Pragmatic Reproducible Research for Data Scientists

Biomedical Data Science Day
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Acknowledgements

- This represents joint work with:
  - Dr. Leah J. Welty, Project Director
  - Abigail S. Baldridge, Biostatistician
  - Eric Whitley, Developer

https://sites.northwestern.edu/stattag/
https://github.com/StatTag

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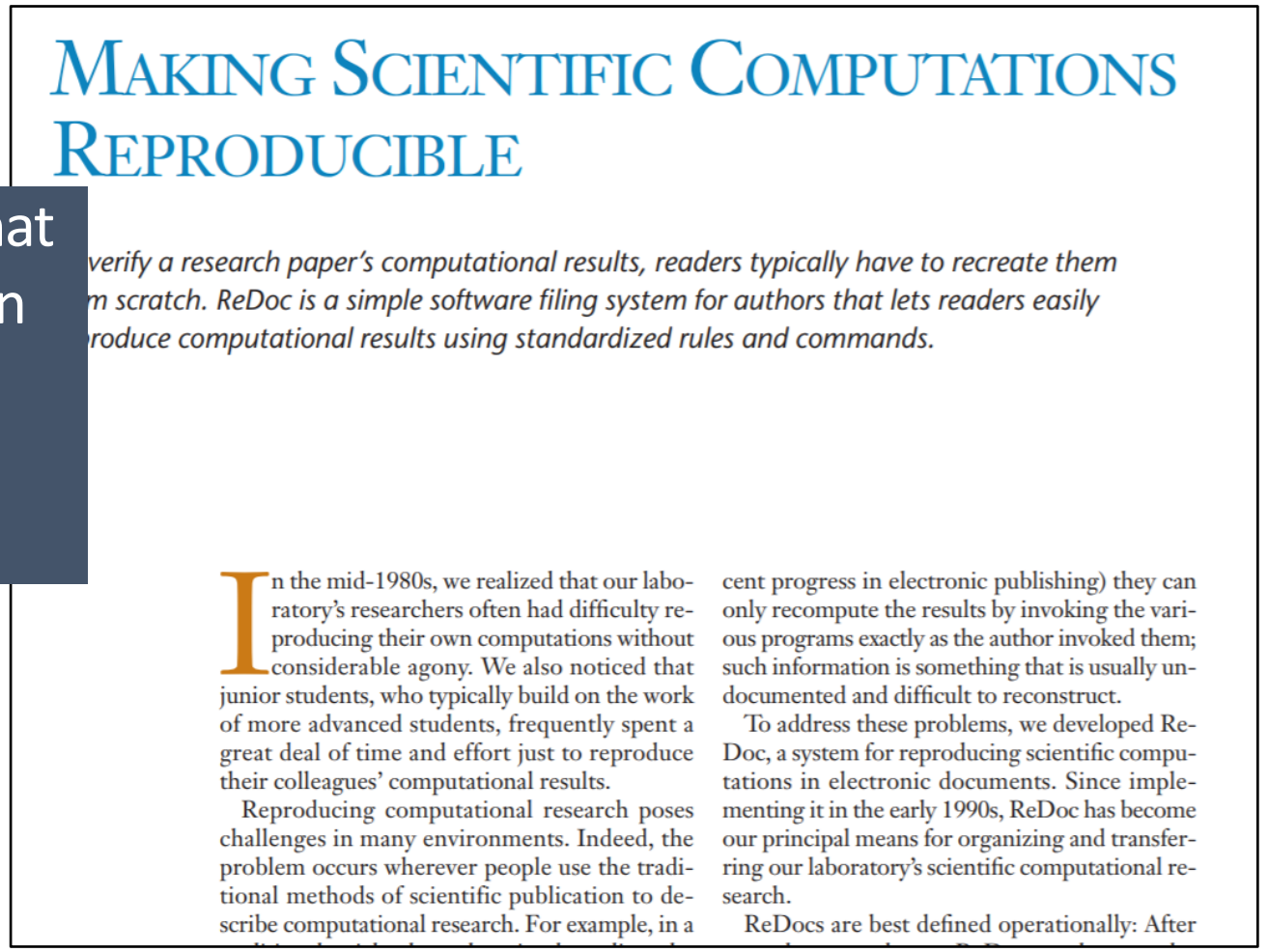
Overview of Reproducible Research

Introduction

Origins lie in the inconvenience of irreproducible research

"In the mid-1980s, we realized that our laboratory's researchers often had difficulty reproducing their own computations without considerable agony."

Schwab M, Karrenbach M, Claerbout J. "Making Scientific Computations Reproducible". Computing in Science & Engineering 2000 2:6, 61-67



MAKING SCIENTIFIC COMPUTATIONS REPRODUCIBLE

verify a research paper's computational results, readers typically have to recreate them m scratch. ReDoc is a simple software filing system for authors that lets readers easily roduce computational results using standardized rules and commands.

In the mid-1980s, we realized that our laboratory's researchers often had difficulty reproducing their own computations without considerable agony. We also noticed that junior students, who typically build on the work of more advanced students, frequently spent a great deal of time and effort just to reproduce their colleagues' computational results.

Reproducing computational research poses challenges in many environments. Indeed, the problem occurs wherever people use the traditional methods of scientific publication to describe computational research. For example, in a

cent progress in electronic publishing) they can only recompute the results by invoking the various programs exactly as the author invoked them; such information is something that is usually undocumented and difficult to reconstruct.

To address these problems, we developed ReDoc, a system for reproducing scientific computations in electronic documents. Since implementing it in the early 1990s, ReDoc has become our principal means for organizing and transferring our laboratory's scientific computational research.

ReDocs are best defined operationally: After

Kinds of Reproducible Research

- Computational Reproducibility
  - Have all of the information about the code, software and hardware.
  - Can re-run it on the same data set
- Empirical Reproducibility
  - Able to reproduce the non-computational experiments
  - Requires very clear methods
- Statistical Reproducibility
  - Full details about statistical tests
  - Pre-registration of studies to prevent p-value hacking

Stodden, 2014 - https://www.edge.org/response-detail/25340

Definition For Today

"…the ability to recompute data analytic results given an observed dataset and knowledge of the data analysis pipeline…"

Leek & Peng, PNAS February 10, 2015; 112 (6)
https://doi.org/10.1073/pnas.1421412111

What Isn't Reproducible Research?

- There are many best practices and concepts that can be confused with it:

Open Science

- Open data
- Open source
- Preregistration of studies
- Prepublication servers

Reproducible research can be disseminated openly.

Replication

- "*…the chances other experimenters will achieve a consistent result…*" – Leek & Peng (2015)

Reproducible research can help others replicate your work.

Tools / Software Engineering

- Unit tests
- Bash scripts
- Any specific programming language (Python, C++)
- Any specific tool (Jupyter Notebooks, Docker)

Reproducible research can be automated.

Scientific Rigor

- Are the methods used the right ones?
- Quality of the data collected and used
- "*…invalid reports can do more harm than irreproducible reports*" – Shiffren, Borner & Stigler 2018

Reproducible research can help us evaluate our methods.

Pragmatic Benefits

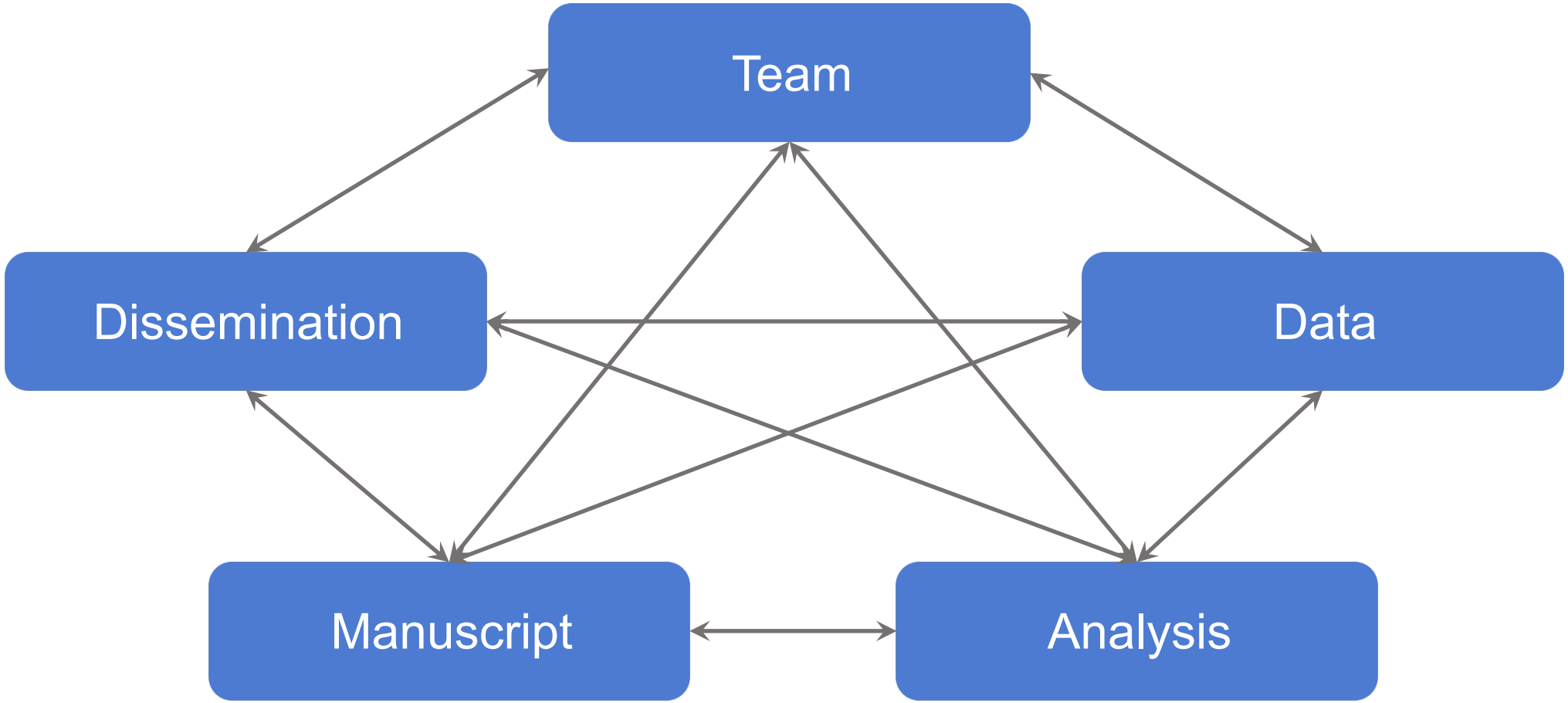
- Allows us to go back and know exactly what we did
  - 2015 Luke – “I’ll totally remember where I put that data set”
  - 2020 Luke – ”AGGGH, 2015 LUKE!!!”
- Guides us to being better scientists
  - Forces us to think through parts of the process
  - Still doesn’t guarantee accuracy
- A little can go a long way
  - Not an all-or-nothing endeavor
- Benefits come with a cost
  - Willingness to change

Why Is Reproducibility Difficult?

- People
- Data
- Project-specific analysis code
- Supporting software – statistical package, compiler, interpreter
- Operating system
- Hardware

It is about reducing or controlling **variation**

It’s a Complicated Process



Pragmatic Reproducible Research

Teams

Pragmatic RR for Teams

Why It's Tricky

- Teams are variable
  - Who is on it (even N=1)
  - What tools / workflows people like to use
- RR is a cultural change
  - Be the leader
  - Don't worry if you can't win them all over

What You Can Do

- Have **a** structure and describe it
  - There is no universal "best" structure
- Write down what you do
  - You'll need this for your Methods section anyway

Structuring Your Project

Having a central storage location and systematic file/path structure: (1) assists BCC faculty and staff who are collaborating on the same project; (2) protects against transitions in a project team; and (3) provides a long term record of work provided to investigators.

Location:

BCC Project Folders should reside in the following location:

- \\fsmresfiles.fsm.northwestern.edu\fsmresfiles\PrevMed\Projects\BCC\Projects

Project Folder Naming Convention:

Within the above folder, the Project Folder should follow this naming convention:

PILastNameFirstInitial_REDCap Project Number

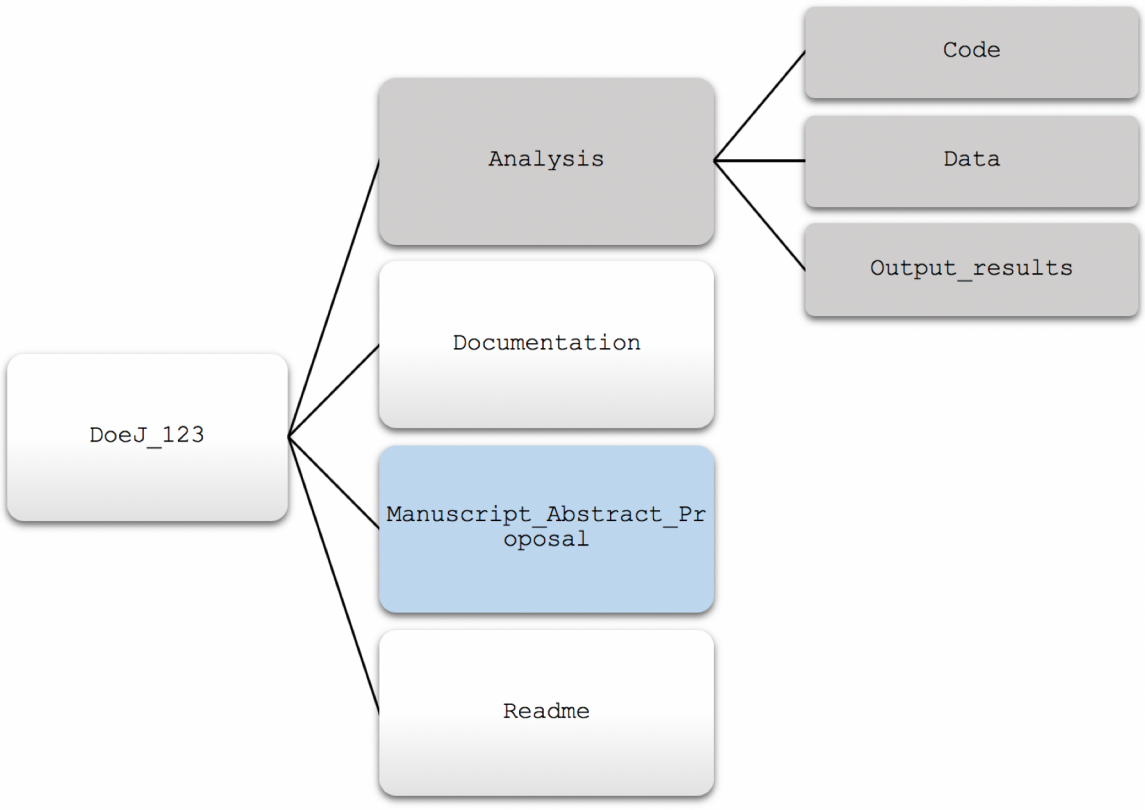
Example: For PI Jane Doe, and REDCap Project Number 123, the file name should be DoeJ_123

- The folder name does not include the project description - this avoids lengthy path/folder names. Project descriptions can be found in the Readme subfolder.
- Do not include leading zeros in the Project Number.

The diagram which follows illustrates the recommended folder structure and substructure. Additional folders may certainly be added as needed.

Date Requirements for Code/Programs/Manuscripts

Code/programs/manuscript files should include date information either inside the programs or as part of the file names. The code header should also include at the minimum the authors' names and the date last updated.



Northwestern Biostatistics Collaborative Core
L. Welty, personal communication, March 21, 2019

Pragmatic Reproducible Research

Data

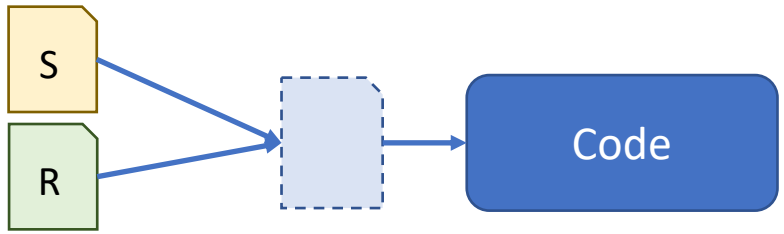
Pragmatic RR for Data

Why It's Tricky

- Data is variable
  - Changes - updates from EHR/EDW
- Provenance matters
  - Local file
  - Institution database server
  - External API
- Distribution and storage
  - Sensitivity of data

What You Can Do

- Human checks
  - Document date accessed, version, etc.
- Computable checks
  - Checksum (e.g., MD5 hash)
  - Assert Your Assumptions (AYA)
- Design for missingness
  - Well-described placeholder



Pragmatic Reproducible Research

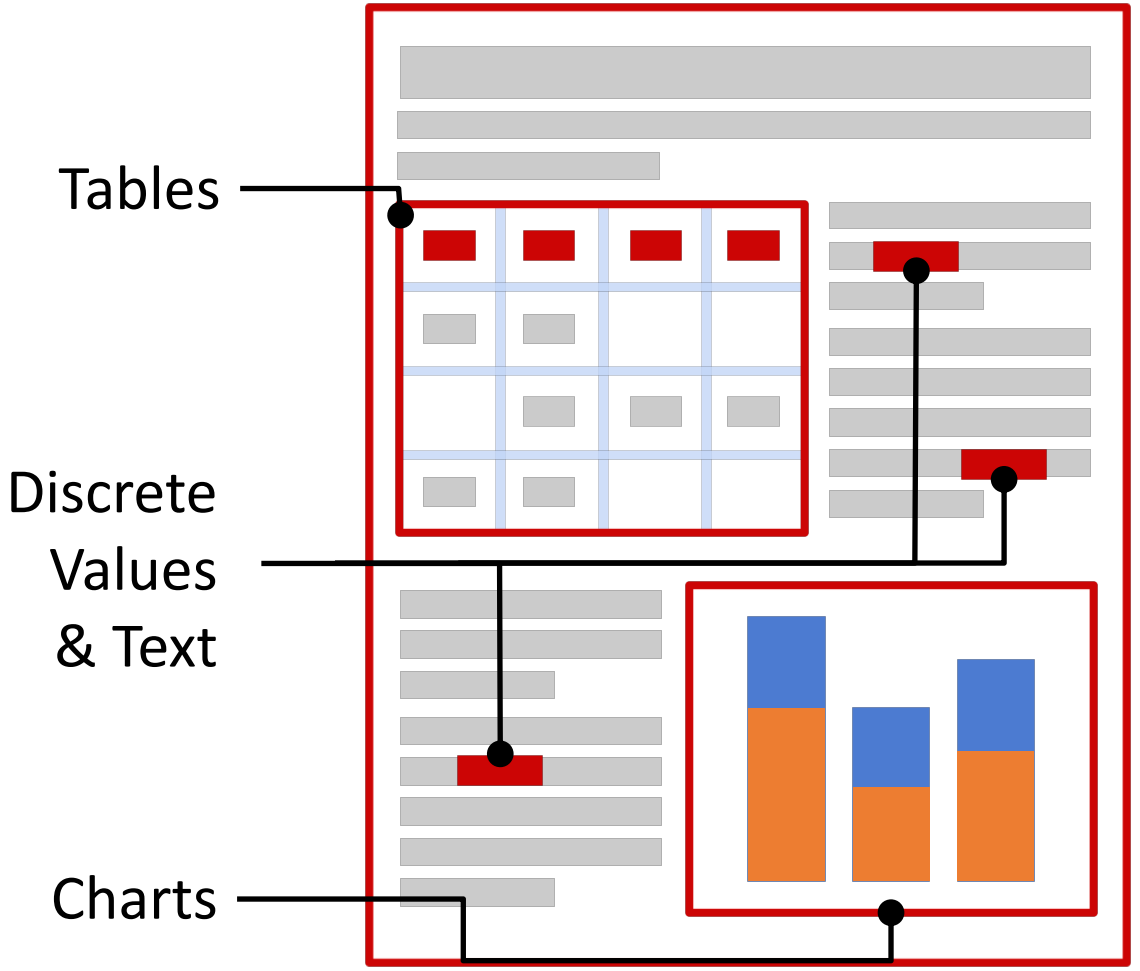
Analysis

Lab Notebook Platforms

"Weave" code chunks and text into a dynamic document

jupyter & rmarkdown

These tools provide an interactive environment that allows you to run multiple languages in a single session – with several forms of visual output



Lab Notebook Platforms

Acts as a Process Pipeline

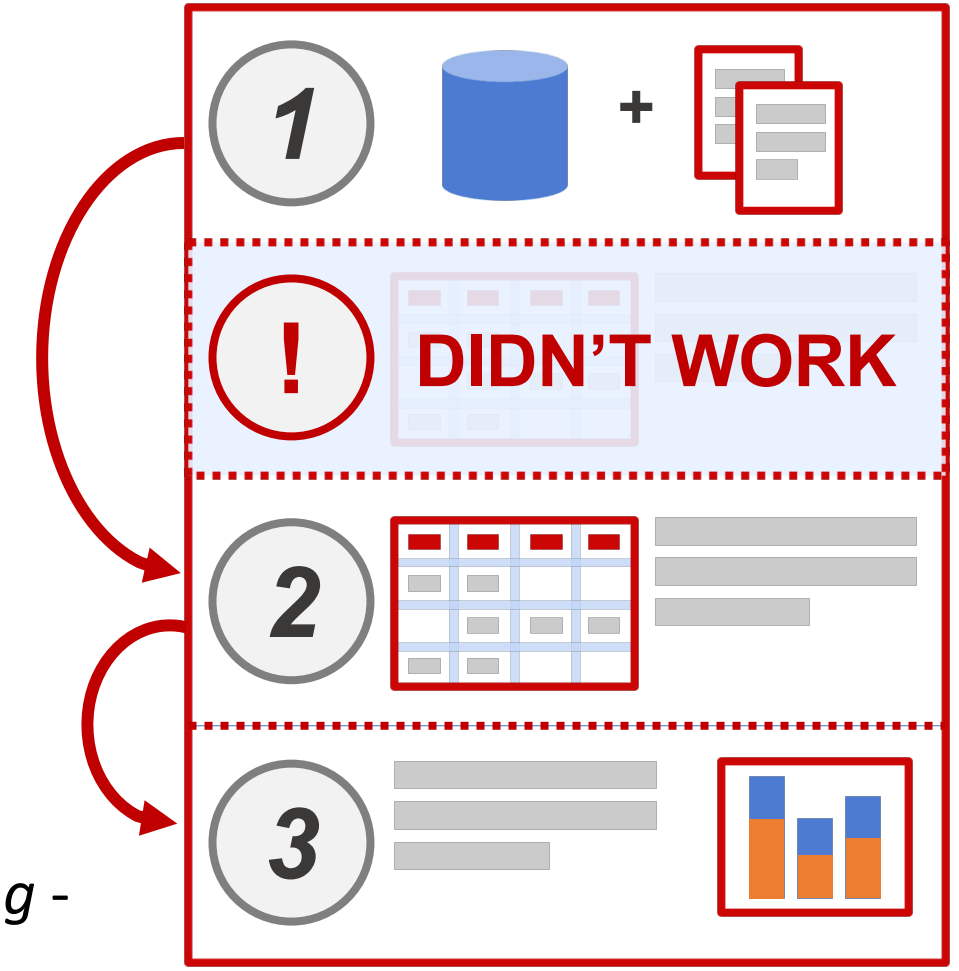
- Automates & consolidates discrete processes
- Easy to review – highly visual

Shows Provenance

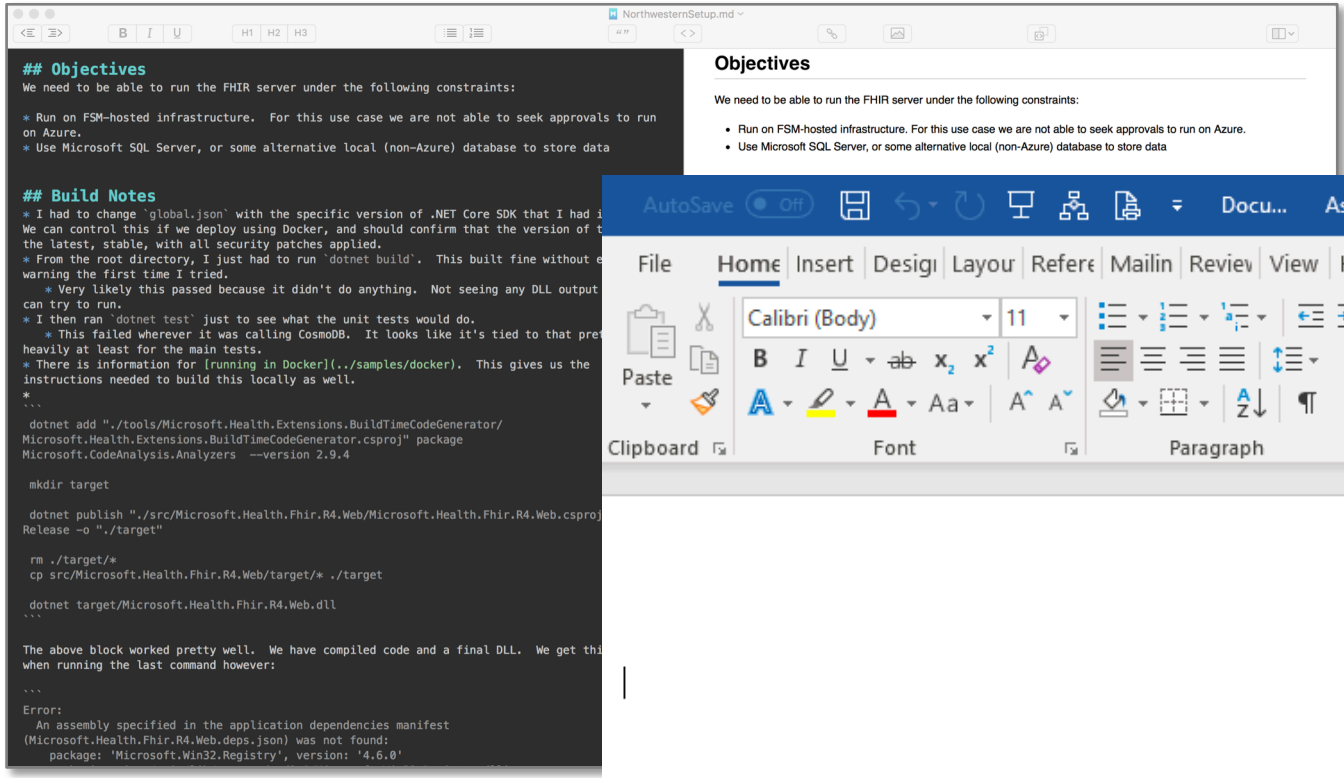
- Trace your work
- See unsuccessful paths
- Trace the ultimate right path

Supports Exploration and Creativity

- Interactive – feedback for faster, easier work
- Doesn't mandate "perfection" – keep *everything* - that's part of the value



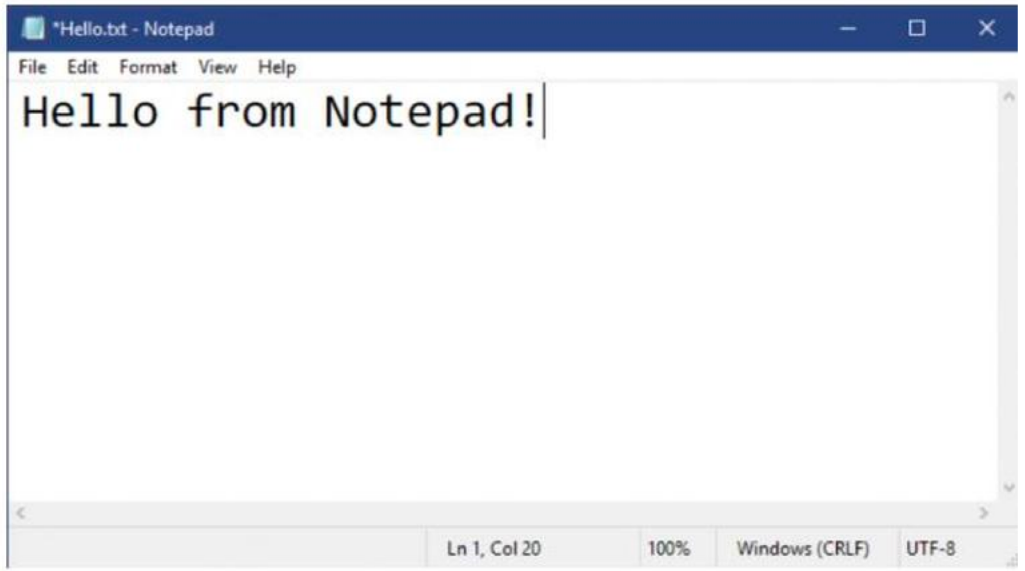
Other Pragmatic Lab Notebook Platforms



Ma

Microsoft Word

Having the discipline to document
- Your environment
- What you did
- What you expected
- What you got



Analysis

- Think of your work as a series of **variables**

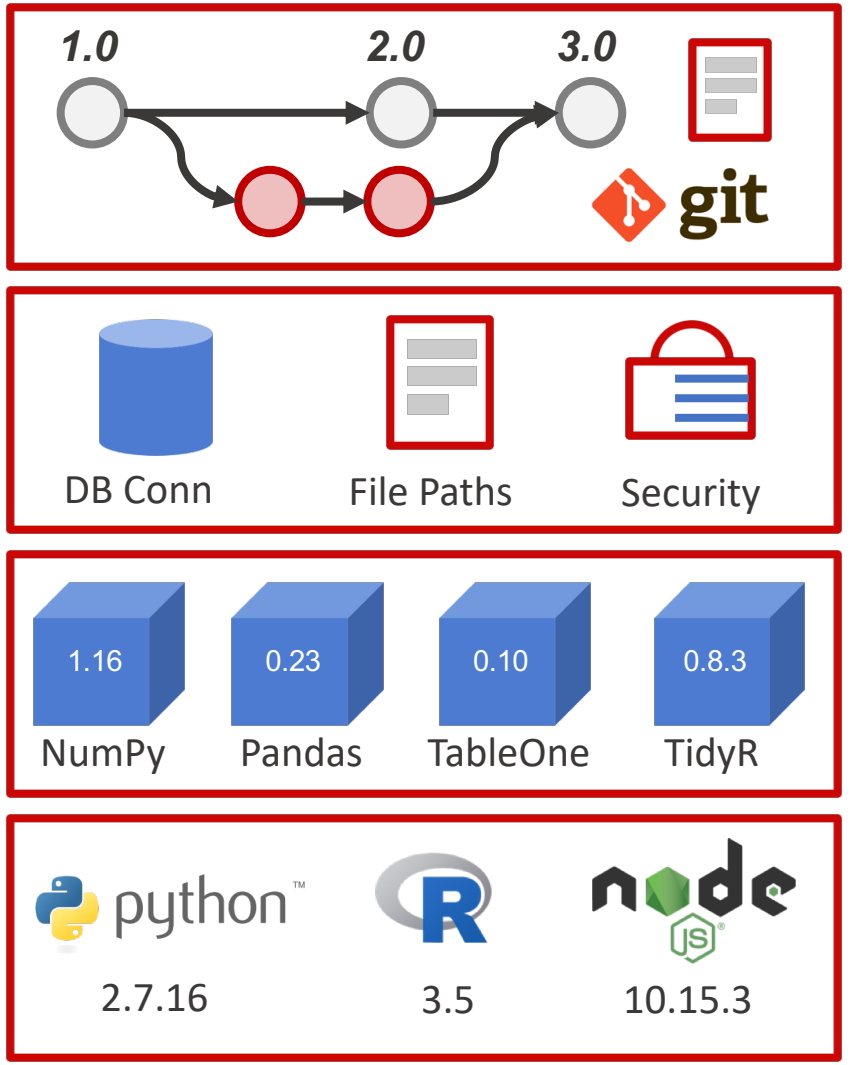
✚ Source code revision

✚ System / application / user configuration

✚ Module / package versions

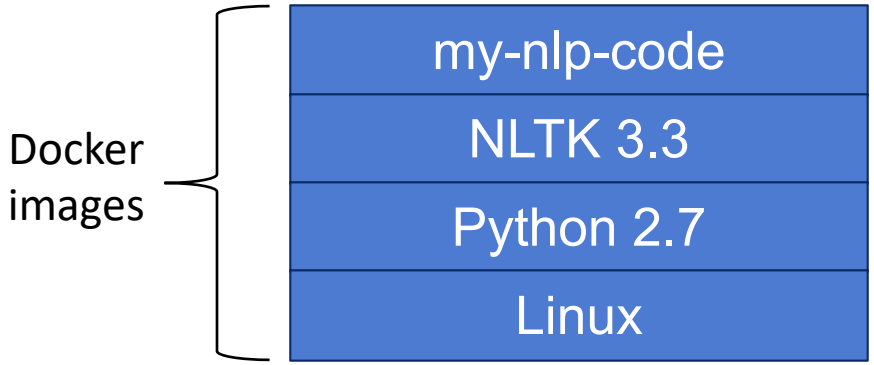
✚ Language / framework versions

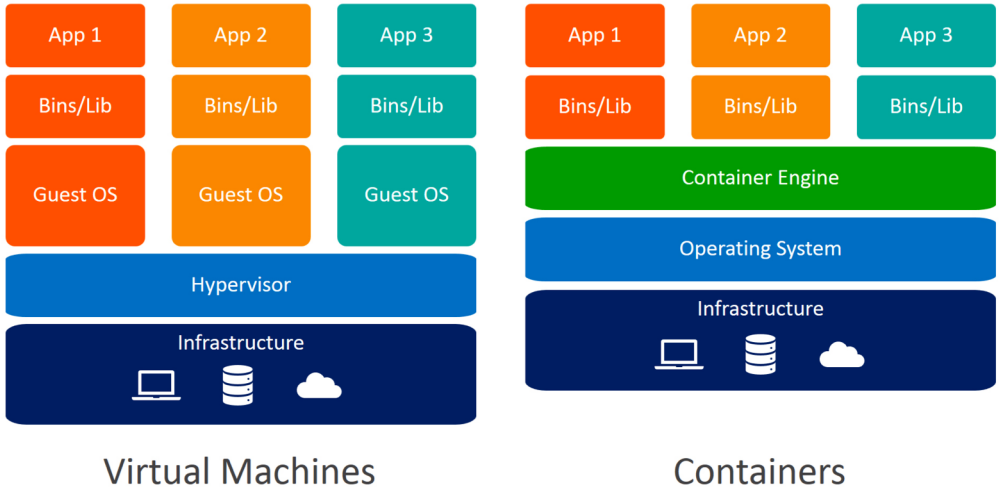
- The variables are **combined** to create a single overall analysis pipeline
- A change to even a *single* variable can influence reproducibility



Automating Reproducible Analyses

- Scripted execution
  - Guarantees (and documents) the same commands are run
  - Long-running processes… go get a cup of [coffee | tea]!
  - Running on my laptop today vs. 5 years from now
- Virtual machines and containers
  - Capture the software environment





Virtual Machines Containers

https://www.bmc.com/blogs/containers-vs-virtual-machines/

Pragmatic Reproducible Research

Manuscripts

Dynamic Documents: R Markdown

NHANES Example.Rmd

Knit

```
---
title: 'Association of Education with Anthropometrics in US Adults: National H
  and Nutrition Examination Study 2013-2014'
geometry: margin=.75in
output: html_document
sansfont: Calibri Light
fontsize: 11pt
---

<style type="text/css">
h1.title {
  font-size: 11pt;
  font-weight: bold;
}
</style>

```{r setup, include=FALSE}
knitr::opts_chunk$set(echo = FALSE)
setwd("R:/NUCATS/NUCATS_Shared/BERDShared/Analysis Manager/Data and Programs/R
analysis<-read.csv("Analysis.csv")
attach(analysis)
library(tableone)

**Methods:** This study included adult ($\geq$ 30 years) participants from the
Examination Study (NHANES). Education and demographic information were assesse
measurements were taken by study personnel. Education was dichotomized based o
Associations were estimated using T-tests or Wilcoxon rank sum tests for conti
data. We examined the association between BMI and education level using multiv

```{r, echo=FALSE}
ps<- table(analysis$PostSecondary)
percents<-100*prop.table(ps)
model <- lm(BMXBMI ~ PostSecondary, data = analysis)
BetaUnivariable <- summary(model)$coefficients[2, 1]
LBUnivariable <- (summary(model)$coefficients[2, 1]) - 1.96 * (summary(model)$
UBUnivariable <- (summary(model)$coefficients[2, 1]) + 1.96 * (summary(model)$
myVars <- c("Gender", "Race", "RIDAGEYR", "Married", "BMXBMI", "LBXTC", "LBXGL
TableOne <- CreateTableOne(data = analysis, vars=myVars, strata= "PostSecondar
```

Association of Education with Anthropometrics in US Adults: National Health and Nutrition Examination Study 2013-2014

Introduction: Education level has been shown to be associated with body mass index (BMI). Gender, race, marital status and metabolic characteristics may alter this association.

Methods: This study included adult (≥ 30 years) participants from the 2013-2014 National Health and Nutrition Examination Study (NHANES). Education and demographic information were assessed by questionnaire and anthropometric measurements were taken by study personnel. Education was dichotomized based on matriculation to post-secondary education. Associations were estimated using T-tests or Wilcoxon rank sum tests for continuous data and chi-squared tests for categorical data. We examined the association between BMI and education level using multivariate linear regression

(Beta: -0.19, 95% CI: -0.79 to 0.41).

Table 1. Association of Education with Participant Characteristics among 2013-2014 NHANES Participants

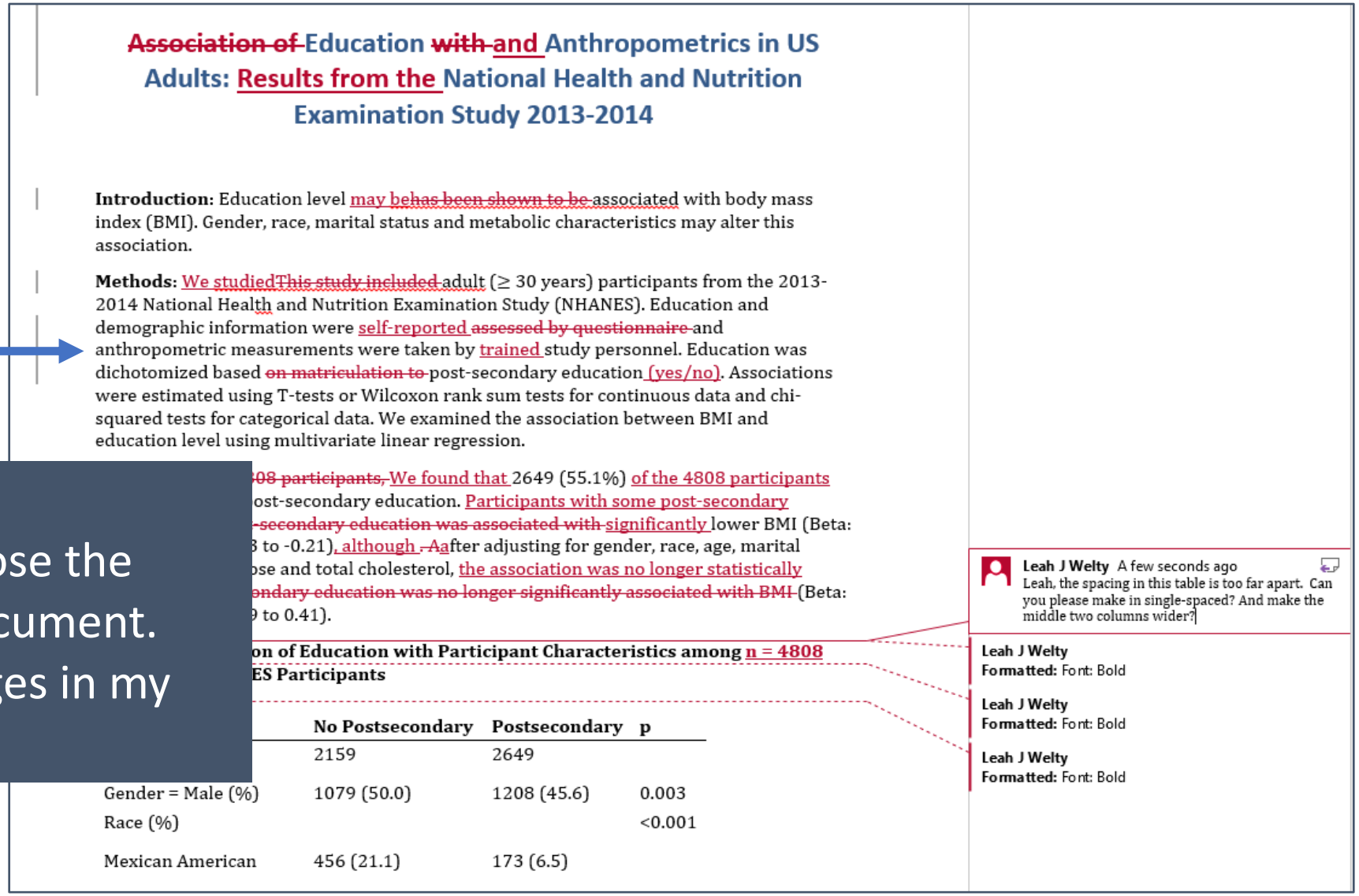
	No Postsecondary	Postsecondary	p
n	2159	2649	
Gender = Male (%)	1079 (50.0)	1208 (45.6)	0.003
Race (%)			<0.001
Mexican American	456 (21.1)	173 (6.5)	
Non-Hispanic Asia	161 (7.5)	411 (15.5)	

Do you have non-technical collaborators who are willing to work this way? Think of a clinical expert working on a phenotype algorithm paper.

Dynamic Documents and Track Changes

I create a dynamic document, generate the Word file and send it to collaborators.

They send back this



~~Association of~~ Education ~~with~~ and Anthropometrics in US Adults: Results from the National Health and Nutrition Examination Study 2013-2014

Introduction: Education level may ~~be~~has been shown to be associated with body mass index (BMI). Gender, race, marital status and metabolic characteristics may alter this association.

Methods: We ~~studied~~This study included adult (≥ 30 years) participants from the 2013-2014 National Health and Nutrition Examination Study (NHANES). Education and demographic information were self-reported ~~assessed by questionnaire~~ and anthropometric measurements were taken by trained study personnel. Education was dichotomized based ~~on matriculation to~~ post-secondary education (yes/no). Associations were estimated using T-tests or Wilcoxon rank sum tests for continuous data and chi-squared tests for categorical data. We examined the association between BMI and education level using multivariate linear regression.

~~08 participants,~~ We found that 2649 (55.1%) of the 4808 participants ost-secondary education. Participants with some post-secondary ~~secondary education was associated with~~ significantly lower BMI (Beta: 3 to -0.21), although ~~,Aa~~fter adjusting for gender, race, age, marital ose and total cholesterol, the association was no longer statistically ~~ondary education was no longer significantly associated with BMI~~ (Beta: 9 to 0.41).

on of Education with Participant Characteristics among n = 4808 ES Participants

	No Postsecondary	Postsecondary	p
	2159	2649	
Gender = Male (%)	1079 (50.0)	1208 (45.6)	0.003
Race (%)			<0.001
Mexican American	456 (21.1)	173 (6.5)	

Leah J Welty A few seconds ago
Leah, the spacing in this table is too far apart. Can you please make in single-spaced? And make the middle two columns wider?

Leah J Welty
Formatted: Font: Bold

Leah J Welty
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Leah J Welty
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I have two choices:

1. Continue in Word, and loose the dynamic nature of the document.
2. Re-enter all of their changes in my source file.

Alternative Approach: StatTag

- StatTag creates a link between a statistical code file and a Word document
- Embeds output (values, tables, figures, verbatim) in document
- Can work separately on the code and the Word document but retain link
- Software agnostic: connects Stata, SAS or R code and Word document
- Can connect multiple code files (of different types) to the same document

https://sites.northwestern.edu/stattag/

Conclusion

Continue the Momentum

"The most important tool is the *mindset*, when starting, that the end product will be reproducible."

– Keith Baggerly

There are a lot of opinions, but there is no wrong way

Identify what could change, and how to control for it

Start somewhere, but **start**

Thank You!

Resources

- Karl Broman – Initial Steps Toward Reproducible Research (https://kbroman.org/steps2rr/)
- Victoria Stodden – Enabling Reproducible Research: Open Licensing for Scientific Innovation (March 3, 2009). International Journal of Communications Law and Policy, Forthcoming. Available at SSRN: https://ssrn.com/abstract=1362040
- Carl Boettiger - An introduction to Docker for reproducible research, with examples from the R environment. (2015) ACM SIGOPS Operating Systems Review, Special Issue on Repeatability and Sharing of Experimental Artifacts. 49(1), 71-79. DOI: 10.1145/2723872.2723882. arXiv:1410.0846 [cs.SE]
- Jeffrey Leek & Richard Peng - Opinion: Reproducible research can still be wrong: Adopting a prevention approach. PNAS February 10, 2015 112 (6) 1645-1646; https://doi.org/10.1073/pnas.1421412111
- Suzanne Bakken - The journey to transparency, reproducibility, and replicability. JAMIA, 26(3) 185-187. https://doi.org/10.1093/jamia/ocz007
- Leslie McIntosh et al., Repeat: a framework to assess empirical reproducibility in biomedical research. BMC Medical Research Methodology. 201717:143. https://doi.org/10.1186/s12874-017-0377-6
- Enrico Coiera et al. Does health informatics have a replication crisis? Journal of the American Medical Informatics Association, Volume 25, Issue 8, 1 August 2018, Pages 963–968, https://doi.org/10.1093/jamia/ocy028

Resources

- Anaconda (https://www.anaconda.com/distribution/)
- Code Ocean (https://codeocean.com/)
- Docker (https://www.docker.com/)
- Dryad (https://datadryad.org/)
- Jupyter Notebook (https://jupyter.org)
- NLM UMLS (https://uts.nlm.nih.gov)
- Natural Language Toolkit (https://www.nltk.org/)
- Python (https://www.python.org)
- R (https://www.r-project.org)
- R Markdown (https://rmarkdown.rstudio.com)
- StatTag (http://stattag.org)