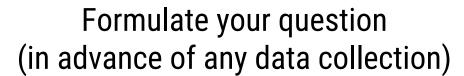
# Experimental design

The Data Scientist's Toolbox





Design your experiment



Identify problems and sources of error



Collect the data

### medicine



Article

# Genomic signatures to guide the use of chemotherapeutics

Anil Potti, Holly K Dressman, Andrea Bild, Richard F Riedel, Gina Chan, Robyn Sayer, Janiel Cragun, Hope Cottrill, Michael J Kelley, Rebecca Petersen, David Harpole, Jeffrey Marks, Andrew Berchuck, Geoffrey S Ginsburg, Phillip Febbo, Johnathan Lancaster & Joseph R Nevins 

■



### medicine



Article

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■



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#### DERIVING CHEMOSENSITIVITY FROM CELL LINES: FORENSIC BIOINFORMATICS AND REPRODUCIBLE RESEARCH IN HIGH-THROUGHPUT BIOLOGY

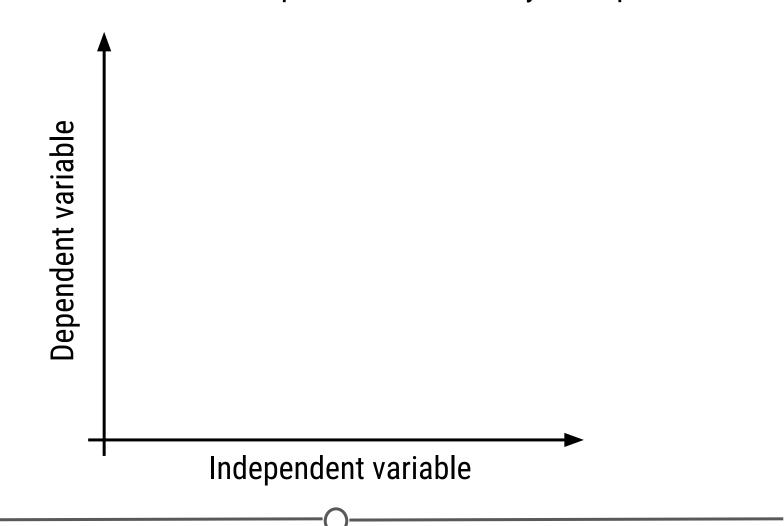
By Keith A. Baggerly<sup>1</sup> and Kevin R. Coombes<sup>2</sup>

#### University of Texas

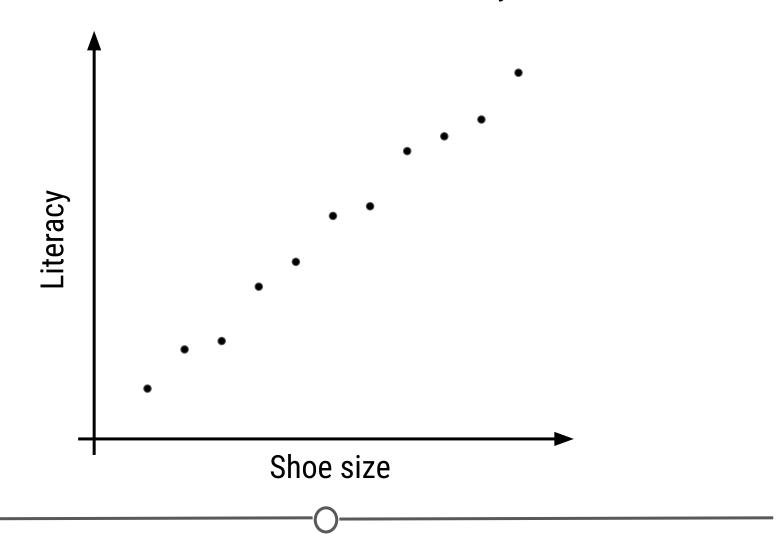
High-throughput biological assays such as microarrays let us ask very detailed questions about how diseases operate, and promise to let us personalize therapy. Data processing, however, is often not described well enough to allow for exact reproduction of the results, leading to exercises in "forensic bioinformatics" where aspects of raw data and reported results are used to infer what methods must have been employed. Unfortunately, poor documentation can shift from an inconvenience to an active danger when it obscures not just methods but errors. In this report we examine several related papers purporting to use microarray-based signatures of drug sensitivity derived from cell lines to predict patient response. Patients in clinical trials are currently being allocated to treatment arms on the basis of these results. However, we show in five case studies that the results incorporate several simple errors that may be putting patients at risk. One theme that emerges is that the most common errors are simple (e.g., row or column offsets); conversely, it is our experience that the most simple errors are common. We then discuss steps we are taking to avoid such errors in our own investigations.

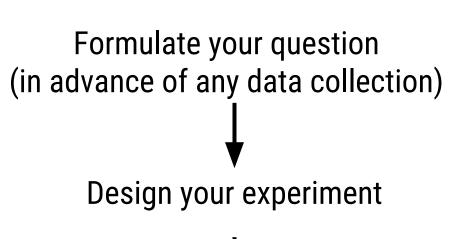
"Poor documentation hid both sensitive/resistant label reversal, and the incorrect use of duplicate (and in some cases mislabeled) samples."

**Hypothesis:** What is the expected outcome of your experiment?



#### **Hypothesis:** As shoe size increases, literacy also increases





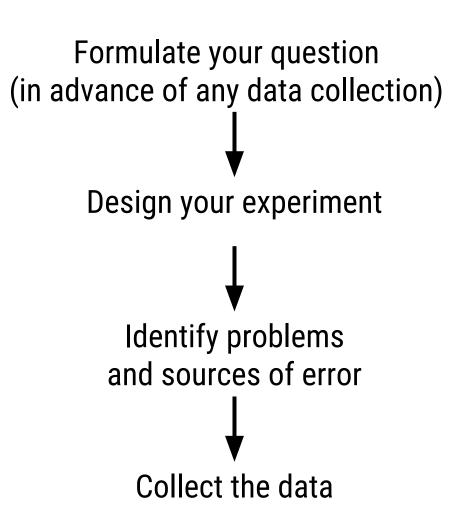
Identify problems and sources of error

Collect the data

Does shoe size affect literacy?



Measure 100 individuals shoe size and test their literacy level



Does shoe size affect literacy?

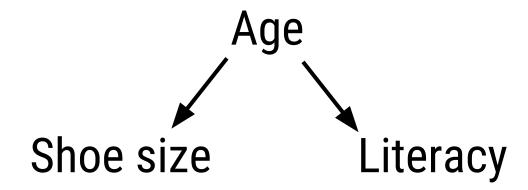
Measure 100 individuals shoe size and test their literacy level

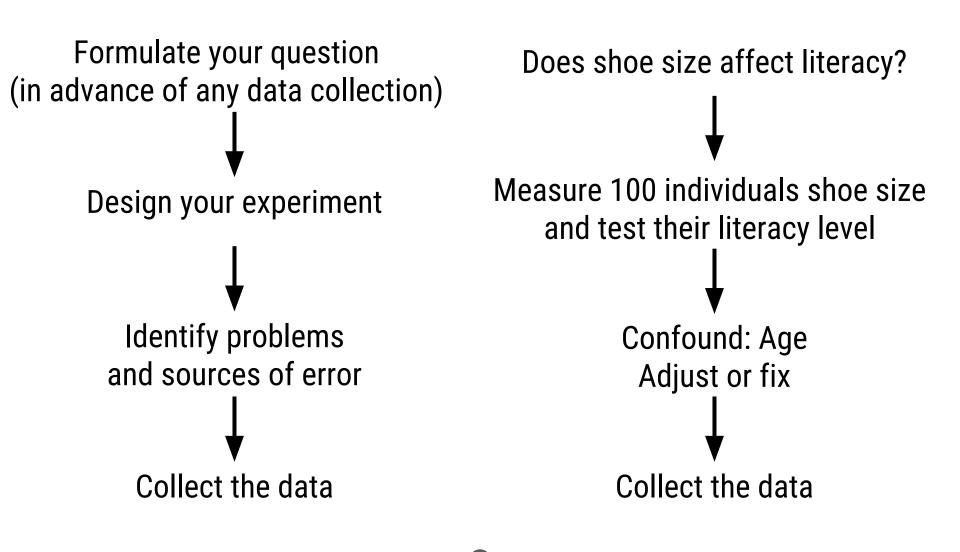
Confound?

## **Hypothesis**

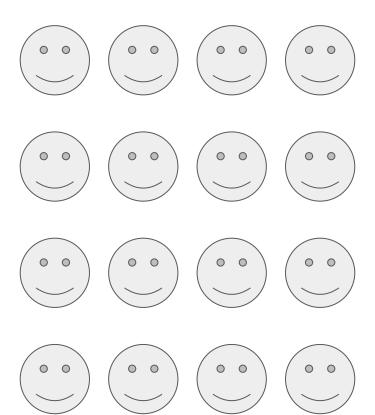
Shoe size → Literacy

### Confounder

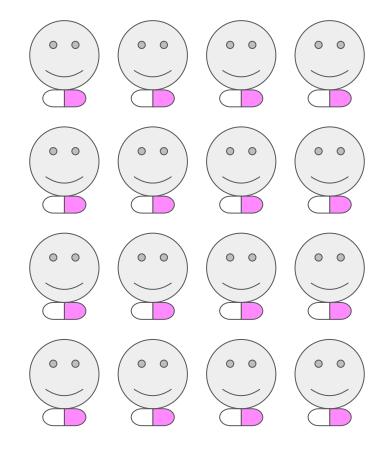




## **Control group**



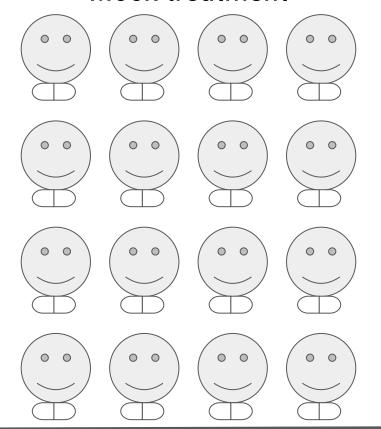
### **Treatment group**



Blinded: Subjects don't know what group they are in

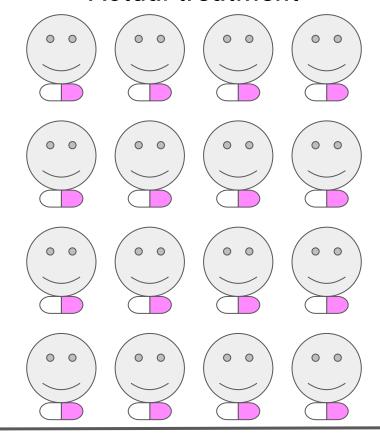
### **Control group**

Mock treatment



### **Treatment group**

Actual treatment



### **Subjects**



#### **Confounded**

#### **Control group Treatment group**









#### Randomized

#### **Control group**









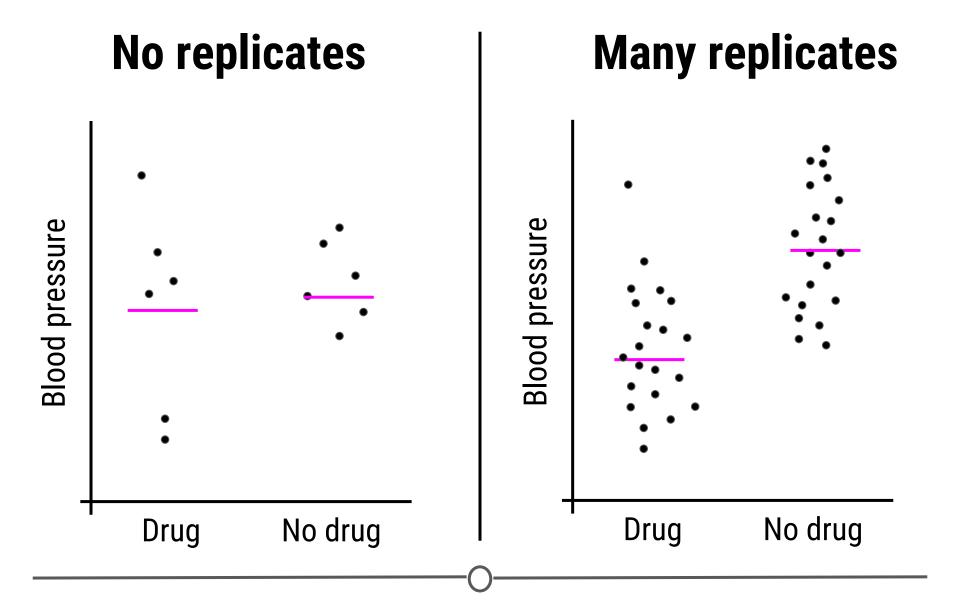
#### Treatment group

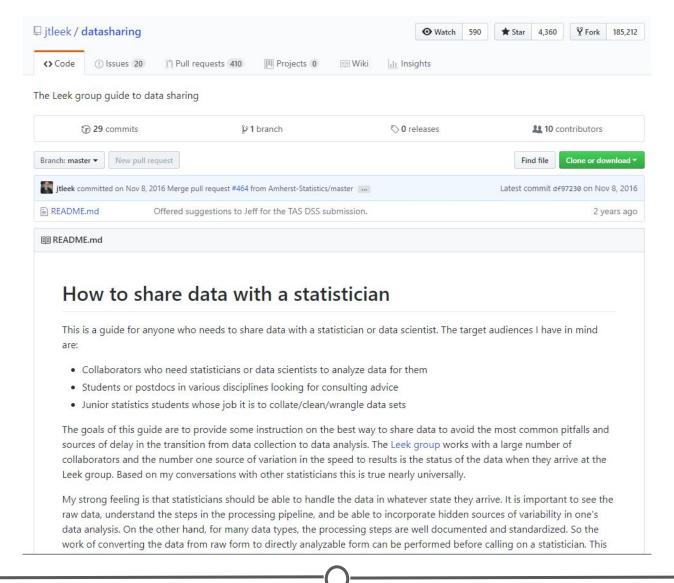












#### **Hack Your Way To Scientific Glory**

You're a social scientist with a hunch: **The U.S. economy is affected by whether Republicans or Democrats are in office.** Try to show that a connection exists, using real data going back to 1948. For your results to be publishable in an academic journal, you'll need to prove that they are "statistically significant" by achieving a low enough p-value.

CHOOSE A Republicans **Democrats POLITICAL PARTY DEFINE TERMS** IS THERE A RELATIONSHIP? IS YOUR RESULT SIGNIFICANT? Given how you've defined your terms, does the economy do better, worse If there were no connection between the economy Which politicians do you want or about the same when more Democrats are in office? Each dot below and politics, what is the probability that you'd get to include? results at least as strong as yours? That probability represents one month of data. is your p-value, and by convention, you need a p-Presidents value of 0.05 or less to get published. Governors Senators Representatives Result: Almost How do you want to measure Your 0.08 p-value is close to the economic performance? 0.05 threshold. Try tweaking your ECONOMY **Employment** variables to see if you can push it Inflation over the line! × GDP Stock prices Other options Factor in power If you're interested in reading real (and more rigorous) studies on the connection between politics and the economy, Weight more powerful see the work of Larry Bartels and Alan Blinder and Mark positions more heavily **Exclude recessions** Data from The @unitedstates Project, National Governors Don't include economic Association, Bureau of Labor Statistics, Federal Reserve MORE DEMOCRATS IN OFFICE → recessions Bank of St. Louis and Yahoo Finance.

# Summarizing: Experimental design

The Data Scientist's Toolbox