Enhancement of Research Findings:
The Significance of Well-Designed Experiments

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ANNALS OF SCIENCE

THE TRUTH WEARS OFF

Is there something wrong with the scientific method?

BY JONAH LEHRER

December 13, 2010

Many Results that are rigorously proved and accepted start shrinking in later studies

The Economist

Unreliable research

Trouble at the lab

Scientists like to think of science as self-correcting. To an alarming degree, it is not

Oct 19th 2013 |
From the print edition

NIH plans to enhance reproducibility

Francis S. Collins and **Lawrence A. Tabak** discuss initiatives that the US National Institutes of Health is exploring to restore the self-correcting nature of preclinical research.

Nature 505: 612-613, 2014

1. *Poor training in experimental design*
2. *Lack of disclosure of basic elements of methods*
3. *Policies and attitudes of funding agencies, institutions and publishers*

Survey of the Quality of Experimental Design, Statistical Analysis and Reporting of Research Using Animals

Carol Kilkenny[1]*, Nick Parsons[2], Ed Kadyszewski[3], Michael F. W. Festing[4], Innes C. Cuthill[5], Derek Fry[6], Jane Hutton[7], Douglas G. Altman[8] PLoS ONE 4:e7824, 2009

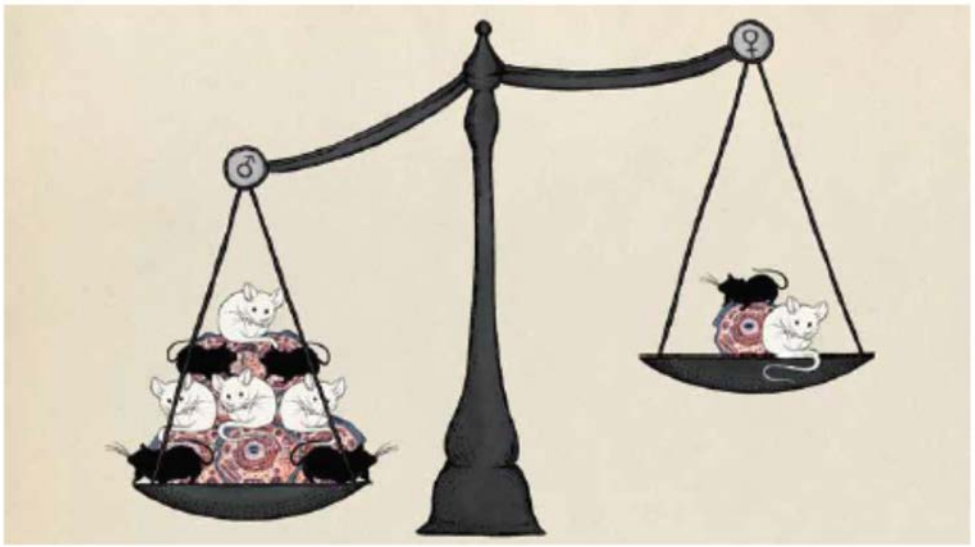
Table 7. Number of studies reporting the sex of the animals.

Species	No	Yes	Unclear	Yes (%)
Mouse (n = 72)	24	47	1	65
Primate (n = 86)	30	55	1	64
Rat (n = 113)	15	98	0	87

nature

May 15, 2014

COMMENT



NIH to balance sex in cell and animal studies

Janine A. Clayton and **Francis S. Collins** unveil policies to ensure that preclinical research funded by the US National Institutes of Health considers females and males.

How to include sex in an experimental design?

1. ***If sex factor is your research interest:***
   Including sex as one of the independent variable

2. ***If sex factor is NOT your research interest:***
   Including both male and female subjects to avoid generalization bias

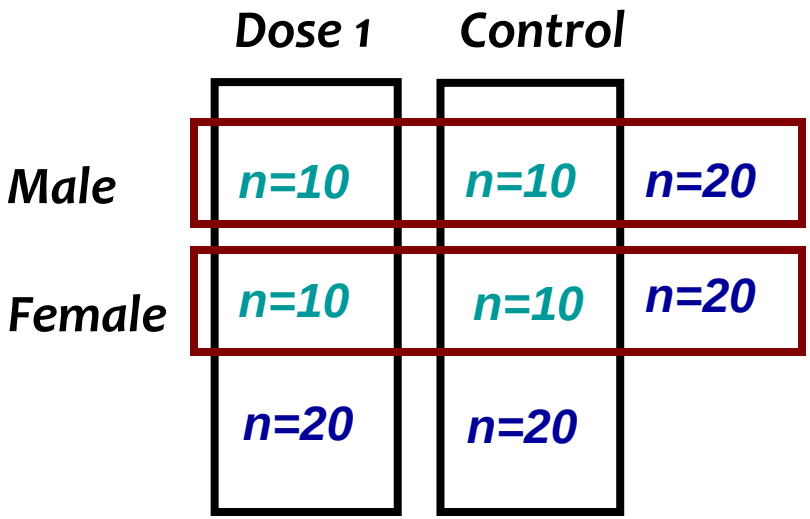
The Real Story		Your Decision: Accept the Null Hypothesis	Your Decision: Reject the Null Hypothesis
	Null Hypothesis is true (the data came from the same population)	You are correct!	You made a Type I error α
	Null Hypothesis is false (the data came from two different populations)	You made a Type II error ~~β~~ ↑	You are correct! 1-β

How to analyze data if sex is one of the independent variables in an experimental design?

1. ***If sex is the only independent variable:***
   student t-test or Mann-Whitney U
2. ***If sex is one of the two independent variables:***
   two-way ANOVA or Mixed ANOVA
3. ***If sex is one of multiple (more than three) independent variables:***
   consider revising the experimental design

Advantages of including sex as one of the independent variables

1. Factorial designs reduce the variability for all levels of the independent variables (by increasing the sample size)



Advantages of including sex as one of the independent variables

2. Factorial designs allow the assessment of interactions between/among independent variables

An experiment designs to evaluate the effect of a drug on locomotive activity in a mouse model system (dependent variable: distance travelled, meter, in an open field)

	Dose 1	Dose 2	Control
Male	2.0m	0.8m	0.4m
Female	0.7m	2.1m	0.3m

What is the adequate sample size for an experiment?

1. ***Power (real effect of the independent variable)***
2. ***Effect size***
    a. *Prior research*
    b. *Preliminary/pilot studies*
3. ***Significance level (α value)***

Sample Size as a function of Power, Effect Size and Significance

Power (α = 0.05 (0.01))

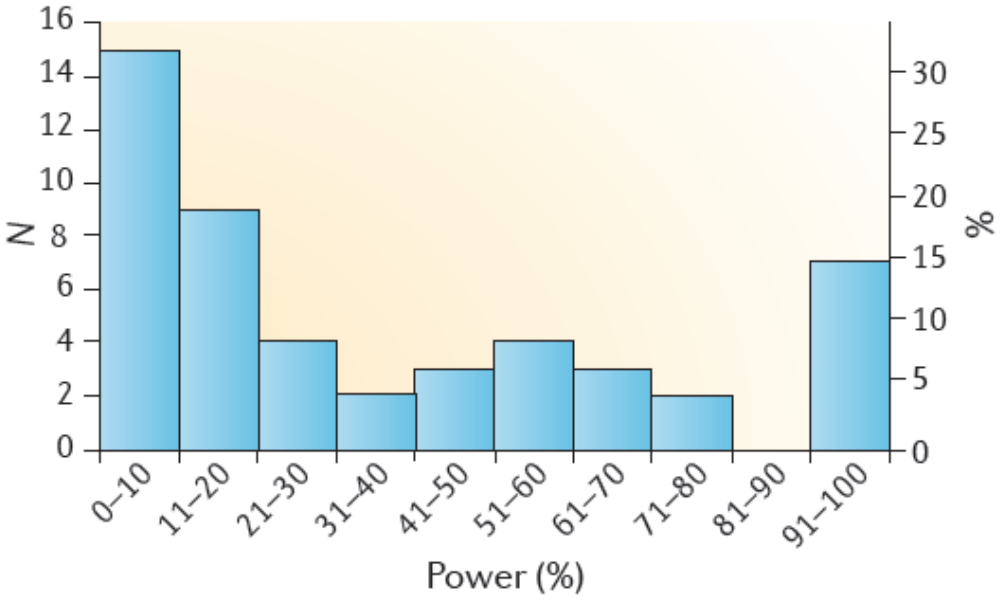
Effect Size	0.1	0.3	0.5	0.7	0.8
Small	21 (70)	83 (156)	144 (232)	219 (323)	271 (385)
Medium	5 (13)	14 (26)	24 (38)	36 (53)	44 (62)
Large	3 (6)	6 (11)	10 (15)	14 (20)	17 (24)

Modified from Geoffrey Keppel, "Design and Analysis: A Researcher's Handbook", 3rd Ed. 1991.

Power failure: why small sample size undermines the reliability of neuroscience

Katherine S. Button[1,2], John P. A. Ioannidis[3], Claire Mokrysz[1], Brian A. Nosek[4], Jonathan Flint[5], Emma S. J. Robinson[6] and Marcus R. Munafò[1]

Nature Review Neuroscience 14: 365-376, 2013



How to increase the statistical power of a study?

1. ***Reducing confounding variables***
    a. *equipment/chemicals/testing environment*
    b. *Experimenters*
        i. *experienced/seasoned vs. new*
        ii. *male vs. female experimenters*

How to increase the statistical power of a study?

2. Reducing subject variability

a. *Random assignment of subjects*
b. *Matching specific/relevant characteristics*
c. *Employ within-subject design (repeated measures)/mixed subject design*

What can we do as faculty, mentors or researchers to enhance research findings?

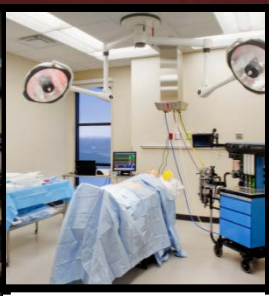
Education & training – in experimental design & application of appropriate statistical analyses

COURSE TITLE: *Experimental Design for Biomedical Science*

COURSE DESCRIPTION: *This course will explore many facets of experimental design including experimental control, hypothesis testing, and complex designs. The course will begin with a review of the basic principles of observation and developing a hypothesis, and subsequently lead to a critical analysis of how experiments may fail to achieve their goal due to flaws in experimental design. Although the principles of experimental design are straightforward and simple, a review of this material is essential for developing increasingly complex research designs and hypothesis testing.*







Thank you!