Opening up Clinical Trials: 7 Trends Towards Open Source

Jeremy Wildfire, Rho

PhUSE Single Day Event, 12/1/2016

Chapel Hill, NC

What is Open Source?

The Open Source Initiative has a good definition:

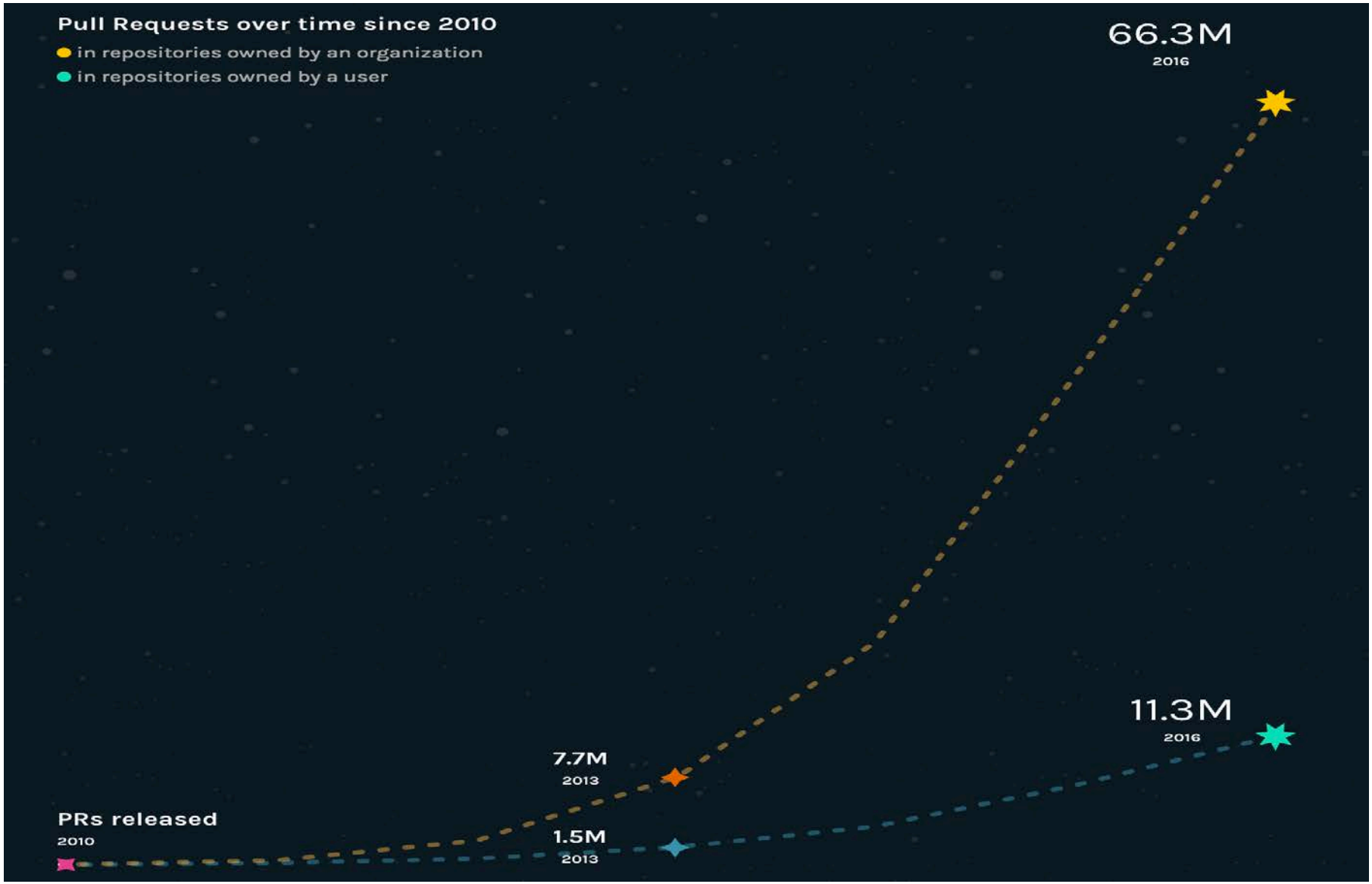
> Generally, Open Source software is software that can be freely accessed, used, changed, and shared (in modified or unmodified form) by anyone.

7 Trends Towards Open Source

(relevant to medical research in the last 10 years or so)

1. Mature Open Source Ecosystem
2. Data Science
3. Regulatory Guidance Updates
4. Reproducible Research
5. Slow (but accelerating) Industry Adoption
6. R can’t be ignored
7. Open Source and SAS

Trend 1: Mature Open Source Ecosystem



Link: State of the Octoverse (aka github)

Example 1 – GitHub Guides

Hello World

10 minute read

The **Hello World** project is a time-honored tradition in computer programming. It is a simple exercise that gets you started when learning something new. Let's get started with GitHub!

You'll learn how to:

- Create and use a repository
- Start and manage a new branch
- Make changes to a file and push them to GitHub as commits
- Open and merge a pull request

What is GitHub?

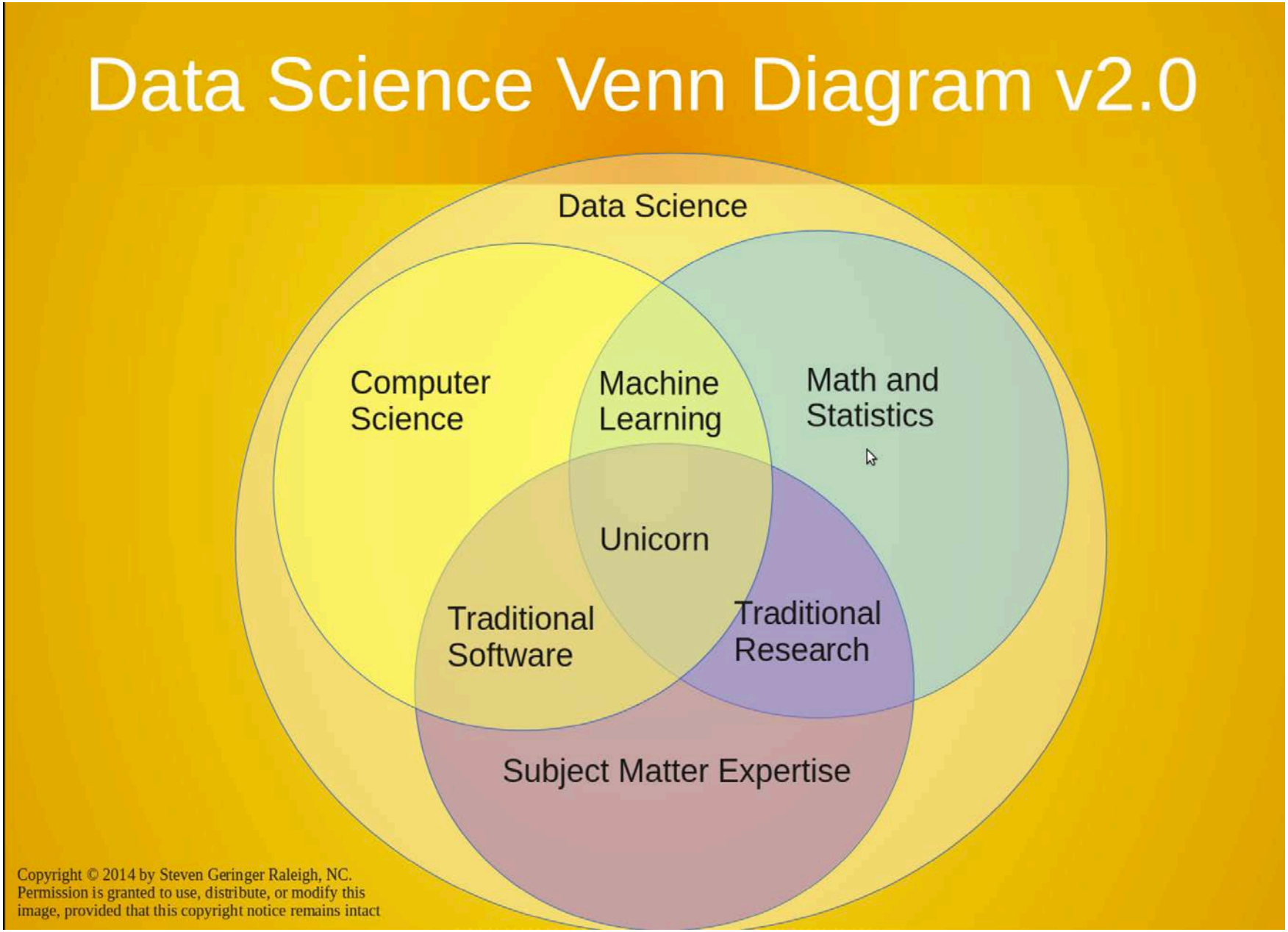
GitHub is a code hosting platform for version control and collaboration. It lets you and others work together on projects from anywhere.

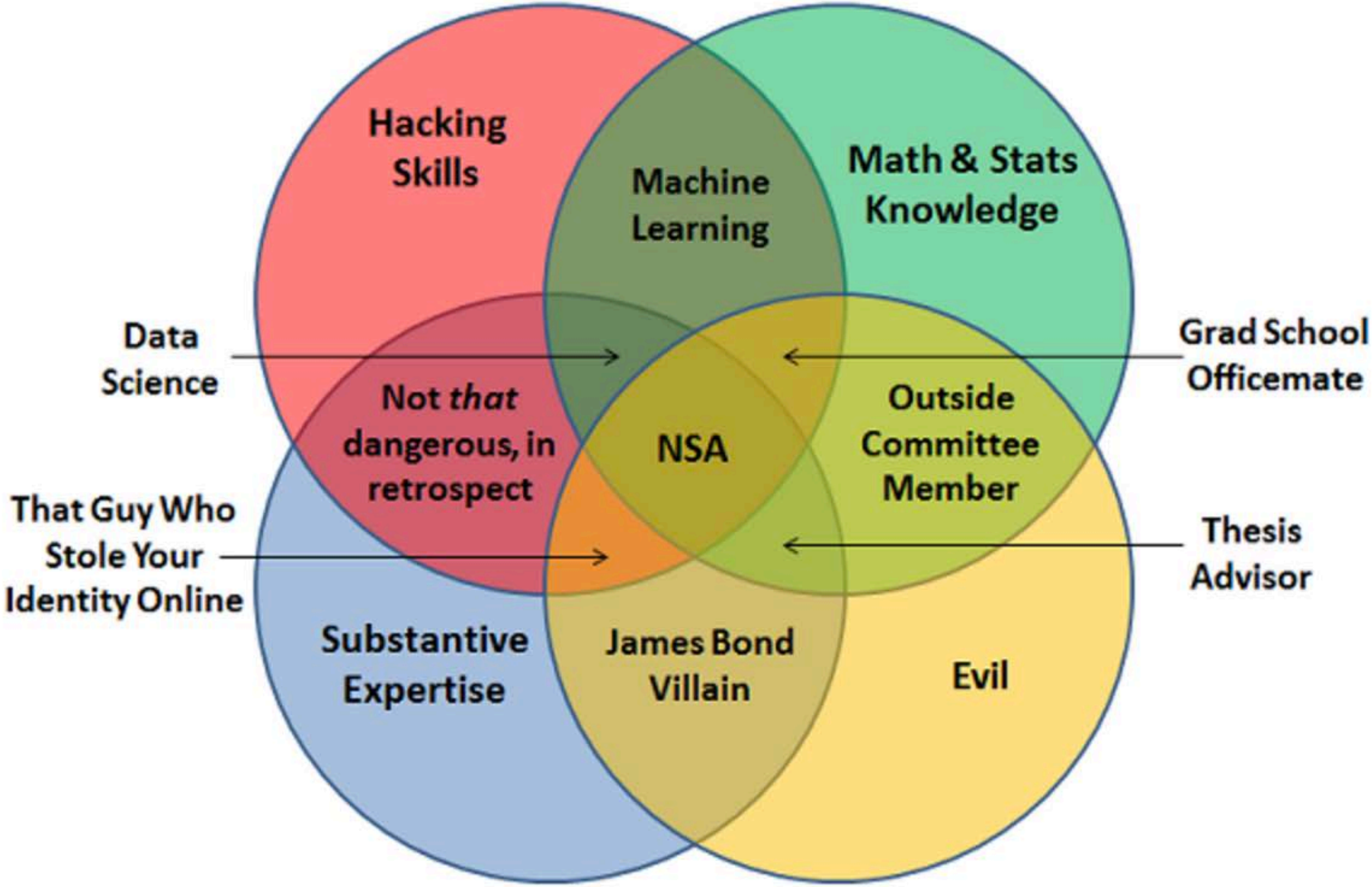
This tutorial teaches you GitHub essentials like *repositories*, *branches*, *commits*, and *Pull Requests*. You'll create

Links: Rho GitHub & GitHub Guides

GitHub's Pull Request workflow, a popular way to create and review code.

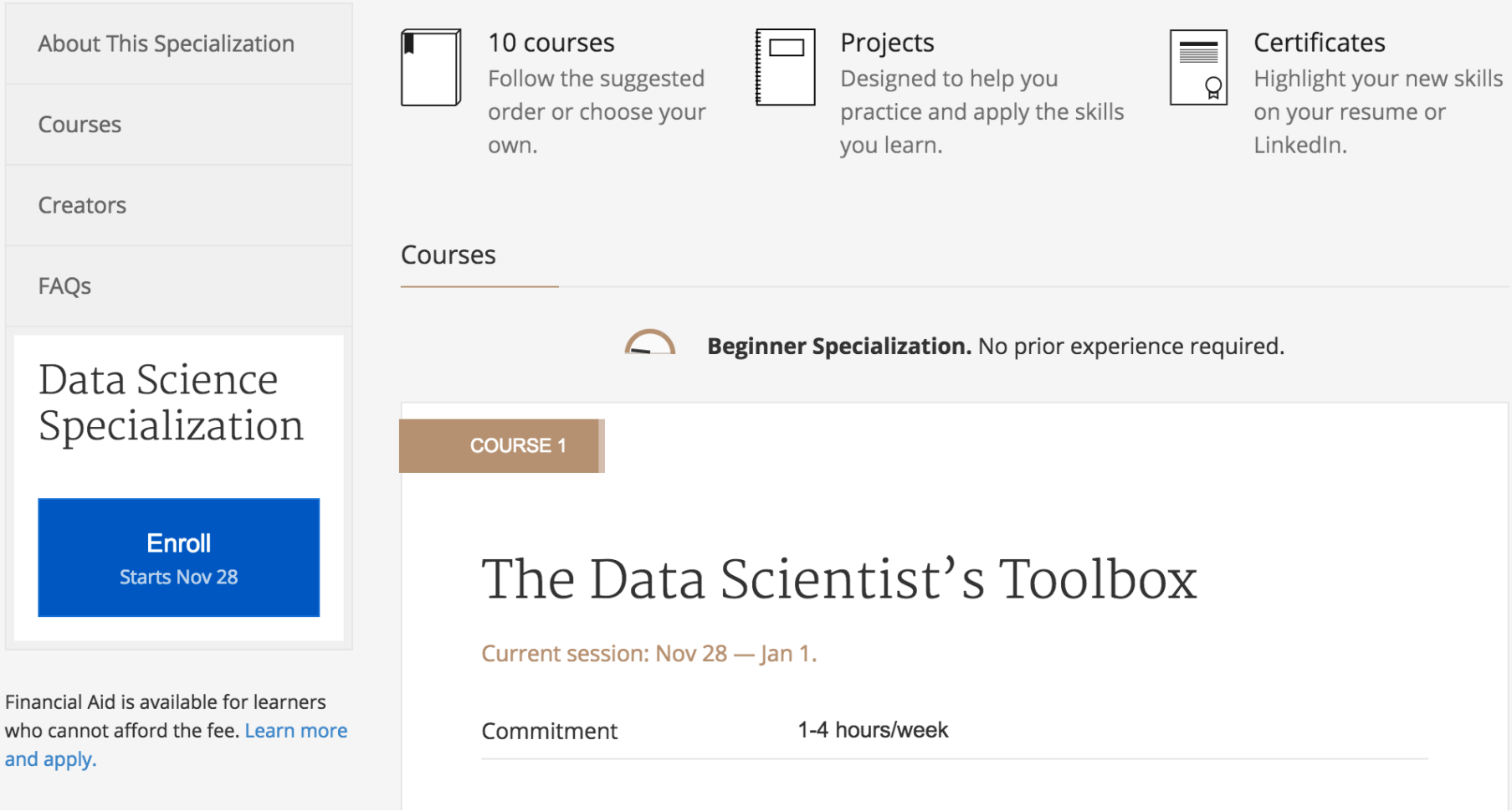
Trend 2: Data Science





Link: [Battle of the Data Science Venn Diagrams]

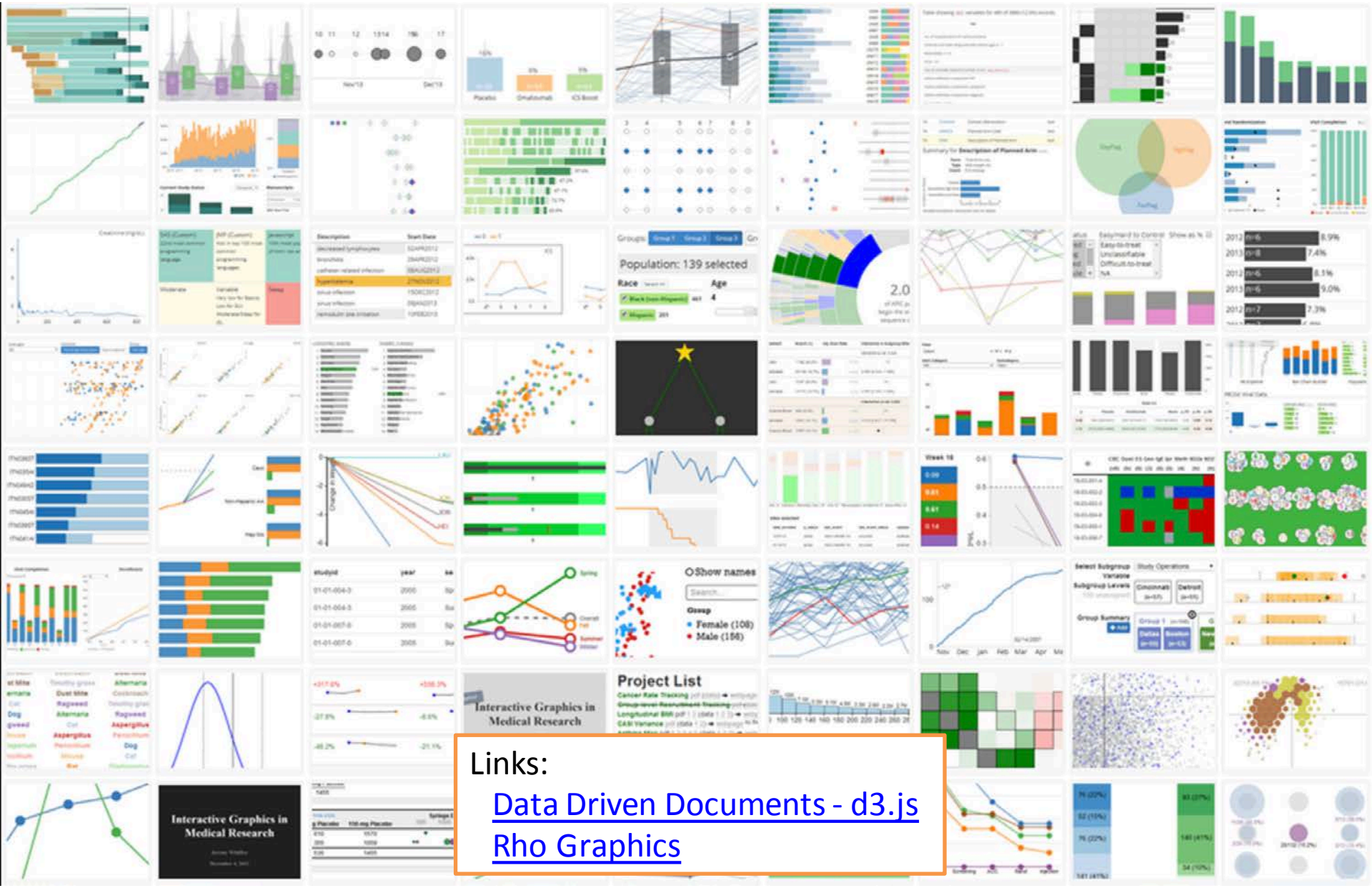
Hopkins/Coursera
Data Science Specialization



Link: [Coursera Data Science Specialization]


Repositories with the most forks
jtleek/datasharing 38,020
octocat/Spoon-Knife 28,738
rdpeng/ProgrammingAssignment2 27,499
twbs/bootstrap 15,669
tensorflow/tensorflow 14,070
rdpeng/ExData_Plotting1 12,458
udacity/frontend-nanodegree-resume 11,553
LarryMad/recipes 10,229
barryclark/jekyll-now 10,070
angular/angular.js 9,334
Link: State of the Octoverse (aka github)

Trend 2.1: Interactive Data Visualization

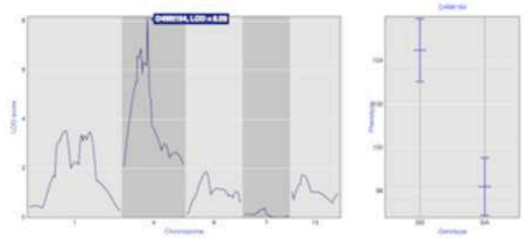


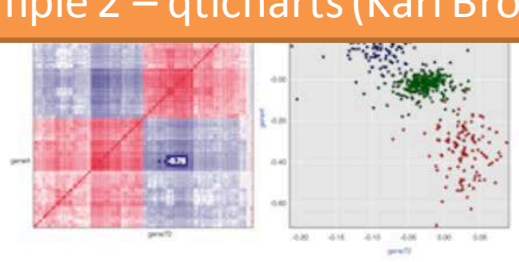
Links:

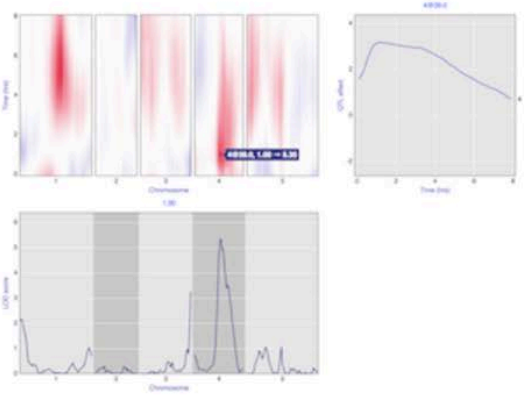
[Data Driven Documents - d3.js]

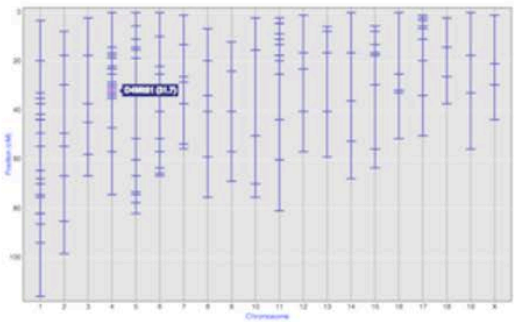
[Rho Graphics]

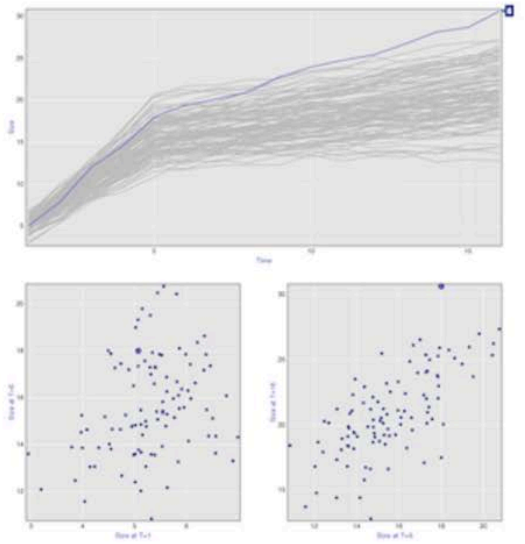
Example 2 – qtlcharts (Karl Broman, UW-Madison)

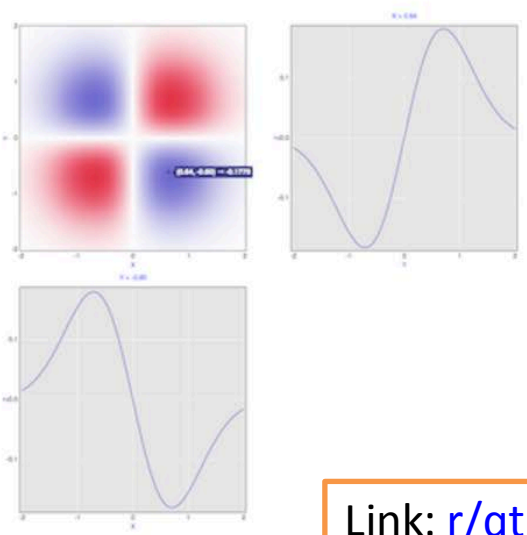






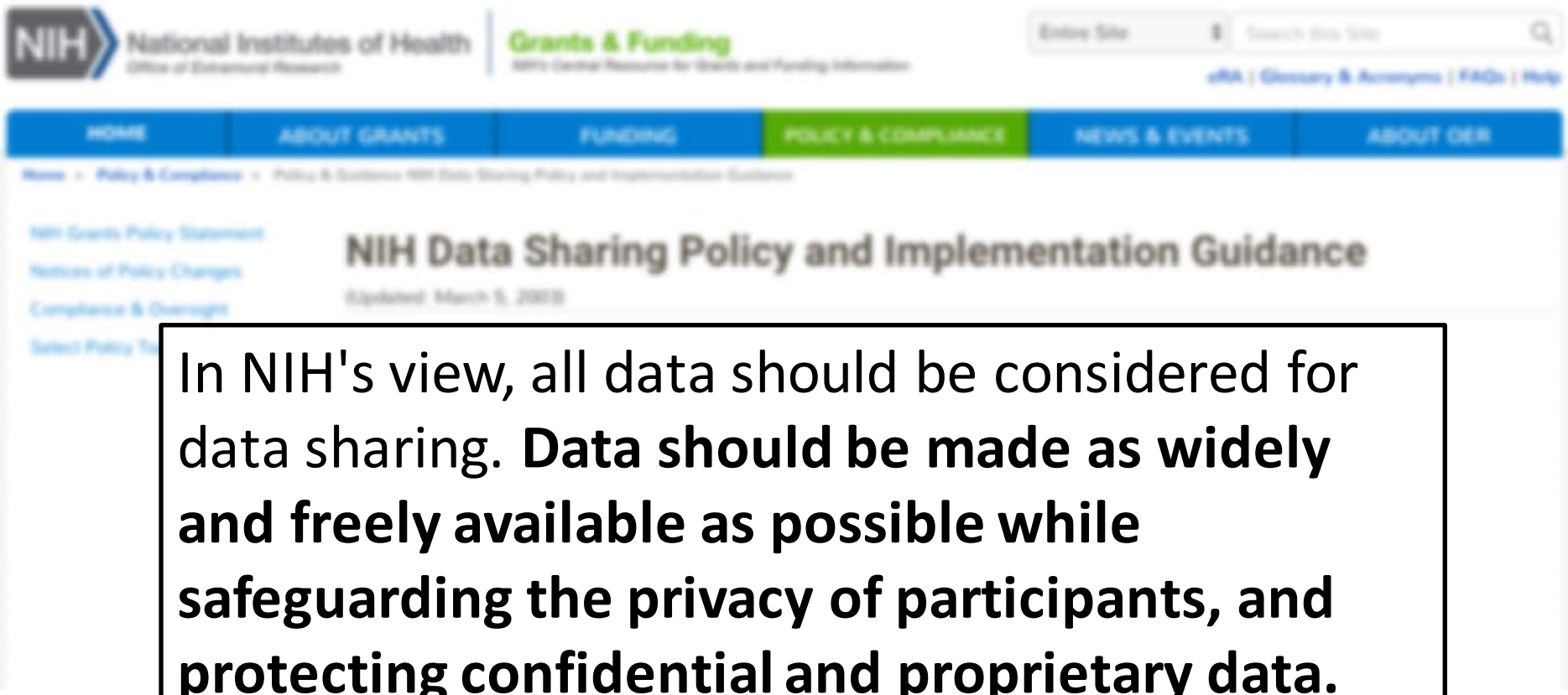






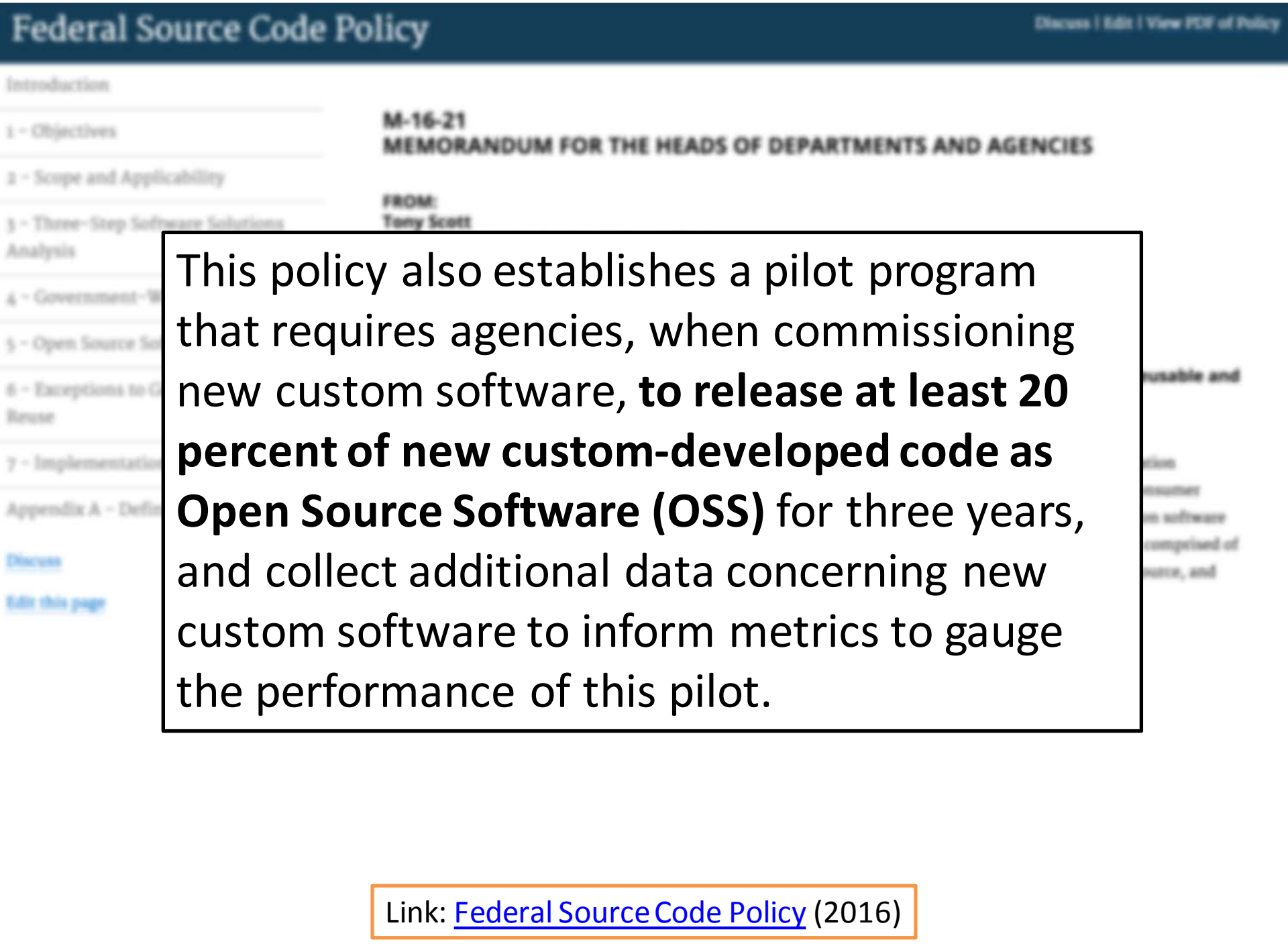
Link: r/qtlcharts

Trend 3: Regulatory Guidance Updates

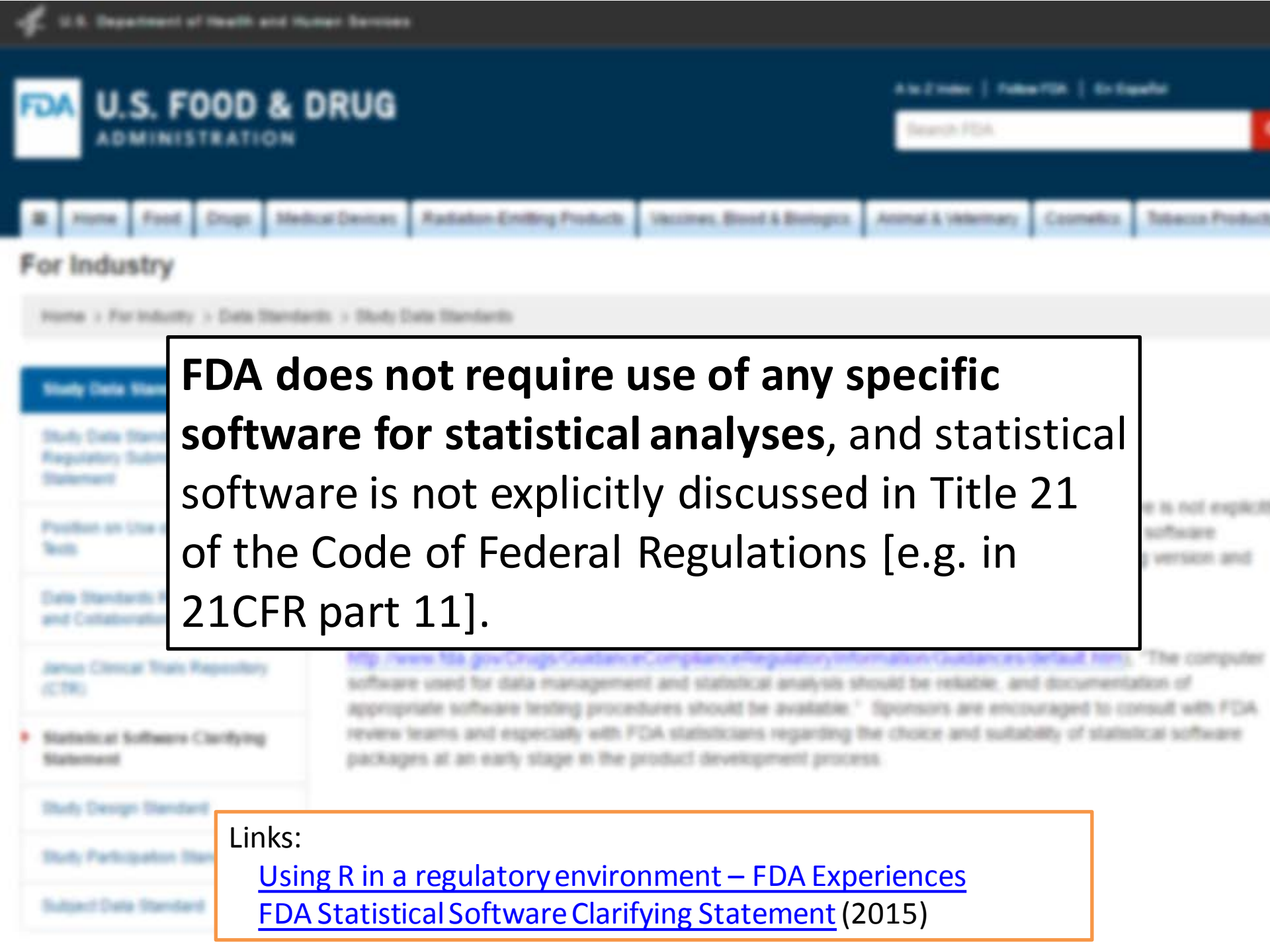


In NIH's view, all data should be considered for data sharing. **Data should be made as widely and freely available as possible while safeguarding the privacy of participants, and protecting confidential and proprietary data.**

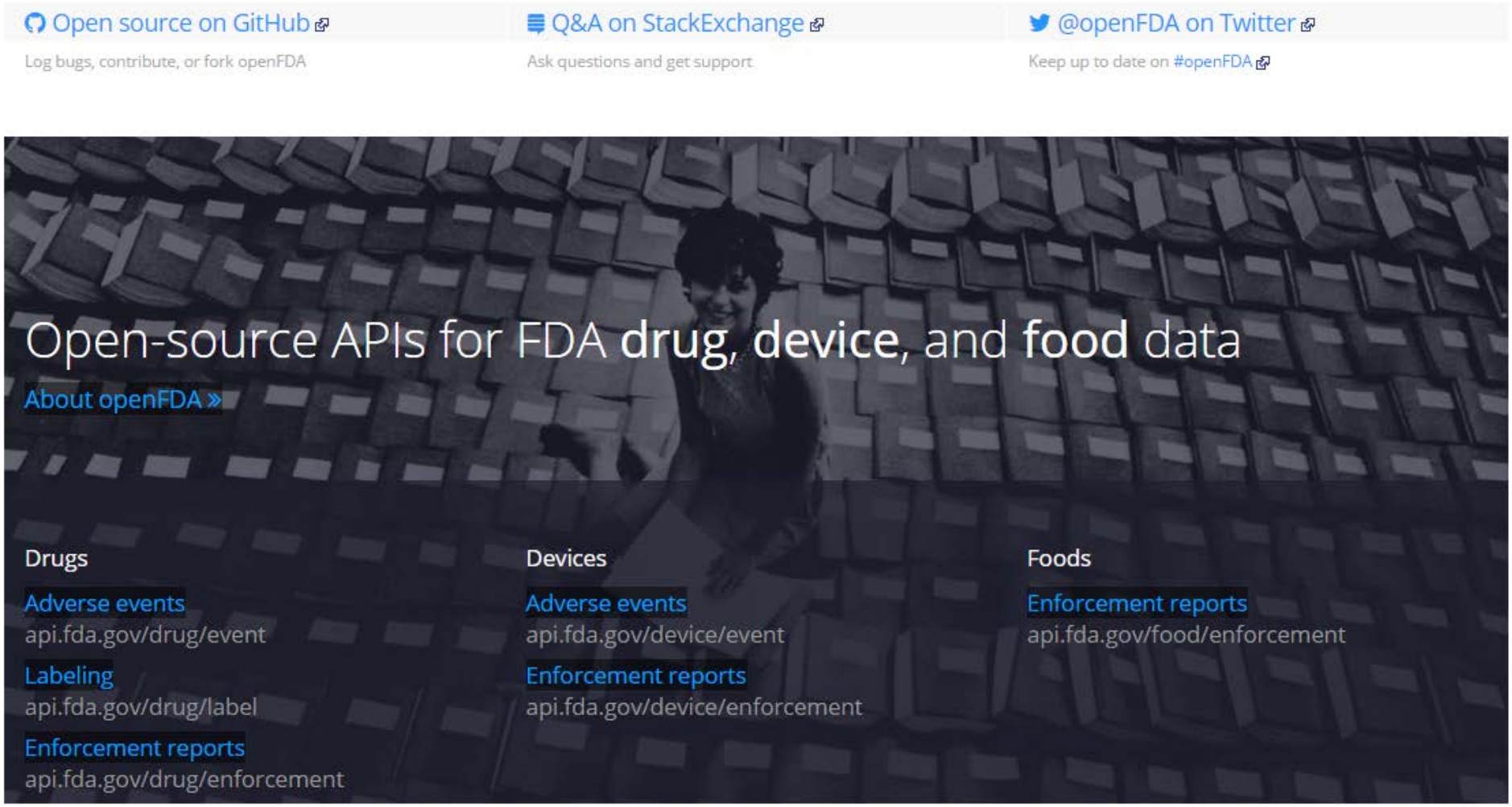
Link: NIH Data Sharing Policy (2003)



Link: [Federal Source Code Policy](#) (2016)

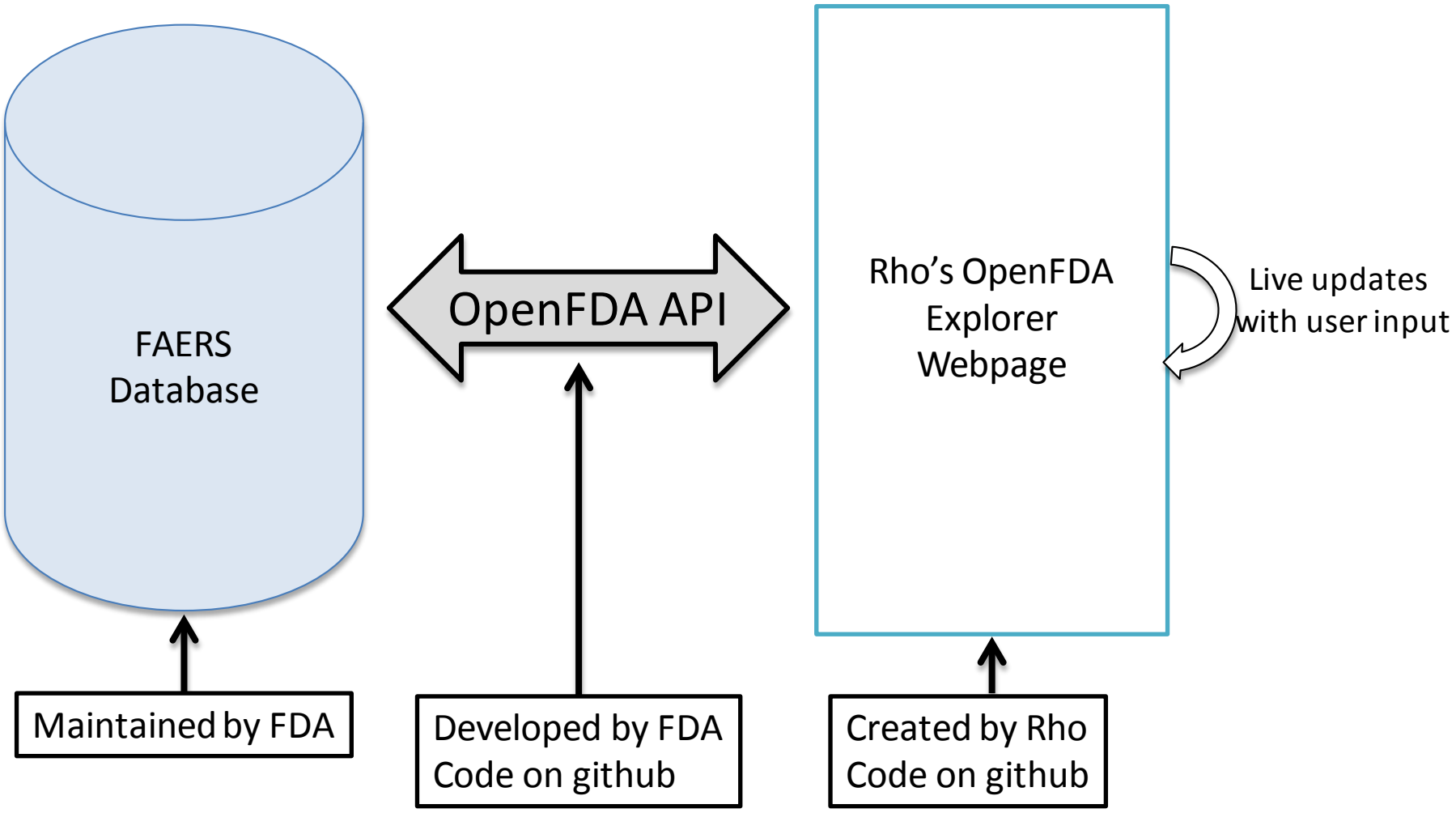

U.S. FOOD & DRUG
ADMINISTRATION
For Industry
FDA does not require use of any specific software for statistical analyses, and statistical software is not explicitly discussed in Title 21 of the Code of Federal Regulations [e.g. in 21CFR part 11].
Links:
Using R in a regulatory environment – FDA Experiences
FDA Statistical Software Clarifying Statement (2015)

Example 3 – OpenFDA (FDA)

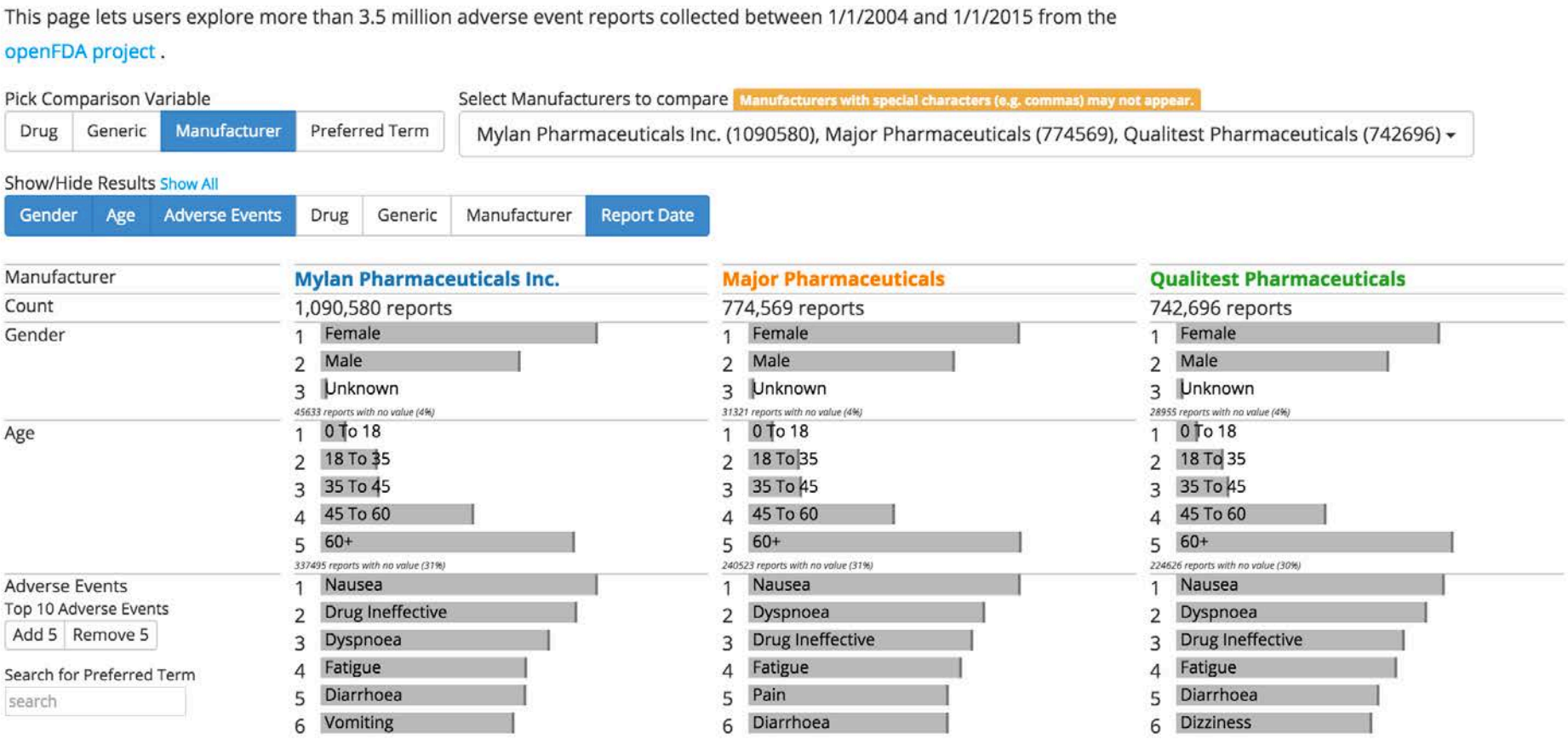


Link: [OpenFDA homepage]

OpenFDA Explorer – System Design



Demo: OpenFDA AE Explorer



Link: [Rho's OpenFDA AE Explorer]

Example 3 - OpenFDA

Pull requests Issues Gist

Search openfda Search

- Repositories 89
- Code 3,954
- Issues 324
- Wikis 49
- Users 1

Languages

JavaScript	26
CSS	9
R	9
HTML	7
Java	7
Python	6
Go	2
Jupyter Notebook	2
Ruby	2

We've found 89 repository results

Sort: Best match

FDA/*openfda*

openFDA is a research project to provide open APIs, raw data downloads, documentation and examples, and a developer c...

Python ★ 254 60 Updated on Feb 9

rOpenHealth/*openfda*

Convenient access to the *OpenFDA* API

R ★ 34 10 Updated on Nov 2, 2015

esridc/*openfda*

Demonstration of Agile Process

JavaScript ★ 2 6 Updated on Jul 7, 2015

Link: OpenFDA repositories on Github

Trend 4: Reproducible Research

nature International weekly journal of science

Availability of data, material and methods

An inherent principle of publication is that others should be able to replicate and build upon the authors' published claims. A condition of publication in a Nature journal is that **authors are required to make materials, data, code, and associated protocols promptly available to readers without undue qualifications**. Any restrictions on the availability of materials or information must be disclosed to the editors at the time of submission. Any restrictions must **also** be disclosed in the submitted manuscript.

After publication, readers who encounter refusal by the authors to comply with these policies should contact the chief editor of the journal. In cases where editors are unable to resolve a complaint, the journal may refer the matter to the authors' funding institution and/or publish a formal statement of correction, attached online to the publication, stating that readers have been unable to obtain necessary materials to replicate the findings.

See sections below for details on:

- reporting requirements
- availability of data
- availability of materials
- availability of computer code
- experimental protocols
- clinical trials
- futher reading

Link: Nature Policies for Publication

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 FEBRUARY 26, 2015 VOL. 372 NO. 9

Randomized Trial of Peanut Consumption in Infants at Risk for Peanut Allergy

George Du Toit, M.B., B.Ch., Graham Roberts, D.M., Peter H. Sayre, M.D., Ph.D., Henry T. Bahnson, M.P.H., Suzana Radulovic, M.D., Alexandra F. Santos, M.D., Helen A. Brough, M.B., B.S., Deborah Phippard, Ph.D., Monica Basting, M.A., Mary Feeney, M.Sc., R.D., Victor Turcanu, M.D., Ph.D., Michelle L. Sever, M.S.P.H., Ph.D., Margarita Gomez Lorenzo, M.D., Marshall Plaut, M.D., and Gideon Lack, M.B., B.Ch., for the LEAP Study Team*

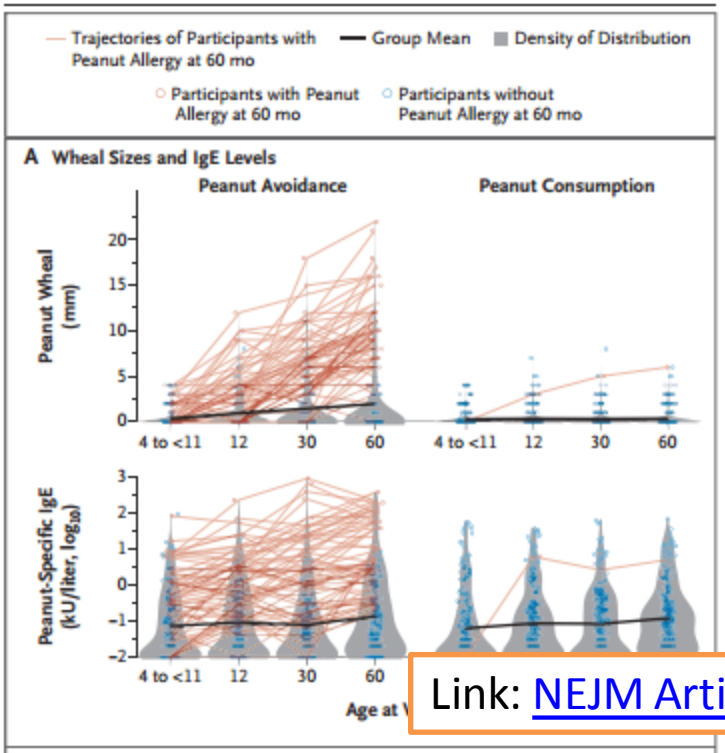
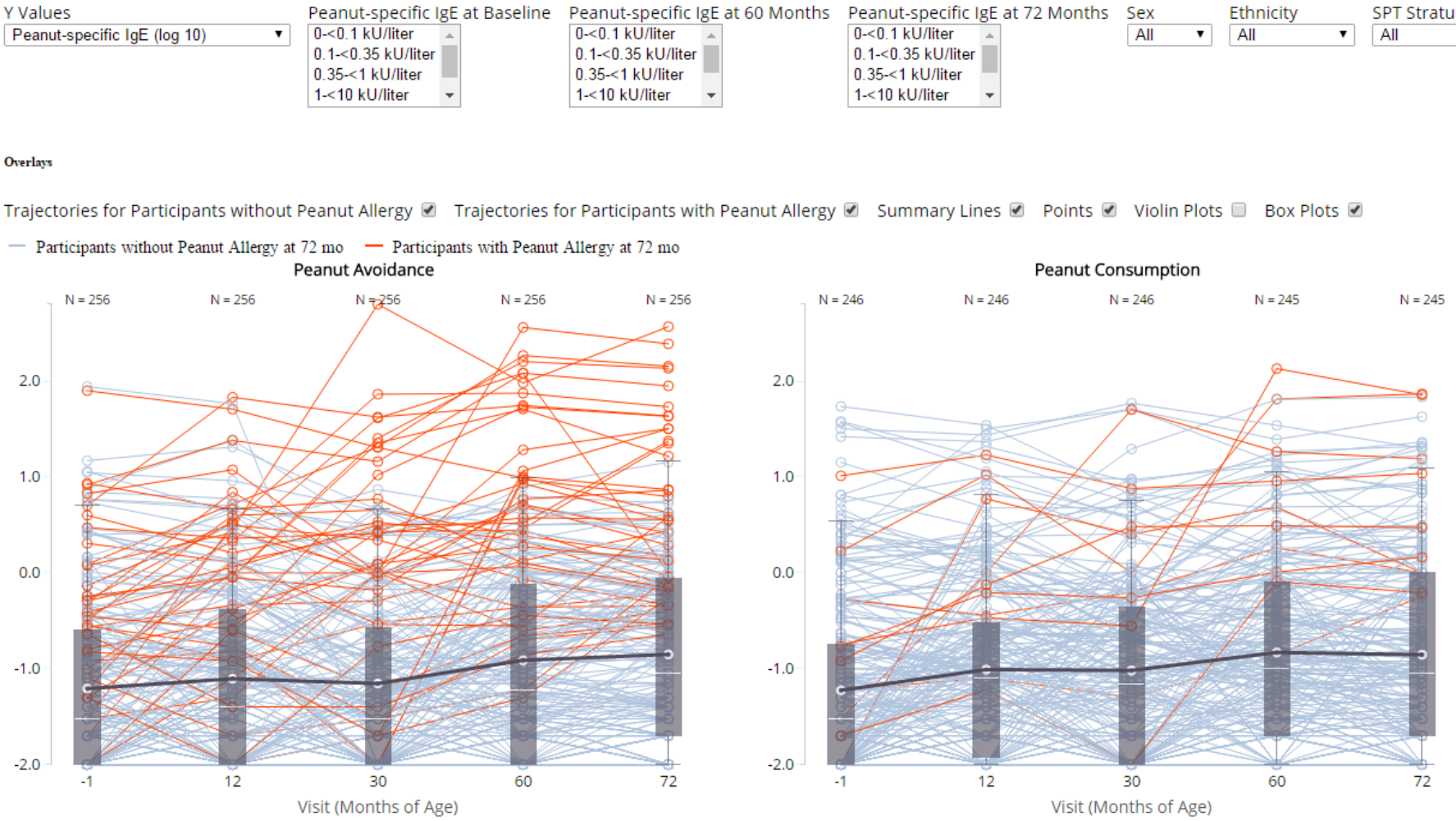


Figure 3. Immunologic Outcomes for the Peanut-Avoidance and Peanut-Consumption Groups at Baseline (4 to <11 Months of Age) and at 12, 30, and 60 Months of Age.

Panel A shows wheal sizes after the peanut-specific skin-prick test and the levels of peanut-specific IgE in participants in the avoidance and consumption groups who met the per-protocol criteria. The solid black lines show the group mean over the course of the study period; the mean wheal size after the peanut-specific skin-prick test differed significantly between the randomized groups at all time points after baseline ($P=0.002$ at 12 months and $P<0.001$ at 30 months and 60 months). The thin red lines represent the trajectory of the development of allergic responses among participants who were allergic at 60 months of age. Panel B shows the levels of peanut-specific IgG and IgG4 and the peanut-specific IgG4:IgE ratio over the course of the study period. The means of each of these measures differed significantly between the two study groups at all postbaseline time points ($P<0.001$). The $\log_{10}$ of the ratio of peanut-specific IgG4:IgE was calculated after the peanut-specific IgG4 levels were converted from micrograms per liter to nanograms per milliliter and the peanut-specific IgE levels from kilo unit per liter to nanograms the use of the formula IgG4 ÷ (IgE×2.4).

Link: NEJM Article (pdf)

Example 4 – LEAP Article (ITN with Rho)



Links:

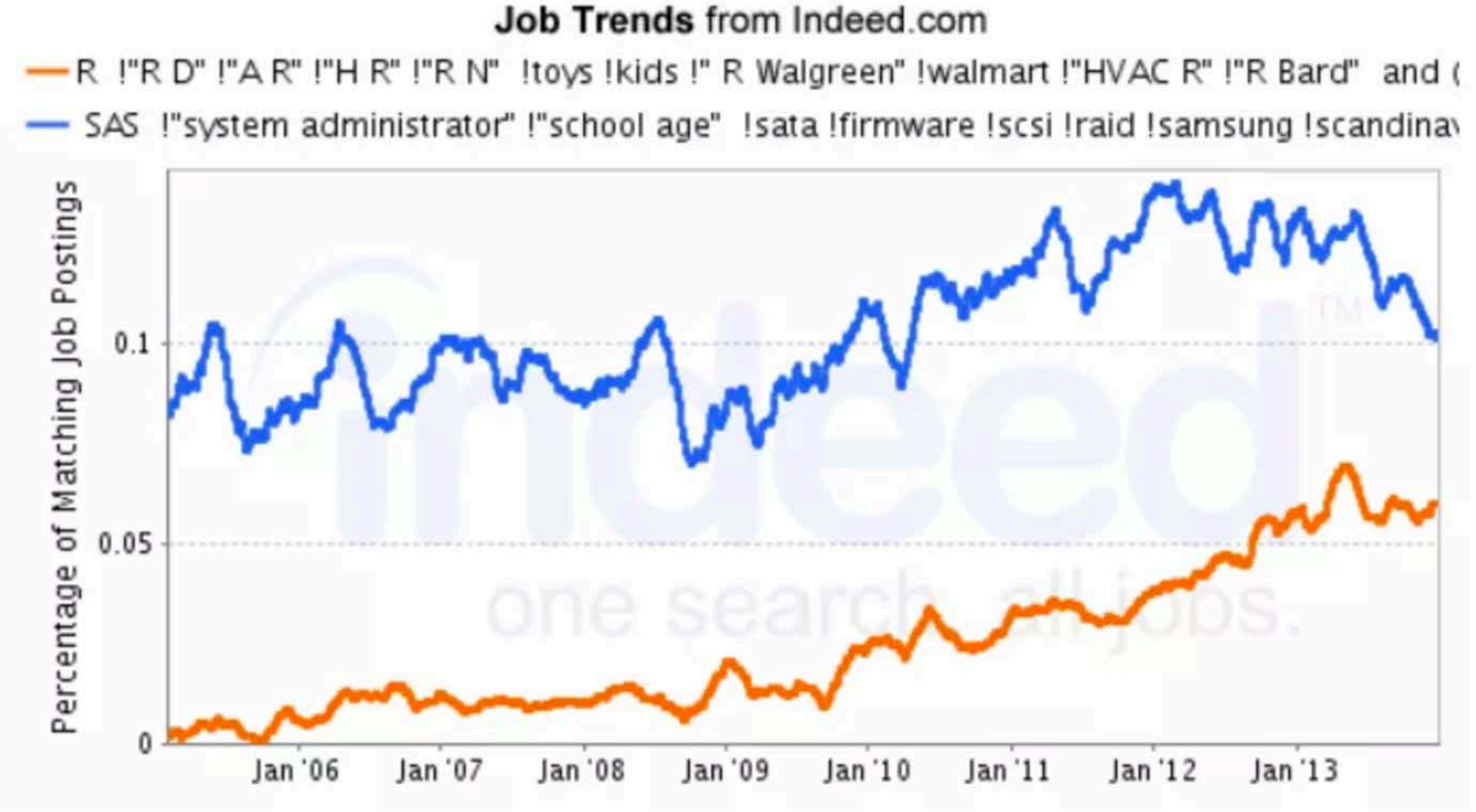
[TrialShare Repository](#) (sign up required)

[Interactive Figure](#)

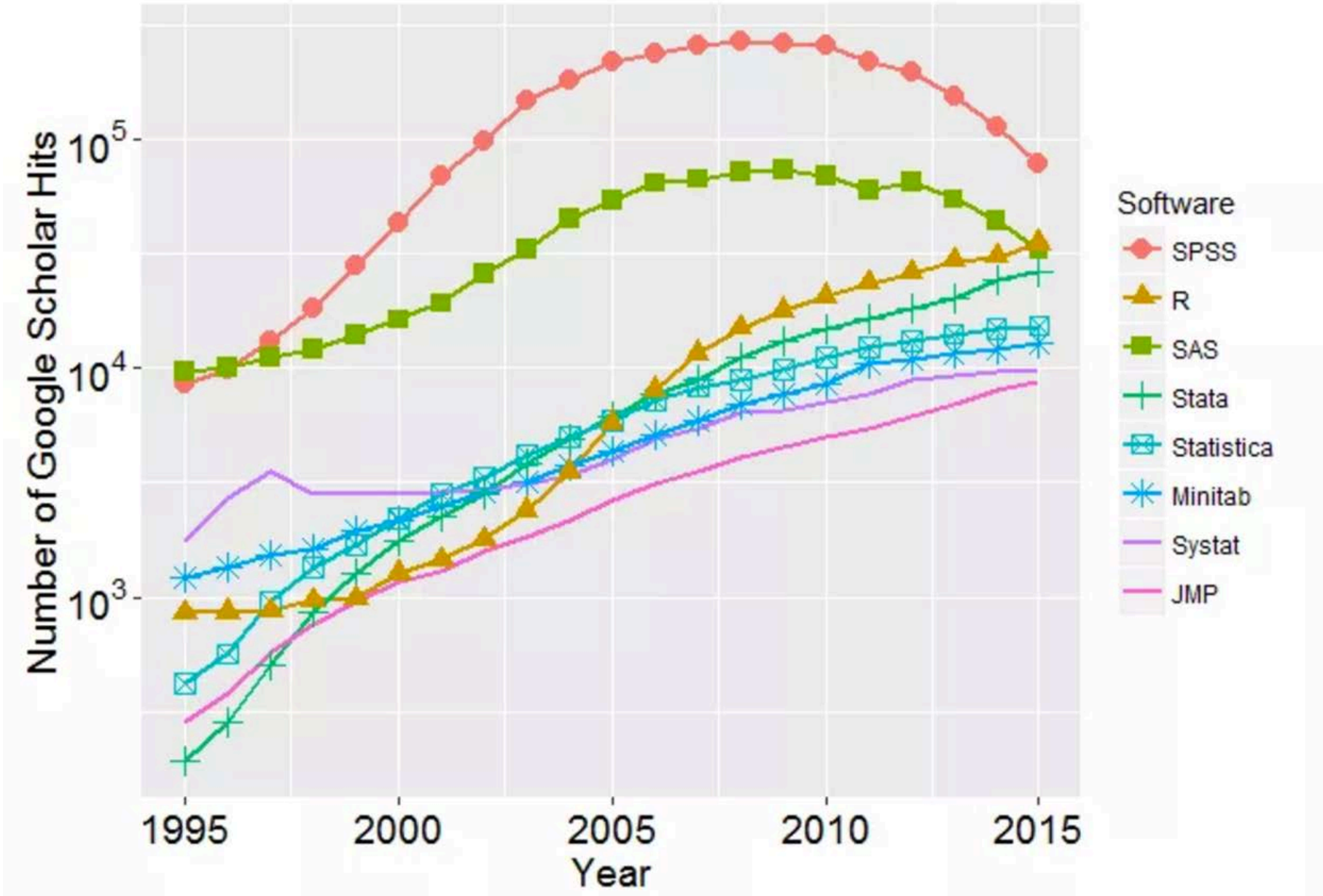
Interlude: SAS vs. R


Seinfeld
hulu

Trend 5: R can no longer be ignored



Link: [The Popularity of Data Analysis Software]



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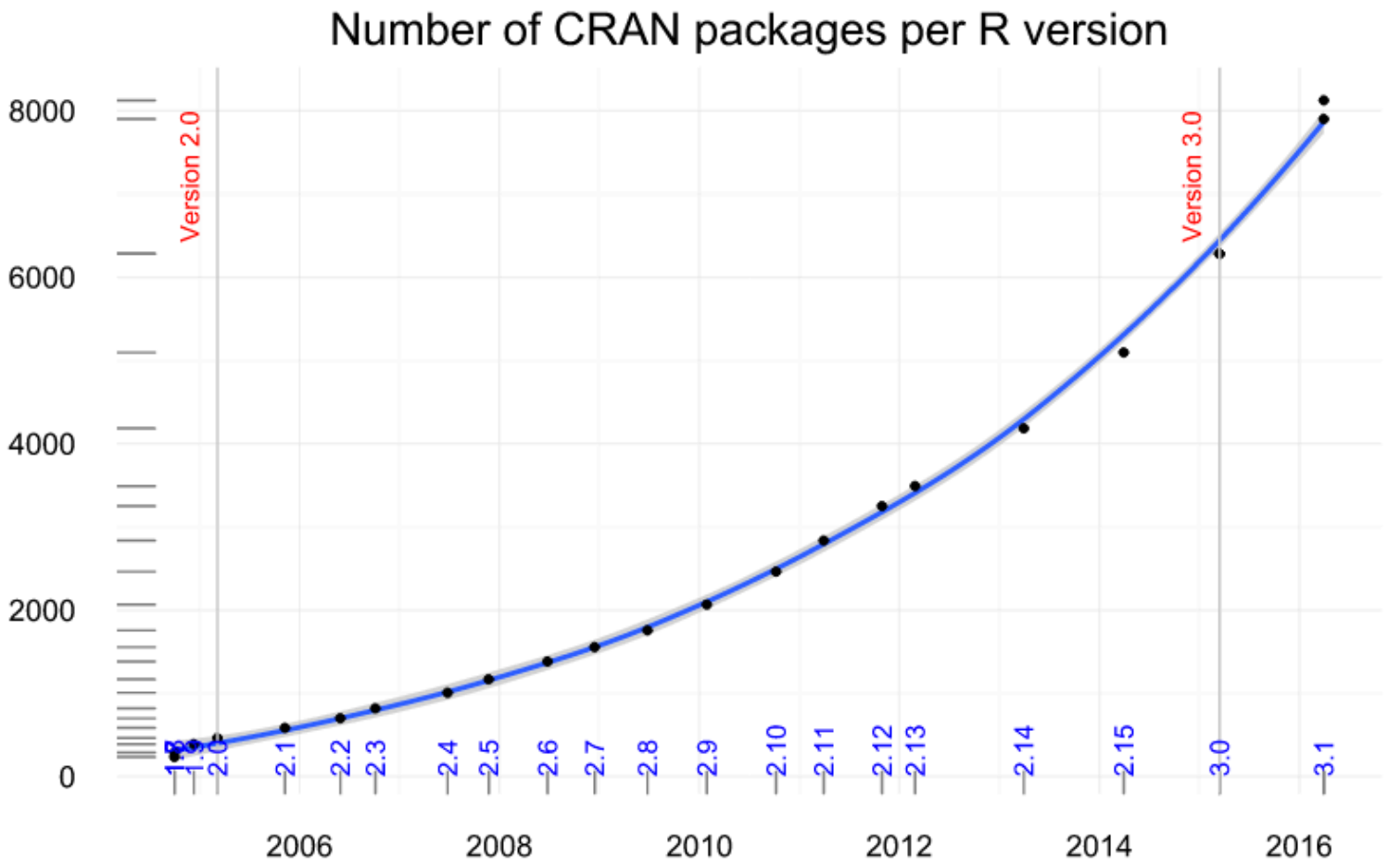
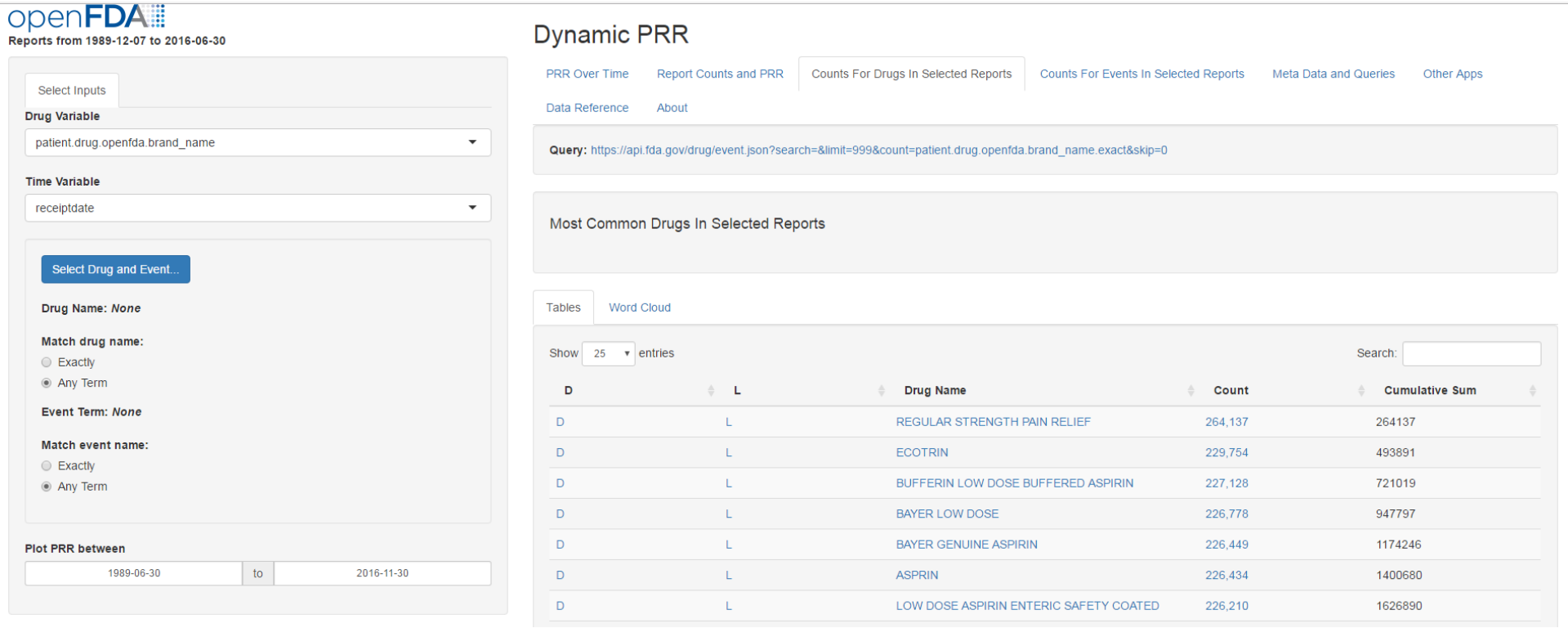


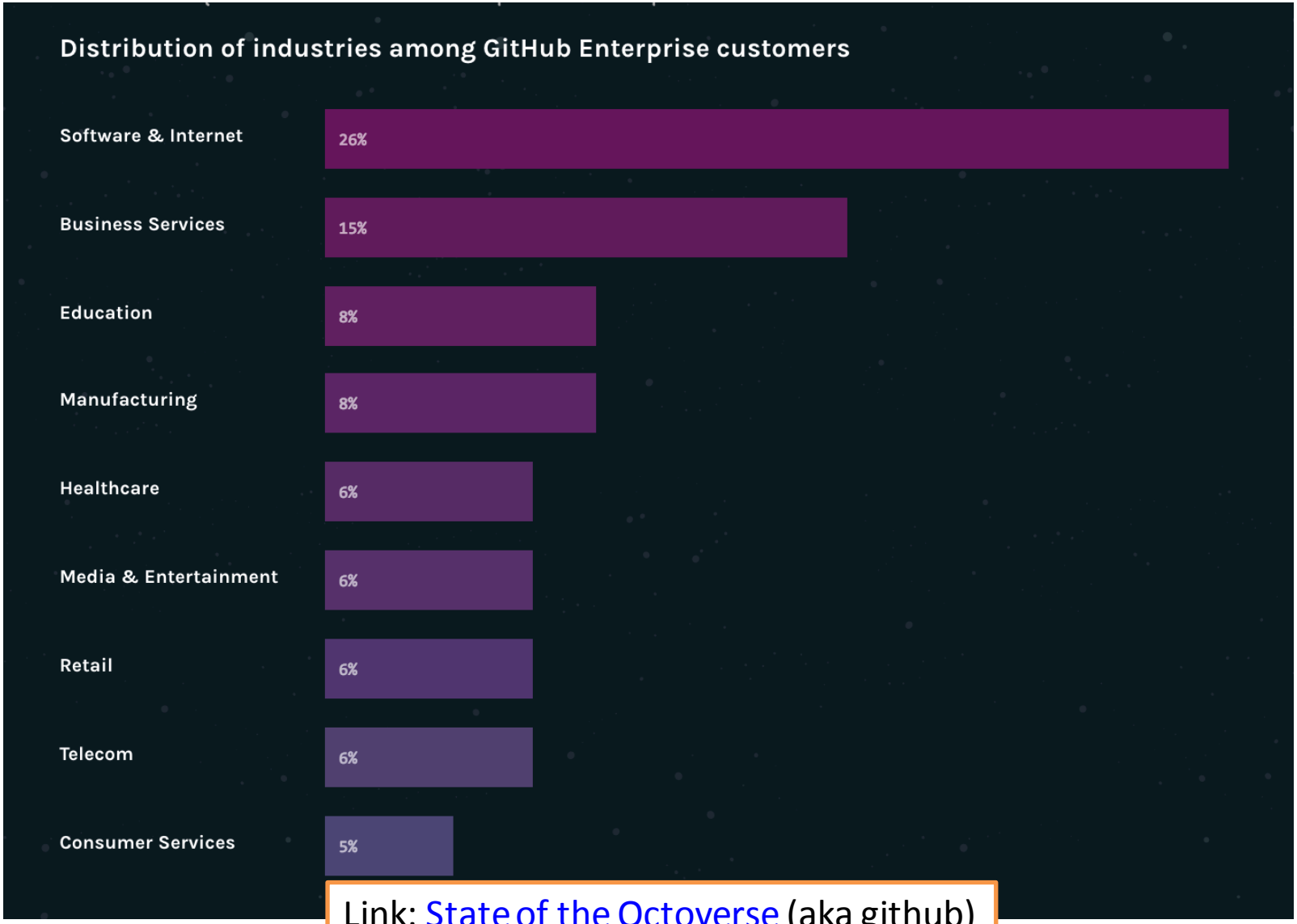
Link: [On the Growth of CRAN Packages]

Example 5 – OpenFDA Shiny Suite (FDA)



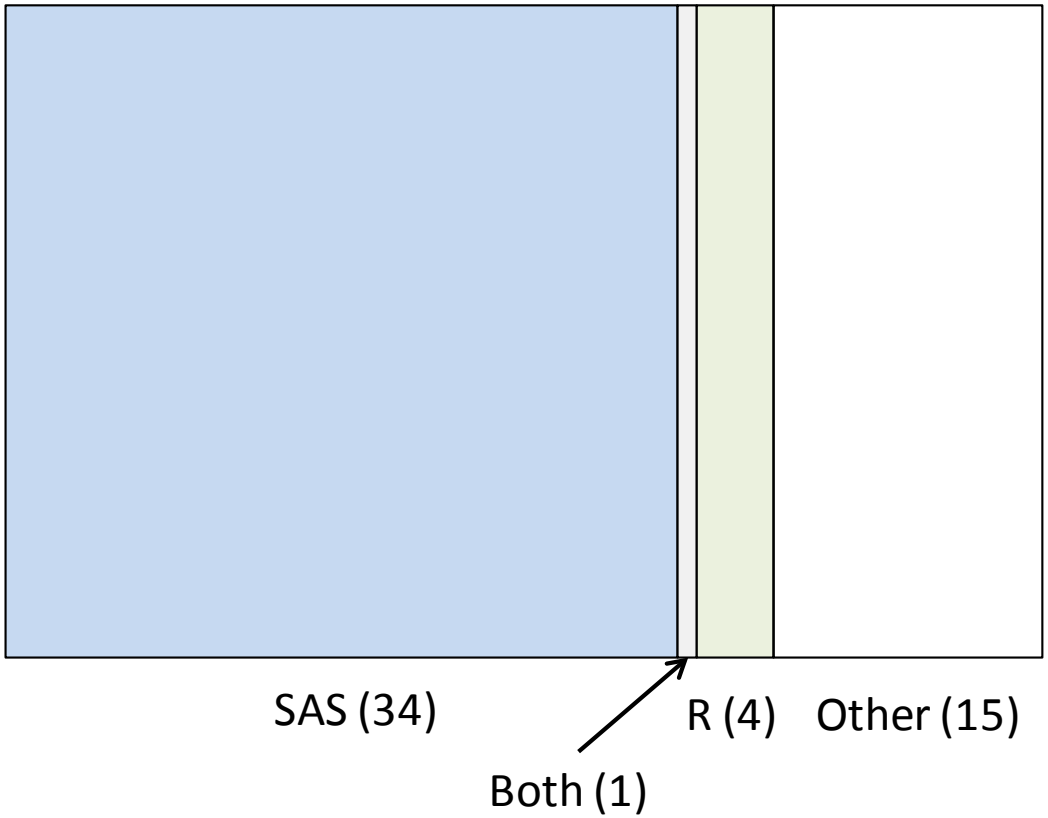
Link: [OpenFDA Analytic and Research Tools]

Trend 6: Slow (but accelerating) Industry Adoption



Link: State of the Octoverse (aka github)

> 60% of Articles from PhUSE 2016 focused on SAS



I reviewed 54 abstracts from PHUSE 2016 under “Applications and Software development”, “Coder’s Corner”, “Data Visualization”, “Coding Solutions”, “Industry Starters” and “Trends and Technology”

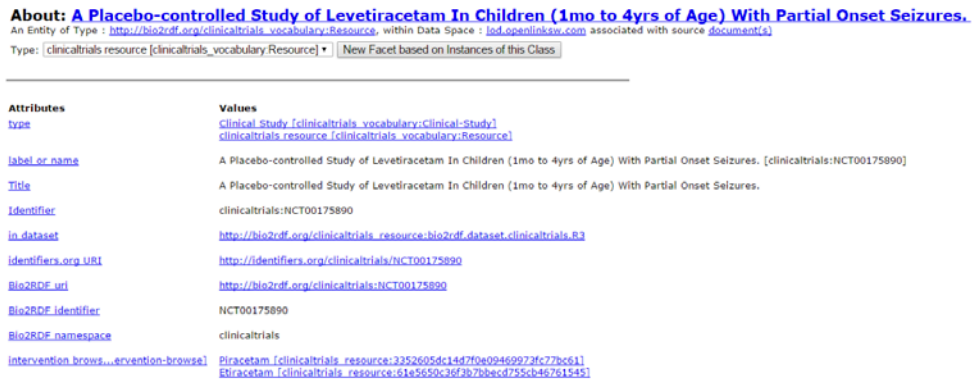
Link: PhUSE 2016 papers

Example 6 – Interactive Visualization of Linked Data (Tim Williams, UCB)

Paper DV06

Interactive Visualization of Linked Data

Tim Williams, UCB Biosciences Inc., Raleigh, USA



About: A Placebo-controlled Study of Levetiracetam In Children (1mo to 4yrs of Age) With Partial Onset Seizures.
An Entity of Type : http://bio2rdf.org/clinicaltrials_vocabulary:Resource, within Data Space : lod.openlinksw.com associated with source document(s)
Type: clinicaltrials resource [clinicaltrials_vocabulary:Resource] ▾ New Facet based on Instances of this Class

Attributes	Values
type	Clinical Study [clinicaltrials_vocabulary:Clinical-Study] clinicaltrials resource [clinicaltrials_vocabulary:Resource]
label or name	A Placebo-controlled Study of Levetiracetam In Children (1mo to 4yrs of Age) With Partial Onset Seizures. [clinicaltrials:NCT00175890]
Title	A Placebo-controlled Study of Levetiracetam In Children (1mo to 4yrs of Age) With Partial Onset Seizures.
Identifier	clinicaltrials:NCT00175890
in dataset	http://bio2rdf.org/clinicaltrials_resource:bio2rdf.dataset.clinicaltrials.R3
identifiers.org URI	http://identifiers.org/clinicaltrials/NCT00175890
Bio2RDF uri	http://bio2rdf.org/clinicaltrials:NCT00175890
Bio2RDF identifier	NCT00175890
Bio2RDF namespace	clinicaltrials
intervention brows...ervention-browse]	Piracetam [clinicaltrials_resource:3352605dc14d7f0e09469973fc77bc61] Etiracetam [clinicaltrials_resource:61e5650c36f3b7bbecd755cb467615451

Figure 7 Virtuoso faceted browser view of clinical trial information from ClinicalTrials.Gov, hosted on OpenLinkSW.

The network graph in **Figure 8** displays information about studies that contributed to two data pools used for submissions. Study phase and contribution are easily identified in the display, with drill-down to study information available by clicking on the study nodes. The legend is also interactive. A click on "Phase 1" opens a faceted browser view listing all Phase 1 studies. From there the user can follow the hyperlinked data to obtain details about each of Phase 1 study.

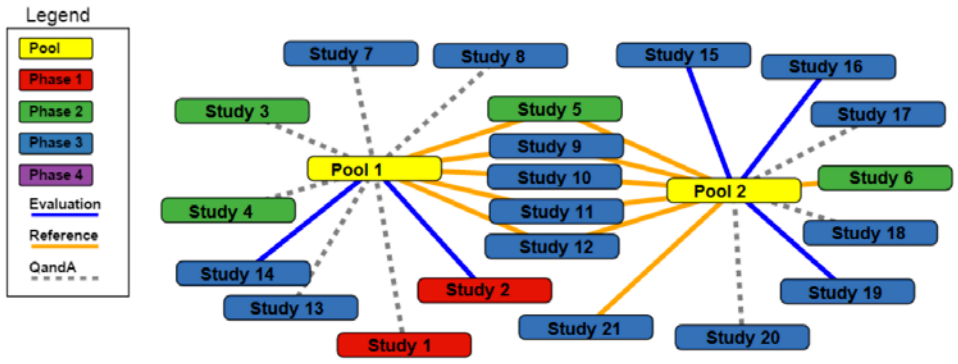
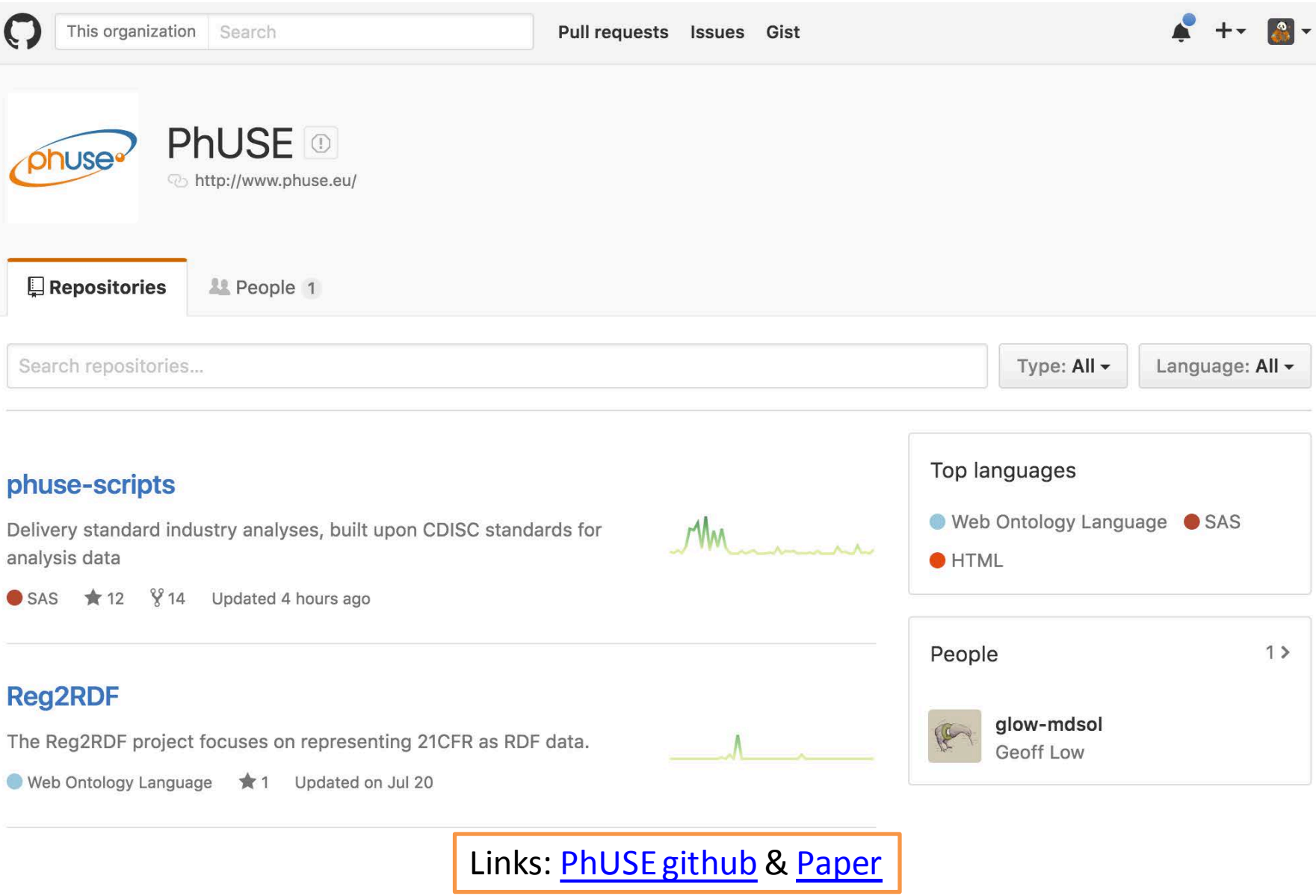


Figure 8 Force network graph showing studies that contribute to data pools.

Link: PhUSE Paper

Trend 7: Open Source and SAS



Links: [PhUSE github](#) & [Paper](#)

Rho Inc.

The contract research organization with unsurpassed expertise, integrity, and passion for clinical research.

Chapel Hill, NC http://graphics.rhoworl... graphics@rhoworld.com

Repositories People 27 Teams 11 Projects 0 Settings

Search repositories... Type: All Language: SAS Customize pinned repositories New

11 results for repositories written in **SAS** Clear filter

sas-violinPlot

Violin Plots in SAS

SAS 1 Updated 6 days ago

sas-snapshotCompare Private

Compare dataset-level, variable-level, and ID-level metadata with SAS

SAS Updated 8 days ago

sas-consort Private

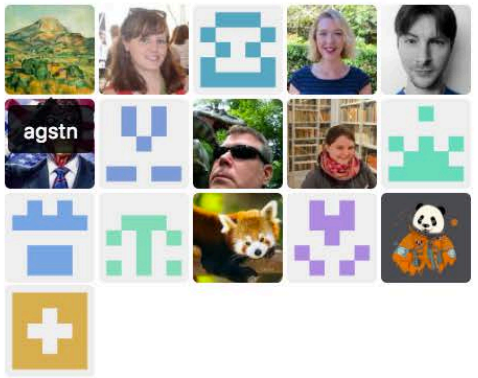
A SAS-based tool to aid in the production of CONSORT diagrams.

SAS Updated 9 days ago

Top languages

JavaScript SAS R HTML

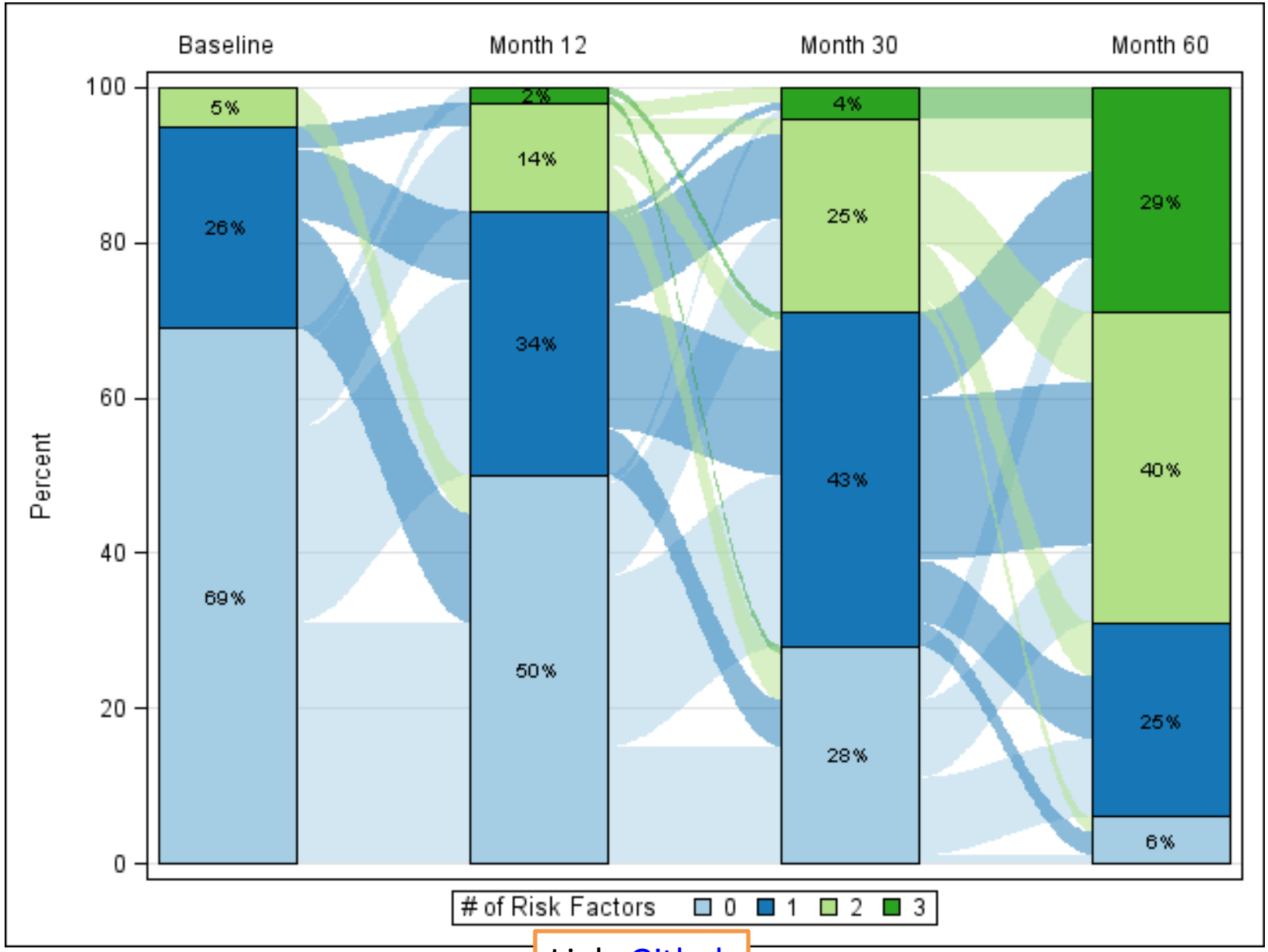
People 27 >



Invite someone

Link: Github

Example 7 – SAS Sankey Diagram Macro (Rho)



Link: [Github]

7 Trends Towards Open Source

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Open Source at Rho

Open source development reflects Rho's Core values. *A team culture*, *critical and creative thinking*, and *innovation* are at the heart of the open source philosophy. We demonstrate our *integrity* and *quality* by releasing the details of our process and allowing others to examine and enhance our work. The open source process encourages *agility and adaptability*, *profitability*, and *stability* by encouraging thorough documentation, reducing rework, and increasing the visibility of our work.

Link: Rho's Open Source Handbook

Guiding Principle

When possible, code should be made public.

Rho Inc.

The contract research organization with unsurpassed expertise, integrity, and passion for clinical research.

Chapel Hill, NC http://graphics.rhow... graphics@rhoworld.c...

Repositories People 1

Search repositories... Type: All Language: All

sas-sankeybarchart

A set of SAS macros for creating longitudinal bar charts with Sankey-style overlays.

SAS ★ 1 Updated 7 hours ago

sas-violinPlot

Violin Plots in SAS

SAS 1 Updated 6 days ago

Webcharts

Reusable, flexible, interactive charts with JavaScript

JavaScript ★ 9 1 Updated 7 days ago

open-source-handbook

Open Source Guidelines for Rho Inc.

1 Updated 7 days ago

Top languages

JavaScript SAS R

People 1 ›

qspencer
Quentin Spencer

Link: Rho Github

Software Sustainability Institute
Journal of open research software
Start Submission
Become a Reviewer

Software Metapapers

Webcharts – A Web-based Charting Library for Custom Interactive Data Visualization

Authors: Nathan Bryant, Jeremy Wildfire

Abstract

Webcharts is a JavaScript library built on top of D3.js that creates reusable, flexible, interactive charts that are highly customizable. Webcharts provides a method for creating commonly-used charts, including bar charts, scatterplots, and timelines, through a simple configuration scheme. Charts created with Webcharts allow users to dynamically manipulate chart data, appearance, and behavior both through callback functions and input elements that are tied to chart objects. This approach allows users to create reusable charts that range from simple static graphics to complex interactive data exploration tools with custom user interfaces, all using the same library.

Keywords: Data Visualization, Javascript, d3.js

Link: Journal of Open Research Software Manuscript

Speed Bumps

- New skills to master
- Integrating open source and commercial systems is complex
- Invites scrutiny … which can lead to work
- Rethinking benefits of proprietary work
- Regulatory environment is a work in progress