



Reproducible Research with Evidence-based Data Analysis

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Replication and Reproducibility

Replication

- Focuses on the validity of the scientific claim
- "Is this claim true?"
- The ultimate standard for strengthening scientific evidence
- New investigators, data, analytical methods, laboratories, instruments, etc.
- Particularly important in studies that can impact broad policy or regulatory decisions

Replication and Reproducibility

Reproducibility

- Focuses on the validity of the data analysis
- "Can we trust this analysis?"
- Arguably a minimum standard for any scientific study
- New investigators, same data, same methods
- Important when replication is impossible

Background and Underlying Trends

- Some studies cannot be replicated: No time, No money, Unique/opportunistic
- Technology is increasing data collection throughput; data are more complex and high-dimensional
- Existing databases can be merged to become bigger databases (but data are used off-label)
- Computing power allows more sophisticated analyses, even on "small" data
- For every field "X" there is a "Computational X"

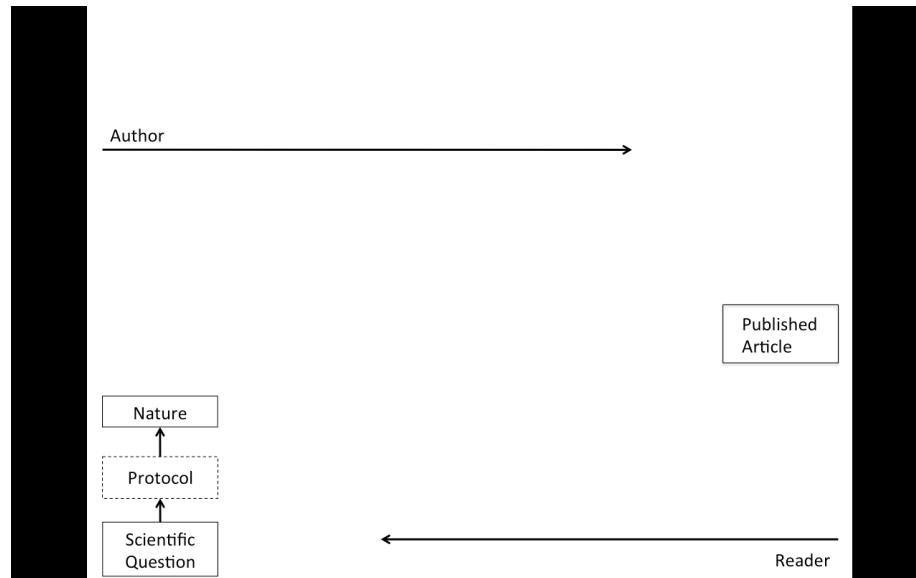
The Result?

- Even basic analyses are difficult to describe
- Heavy computational requirements are thrust upon people without adequate training in statistics and computing
- Errors are more easily introduced into long analysis pipelines
- Knowledge transfer is inhibited
- Results are difficult to replicate or reproduce
- Complicated analyses cannot be trusted

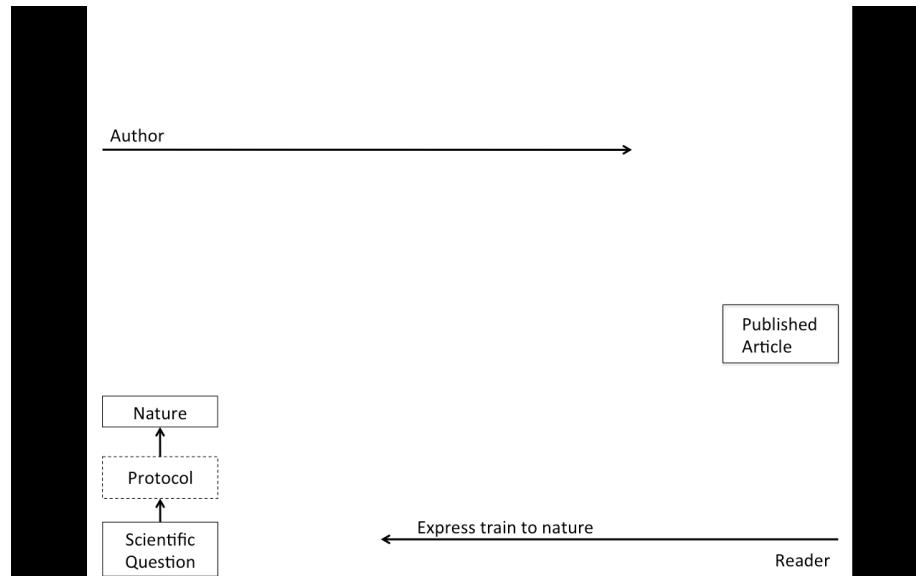
What is Reproducible Research?



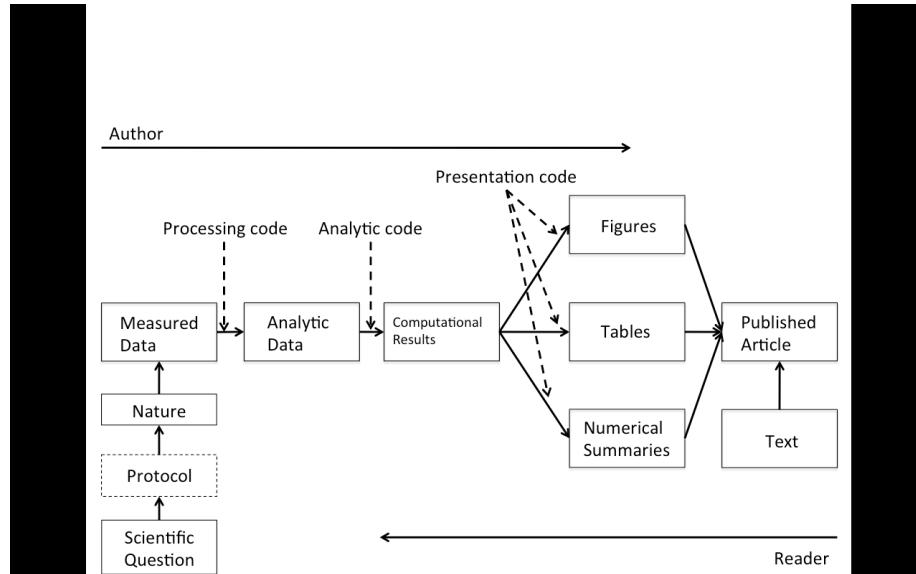
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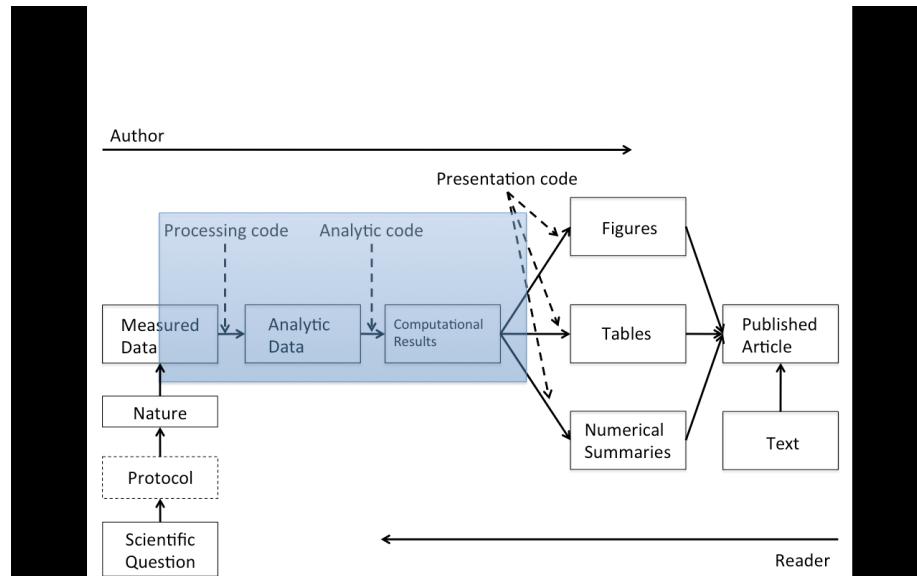
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What Problem Does Reproducibility Solve?

What we get

- Transparency
- Data Availability
- Software / Methods Availability
- Improved Transfer of Knowledge

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An analysis can be reproducible and still be wrong

We want to know “can we trust this analysis?”

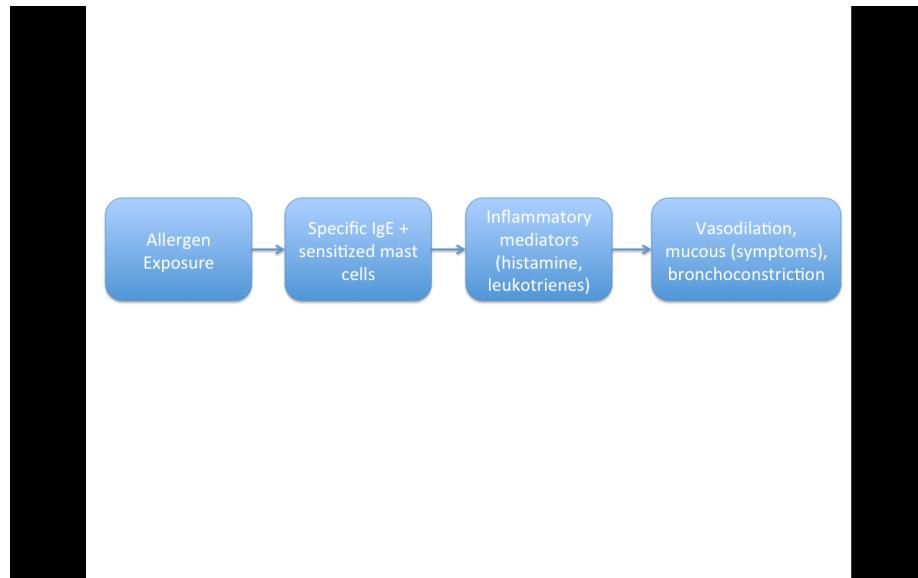
Does requiring reproducibility deter bad analysis?

Problems with Reproducibility

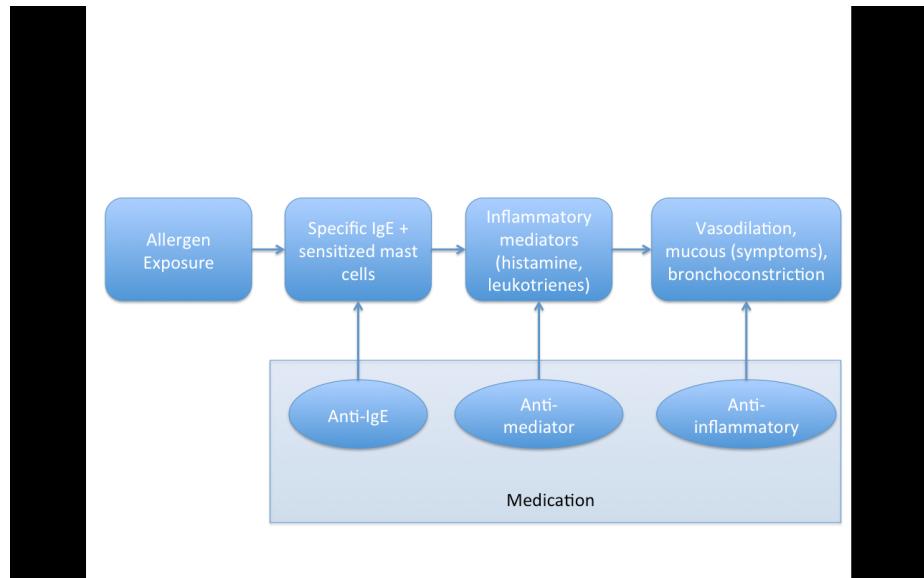
The premise of reproducible research is that with data/code available, people can check each other and the whole system is self-correcting

- Addresses the most “downstream” aspect of the research process – post-publication
- Assumes everyone plays by the same rules and wants to achieve the same goals (i.e. scientific discovery)

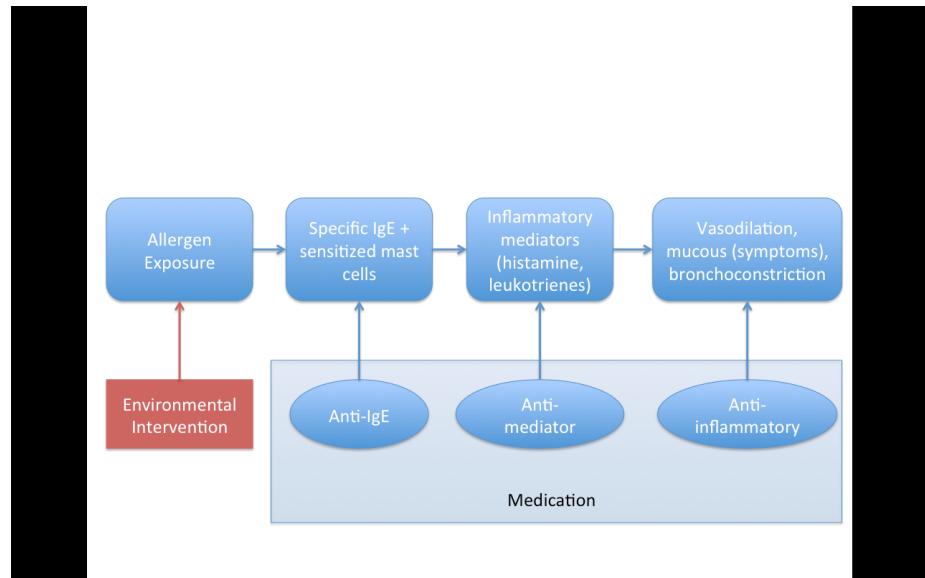
An Analogy from Asthma



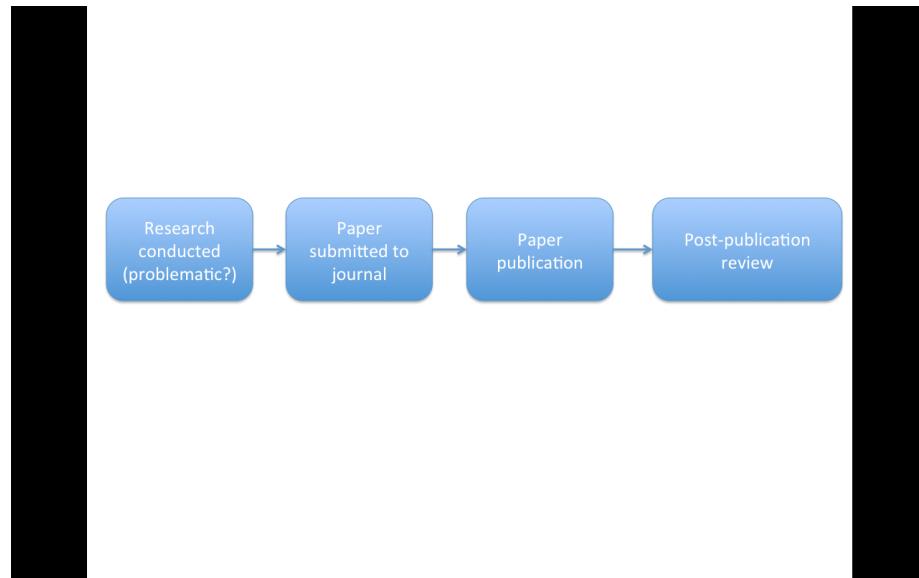
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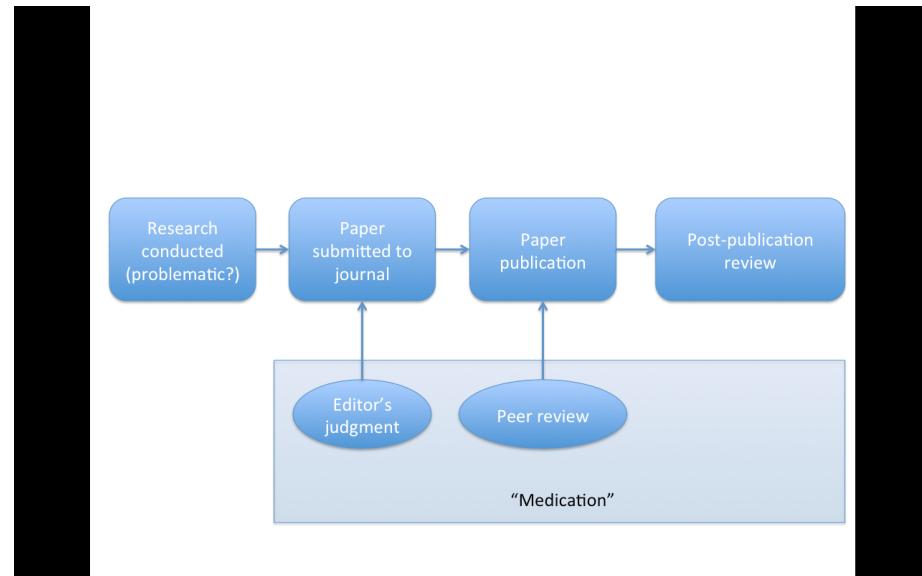
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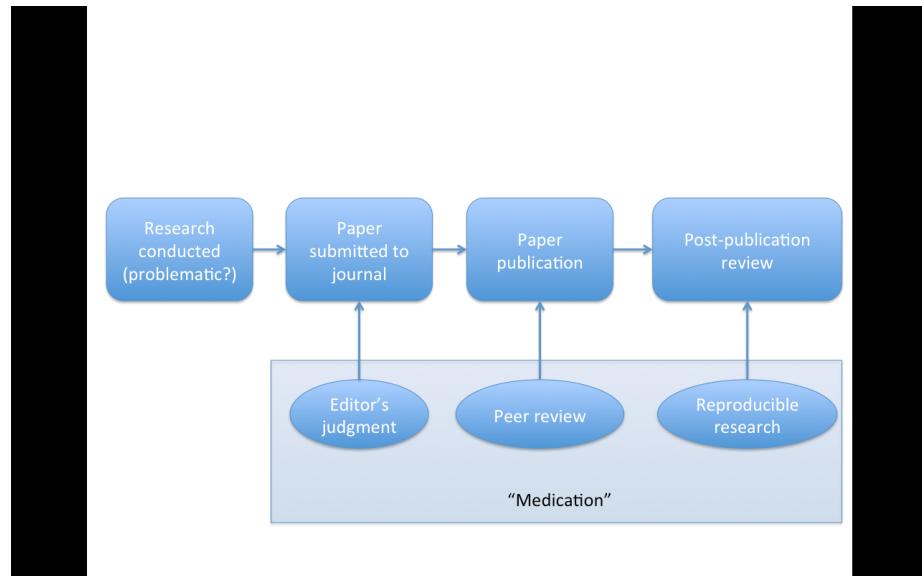
Scientific Dissemination Process



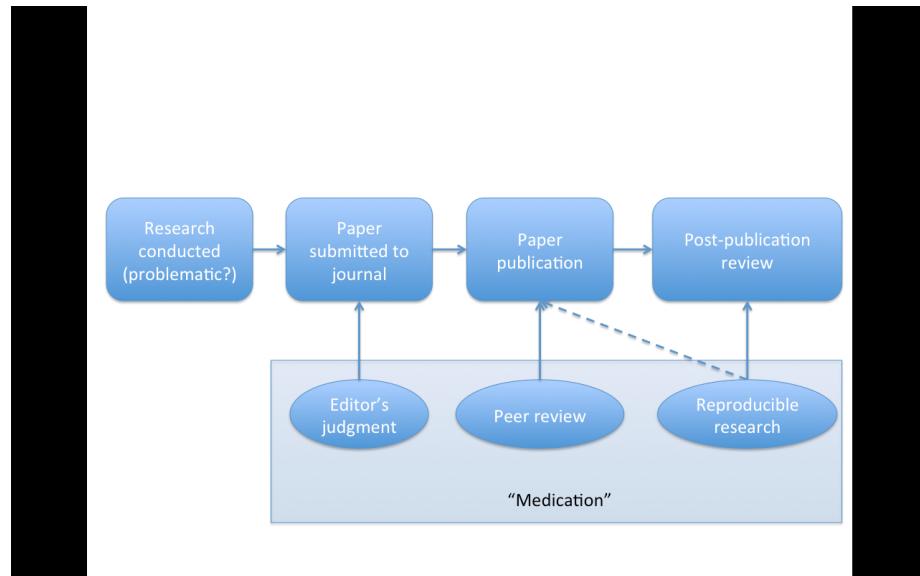
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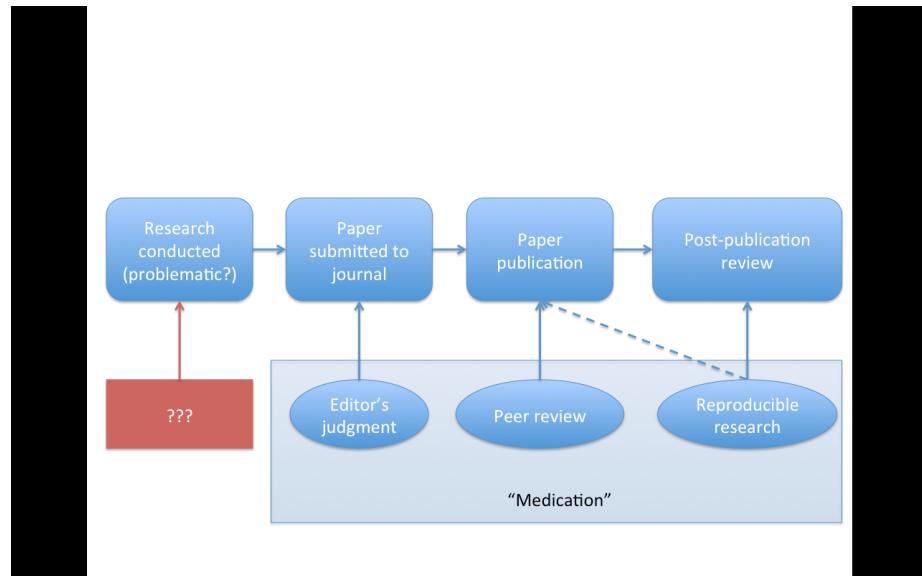
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Scientific Dissemination Process



Scientific Dissemination Process



At Biostatistics

Biostatistics (2009), **10**, 4, pp. 756–772
doi:10.1093/biostatistics/kxp029
Advance Access publication on July 27, 2009

C

Second-order estimating equations for the analysis of clustered current status data

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Biostatistics (2009), **10**, 3, pp. 409–423
doi:10.1093/biostatistics/kxp010
Advance Access publication on April 17, 2009

R

Air pollution and health in Scotland: a multicity study

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At Biostatistics

The image displays a grid of academic journal article snippets from the *Biostatistics* journal, arranged in two columns and three rows. The articles are presented in a light blue box with black text. Each snippet includes the journal title, volume, issue, page numbers, DOI, publication date, abstract, author information, and a small letter identifier.

Top Row:

- Biostatistics (2009), 10, 4, pp. 756–772**
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Advance Access publication on July 27, 2009
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- Second-order estimating equations for the analysis of clustered current status data**

Middle Row:

- Biostatistics (2012), 13, 1, pp. 166–178**
doi:10.1093/biostatistics/xxr113
Advance Access publication on June 17, 2011
R
- Significance analysis and statistical dissection of variably methylated regions**

Bottom Row:

- ANDREW P. FEINBERG***
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Health and Health Policy, University of Glasgow, Glasgow, G12 8QQ UK

Who Reproduces Research?

- For reproducibility to be effective as a means to check validity, someone needs to do something
 - Re-run the analysis; check results match
 - Check the code for bugs/errors
 - Try alternate approaches; check sensitivity
- The need for someone to do something is inherited from traditional notion of replication
- Who is "someone" and what are their goals?

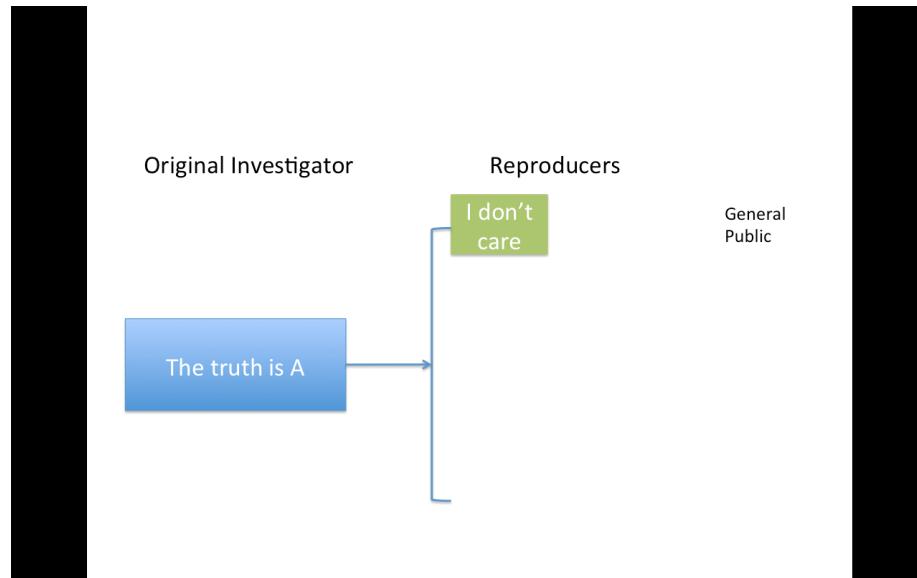
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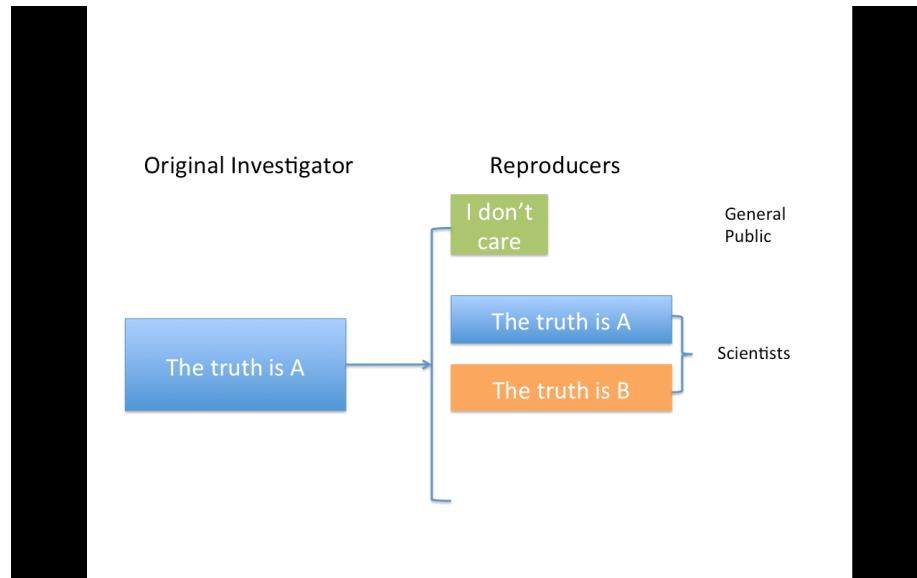
Original Investigator

The truth is A

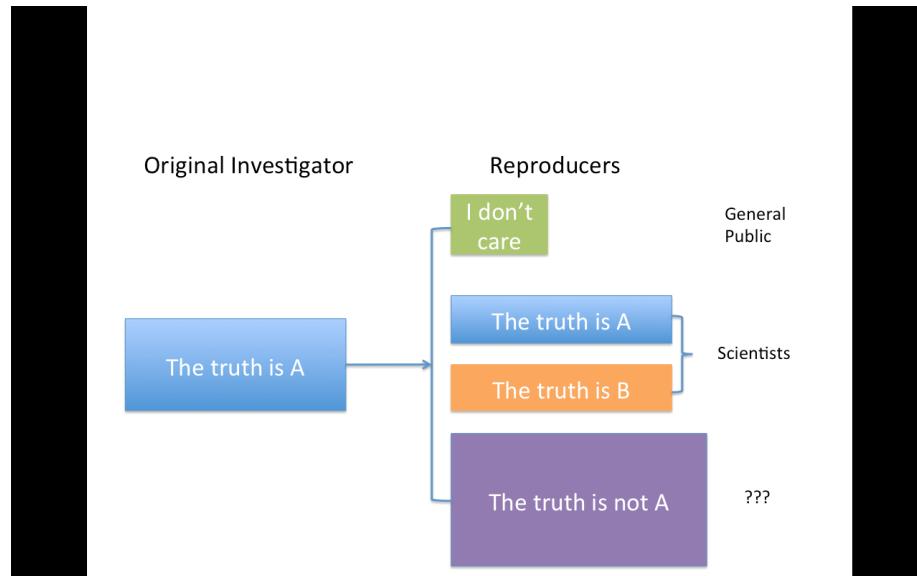
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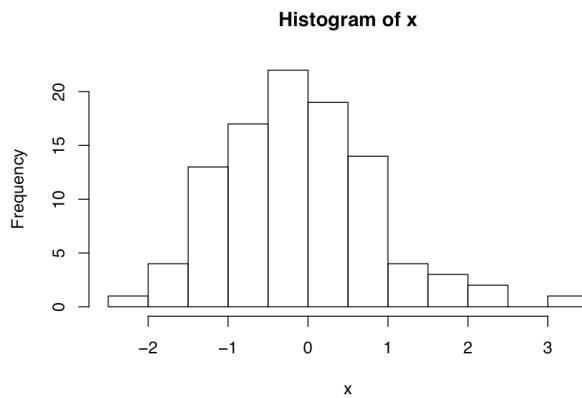
The Story So Far

- Reproducibility brings transparency (wrt code+data) and increased transfer of knowledge
- A lot of discussion about how to get people to share data
- Key question of "can we trust this analysis?" is not addressed by reproducibility
- Reproducibility addresses potential problems long after they've occurred ("downstream")
- Secondary analyses are inevitably coloured by the interests/motivations of others

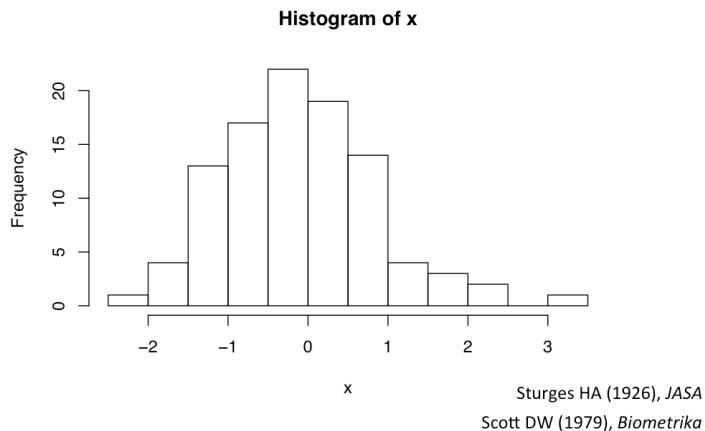
Evidence-based Data Analysis

- Most data analyses involve stringing together many different tools and methods
- Some methods may be standard for a given field, but others are often applied ad hoc
- We should apply thoroughly studied (via statistical research), mutually agreed upon methods to analyze data whenever possible
- There should be evidence to justify the application of a given method

Evidence-based Data Analysis



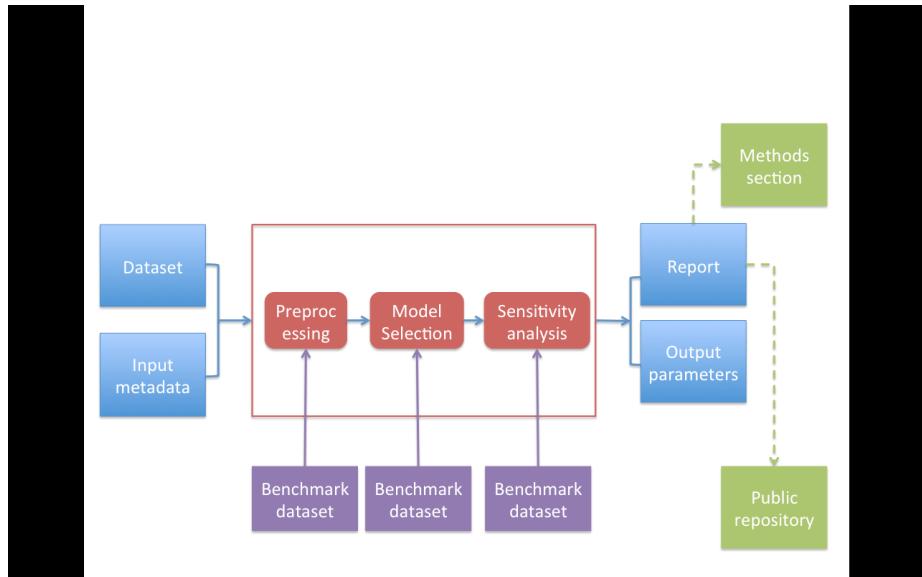
Evidence-based Data Analysis



Evidence-based Data Analysis

- Create analytic pipelines from evidence-based components – standardize it
- A Deterministic Statistical Machine <http://goo.gl/Qvlhuv>
- Once an evidence-based analytic pipeline is established, we shouldn't mess with it
- Analysis with a “transparent box”
- Reduce the "researcher degrees of freedom"
- Analogous to a pre-specified clinical trial protocol

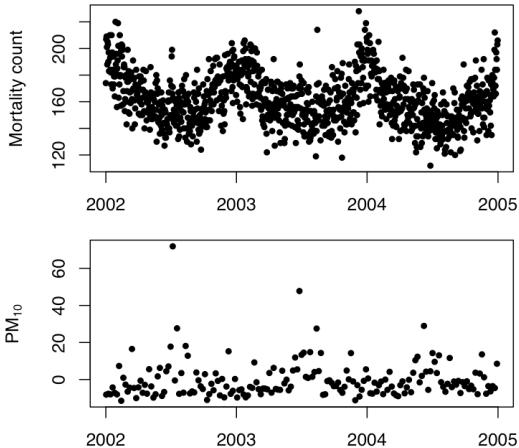
Deterministic Statistical Machine



Case Study: Estimating Acute Effects of Ambient Air Pollution Exposure

- Acute/short-term effects typically estimated via panel studies or time series studies
- Work originated in late 1970s early 1980s
- Key question: "Are short-term changes in pollution associated with short-term changes in a population health outcome?"
- Studies usually conducted at community level
- Long history of statistical research investigating proper methods of analysis

Data from New York City



Case Study: Estimating Acute Effects of Ambient Air Pollution Exposure

- Can we encode everything that we have found in statistical/epidemiological research into a single package?
- Time series studies do not have a huge range of variation; typically involves similar types of data and similar questions
- We can create a deterministic statistical machine for this area?

DSM Modules for Time Series Studies of Air Pollution and Health

1. Check for outliers, high leverage, overdispersion
2. Fill in missing data? NO!
3. Model selection: Estimate degrees of freedom to adjust for unmeasured confounders
 - Other aspects of model not as critical
4. Multiple lag analysis
5. Sensitivity analysis wrt
 - Unmeasured confounder adjustment
 - Influential points

Where to Go From Here?

- One DSM is not enough, we need many!
- Different problems warrant different approaches and expertise
- A curated library of machines providing state-of-the art analysis pipelines
- A CRAN/CPAN/CTAN/... for data analysis
- Or a “Cochrane Collaboration” for data analysis

A Model: Cochrane Collaboration

The screenshot shows the homepage of the Cochrane Summaries website. At the top left is the Cochrane logo and the text "COCHRANE SUMMARIES Independent high-quality evidence for health care decision making". At the top right are language links: English | 简体中文 | Hrvatski | Français | Português | Español. Below these are links to "Cochrane.org" and "The Cochrane Library". A search bar at the top center contains the placeholder text "Enter words like 'aspirin for headaches' or 'vaccines for influenza'". To the right of the search bar is a "Search" button. Below the search bar are links for "Browse health topics" and "New and updated". A note below the search bar states "A product of The Cochrane Collaboration". On the right side of the header is a link to "How to use this site". In the center of the page is a quote: "If you are looking for information you can trust, to help you make choices about health care, this site is for you."

A Model: Cochrane Collaboration

Vitamin C supplementation for asthma

Kaur B, Rowe BH, Stovold E

Published Online: August 15, 2012

Asthma is a chronic inflammatory disease of the airways characterised by wheeze and breathlessness. One theory for the observed increase in the number of people with asthma is the 'western' diet with its lack of nutrients from fresh food. We reviewed evidence from nine trials of the antioxidant vitamin C as a treatment for asthma. In general the trials were small, varied greatly in their design and the reporting was poor. From the available evidence it is not possible to recommend either the use or avoidance of vitamin C supplements in asthma.

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A Curated Library of Data Analysis

- Provide packages that encode data analysis pipelines for given problems, technologies, questions
- Curated by experts knowledgeable in the field
- Documentation/references given supporting each module in the pipeline
- Changes introduced after passing relevant benchmarks/unit tests

Summary

- Reproducible research is important, but does not necessarily solve the critical question of whether a data analysis is trustworthy
- Reproducible research focuses on the most "downstream" aspect of research dissemination
- Evidence-based data analysis would provide standardized, best practices for given scientific areas and questions
- Gives reviewers an important tool without dramatically increasing the burden on them
- More effort should be put into improving the quality of "upstream" aspects of scientific research