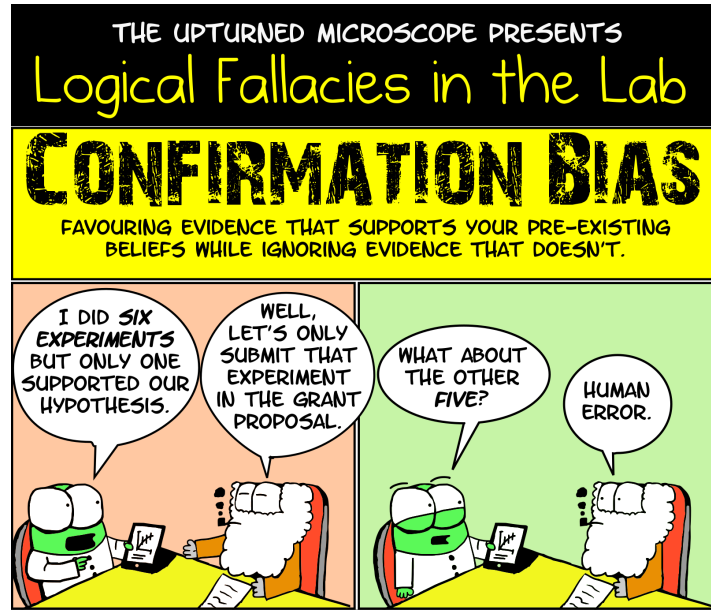


Scientists should be **blind** ... if they want to be **objective**!

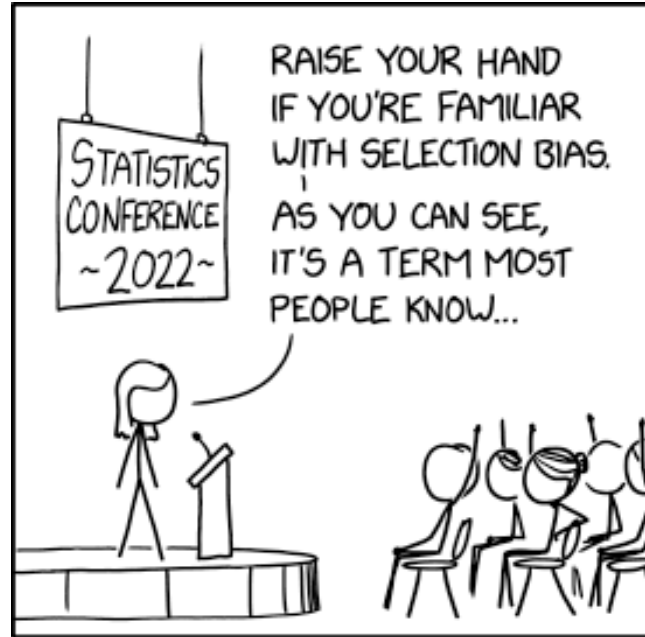


- Accountability
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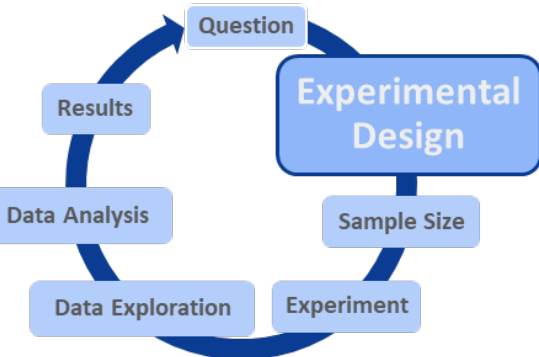
Blinding is important to avoid Confirmation bias



Selection Bias

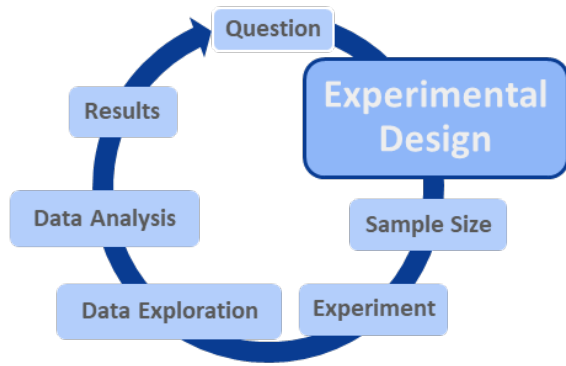


Biases in our sample populations can impact on our conclusions too

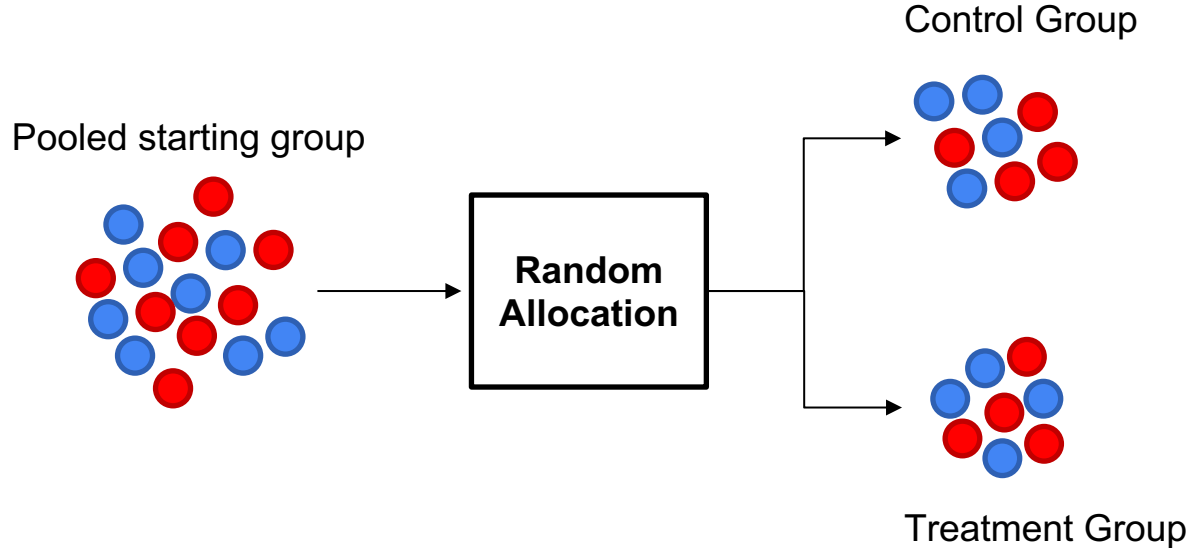


- Accountability
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Randomisation



- Accountability
- Accurate
- Care
- Collegiality
- Cooperation
- Ethics
- Fair**
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- Quality
- Reliability**
- Reproducibility**
- Respect
- Responsibility
- Rigor**
- Transparency



Each experimental unit has equal probability of receiving a treatment

- Minimises Selection Bias
- Reduces systematic differences between groups

Random Allocation

CLINICAL TRIALS RANDOMIZATION



Patient information is entered into a computer



The computer randomly assigns patients to two or more groups, helping to prevent bias



Control group receives standard therapy



Investigational group receives new treatment

Question

Results

Experimental Design

Sample Size

Data Analysis

Data Exploration

Experiment

Accountability

Accurate

Care

Collegiality

Cooperation

Ethics

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Objectivity

Openness

Quality

Reliability

Reproducibility

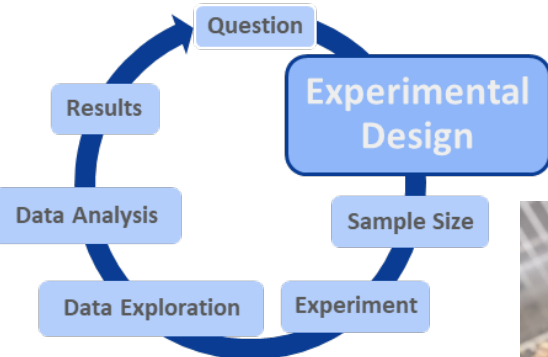
Respect

Responsibility

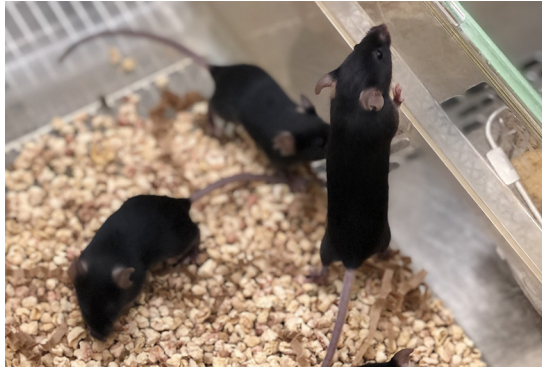
Rigor

Transparency

Random Allocation



- Accountability
- Accurate
- Care
- Collegiality
- Cooperation
- Ethics
- Fair**
- Honesty**
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- Reproducibility**
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- Responsibility
- Rigor**
- Transparency



Pick out a mouse at random, first 3 get the treatment

Is this random?

Does it have the potential to introduce bias?

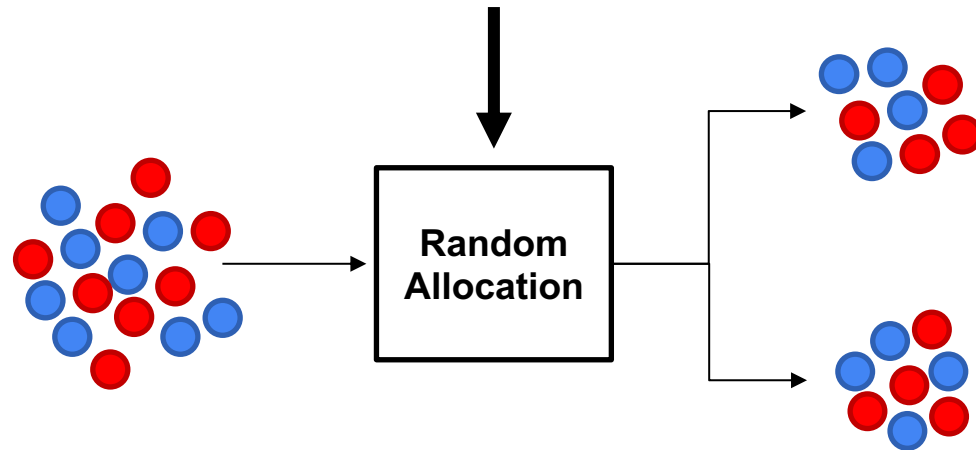
A Biased

B Not Biased

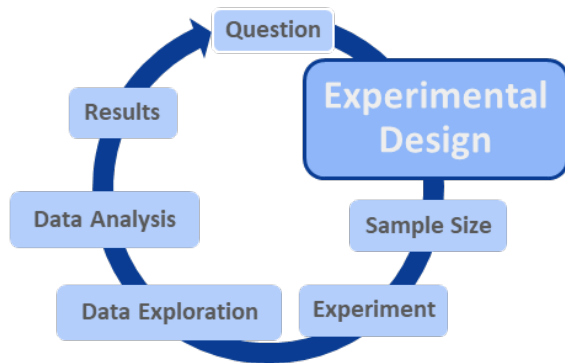


Randomisation More Broadly

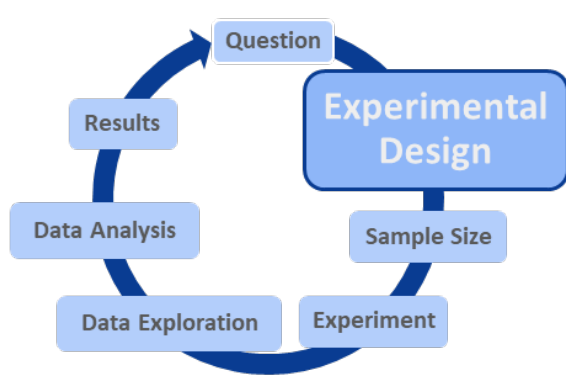
Consider Nuisance Factors



Also consider randomisation **throughout** the experiment



Accountability
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Transparency



In a nutshell

Good experimental design...

- Translates the scientific question into lab work
- Prevents subjectivity
- Reduces effects of nuisance variables

...Is a fair way to do science

Accountability

Accurate

Care

Collegiality

Cooperation

Ethics

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Honesty

Objectivity

Openness

Quality

Reliability

Reproducibility

Respect

Responsibility

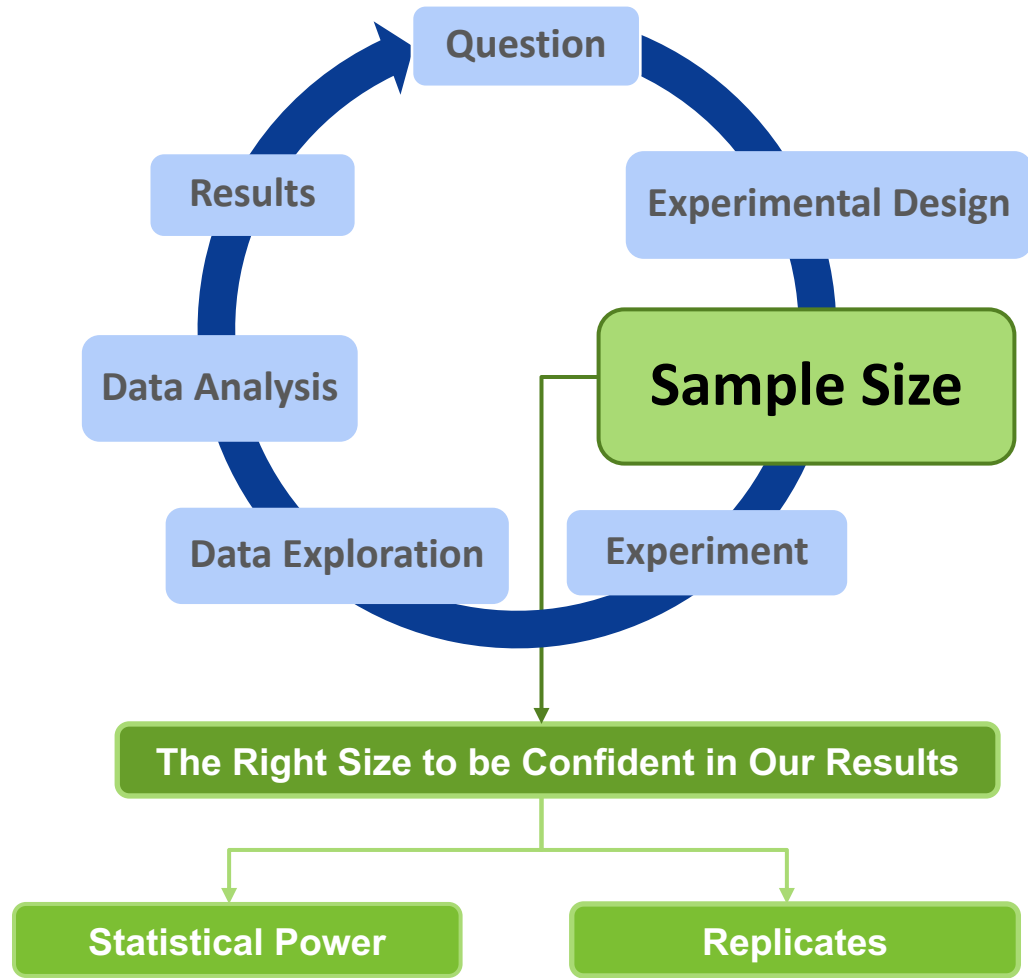
Rigor

Transparency

Research Integrity in practice

Sample size

- Accountability
- Accurate
- Care
- Collegiality
- Cooperation
- Ethics
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- Openness
- Quality
- Reliability
- Reproducibility
- Respect
- Responsibility
- Rigor
- Transparency



Statistical power: an analogy

You send your child into the basement to find a tool. The child comes back and says "it isn't there".

What do you conclude?

In the house

"If the tool really is in the basement, what are the chances that your child would have found it?"

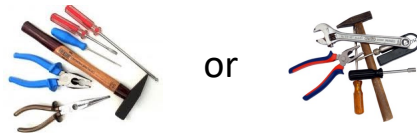
How long did the child spend looking?



How big is the tool?



How messy is the basement?



In the lab

"If there is a difference between 2 conditions, what are the chances that your experiment will pick it up ($p < 0.05$)?"

How many mice do you look at? **Sample size**



How big is the difference? **The absolute effect**



How messy the data are? **Variability**



Accountability

Accurate

Care

Collegiality

Cooperation

Ethics

Fair

Honesty

Objectivity

Openness

Quality

Reliability

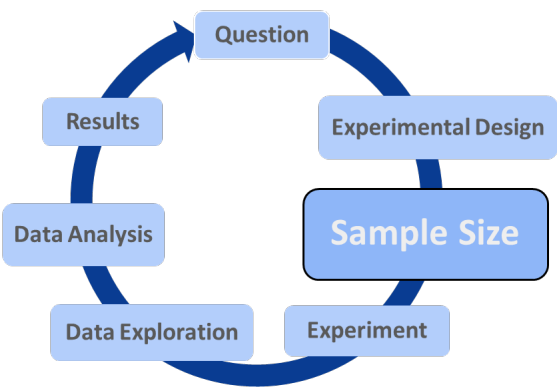
Reproducibility

Respect

Responsibility

Rigor

Transparency



- Accountability
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The Importance of Statistical Power

“If there is a difference between 2 conditions, what are the chances that your experiment will pick it up ($p < 0.05$)?”

Increase **Sample size** to increase **Power** →

How many mice do you look at? **Sample size**



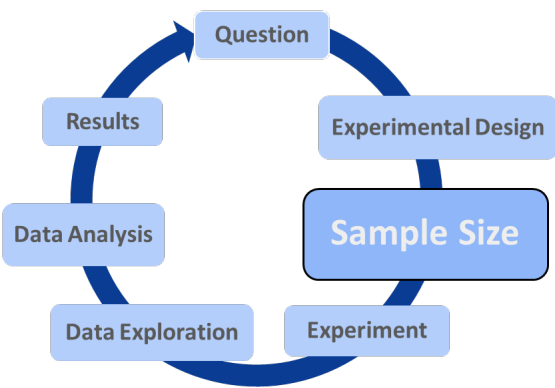
Little to no control

How big is the difference? **The absolute effect**



How messy the data are? **Variability**





- Accountability
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The Importance of Statistical Power

Low Powered Studies have a greater chance of failing to detect a real effect

BUT that's all probability...

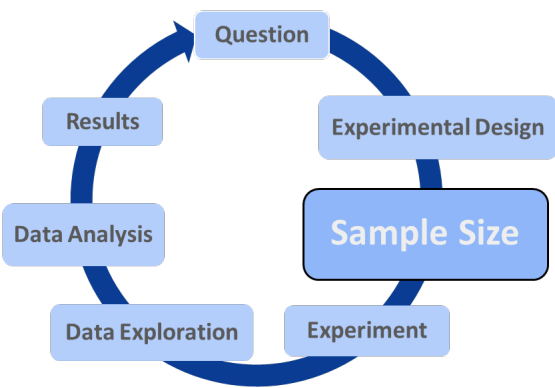
So some underpowered studies will detect a real effect

Are these results trustworthy?

A Yes

B No



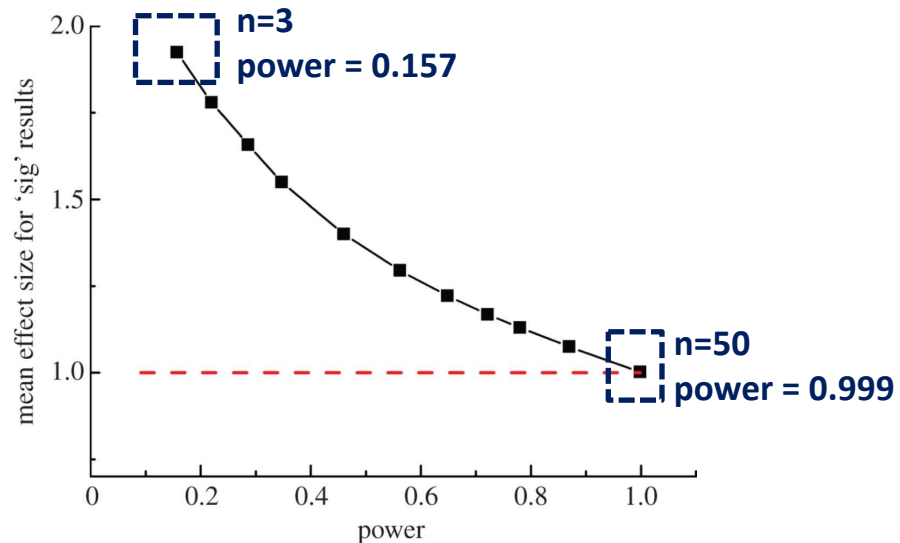
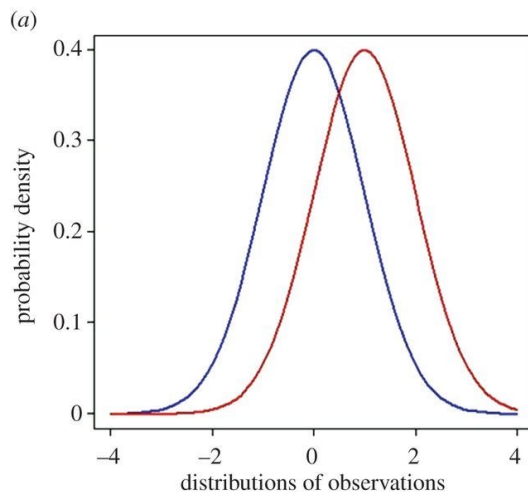


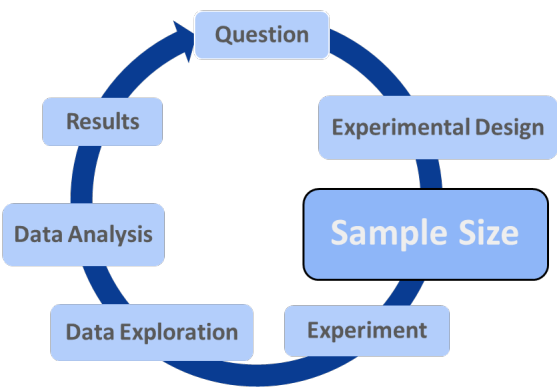
The Importance of Statistical Power

The Problem of the “Inflation Effect”...

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The TRUE effect size = 1



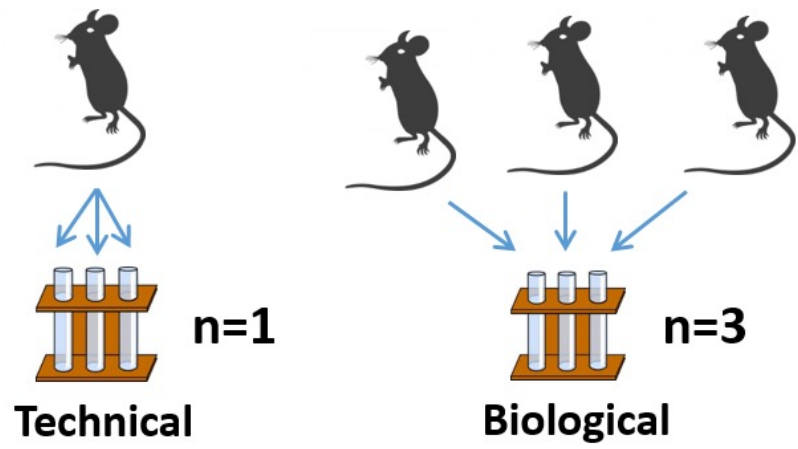


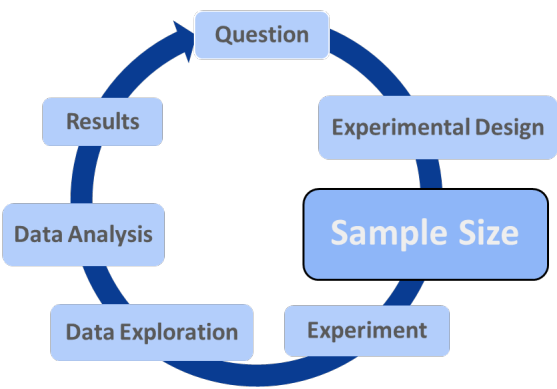
- Accountability
- Accurate
- Care
- Collegiality
- Cooperation
- Ethics
- Fair
- Honesty
- Objectivity
- Openness
- Quality
- Reliability
- Reproducibility
- Respect
- Responsibility
- Rigor
- Transparency

Defining Replicates

By the way: *replicates* = repeat = sample = library

Technical versus biological replicates





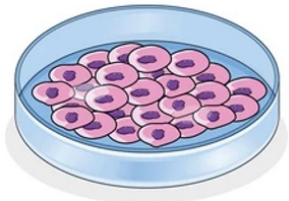
- Accountability
- Accurate
- Care
- Collegiality
- Cooperation
- Ethics
- Fair
- Honesty
- Objectivity
- Openness
- Quality
- Reliability
- Reproducibility
- Respect
- Responsibility
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- Transparency

What is a Biological Replicate in Practice?



1 biological replicate:

- A** 1 mouse
- B** 1 cage



1 biological replicate:

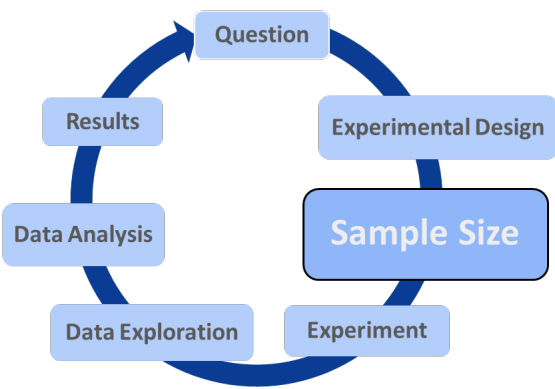
- A** 1 cell
- B** 1 petri dish



1 biological replicate:

- A** 1 worm
- B** 1 petri dish





In a nutshell

Sample Size & Power are key to confident results

Underpowered Studies are more likely to:

- Fail to detect real effects
- Overestimate the effect size of detected effects

More biological replicates increase our evidence

How Many?

Formalise with power calculations....

Accountability
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Reliability
Reproducibility
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Responsibility
Rigor
Transparency



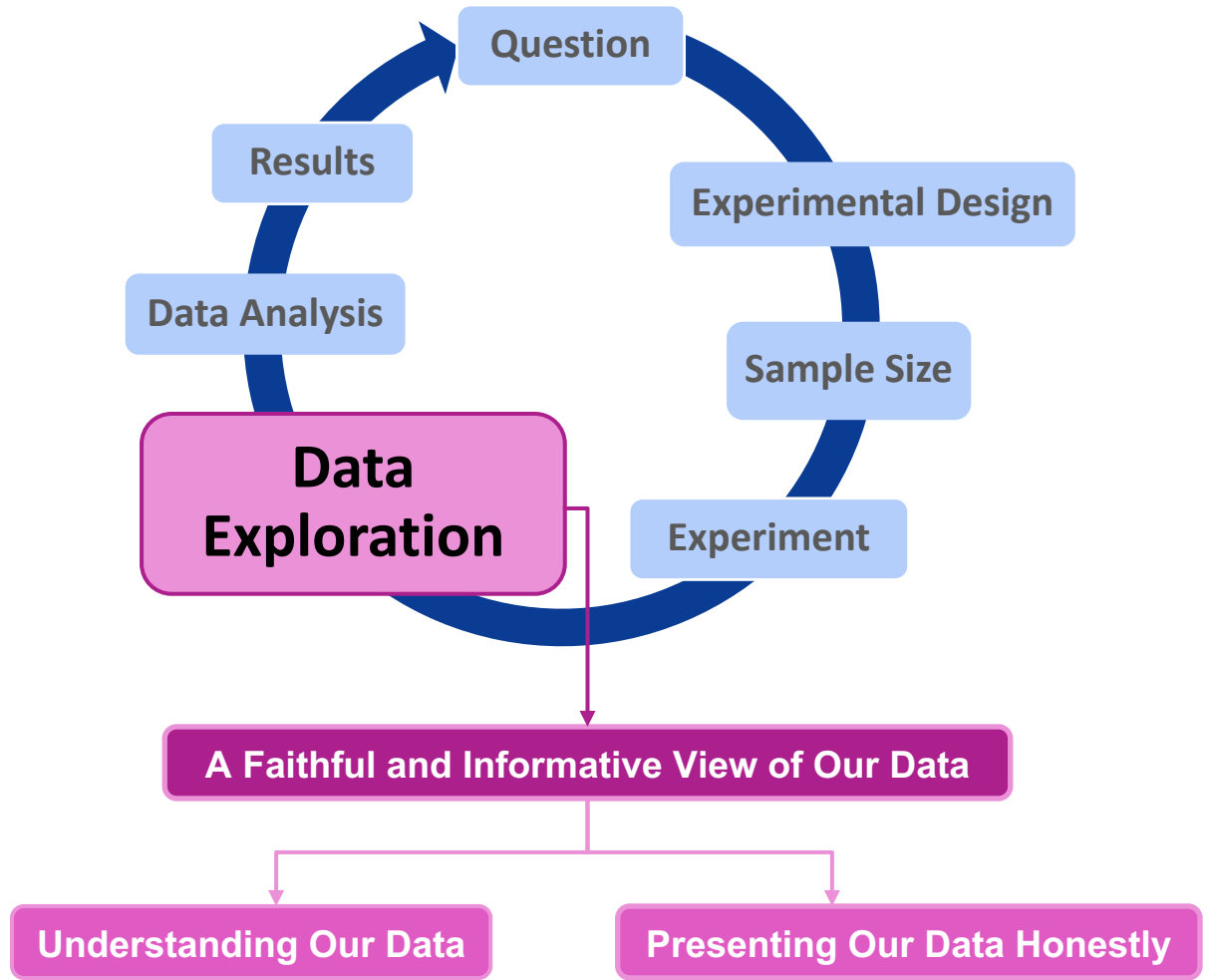


Research Integrity in practice

Data Exploration & Data Analysis



- Accountability
- Accurate**
- Care
- Collegiality**
- Cooperation**
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- Objectivity
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- Rigor
- Transparency**



Data Exploration

Accountability

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Care

Collegiality

Cooperation

Ethics

Fair

Honesty

Objectivity

Openness

Quality

Reliability

Reproducibility

Respect

Responsibility

Rigor

Transparency

Understanding Our Data:

- The Biology

- The Quality

Builds Our Understanding and Confidence



Data Exploration: Understanding Our Data

Often we summarise our data to key values

N	182
X Mean	54.26
Y Mean	47.83
X SD	16.76
Y SD	26.93
Correlation	-0.06

Can be really useful...
...And also really not!

Accountability

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Cooperation

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Reliability

Reproducibility

Respect

Responsibility

Rigor

Transparency

Data Exploration: Anscombe's Quartet

Accountability

Accurate

Care

Collegiality

Cooperation

Ethics

Fair

Honesty

Objectivity

Openness

Quality

Reliability

Reproducibility

Respect

Responsibility

Rigor

Transparency

"A computer should make both calculations *and* graphs"

Dataset 1		Dataset 2		Dataset 3		Dataset 4	
X1	Y1	X2	Y2	X3	Y3	X4	Y4
10.00	8.04	10.00	9.14	10.00	7.46	8.00	6.58
8.00	6.95	8.00	8.14	8.00	6.77	8.00	5.76
13.00	7.58	13.00	8.74	13.00	12.74	8.00	7.71
9.00	8.81	9.00	8.77	9.00	7.11	8.00	8.84
11.00	8.33	11.00	9.26	11.00	7.81	8.00	8.47
14.00	9.96	14.00	8.10	14.00	8.84	8.00	7.04
6.00	7.24	6.00	6.13	6.00	6.08	8.00	5.25
4.00	4.26	4.00	3.10	4.00	5.39	19.00	12.50
12.00	10.84	12.00	9.13	12.00	8.15	8.00	5.56
7.00	4.82	7.00	7.26	7.00	6.42	8.00	7.91
5.00	5.68	5.00	4.74	5.00	5.73	8.00	6.89



**Francis
Anscombe**

4 datasets

Each consisting of X and Y variable

All 4 datasets have the same summary statistics...

Data Exploration: Anscombe's Quartet

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Objectivity

Openness

Quality

Reliability

Reproducibility

Respect

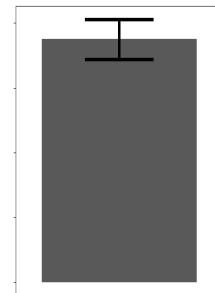
Responsibility

Rigor

Transparency

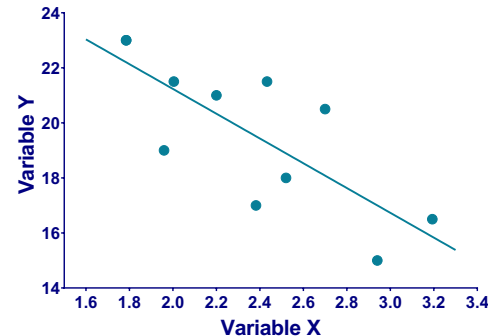
The average and spread of the conditions appears the same

	Dataset 1		Dataset 2		Dataset 3		Dataset 4	
	X1	Y1	X2	Y2	X3	Y3	X4	Y4
N	11	11	11	11	11	11	11	11
Mean	9.00	7.50	9.00	7.50	9.00	7.50	9.00	7.50
STD	3.31	2.03	3.31	2.03	3.31	2.03	3.31	2.03
SEM	1.00	0.612	1.00	0.612	1.00	0.612	1.00	0.612



The relationship between X & Y can be described the same

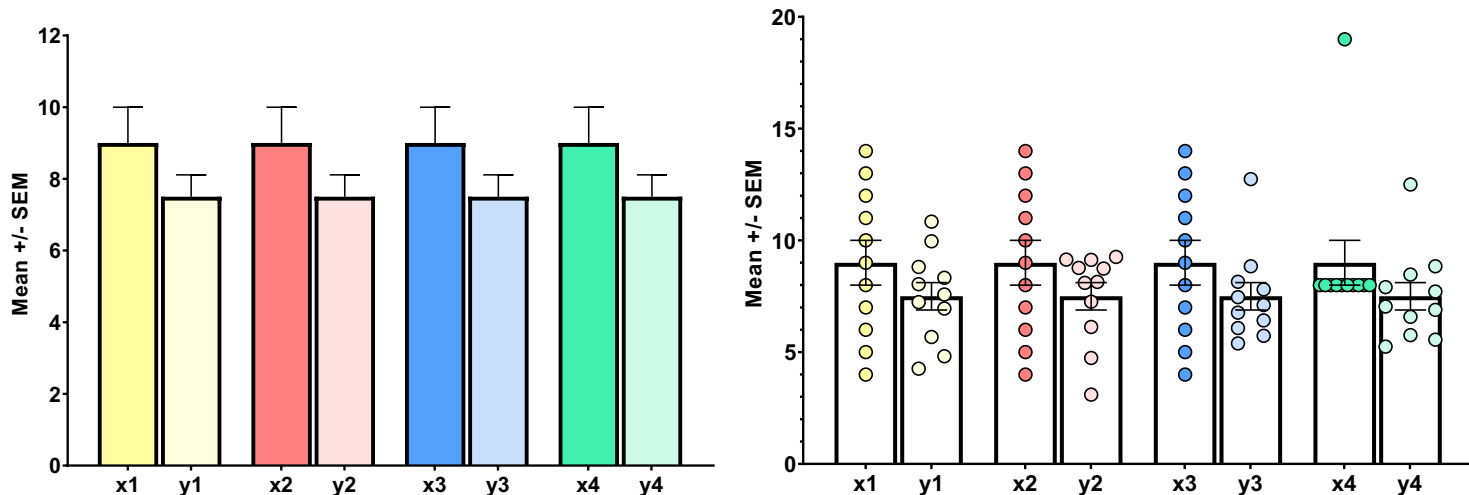
	Correlation (r)	Line of Best Fit
x1 vs. y1	r = 0.8164	Y = 0.5001*X + 3.000
x2 vs. y2	r = 0.8162	Y = 0.5000*X + 3.001
x3 vs. y3	r = 0.8163	Y = 0.4997*X + 3.002
x4 vs. y4	r = 0.8165	Y = 0.4999*X + 3.002



Data Exploration: Anscombe's Quartet

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Transparency

How does the data behave within the groups?

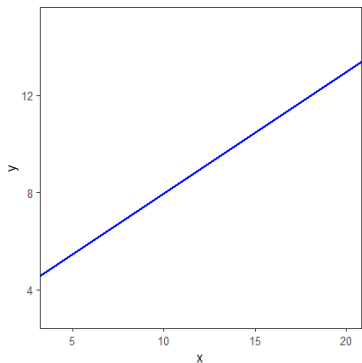


We're still not getting a complete view of the data
What about the relationship between X & Y?

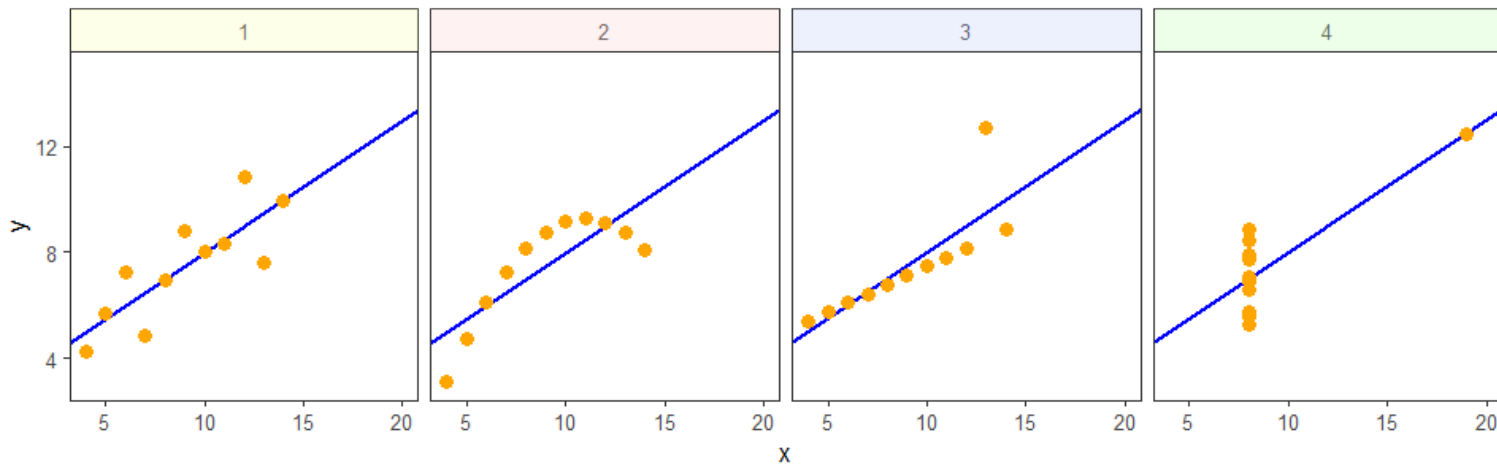
Data Exploration: Anscombe's Quartet

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Reliability
Reproducibility
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What about the relationship between X & Y?



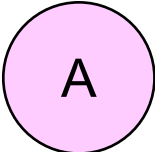
$r = 0.816$ $Y = 0.500 * X + 3.00$

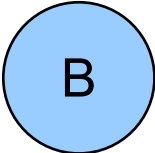


Can You Predict The Data Structure?

We already know what the data will look like...

Accountability
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Transparency

Line 

Circle 

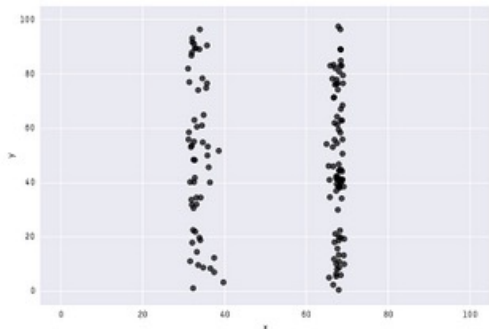
N	182
X Mean	54.26
Y Mean	47.83
X SD	16.76
Y SD	26.93
Correlation	-0.06

 Unstructured

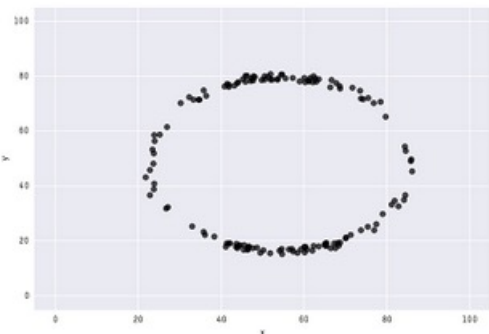
 I Don't Know...
A Dinosaur!



The Datasaurus Dozen



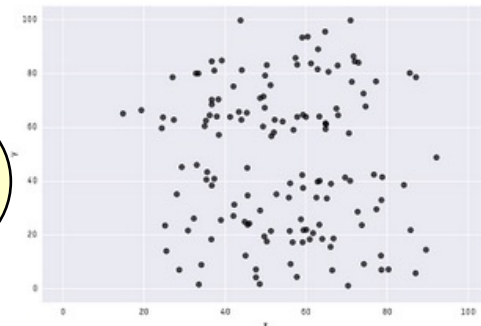
A



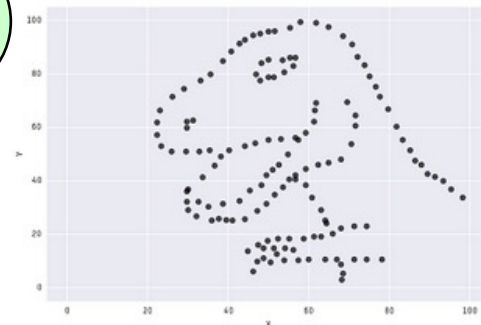
B

N	182
X Mean	54.26
Y Mean	47.83
X SD	16.76
Y SD	26.93
Correlation	-0.06

C



D

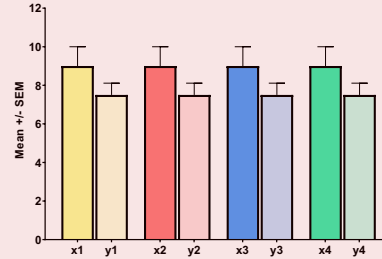


And More!

Data Exploration: Seeing is Believing!

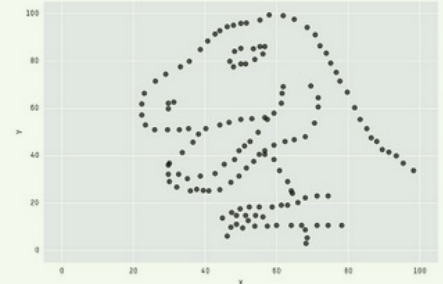
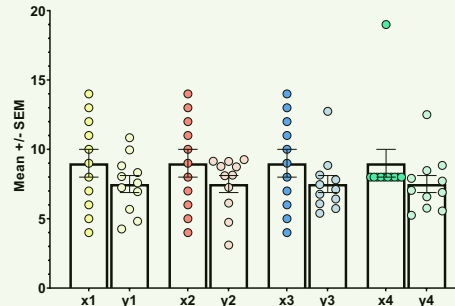
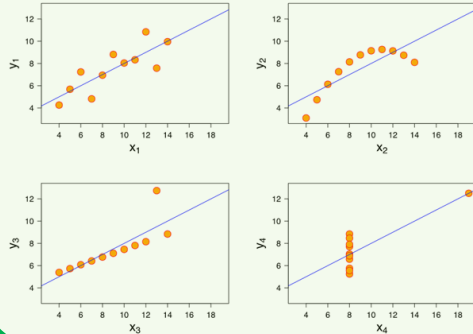
Beware of statistical or graphical summaries...

	Correlation (r)	Line of Best Fit
x1 vs. y1	r = 0.8164	Y = 0.5001*X + 3.000
x2 vs. y2	r = 0.8162	Y = 0.5000*X + 3.001
x3 vs. y3	r = 0.8163	Y = 0.4997*X + 3.002
x4 vs. y4	r = 0.8165	Y = 0.4999*X + 3.002



N	182
X Mean	54.26
Y Mean	47.83
X SD	16.76
Y SD	26.93
Correlation	-0.06

...without proper exploration & visualisation!



Accountability

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Objectivity

Openness

Quality

Reliability

Reproducibility

Respect

Responsibility

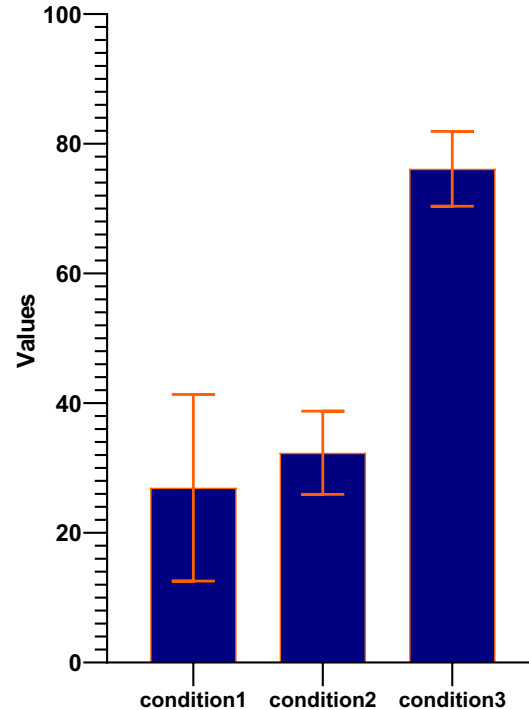
Rigor

Transparency

Data Exploration Exercise



What do you think of this graph?

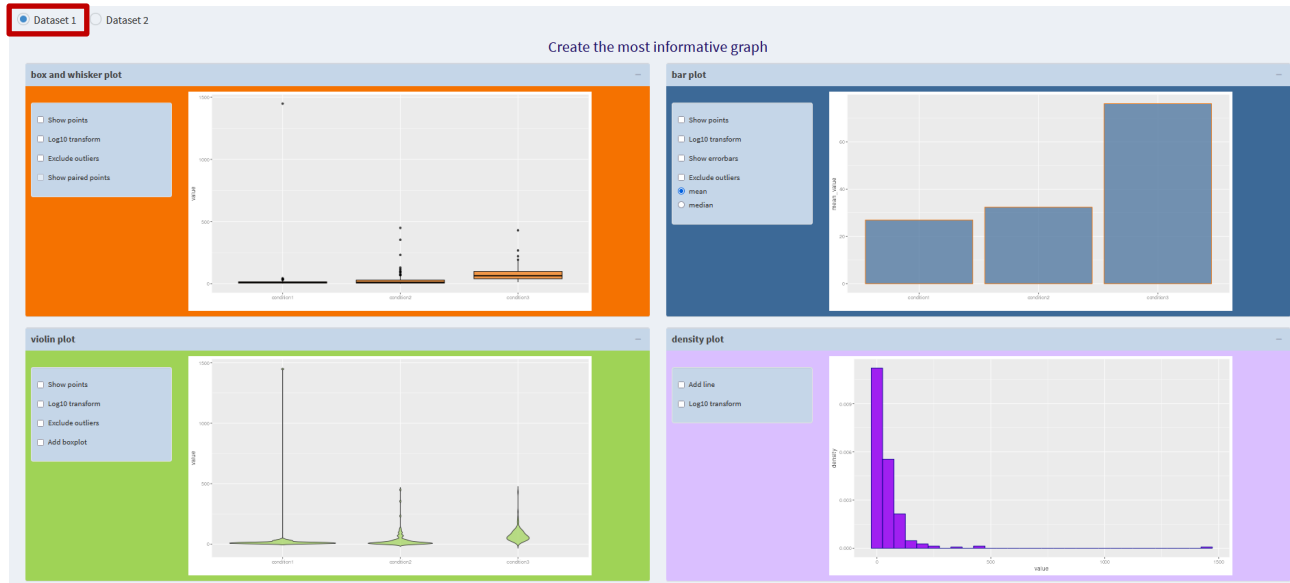


Values from 3 conditions from one experiment



Representing Dataset 1: Create the most informative graph

<https://tinyurl.com/RldataExp> **Make sure you are looking at Dataset 1**

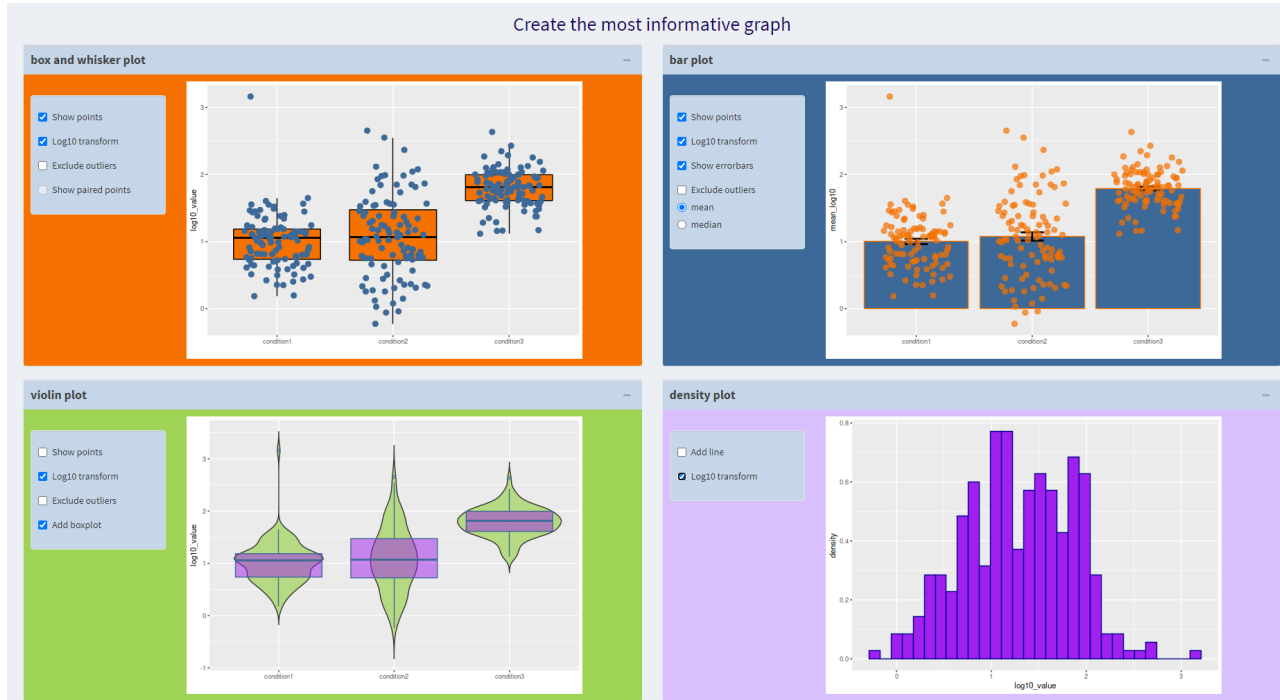


Plot for initial exploration of the data?
Plot for presentation/ publication?



Representing Dataset 1:

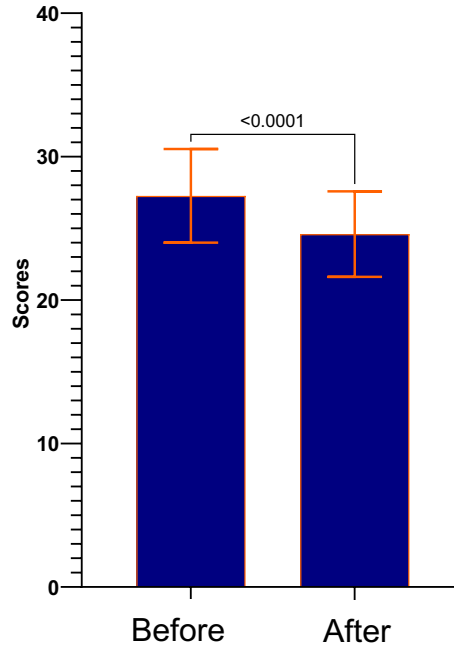
Create the most informative graph



Which plots did we choose and why?
Any differences between initial exploration and presentation?



What do you think of this graph?



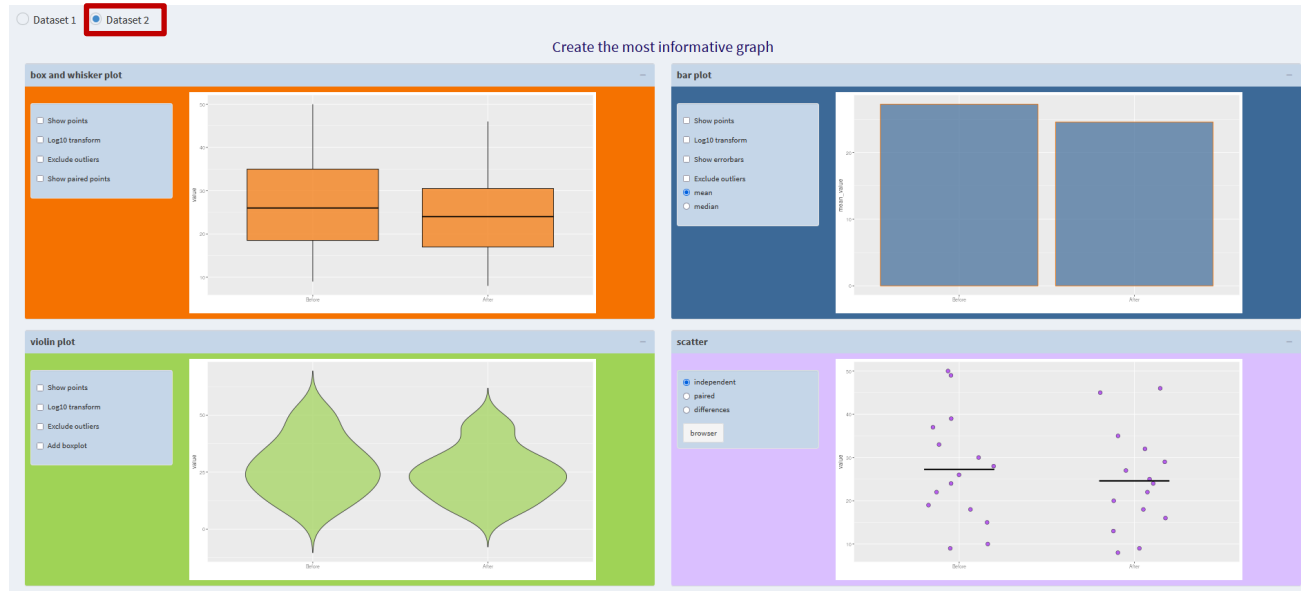
Values for before-after treatment from 4 experiments.



Representing Dataset 2: Create the most informative graph

<https://tinyurl.com/RIDataExp>

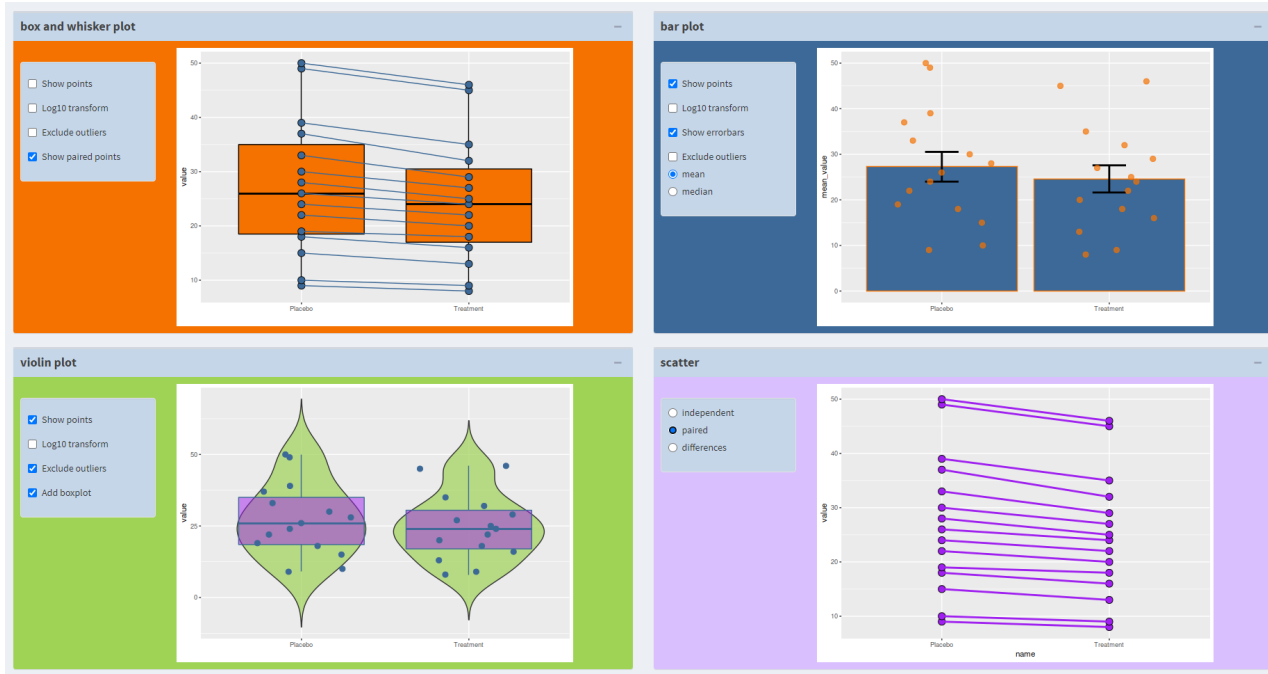
Make sure you are looking at Dataset 2



Create a plot to best represent dataset 2
Think about experimental design and statistics



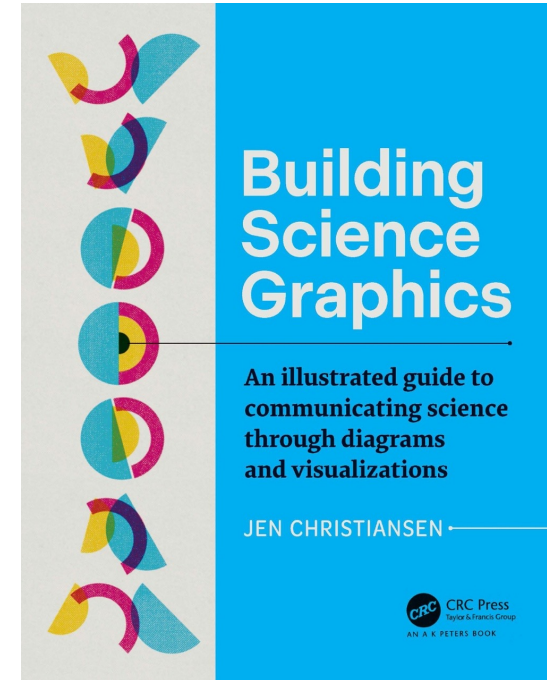
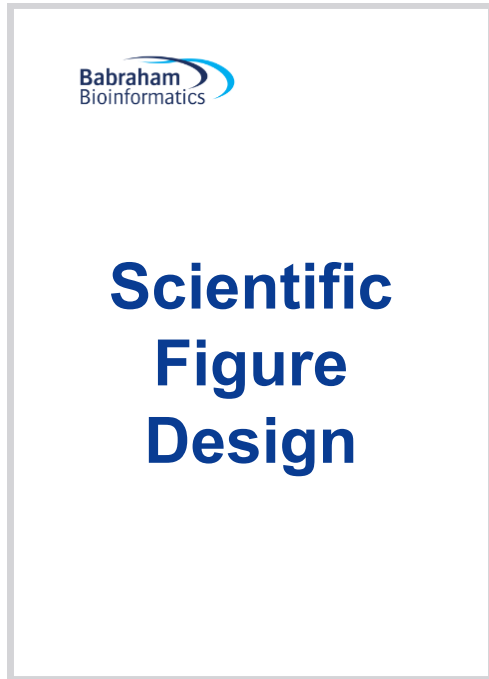
Representing Dataset 2: Create the most informative graph



Which plots did we choose and why?
What do you think about the stats now?



An Aside to Help with Better Figure Design...

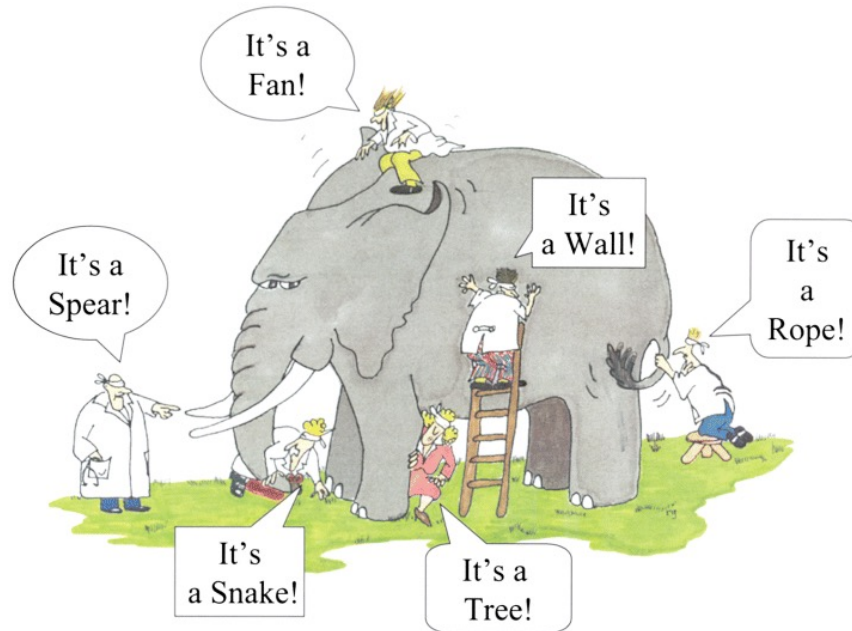


Data exploration

What can go wrong if we don't do it?!

Data exploration

Less Exploring more Assuming!

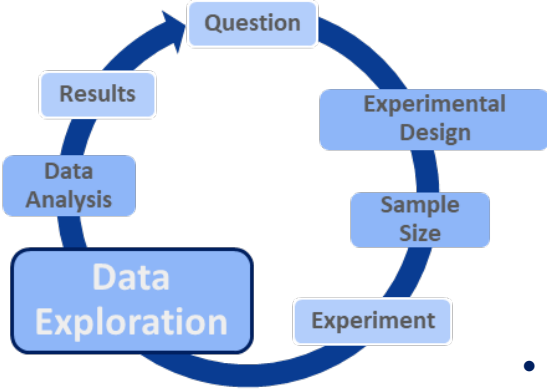


Risk missing the actual story the data is telling...

Data Exploration...



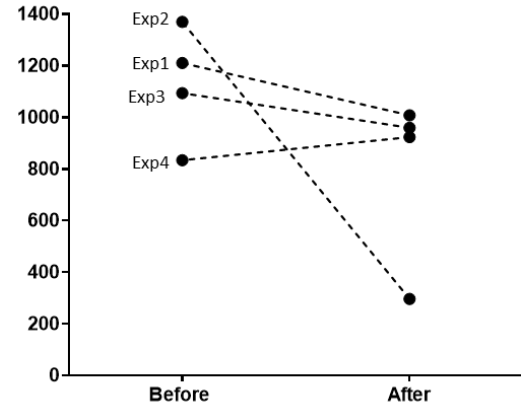
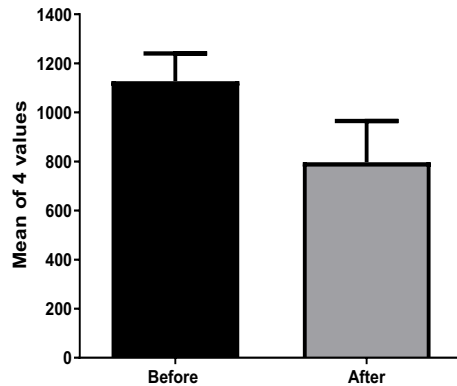
...Suspicious Summaries

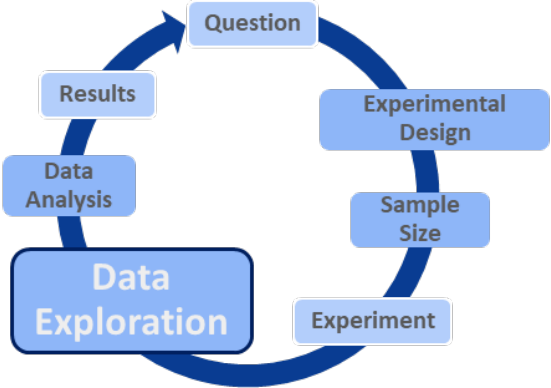


- Accountability**
- Accurate
- Care
- Collegiality
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- Ethics**
- Fair**
- Honesty**
- Objectivity**
- Openness**
- Quality**
- Reliability**
- Reproducibility
- Respect
- Responsibility
- Rigor**
- Transparency**

Example 1

- Four experiments: Before-After treatment effect on a variable of interest.
- Hypothesis: Treatment will decrease the levels of the variable of interest

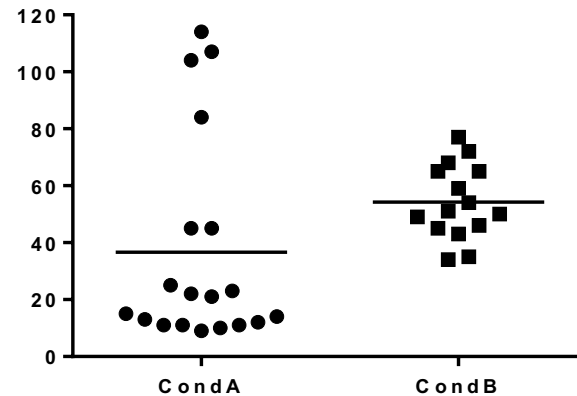
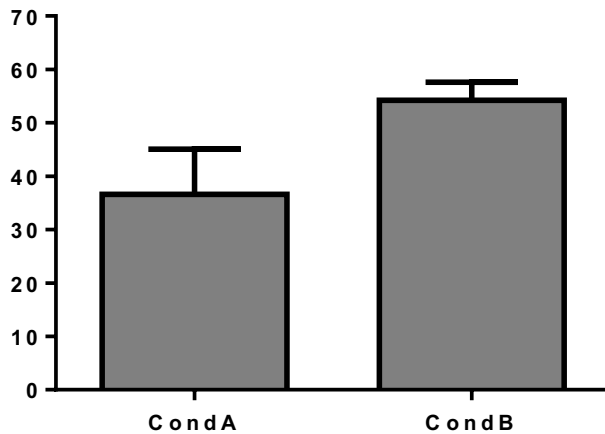


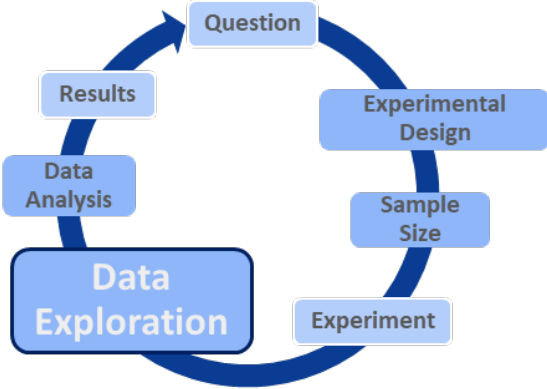


Example 2

Accountability

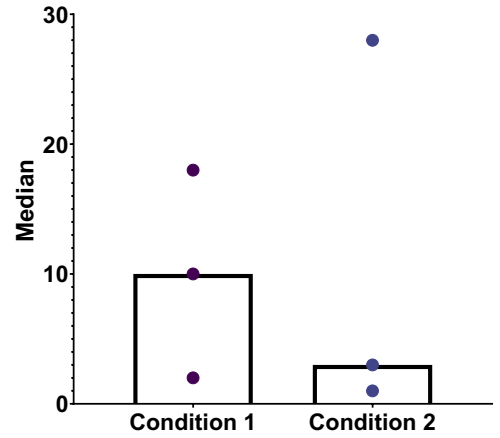
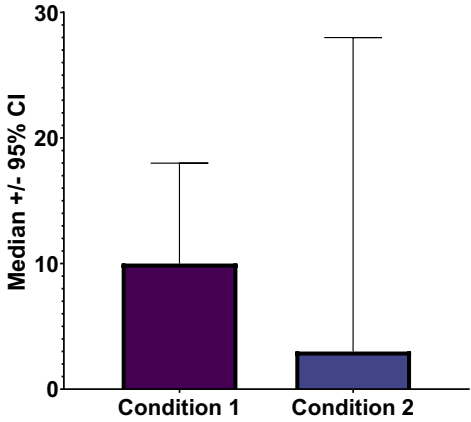
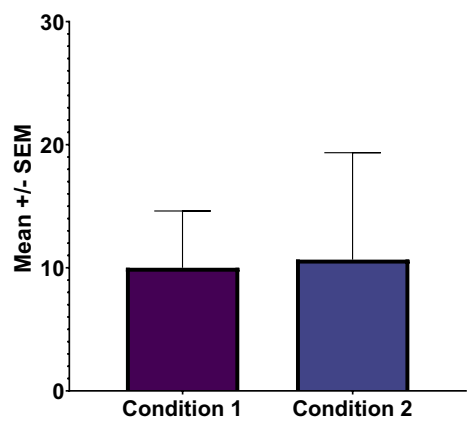
Accurate
 Care
 Collegiality
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 Objectivity
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 Respect
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Rigor
Transparency





Example 3

- Accountability**
- Accurate
- Care
- Collegiality
- Cooperation
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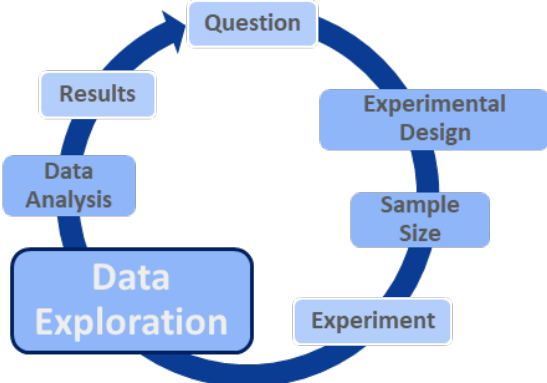


Data Exploration...



...Dubious Datasets

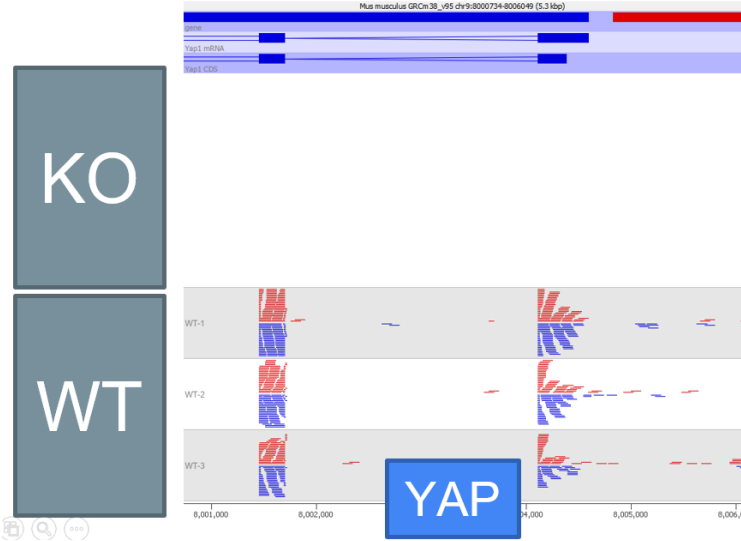
Example 1: A Knockout?

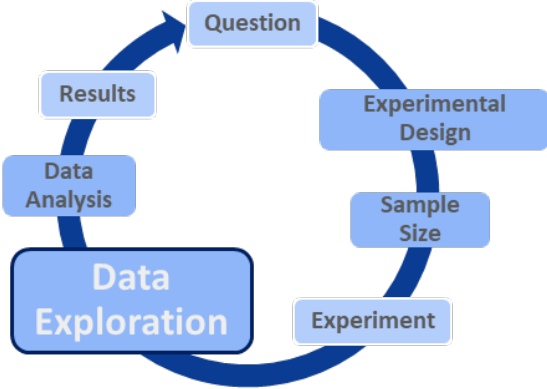


nature
neuroscience

YAP and TAZ control peripheral myelination and the expression of laminin receptors in Schwann cells

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- Ethics**
- Fair
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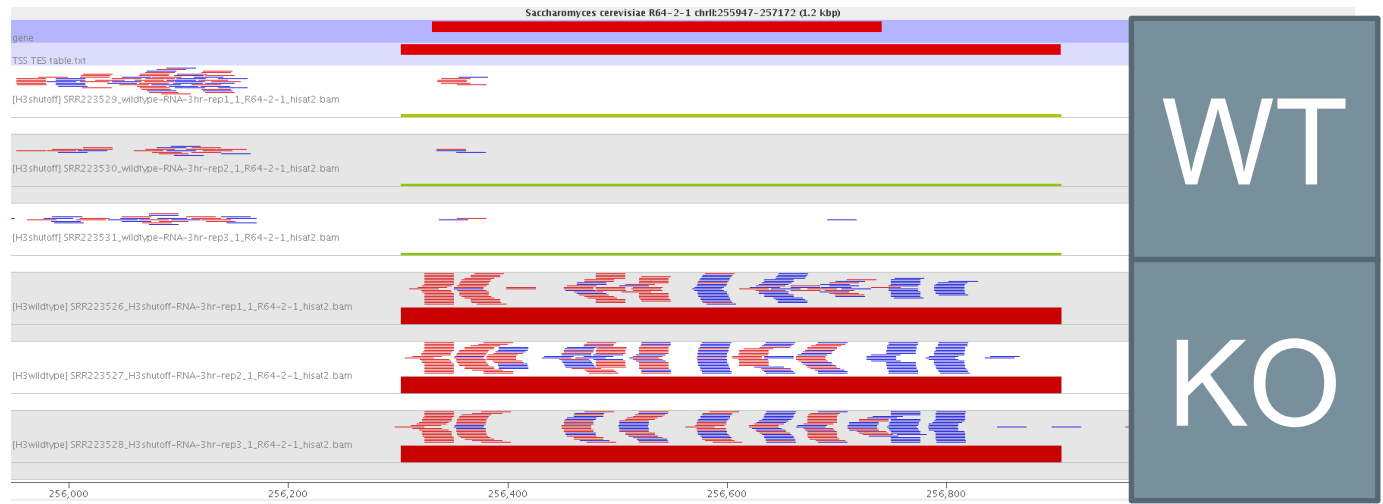
Example 2: A Case of Mistaken Identity

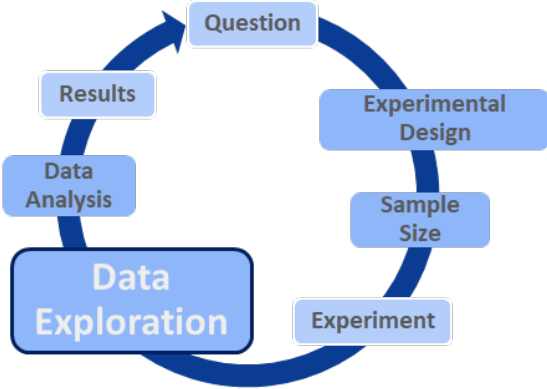
OPEN ACCESS Freely available online

PLOS GENETICS

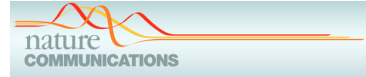
In Vivo Effects of Histone H3 Depletion on Nucleosome Occupancy and Position in *Saccharomyces cerevisiae*

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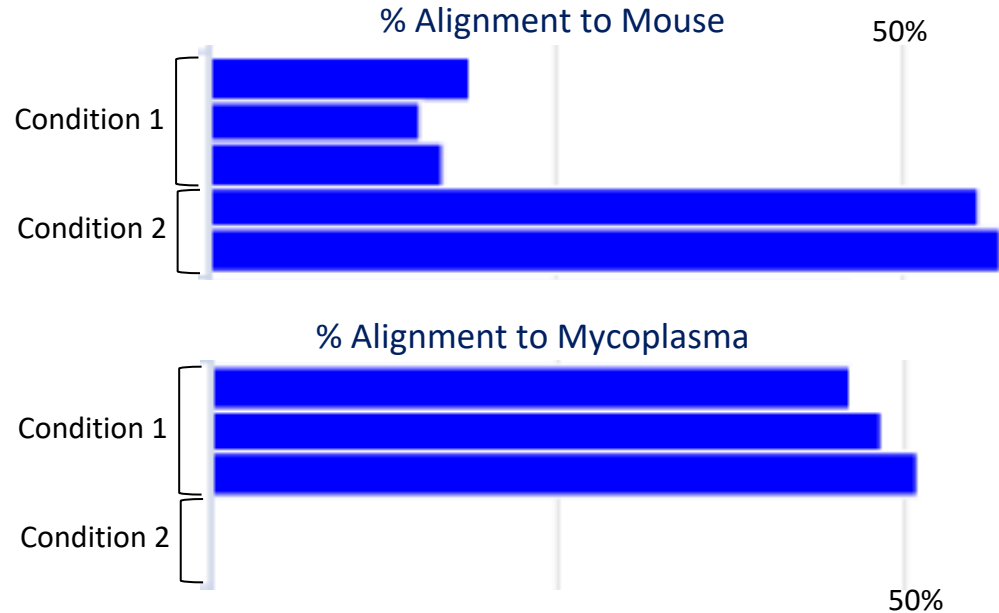


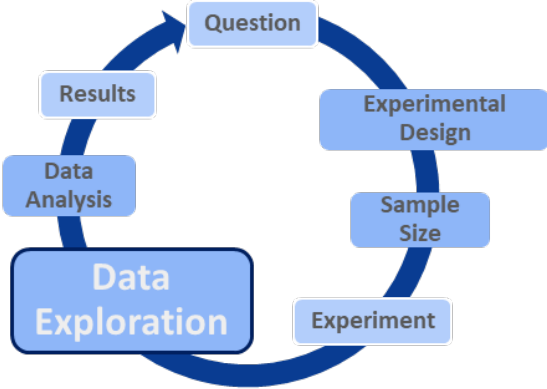
Example 3: Of Mice and Mycoplasma!



DOT1L-mediated murine neuronal differentiation associates with H3K79me2 accumulation and preserves SOX2-enhancer accessibility

- Accountability**
- Accurate
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 - Collegiality
 - Cooperation
- Ethics**
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All highlight the perils of assuming and not exploring....

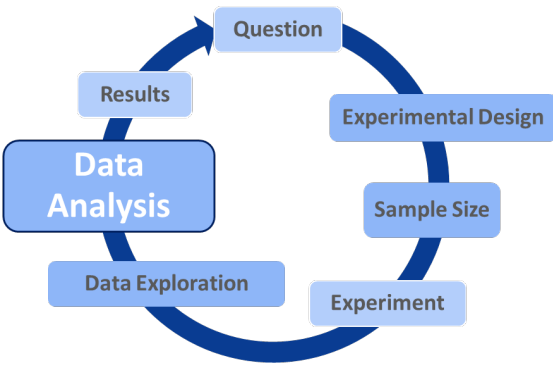


...Is it okay if you don't know there's a problem?

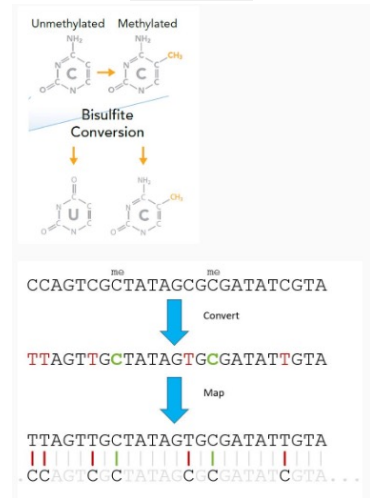
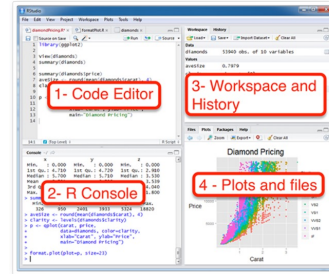
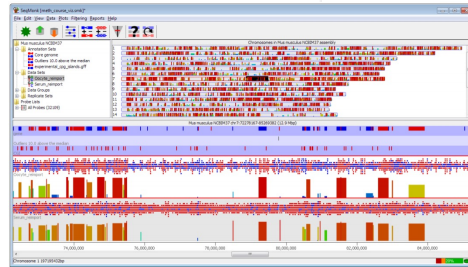
- Accountability**
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- Rigor**
- Transparency**

Analytical Tools

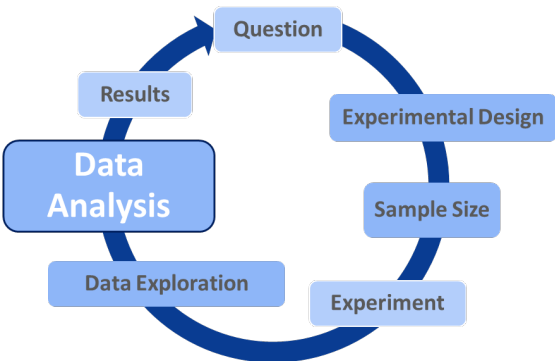
The right tools for the job!



- Accountability
- Accurate
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- Cooperation
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- Honesty
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- Openness
- Quality
- Reliability
- Reproducibility
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- Responsibility
- Rigor
- Transparency




- Know what's out there
- Learn how to use it



- Accountability
- Accurate
- Care
- Collegiality**
- Cooperation**
- Ethics
- Fair
- Honesty
- Objectivity
- Openness
- Quality**
- Reliability**
- Reproducibility**
- Respect
- Responsibility**
- Rigor**
- Transparency

Help With Analytical Tools



Core Skills Courses

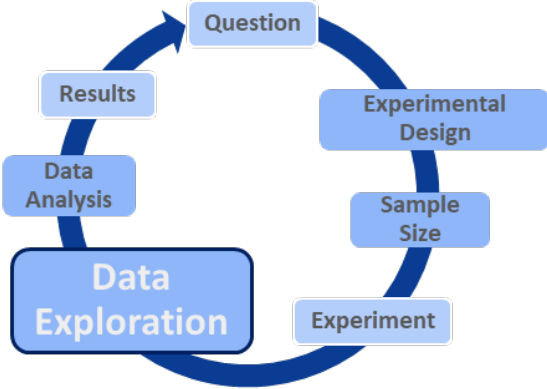
e.g. R Programming



Application Specific Courses

e.g. NGS Analysis

<https://www.bioinformatics.babraham.ac.uk/training.html>



In a nutshell

Data exploration is CRITICAL to:

- Understand our data
- Be confident in our findings

Ensure our results are quality and reliable

... Good for everyone!

Accountability

Accurate
Care
Collegiality
Cooperation

Ethics

Fair
Honesty
Objectivity
Openness

Quality

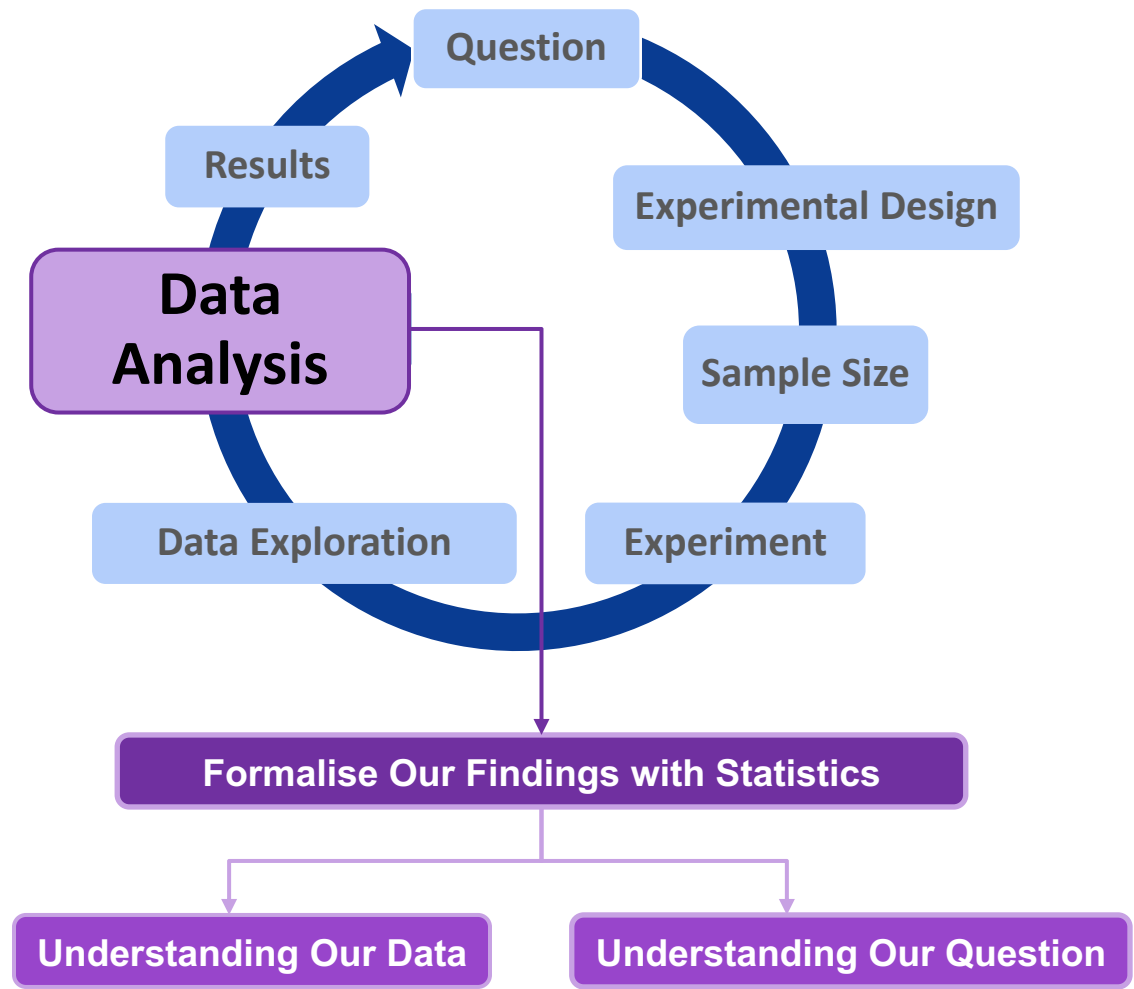
Reliability
Reproducibility
Respect

Responsibility

Rigor

Transparency

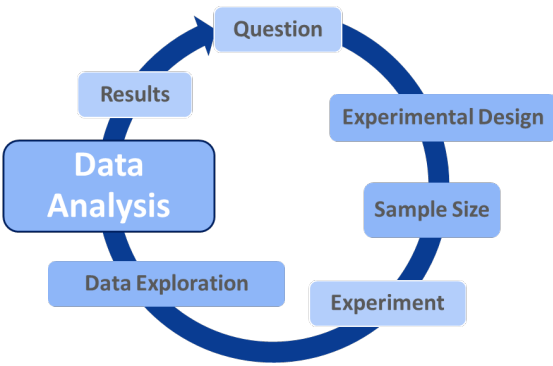
- Accountability**
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- Honesty**
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- Reproducibility**
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Statistical Analysis

Translate the hypothesis/question into statistical questions

By choosing the right test!



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Rigor
Transparency

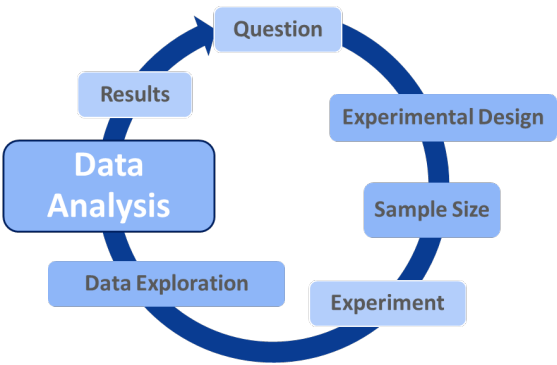
Healthy approach:

“It’s not about knowing the name of the test...”

...It’s knowing what the test should do”



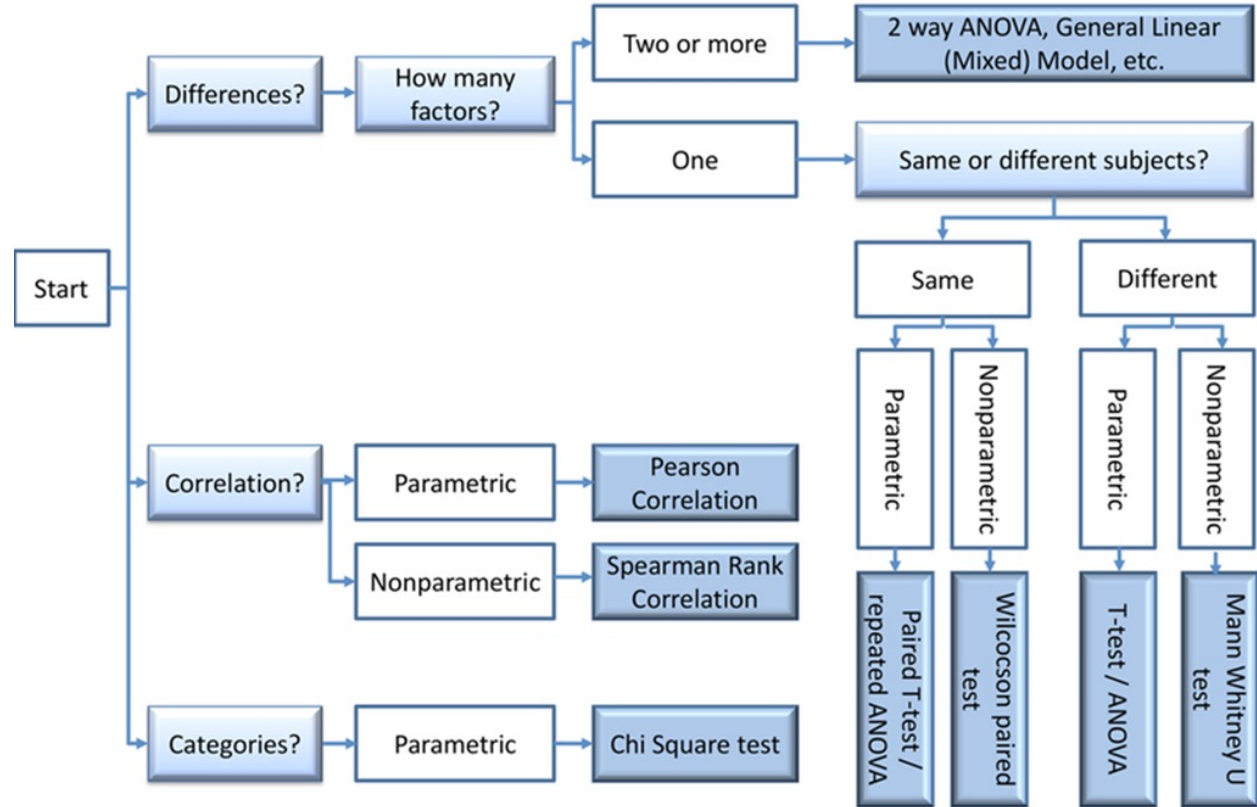
Anne Segonds-Pichon

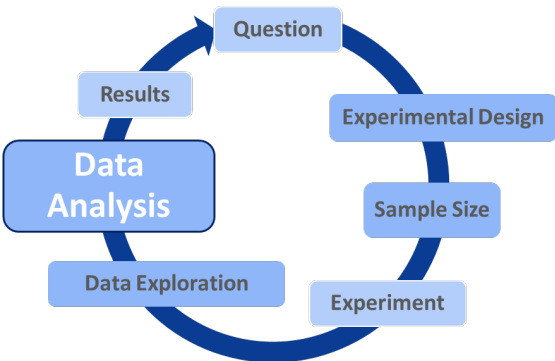


- Accountability
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Knowing what the Test should do...

Statistics Decision tree





- Accountability
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- Reproducibility**
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- Rigor**
- Transparency

Knowing what the Test should do...

Babraham Bioinformatics

Statistics Using R

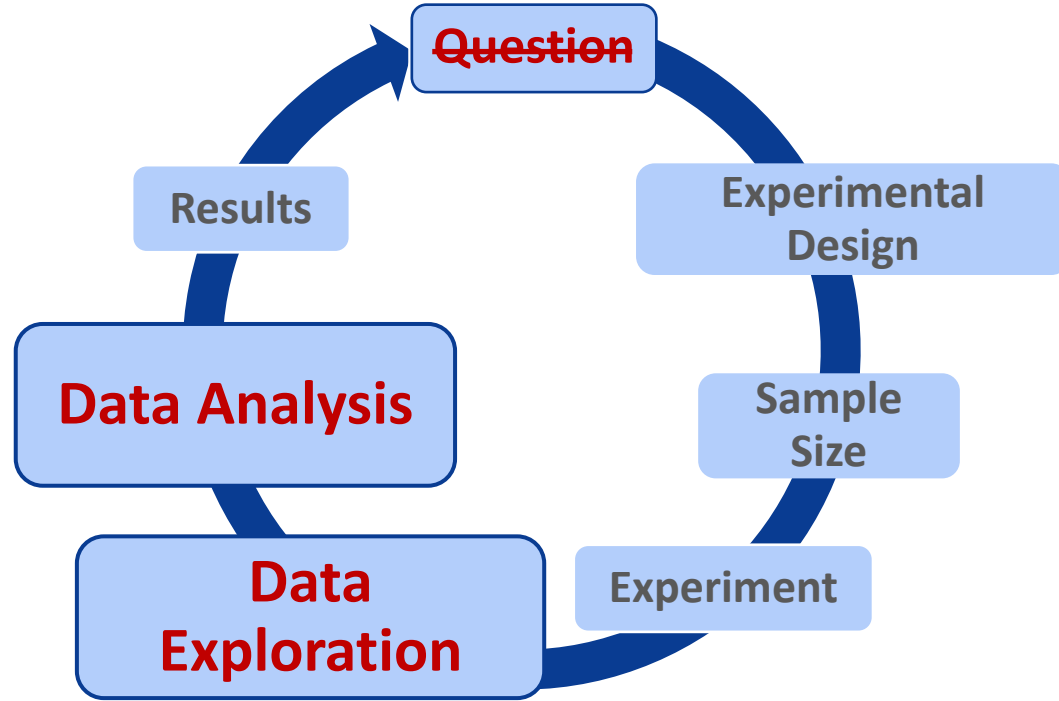
Babraham Bioinformatics

Statistics Using GraphPad Prism

<https://www.bioinformatics.babraham.ac.uk/training.html>

Research Integrity

More than 1 way to Investigate!



Exploratory data analysis

Accountability
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Transparency

In a nutshell



Data exploration should always be a **pivotal step of analysis**

Stats helps us **formalise our findings**





Research Integrity

What does Ethics mean?

Research Integrity

Ethics and Animal Welfare

Accountability

Accurate

Care

Collegiality

Cooperation

Ethics

Fair

Honesty

Objectivity

Openness

Quality

Reliability

Reproducibility

Respect

Responsibility

Rigor

Transparency

- If we need **biological replicates** to be confident in our results, why not have **as many as we can**?
- And what does it have to do with **integrity**?
- Time to talk about the **Home Office**, **ASPA** and the **3 Rs**

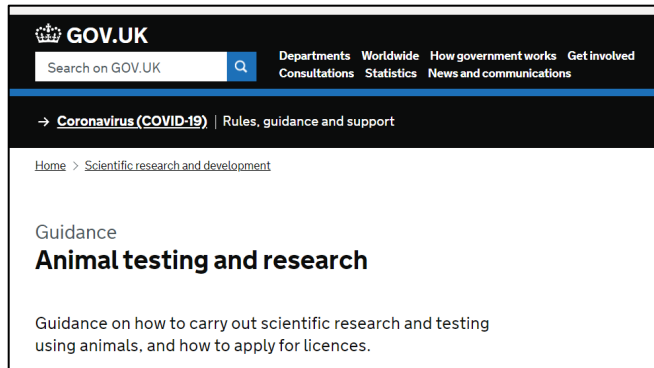


Research Integrity

Home Office

The **Home Office** (HO) is a ministerial department of the Government of the UK, responsible for immigration, security and law and order.

- But more importantly: **animal welfare**



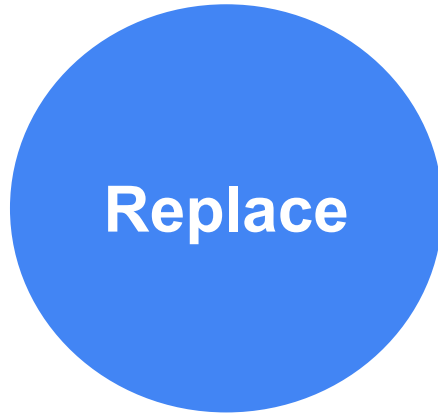
The screenshot shows the GOV.UK website interface. At the top, there is a search bar with the text 'Search on GOV.UK' and a magnifying glass icon. To the right of the search bar are links for 'Departments', 'Worldwide', 'How government works', and 'Get involved'. Below the search bar, there are links for 'Consultations', 'Statistics', and 'News and communications'. A navigation bar below the search bar shows a breadcrumb trail: '→ Coronavirus (COVID-19) | Rules, guidance and support'. Below the navigation bar, there is a breadcrumb trail: 'Home > Scientific research and development'. The main content area has the heading 'Guidance' followed by the sub-heading 'Animal testing and research'. Below this, there is a paragraph of text: 'Guidance on how to carry out scientific research and testing using animals, and how to apply for licences.'



By Steph Gray, CC BY-SA 2.0, <https://commons.wikimedia.org/w/index.php?curid=31387711>

Research Integrity

The 3 Rs



Accountability

Accurate

Care

Collegiality

Cooperation

Ethics

Fair

Honesty

Objectivity

Openness

Quality

Reliability

Reproducibility

Respect

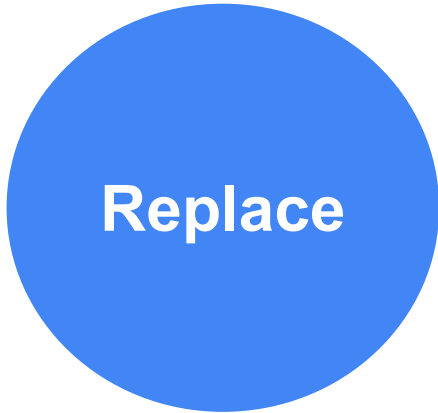
Responsibility

Rigor

Transparency

Research Integrity

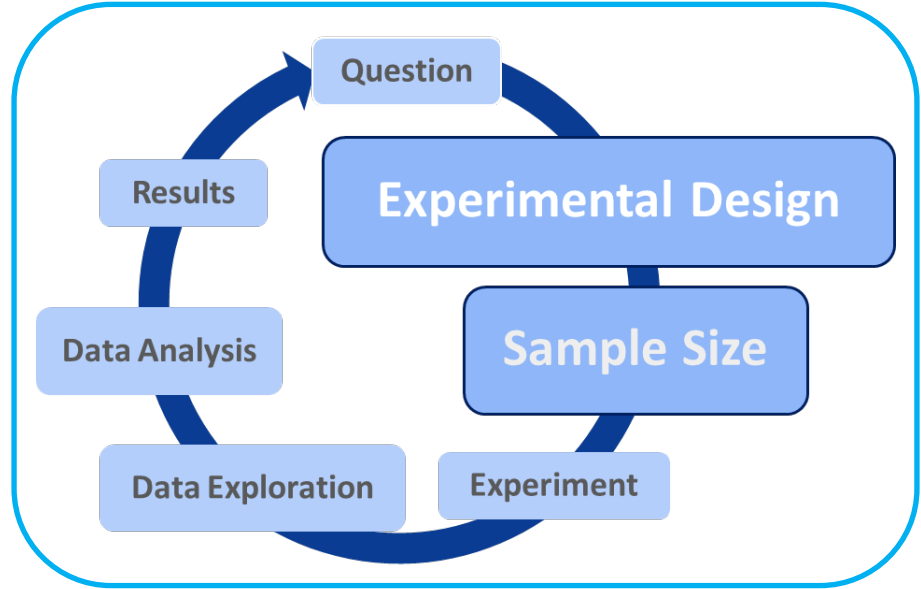
The 3Rs: about animal welfare



Avoiding or replacing the use of animals in areas where they otherwise would have been used.

Research Integrity

The 3Rs: about animal welfare

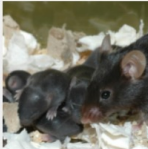
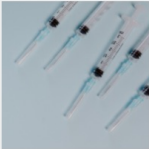
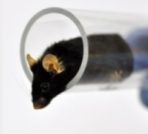

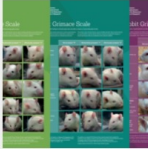



Minimising the number of animals used consistent with scientific aims.

Research Integrity

The 3Rs: about animal welfare



	Breeding and colony management Guidance on re-establishing colonies after a pause (e.g. COVID-19 lockdown).		Blood sampling Techniques for blood sampling in laboratory animal species to ensure the most appropriate technique is chosen.
	Mouse handling: How to pick up a mouse Guidance on non-aversive methods for handling mice, including tutorials, FAQs and practical tips.		Evaluating environmental enrichment Supporting technicians in assessing the welfare impact of new enrichment.
	Grimace scales Posters and other resources on the use of grimace scales to assess pain in laboratory animals.		Rat tickling Resources on rat tickling and how it can be used to promote positive human-animal interactions.

Minimising the pain, suffering, distress or lasting harm that research animals might experience.

Research Integrity

The 3 Rs at Babraham: AWERB

The Hub People Committees ▾ Institute ▾ Science Facilities ▾



Animal Welfare & Ethical Review Body

Remit

To provide the campus with independent ethical advice on the balance of harms to benefits within scientific projects using animals. To monitor standards of animal care and welfare, to support and advise named persons and licensees working under the Animals (Scientific Procedures) Act and to advise the Establishment Licence Holder on the suitability of Project Licence applications. To develop initiatives and guidelines leading to the widest possible application of the 3Rs (refinement, reduction and replacement) both on the campus and amongst the wider scientific community. In accordance with our commitments to the Concordat on Openness in animal research, any staff member with a concern that falls within the AWERB remit is encouraged to speak to the AWERB chair or any other committee member.



Good Research in Practice



Good Research in Practice

Accountability

Accurate

Care

Collegiality

Cooperation

Ethics

Fair

Honesty

Objectivity

Openness

Quality

Reliability

Reproducibility

Respect

Responsibility

Rigor

Transparency

The Research Process

- Responsibilities
- Competence
- Project planning
- Quality Control

Laboratory Practice

- Health and safety
- Handling of samples and materials
- Facilities and equipment
- Documentation of procedures and methods
- Research/work records



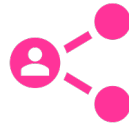
Get a GRiP!

'Good Research in Practice' (GRiP) supports and measures the more practical aspects of Research Integrity standards compliance on the ground in the lab.



Keeping track of the research

How?



Research Integrity

Laboratory Notebooks

Accountability

Accuracy

Care

Collegiality

Cooperation

Ethics

Fair

Honesty

Objectivity

Openness

Quality

Reliability

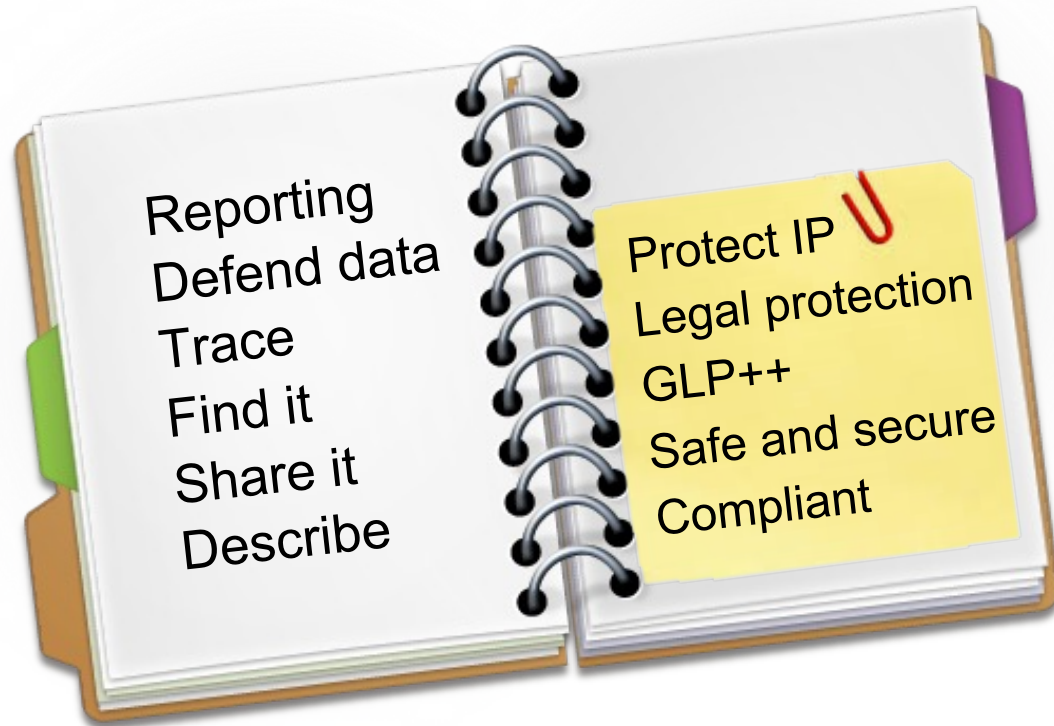
Reproducibility

Respect

Responsibility

Rigor

Transparency



Research Integrity

Laboratory Notebooks

Accountability

Accuracy

Care

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Ethics

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Respect

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Research Integrity

Laboratory Notebooks

Accountability

Accuracy

Care

Collegiality

Cooperation

Ethics

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Openness

Quality

Reliability

Reproducibility

Respect

Responsibility

Rigor

Transparency



Research Data Data Storage



Accountability

Accuracy

Care

Collegiality

Cooperation

Ethics

Fair

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Quality

Reliability

Reproducibility

Respect

Responsibility

Rigor

Transparency

Legal
Requirements

Practicalities

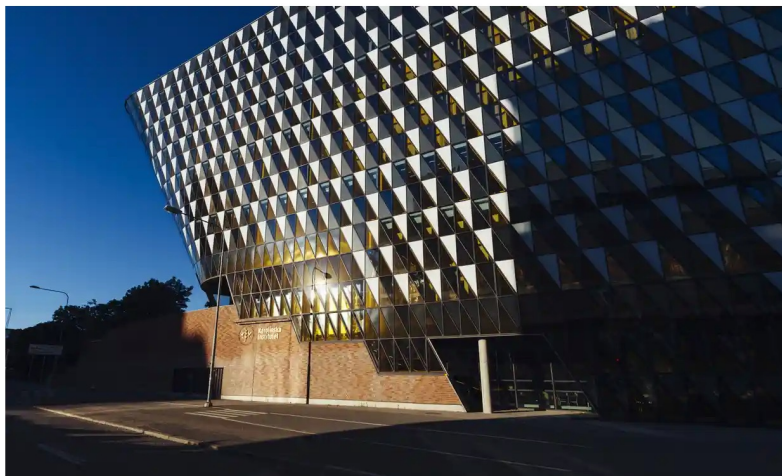
Research Data


Data Storage

Sweden

Decades of research destroyed after freezer fails at Swedish university

Estimated value of the samples thought to be in the millions as incident reported to police



 An internal investigation has been launched at the Karolinska Institutet despite no indication of sabotage. Photograph: Bloomberg/Getty Images

Accountability

Accuracy

Care

Collegiality

Cooperation

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Openness

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Transparency

The Guardian
Newspaper of the year

- Interruption in the supply of liquid nitrogen leading to the destruction of samples from multiple institutions.
- Valued in the millions.
- “Those worst affected are those researching leukaemia, they have gathered samples from patients over as much as 30 years,”

What should we be doing?

Expectations and Responsibilities



Created by Fajar Studio
from Noun Project



Created by Ribbla Team
from Noun Project



Created by Anggara Putra
from Noun Project



Created by shashank singh
from Noun Project



Created by Good Wife
from Noun Project

Research Data

OneNote

Accountability

Accuracy

Care

Collegiality

Cooperation

Ethics

Fair

Honesty

Objectivity

Openness

Quality

Reliability

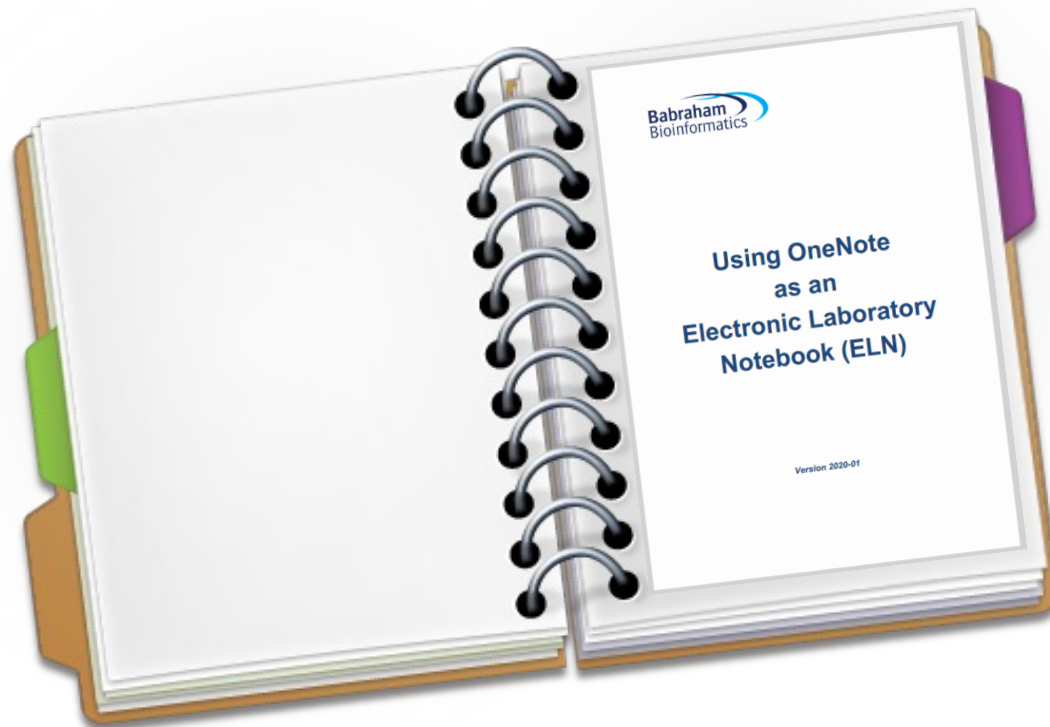
Reproducibility

Respect

Responsibility

Rigor

Transparency



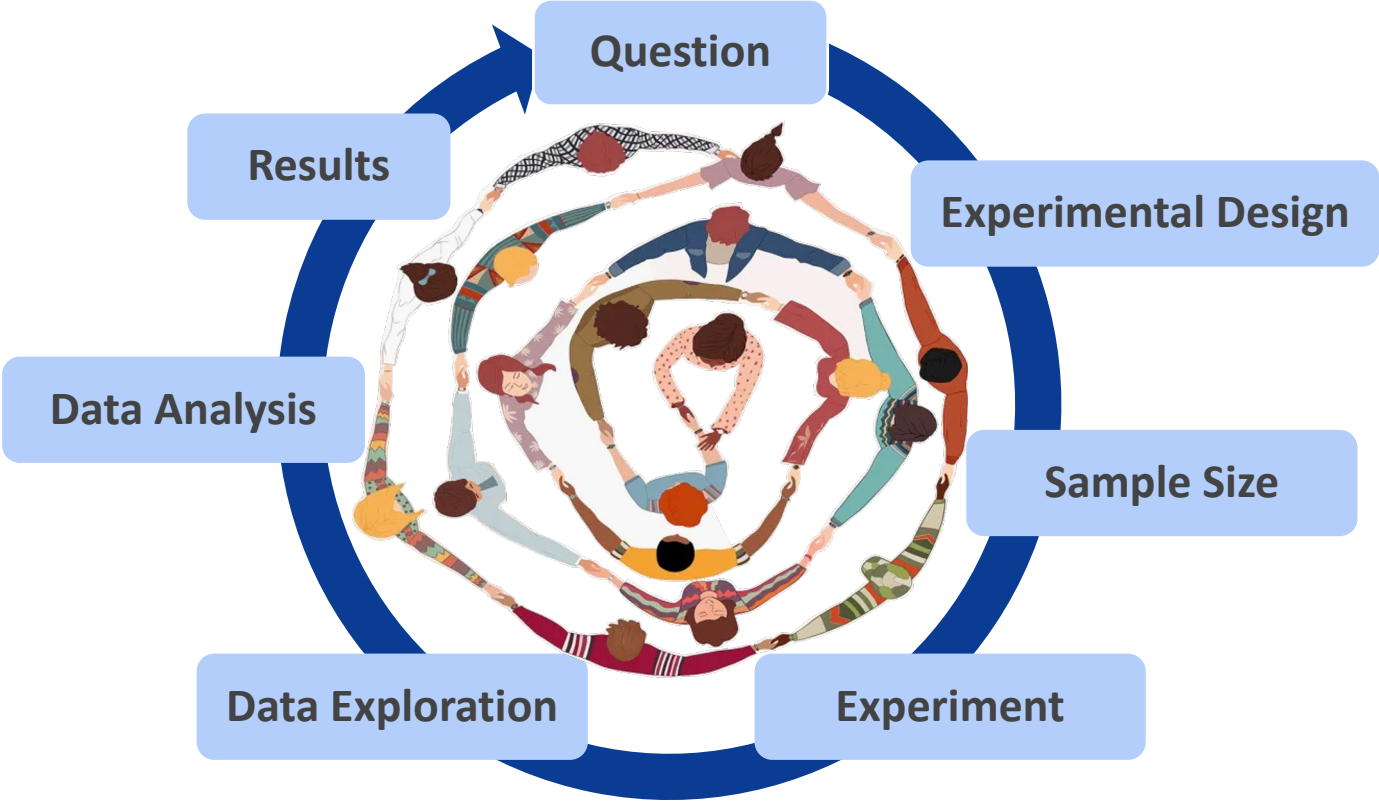


Responsibility



Research Integrity

Wider Responsibility



- Accountability
- Accurate
- Care
- Collegiality
- Cooperation
- Ethics
- Fair
- Honesty
- Objectivity
- Openness
- Quality
- Reliability
- Reproducibility
- Respect
- Responsibility
- Rigor
- Transparency

Research Integrity

Accountability

Accuracy

Care

Collegiality

Cooperation

Ethics

Fair

Honesty

Objectivity

Openness

Quality

Reliability

Reproducibility

Respect

Responsibility

Rigor

Transparency



Photo by Miguel Henriques Unsplash

Research Integrity

Questioning

Accountability

Accuracy

Care

Collegiality

Cooperation

Ethics

Fair

Honesty

Objectivity

Openness

Quality

Reliability

Reproducibility

Respect

Responsibility

Rigor

Transparency



Photo by Ana Municio on Unsplash

Research Integrity

Collaboration and Competition

Accountability

Accuracy

Care

Collegiality

Cooperation

Ethics

Fair

Honesty

Objectivity

Openness

Quality

Reliability

Reproducibility

Respect

Responsibility

Rigor

Transparency



Photo by Natalie Pedigo on Unsplash

Research Integrity

The Game

Accountability

Accuracy

Care

Collegiality

Cooperation

Ethics

Fair

Honesty

Objectivity

Openness

Quality

Reliability

Reproducibility

Respect

Responsibility

Rigor

Transparency



Photo by Karthik Balakrishnan on Unsplash

Research Integrity Wider Responsibility and Scientific Community

- Accountability
- Accuracy
- Care
- Collegiality
- Cooperation
- Ethics
- Fair
- Honesty
- Objectivity
- Openness
- Quality
- Reliability
- Reproducibility
- Respect
- Responsibility
- Rigor
- Transparency

Review

The review path

- Having your work reviewed by others - peer review (journal, paper), conference etc.
- Reviewing other people's work

Reviewing also means more locally: With in your group, department, or within. Colleagues should be positive, not combative.

You may have a vested interest in you and your science being successful and getting the very right cables to them.

Actively work to read and respond

Don't take it personally

Be positive to your colleagues of others' science

It makes you and your science better. Of the people know lots of things, it needs both ways. You don't do them, it may do it for you.

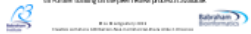
As your science progresses, you pass through milestones, pick up issues, find alternative ways to go.

You don't want to be taken down in public for not doing it as well as you might when a journal scientist took time to look at an abstract and conference without sharing with others. But and their feelings come against the common understanding of research objectives - if you were a professional and did not deny and not intentionally. The idea is that it is to help to you. [Link something, you can be helpful, not to help to you. Be supportive to consider, make mistakes, have the things, get the right before you go to the review/feedback etc.

It will save you from future embarrassment, time and effort to go through this time.

What does reviewing the science mean to you?

It's further building on the science review process is available.



FAIR

**Findable
Accessible
Interoperable
Reusable**

(which could mean replicate the spirit of the analysis, rather than just copy through exactly the same kind)

Findable

Accessible

Interoperable

Reusable

Having your science in **FAIR** can maximize the value of your science and your data.

Your data has value above and beyond what you created it for, especially with big datasets.

Make your data as useful as possible (make it work for you and others) others can put things out of your data.

This is good for others, and all starting with value to your research. Also good for the planet - not depending what has already been done.

This is about data disclosure - how to do it, to make data accessible, it's a process and a skill set and it's to make it as accessible as possible - it benefits everyone.

At it we are going to see (open) data that we generate our data. And we provide a DOI.


It's important that that (FAIR) make use of public data as much as possible. Some time, and energy.

Also, make sure - if your work is based on an existing paper/data, that you do a proper link to the actual data.

This is also being supported (practice standard) and analyzing the type of data you will likely be collecting.

And also good check - it will save you a lot of time and money.

How does this link to research integrity?



Pre-prints

The positives and negatives to pre-prints are a bit more nuanced.

The problem is that published data is often out of date. By the time a paper comes out (6 months +, mostly more), takes time to get published, findings may have moved on.

Now have bioRxiv.

A way to circumvent the delay in getting research out BUT it's not peer reviewed.

It looks like a paper, but it's not:

- Not peer reviewed
- Not fact checked
- A high proportion on bioRxiv never makes it into a paper.


If we consider that about half of all that is published (and peer reviewed) is wrong, this pushes that likelihood up even more with bioRxiv.

However, it is worth thinking about if your data is time critical. You may also need to check with your preferred journal - will they preprint you? Not accept if you've published on bioRxiv first?

pre

print

How does this link to research integrity?



Open Access

This is a bit of a game. Open access can have benefits to you, and others.

There are open access journals, or some which you can pay a fee to make open access. This means your paper is more accessible.

Now have bioRxiv.

Also accessible to automatic text mining, so even more can be gleaned from your data (see FAIR).

Something like PubMed Central will also make papers open access - with about a 6 month delay - on loads of journals, not just open access ones.


Where you can put out information, including API etc (auto program).

Remember: Just because something is in a paper, doesn't mean it's actually true!

pre

print

How does this link to research integrity?





Research Integrity

Review

This means both:

- Having your work reviewed by others – peer review (journals, papers, conferences etc)
- Reviewing other people's work

Reviewing also means more locally: Within your group, department, institute.

Criticism should be positive, not constructive.

Your group have a vested interest in you and your science being successful and getting the necessary right, advice to them.

Actively seek
input and
questioning

Don't take it
personally

Be positive in
your criticism
of others' science

It makes you and your science better. Of we people know lots of things, it works both ways. You do it for them, they do it for you.

As your science progresses, you pass through these barriers, pick up issues, find alternative viewpoints.

You don't want to be taken down in a public forum (see below) as an example where a junior scientist took their work to an internal oral conference without clearing with others first and their findings went against the common understanding of enzyme structure – they were questioned and disproved openly and respectfully. We don't want it to happen to you!
Lab meetings, etc can be a safe general. An opportunity to consider, make mistakes, have the class, get things right before you go to conference/seminar etc.

It will ease you from future embarrassment, time and effort to go through this work.

What does reviewing the science mean to you?

1/3 Further training on the peer review process is available.



UoB Birmingham
Faculty of Science, School of Life Sciences, Birmingham Business School



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Accessible

Interoperable

Reusable

(which could mean replicate the spirit of the analysis, rather than just jump through exactly the same hoops)



Ensuring your science is FAIR maximises the value of your science and your data.
Your data has value above and beyond what you created it for, especially with big datasets.

Make your data as useful as possible (make it work for you and others)

Others can pull things out of your data.

This is good for others, and ultimately adds value to your research.

Also good for the planet – not repeating what has already been done.

This is about data disclosure – so we need to do this, to make data accessible, BUT there's a real selling point for us to make it as accessible as possible – it benefits every one.
At it we reprocess (or generate) data that we generate new data. And we generate a LOT.

It's also important that YOU make use of public data as much as possible. Saves time, and money.

Also, make sure – if your work is based on an existing paper/data, that you do a PMID check on the actual data.

This is also a learning opportunity by (searching, checking and analysing) the type of data you will likely be collecting.

And also a good check – it could save you a lot of time and money!

How does this link to research integrity?



UoB Birmingham
Faculty of Science, School of Life Sciences, Birmingham Business School



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What are the pros and cons?



How does this link to research integrity?



UoB Birmingham
Faculty of Science, School of Life Sciences, Birmingham Business School



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Means you can pull out information, including API etc (auto program).

Remember: Just because something is in a paper, doesn't mean it's actually true!

What are the pros and cons?



How does this link to research integrity?



UoB Birmingham
Faculty of Science, School of Life Sciences, Birmingham Business School



Research Integrity

In a nutshell

Applying **research integrity principles** is our **responsibility as scientists**

Accountability

Accurate

Care

Collegiality

Cooperation

Ethics

Fair

Honesty

Objectivity

Openness

Quality

Reliability

Reproducibility

Respect

Responsibility

Rigor

Transparency



Research Integrity

In the lab

Accountability

Accurate

Care

Collegiality

Cooperation

Ethics

Fair

Honesty

Objectivity

Openness

Quality

Reliability

Reproducibility

Respect

Responsibility

Rigor

Transparency



Research Integrity

Work culture



Accountability
Accurate
Care
Collegiality
Cooperation
Ethics
Fair
Honesty
Objectivity
Openness
Quality
Reliability
Reproducibility
Respect
Responsibility
Rigor
Transparency

Research Integrity

PhD Students



It doesn't matter if it 'doesn't work'

Accountability

Accurate

Care

Collegiality

Cooperation

Ethics

Fair

Honesty

Objectivity

Openness

Quality

Reliability

Reproducibility

Respect

Responsibility

Rigor

Transparency

Research Integrity

Accountability

Accurate

Care

Collegiality

Cooperation

Ethics

Fair

Honesty

Objectivity

Openness

Quality

Reliability

Reproducibility

Respect

Responsibility

Rigor

Transparency

Work hard...



...but what if it is too hard?

Research Integrity

Accountability

Accurate

Care

Collegiality

Cooperation

Ethics

Fair

Honesty

Objectivity

Openness

Quality

Reliability

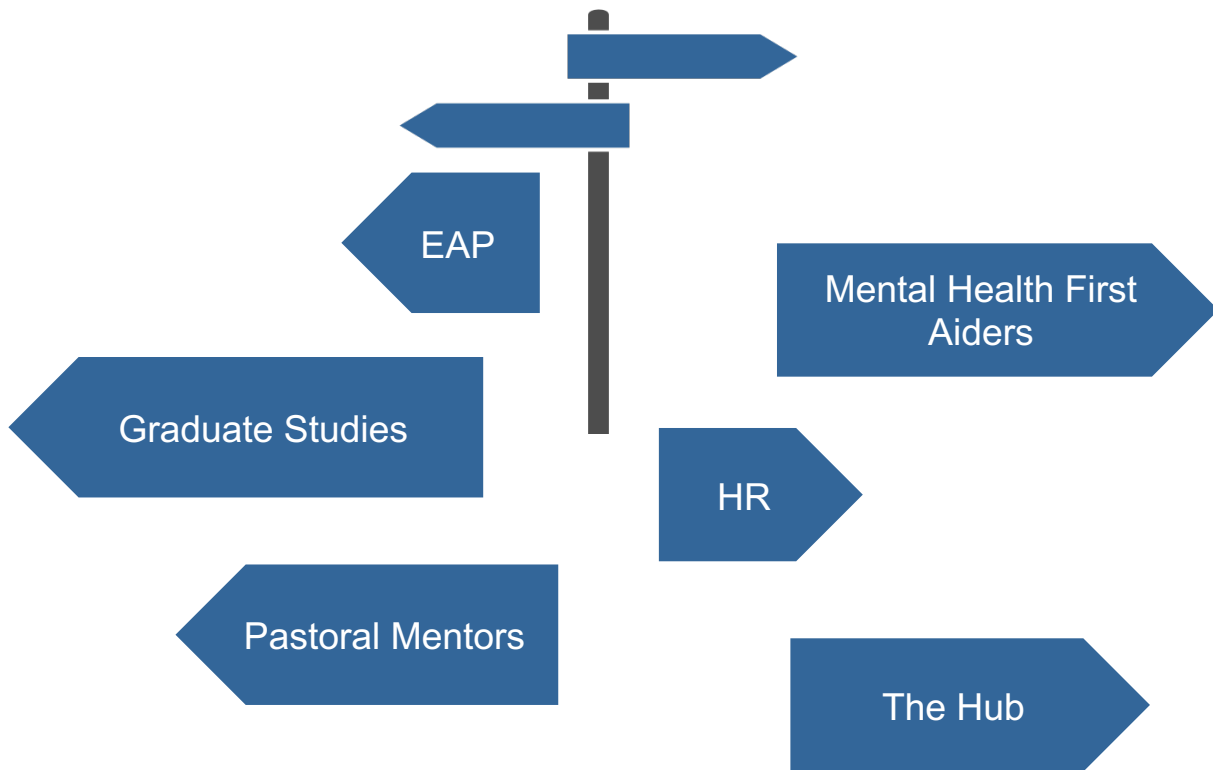
Reproducibility

Respect

Responsibility

Rigor

Transparency



Research Integrity

Accountability

Accurate

Care

Collegiality

Cooperation

Ethics

Fair

Honesty

Objectivity

Openness

Quality

Reliability

Reproducibility

Respect

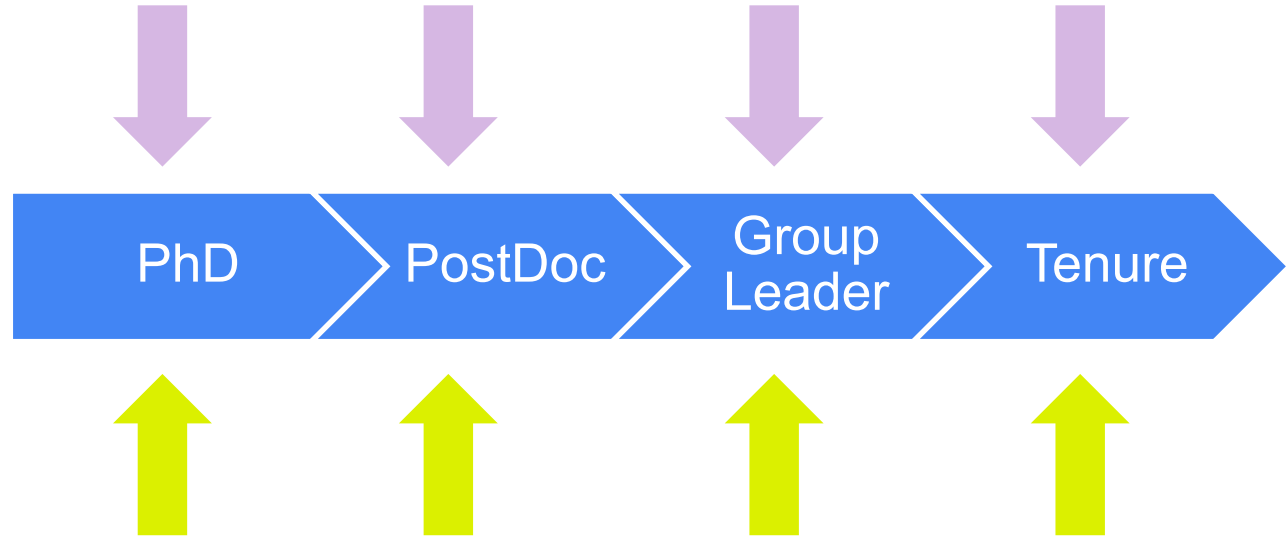
Responsibility

Rigor

Transparency



Research Integrity



Accountability
Accurate
Care
Collegiality
Cooperation
Ethics
Fair
Honesty
Objectivity
Openness
Quality
Reliability
Reproducibility
Respect
Responsibility
Rigor
Transparency

Research Integrity



Which roles are most important or responsible for Research Integrity?

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Cooperation
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Director

PostDoc

PhD student

Head of ISP

Technician

Research Assistant

H&S officer

Lab Manager

Group Leader

Facilities

Animal Technician

Leadership Team

Visiting Scientist

Tenure



How our integrity may be tested





Publications



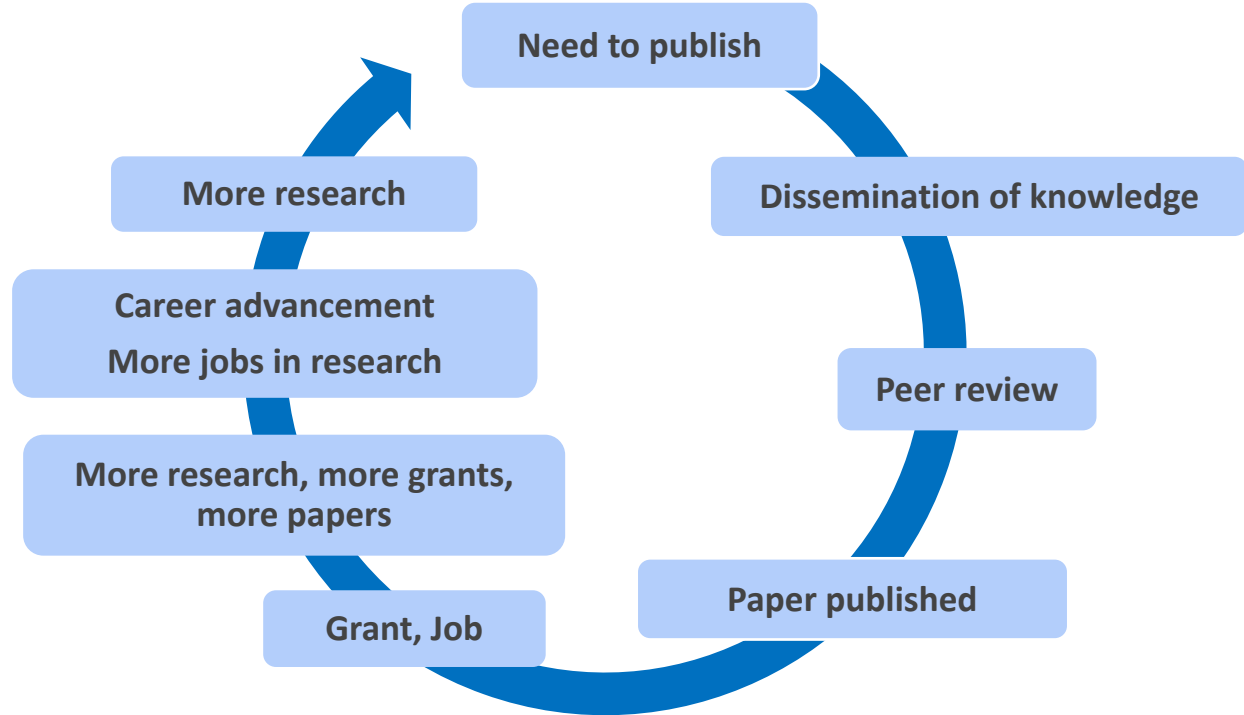


Publish or Perish?



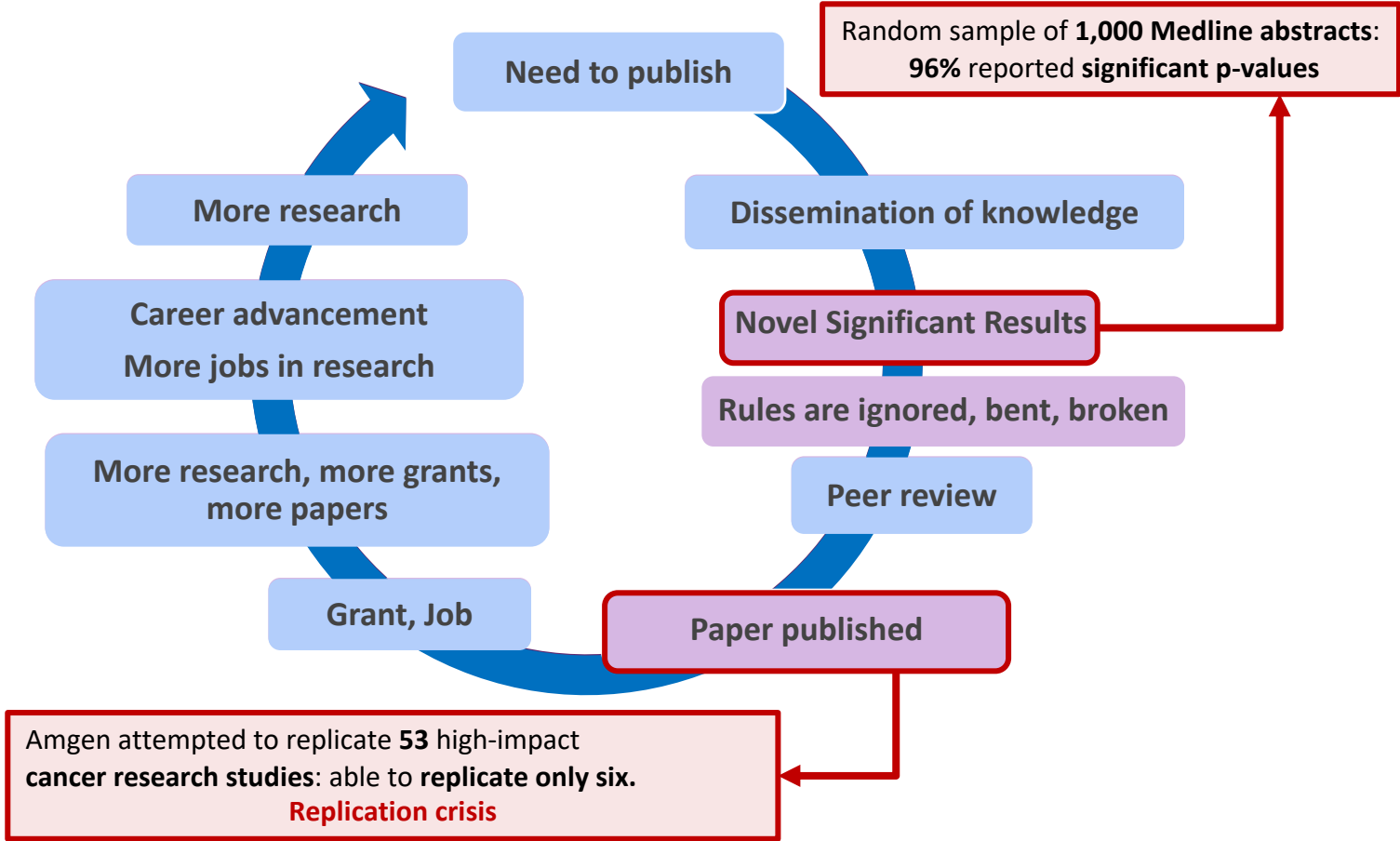
Publications: the good

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Publications: the bad

- Accountability
- Accurate
- Care
- Collegiality
- Cooperation
- Ethics
- Fair
- Honesty
- Objectivity
- Openness
- Quality
- Reliability
- Reproducibility
- Respect
- Responsibility
- Rigor
- Transparency



Publications: the ugly Paper Mills

Accountability

Accurate

Care

Collegiality

Cooperation

Ethics

Fair

Honesty

Objectivity

Openness

Quality

Reliability

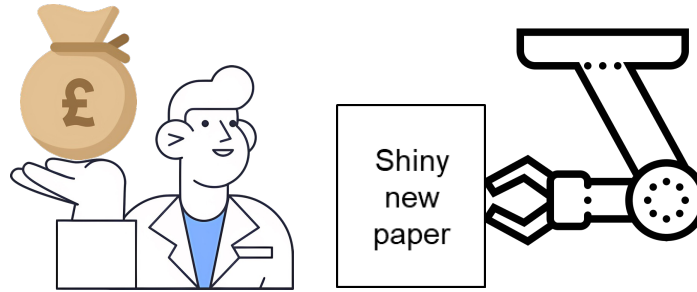
Reproducibility

Respect

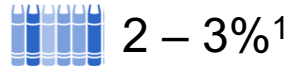
Responsibility

Rigor

Transparency



Estimated Prevalence



1. <https://www.nature.com/articles/d41586-023-03464-x>

2. <https://www.medrxiv.org/content/10.1101/2023.05.06.23289563v2>

3. <https://publicationethics.org/node/55256>



In 2023 Hindawi closed 4 journals because they were “heavily compromised by paper mills”

Publications: the balance

Accountability

Accurate

Care

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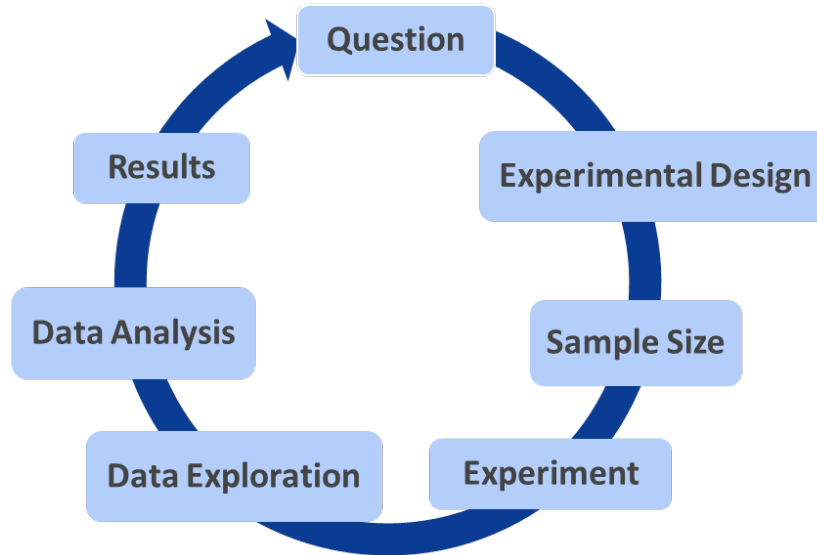


Misconduct

Research Integrity

Misconduct

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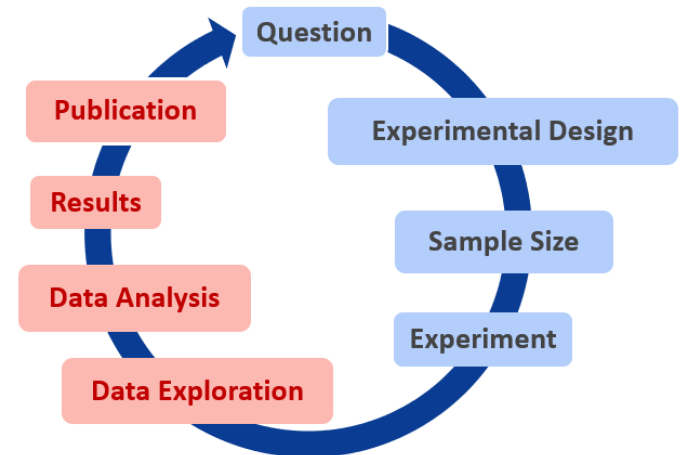
Misconduct: How?

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There are **many ways to misbehave** when it comes to research

Plagiarism
Fabrication and falsification
Inappropriate image manipulation
Non-publication of data
Faulty data-gathering procedures
Poor data storage and retention
Misleading authorship
Sneaky publication practices



Misconduct: Why?

Accountability

Accurate
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Objectivity

Openness

Quality

Reliability

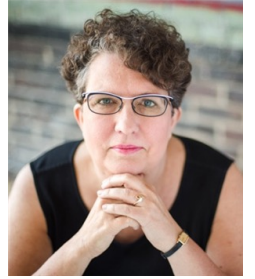
Reproducibility

Respect

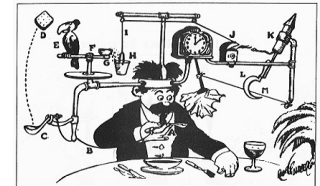
Responsibility

Rigor

Transparency



Tina Gunsalus



Misconduct: Spot the TRAGEDIES



Group and authority pressure

Entitlement

Deception

Ambition

Incrementalism

Rationalisation

Embarrassment

Temptation

Stupid systems

A Simple Request from their Professor

Verify the numbers in a figure matched the spreadsheet

A Questionable Outcome

Paper published with the new student as a co-author

They accept the credit

Why?



The New Student



The Professor

A real case from Tina Gunsalus

<https://www.nature.com/articles/d41586-018-05145-6>

Misconduct: In a nutshell

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“I never met anyone who said, yeah, you know, that was the day I woke up and decided to you know, put my career at risk, potentially go to jail, embarrass my family, lose my job.”



Tina Gunsalus

**We need to be aware of our feelings and circumstances
And acknowledge how they might influence us**

The Only Acceptable Tragedy!*

STEPS

Tragedy • The Dance - How To...



STEP 1 - Put your hands up beside your ears in 'Tragedy' shock!



STEP 2a - Raise your right arm.



STEP 2b - Raise your left arm so both arms are up.



STEP 3 - Clasp both hands together on your heart.



STEP 4 - Stretch both arms out straight in front with your palms up.



STEP 5a - Put your hands to your head as in STEP 1 and then step to your right.



STEP 5b - Repeat the same move to your left. Repeat the same two moves again.



STEP 6a - Step to the left and swing your left arm out with your right hand on your hip.



STEP 6b - Step to the left and swing your right arm out with your left hand on your hip.



STEP 7 - Hold your right arm out and stop the traffic!



STEP 8 - Keep your right arm out, turn to your right and roll your left shoulder three times.

<https://www.youtube.com/watch?v=OiwDHHcHPPh0>

*To be fully transparent we should note the Bee Gees did it first!



The bottom line



Research Integrity

It's about being a good scientist



Research integrity

is about **owning every step of our research, and benefits everyone.**

Research Integrity

What does it mean?

Questioning

Definitions

In Practice

Ethics

Keeping Track

How can we apply it?

Publications

Misconduct

When is it tested?

Responsibility

Bottom line

Good Science



**What do you think now?
Which words are
most important/synonymous with integrity?**



Research Integrity

More than words

Responsibility
Accountability Honesty Fair
Respect Objectivity
Care Scientific integrity Rigor
Openness Ethics Transparency Accurate
Reliability Cooperation Collegiality
Quality

Research Integrity

Useful resources



Training Courses



www.bioinformatics.babraham.ac.uk



MS Teams channel and mailing list. Contact

Richard.Acton@babraham.ac.uk

Research Integrity

Useful resources

nature

Retraction Watch



PUBPEER
The online Journal club

UKRIO
RESEARCH INTEGRITY OFFICE