



University of California  
San Francisco

# Toward leveraging publicly accessible clinical trials data- sharing, dissemination, and repurposing

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Bakar Institute of Computational Health Sciences

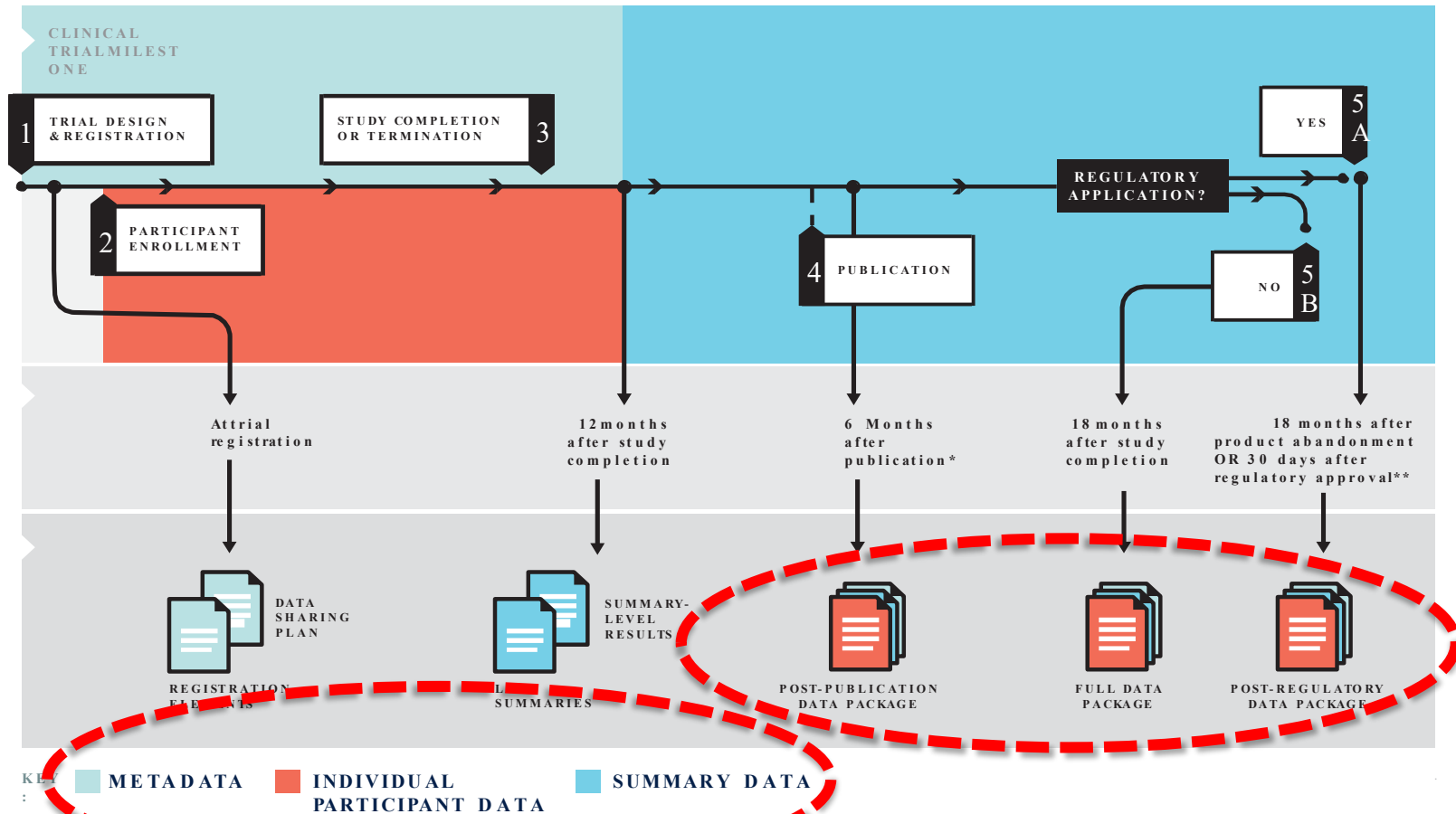
University of California, San Francisco

ASCPT, 03.16.2019



**IMMPORT**  
BIOINFORMATICS FOR THE FUTURE OF IMMUNOLOGY

# Clinical Trial Life Cycle: When to Share Data



Sharing Clinical Trial Data: Maximizing Benefits, Minimizing Risk.

<http://www.fda.gov/Reports/2015/>

# The Landscape of Clinical Trial Data Sharing Initiatives



Pharmaceutical  
Companies

Government Health  
Agencies

Non-Profit  
Organizations

NIH U.S. National Library of Medicine

*ClinicalTrials.gov*



# ImmPort.org

ImmPort data portal was developed to collect and share research and clinical trials data from NIAID/DAIT funded researchers



ImmPort is funded by the NIH, NIAID and DAIT in support of the NIH mission to share data with the public. Data shared through ImmPort has been provided by NIH-funded programs, other research organizations and individual scientists ensuring these discoveries will be the foundation of future research.

**Announcements**

February 28, 2018 - Scientific Data has published the new ImmPort paper: ImmPort, toward repurposing of open access immunological assay data for translational and clinical research.

March 4, 2018 - Atul Butte, ImmPort PI, will present "Systems Immunology: Public Health for the 21st Century" at the National Academies of Sciences, Engineering, and Medicine.



**Private Data**

Upload  
Validator  
Search/Download



**Shared Data**

Tutorials  
Gene Lists  
Search/Download



**Data Analysis**

Analysis Workflow  
Automated Clustering  
Tutorials



**Resources**

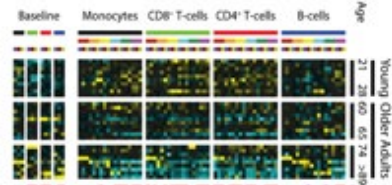
Documentation  
Publications  
Tutorials

Study: Defective signaling in aging

Chronic inflammation that occurs during immunosenescence shares biomarkers with cardiovascular disease however the causality of the two is unclear. This study investigated the invitro stimulation of peripheral blood for activation of the JAK-STAT pathway and compared this activation with measures of cardiovascular health. By longitudinally sampling patients over a range of ages, a cytokine response score was calculated from a panel of molecular measurements. This score was found to be associated with cardiovascular assessments and a predictor of cardiovascular health.

PubMed ID: 27746093 Study: SCY687

Summary



## FAIR Principles

Make your data:

- Findable
- Accessible
- Interoperable
- Reusable

**Findable**

- Descriptive metadata
- Persistent

**Accessible**

- Determining what to share
- Participant consent and risk management
- Access status

**Interoperable**

- XML standards
- Data Documentation Initiative
- CDISC

**Reusable**

- Rights and licence models
- Permitted and non-permitted use

<http://datafairport.org/>

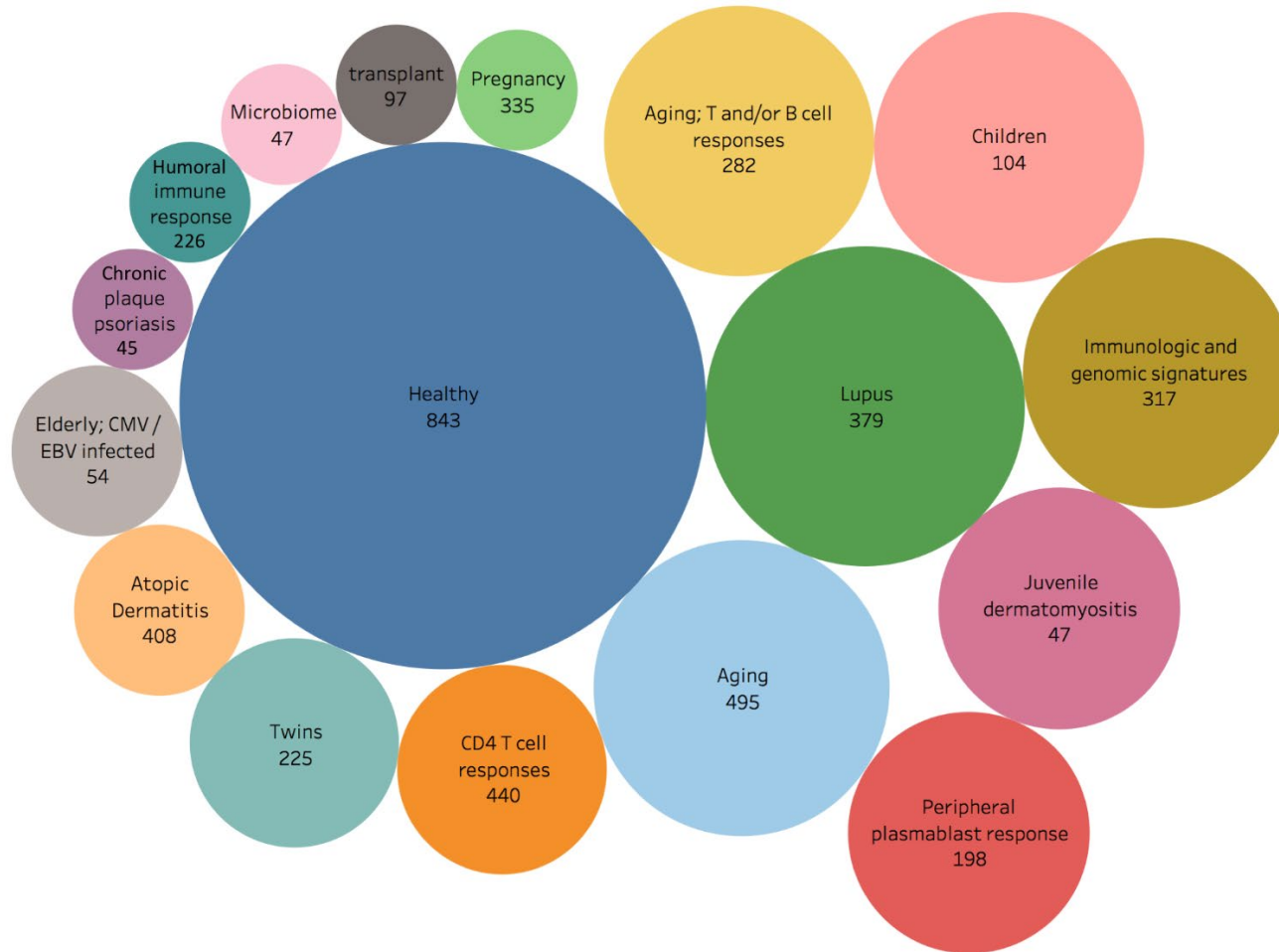
# ImmPort redistributes data from major NIAID-funded programs and more

Data from 300+ trials and studies already released, involving:

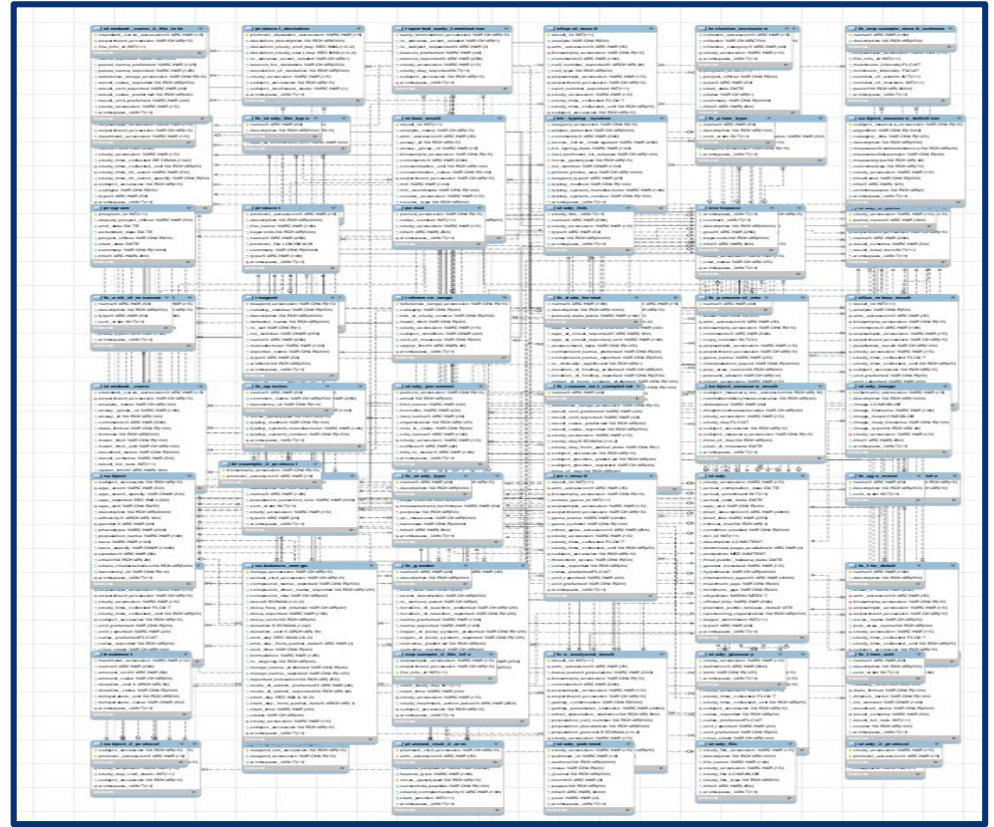
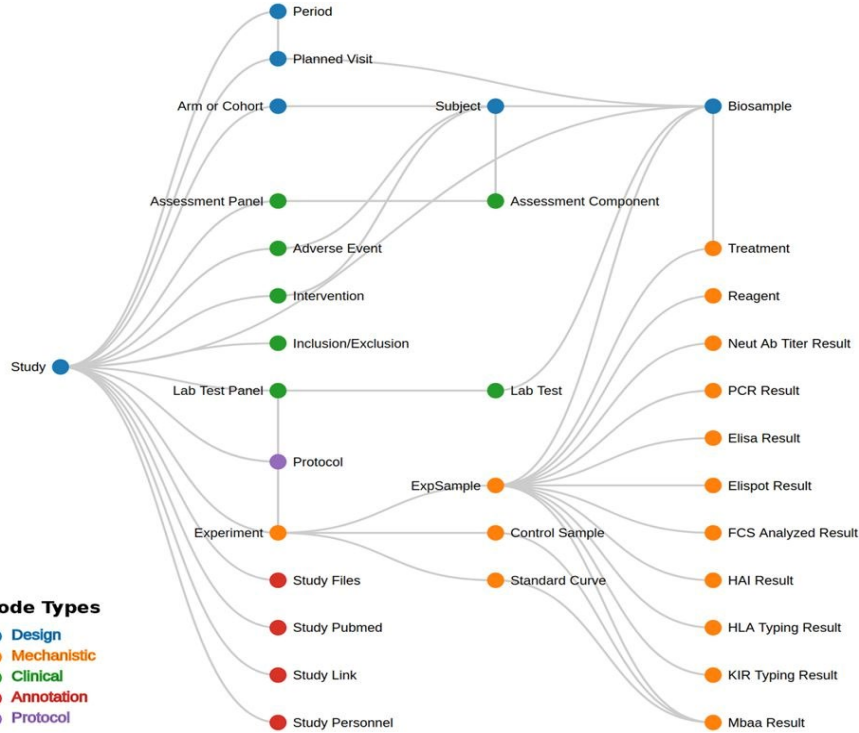
- **Human Immunology Project Consortium (HIPC)**
- **Accelerating Medicines Partnership (AMP) in Rheumatoid Arthritis and Lupus (AMP)**
- **National Cancer Institute, Oncology Models Forum**
- **March of Dimes: Preterm Birth Research**
- Immune Tolerance Network (ITN)
- Atopic Dermatitis Research Network (ADRN)
- Clinical Trials in Organ Transplantation (CTOT) and in Children (CTOT-C)
- Population Genetics Analysis Program
- Protective Immunity for Special Populations
- HLA Region Genomics in Immune-mediated Diseases
- Modeling Immunity for Biodefense
- Reagent Development for Innate Immune Receptors
- Adjuvant Development Program
- Immunity in Neonates and Infants  
Asthma and Allergic Diseases  
Cooperative Research Centers  
HLA and KIR Region Genomics in Immune-Mediated Diseases
- Cooperative Study Group for Autoimmune Disease Prevention
- Immunobiology of Xenotransplantation
- Centers for Medical Countermeasures against Radiation Consortium
- Inner City Asthma Consortium
- Systems Approach to Immunity and Inflammation
- Innate Immune Receptors and Adjuvant Discovery Program
- Maintenance of Macaque Specific Pathogen-Free Breeding Colonies
- Non-human Primate Transplantation Tolerance Cooperative Study Group
- Consortium for Food Allergy Research
- Development of Sample Sparing Assays for Monitoring Immune Responses (U24)



# Influenza Vaccination Studies in ImmPort

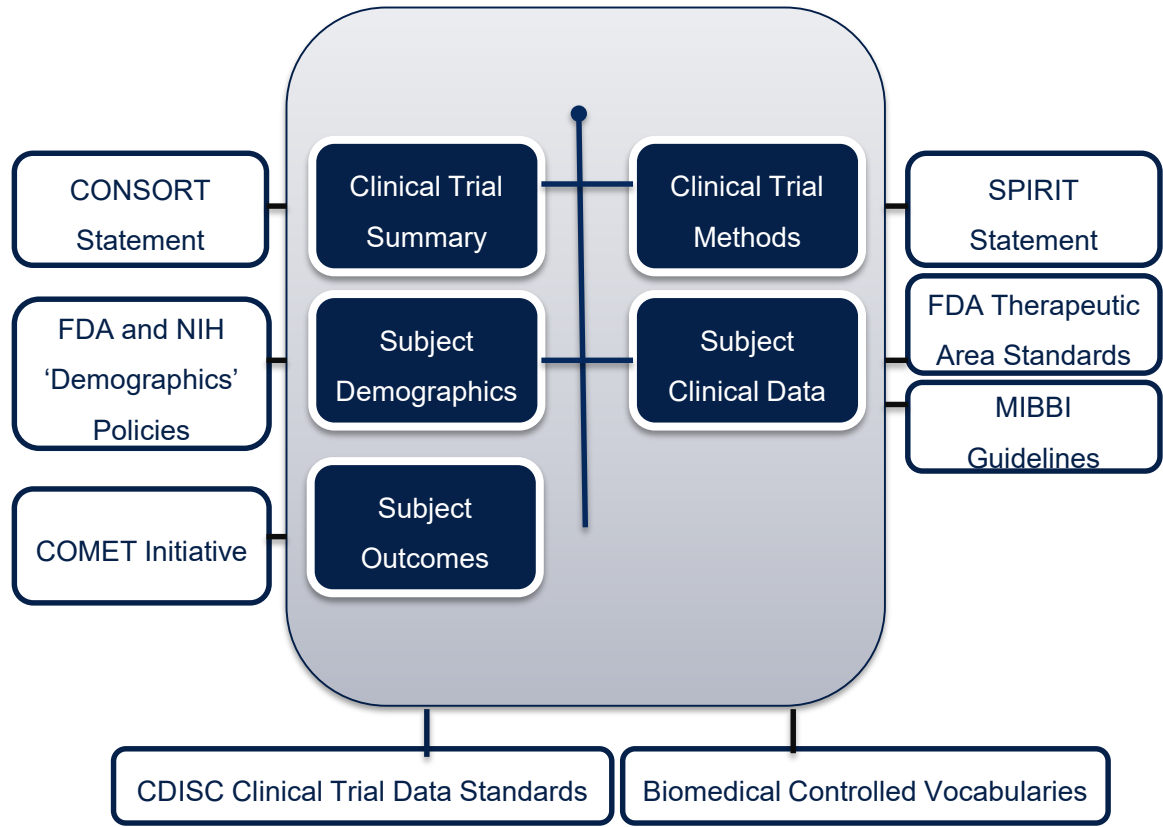


# Data Model





# Leveraging of existing minimum information guidelines and data standards

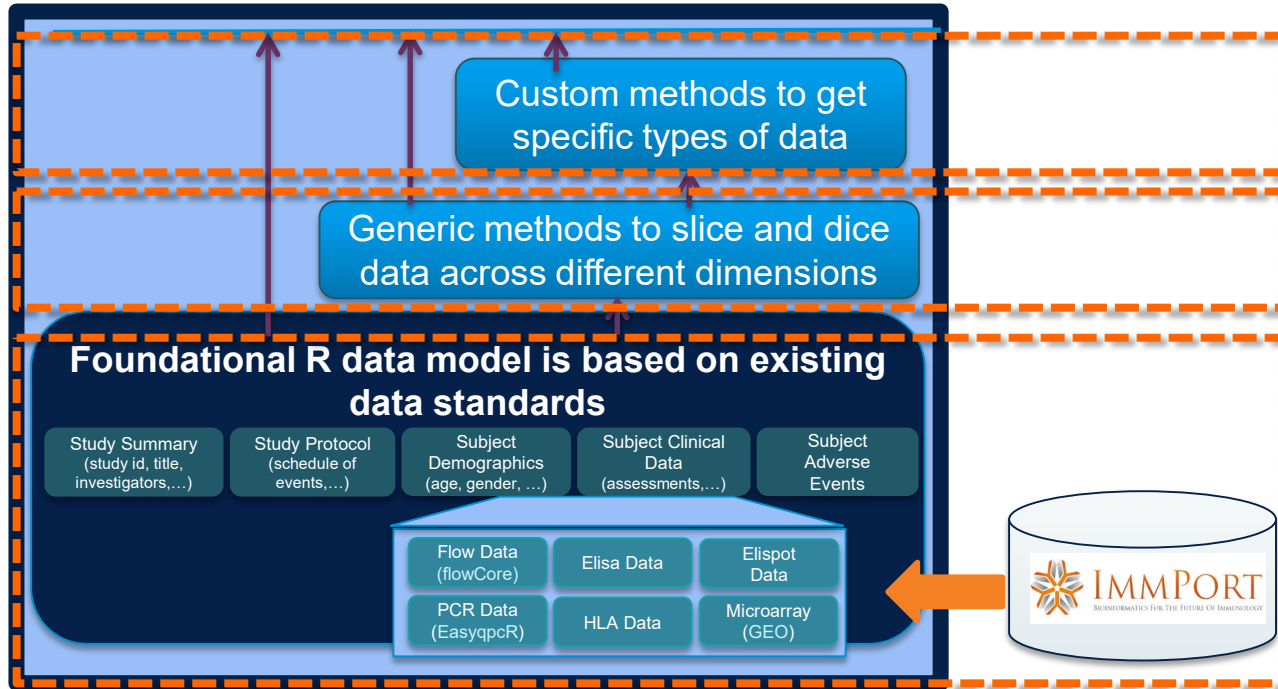


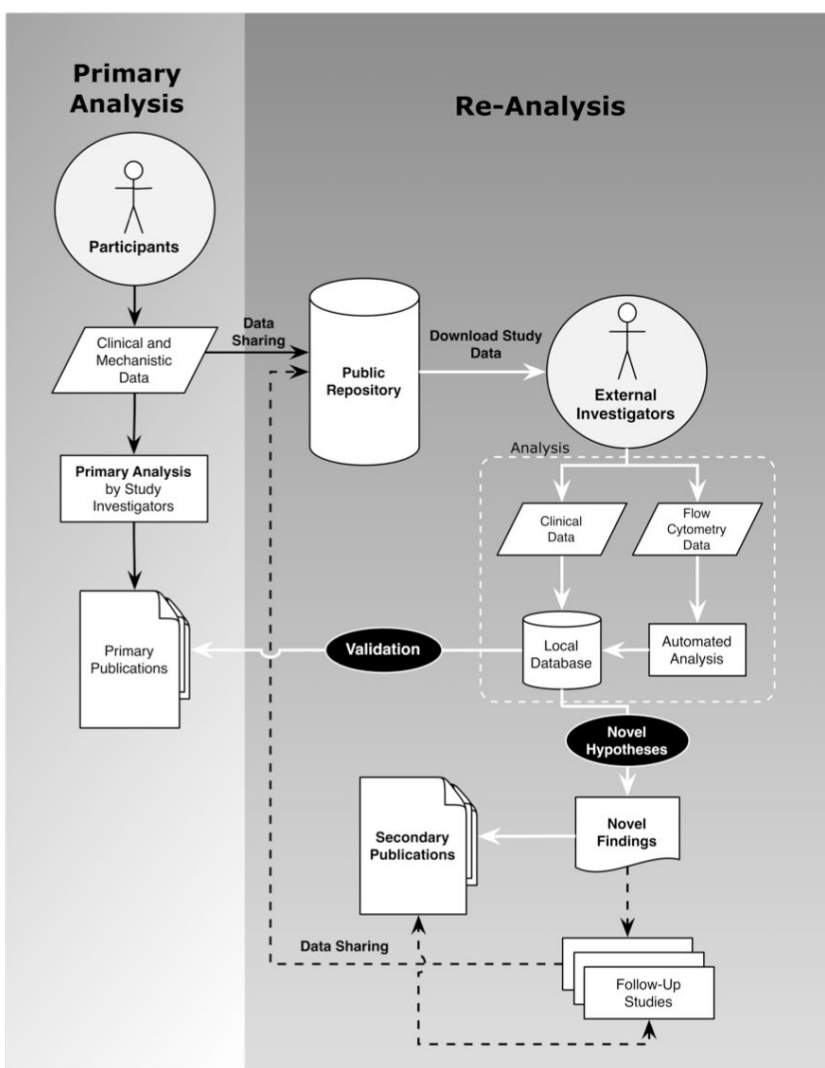
# Data Accessibility

```
sdy212 = getStudy('SDY212',...)
```



RImmPort  
package





**R**eproducibility  
**R**e-Analyze  
**R**epurpose

# RAVE Trial: Rituximab in ANCA-Associated Vasculitis

- 35% of patients treated with rituximab and 47% of patients treated with cyclophosphamide failed to achieve remission.
- **In retrospect, do any measured factors predict response to therapies?**

# Proposed Personalized Treatment on the Basis of Granularity Index

What data is publicly available?

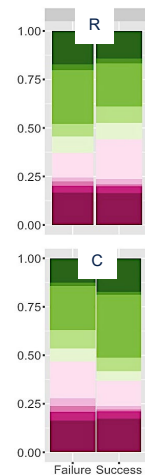
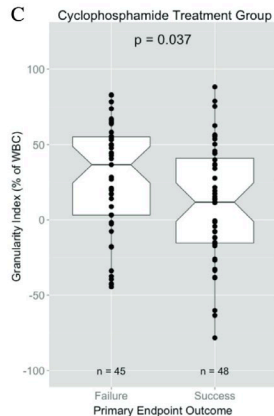
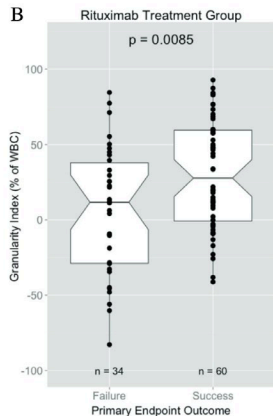
✓ Clinical Data from first 6 months

✓ Mechanistic Data

- Flow Cytometry data
- ANCA titers

Time Point	Visit	Month												Days 6 months after RIT	Outcome (Failure/Success)	
		1	2	3	4	5	6	7	8	9	10	11	12			
Baseline	1	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Week 1	2	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Week 2	3	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Week 3	4	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Week 4	5	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Week 5	6	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Week 6	7	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Week 7	8	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Week 8	9	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Week 9	10	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Week 10	11	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Week 11	12	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Week 12	13	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Week 13	14	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Week 14	15	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Week 15	16	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Week 16	17	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Week 17	18	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Week 18	19	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Week 19	20	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Week 20	21	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Week 21	22	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Week 22	23	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Week 23	24	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Week 24	25	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Week 25	26	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Week 26	27	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Week 27	28	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Week 28	29	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Week 29	30	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Week 30	31	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Week 31	32	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Week 32	33	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Week 33	34	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Week 34	35	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Week 35	36	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Week 36	37	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Week 37	38	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Week 38	39	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Week 39	40	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Week 40	41	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Week 41	42	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Week 42	43	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Week 43	44	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Week 44	45	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Week 45	46	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Week 46	47	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Week 47	48	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Week 48	49	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Week 49	50	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Week 50	51	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Week 51	52	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Week 52	53	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Week 53	54	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Week 54	55	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Week 55	56	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Week 56	57	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Week 57	58	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Week 58	59	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Week 59	60	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Week 60	61	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Week 61	62	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Week 62	63	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Week 63	64	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Week 64	65	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Week 65	66	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Week 66	67	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Week 67	68	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Week 68	69	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Week 69	70	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Week 70	71	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Week 71	72	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Week 72	73	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Week 73	74	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Week 74	75	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Week 75	76	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Week 76	77	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Week 77	78	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Week 78	79	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Week 79	80	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Week 80	81	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Week 81	82	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Week 82	83	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Week 83	84	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Week 84	85	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Week 85	86	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Week 86	87	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Week 87	88	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Week 88	89	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Week 89	90	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Week 90	91	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Week 91	92	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Week 92	93	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Week 93	94	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Week 94	95	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Week 95	96	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Week 96	97	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Week 97	98	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Week 98	99	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Week 99	100	X	X	X	X	X	X	X	X	X	X	X	X	X	X	

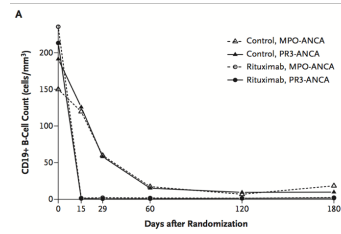
(Open Arthritis Journal, Specks et al., 2011)



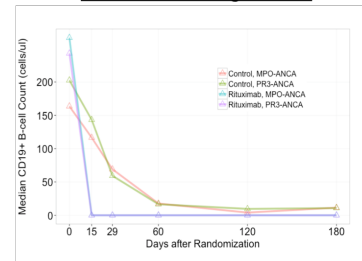
- Subset**
- Lymphocytes
  - Monocytes
  - FSClo Granulocytes
  - FSCloSSClo Granulocytes
  - FSCloSSC+ Granulocytes
  - FSCloSSChi Granulocytes
  - FSC+SSC+ Granulocytes
  - FSCiSSC+ Granulocytes
  - FSCiSSChi Granulocytes

## Manual Gating Results

NEJM, 2010 Stone et al.

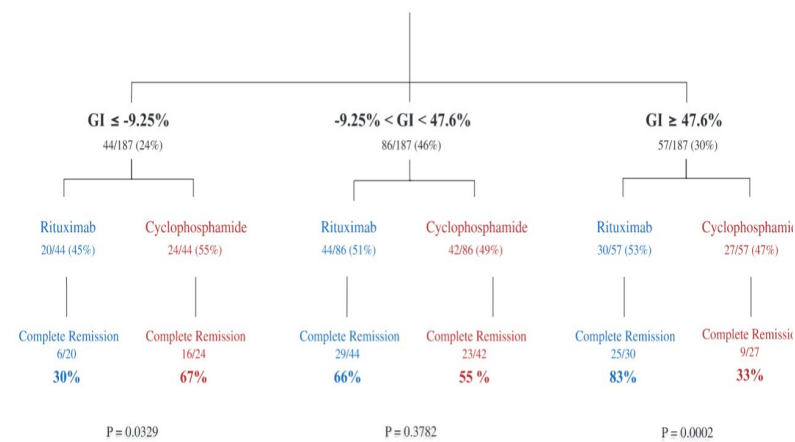


## Automated Gating Results



**A**

187 subjects\*



# Proposed Personalized Treatment on the Basis of Granularity Index

Nasrallah et al. *Arthritis Research & Therapy* (2015) 17:262  
DOI 10.1186/s13075-015-0778-z



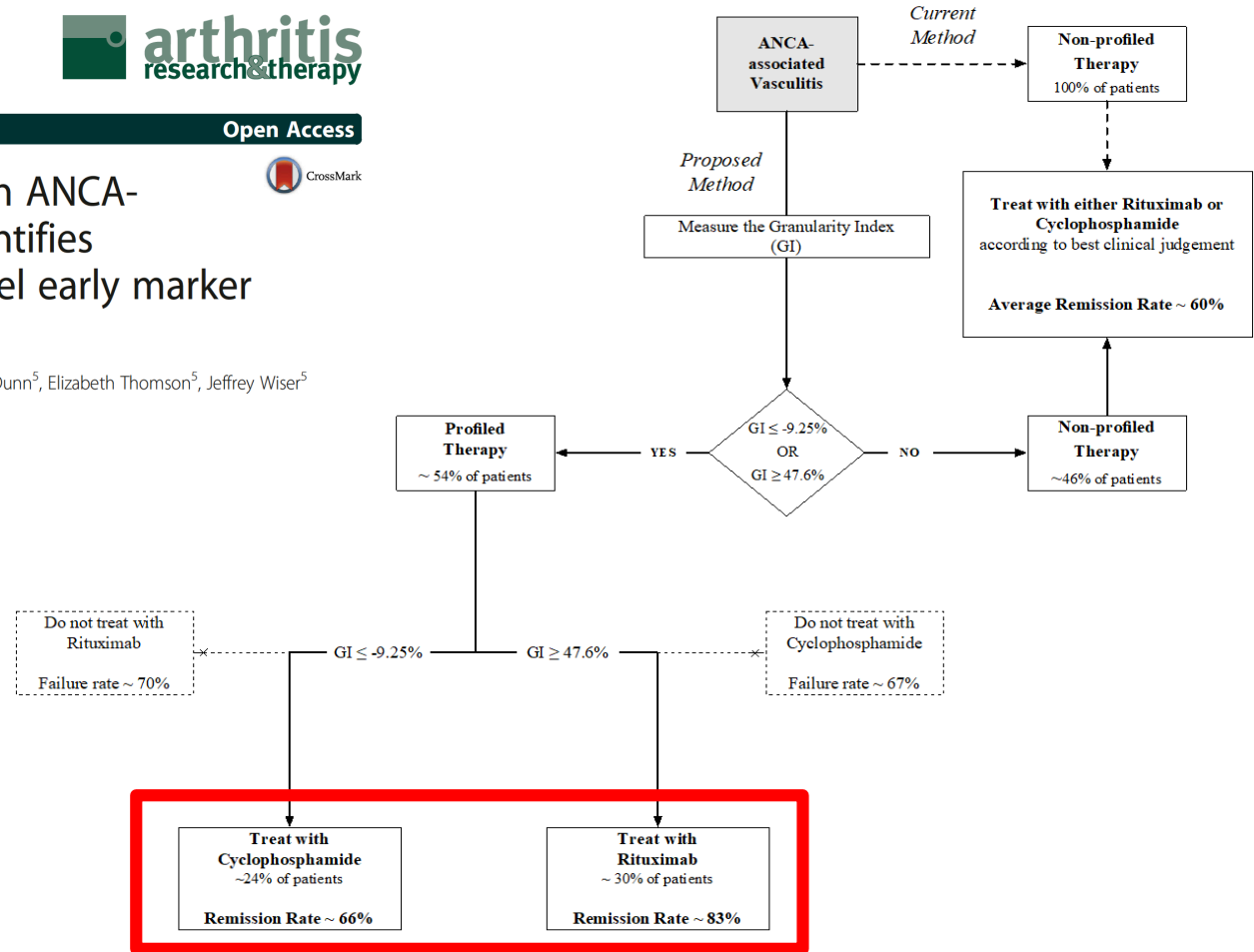
RESEARCH ARTICLE

Open Access



## Reanalysis of the Rituximab in ANCA-Associated Vasculitis trial identifies granulocyte subsets as a novel early marker of successful treatment

Mazen Nasrallah<sup>1,2,3,4</sup>, Yannick Pouliot<sup>3</sup>, Bjoern Hartmann<sup>4</sup>, Patrick Dunn<sup>5</sup>, Elizabeth Thomson<sup>5</sup>, Jeffrey Wiser<sup>5</sup> and Atul J. Butte<sup>1\*</sup>





## Manual curation of studies, arms, and planned visits to filter for normal human subjects

Resource

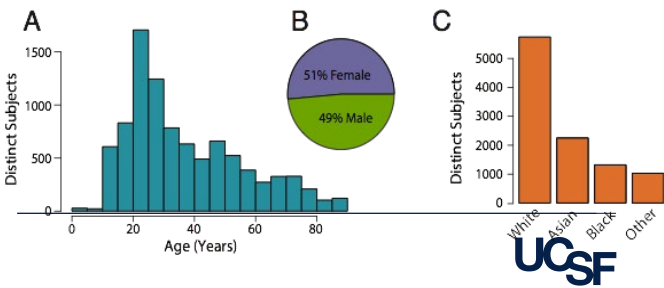
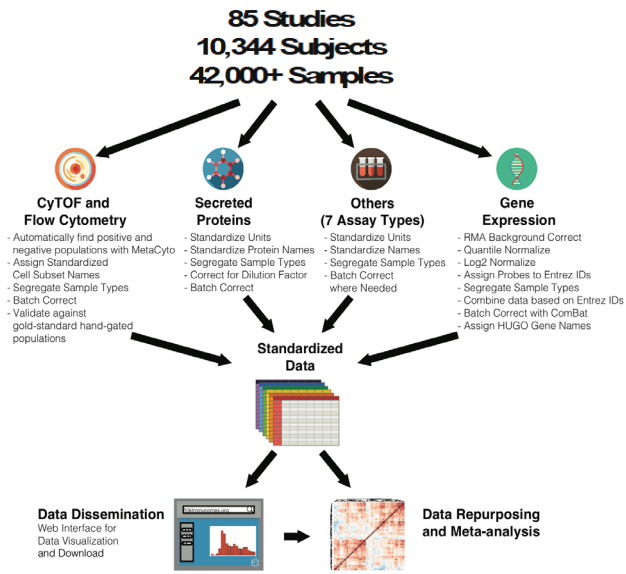
### The 10,000 Immunomes Project: Building a Resource for Human Immunology

Kelly A. Zalocusky<sup>1, 2</sup>, Matthew J. Kan<sup>1, 2</sup>, Zicheng Hu<sup>1, 2</sup>, Patrick Dunn<sup>3</sup>, Elizabeth Thomson<sup>3</sup>, Jeffrey Wiser<sup>3</sup>, Sanchita Bhattacharya<sup>1, 2, 4</sup>, Atul J. Butte<sup>1, 2, 4, 5</sup>

## 10kimmunomes.org

#### Data available in the 10,000 Immunomes Project

<b>Total Samples</b>	<b>42117</b>
<b>Total Distinct Subjects</b>	<b>10344</b>
<hr/>	
<b>MEASUREMENT</b>	<b>SUBJECTS</b>
<u>Secreted Proteins</u>	4835
<i>ELISA</i>	4035
<i>Multiplex ELISA</i>	1286
<u>Virus Titer</u>	3609
<i>Virus Neutralization Titer</i>	2265
<i>HAI Titer</i>	1344
<u>Clinical Lab Tests</u>	2639
<i>Complete Blood Count</i>	1684
<i>Comprehensive Metabolic Panel</i>	664
<i>Fasting Lipid Profile</i>	664
<u>Questionnaire</u>	1422
<u>Cytometry</u>	1415
<i>Flow Cytometry (PBMC)</i>	907
<i>CyTOF (PBMC)</i>	583
<i>Flow Cytometry (Whole Blood)</i>	164
<u>HLA Type</u>	1093
<u>Gene Expression Array</u>	476
<i>Whole Blood</i>	311
<i>PBMC</i>	165



# immTransplant: Visualizing Open-Access Living Donor Transplant Data



**Study Curation:**

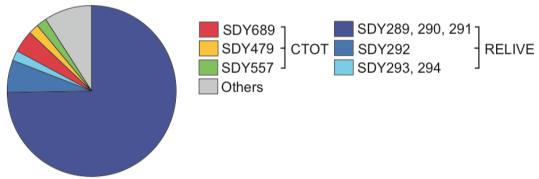
- clinical trials that excluded or have insufficient living donation information

20 Curated clinical trials

**Subject Curation:**

- deceased donors
- living donors with >95% missing data

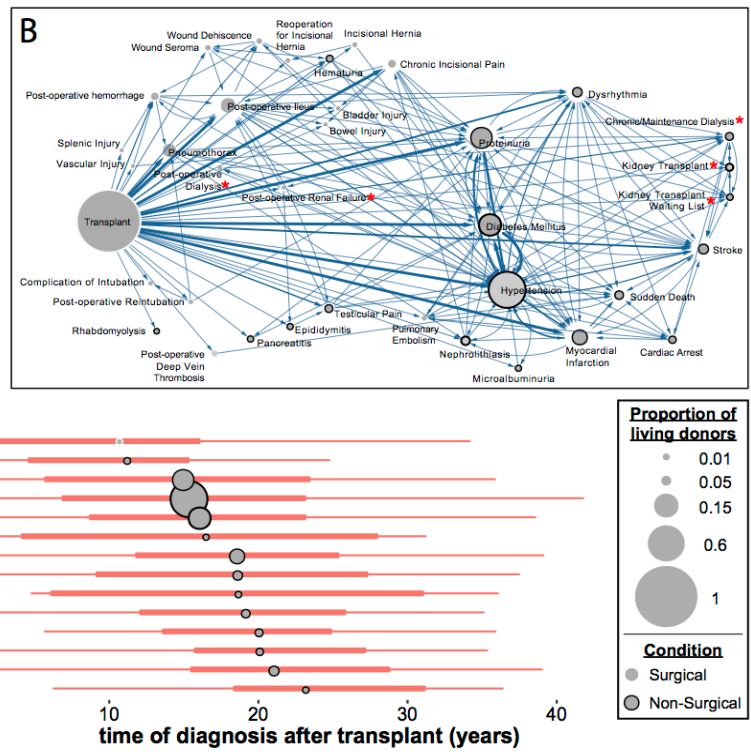
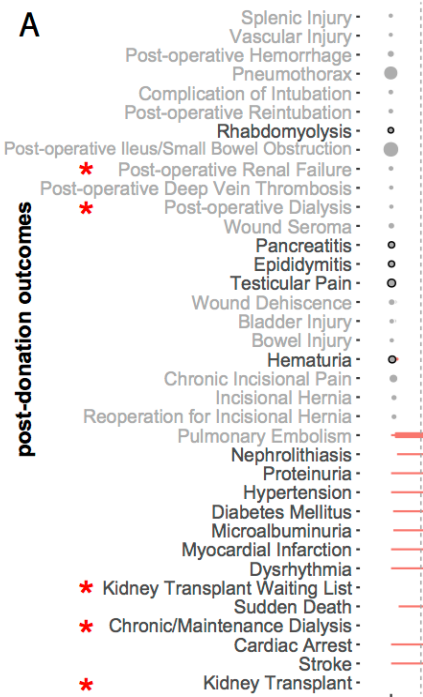
11,263 Subjects



**Data Curation:**

- Data compilation
- Data standardization

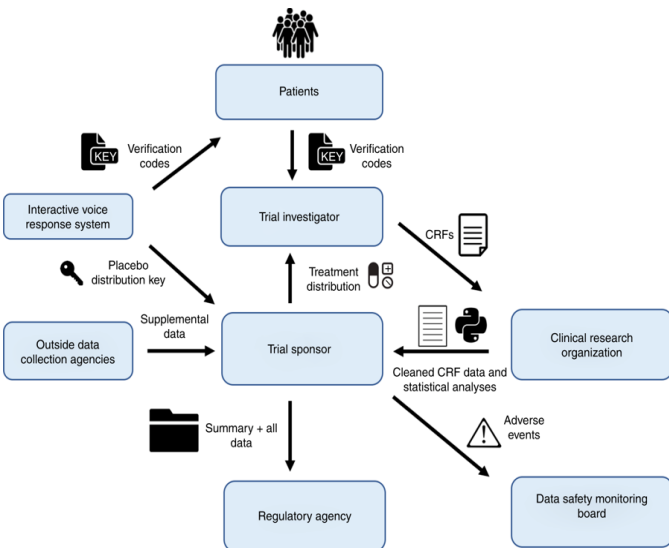
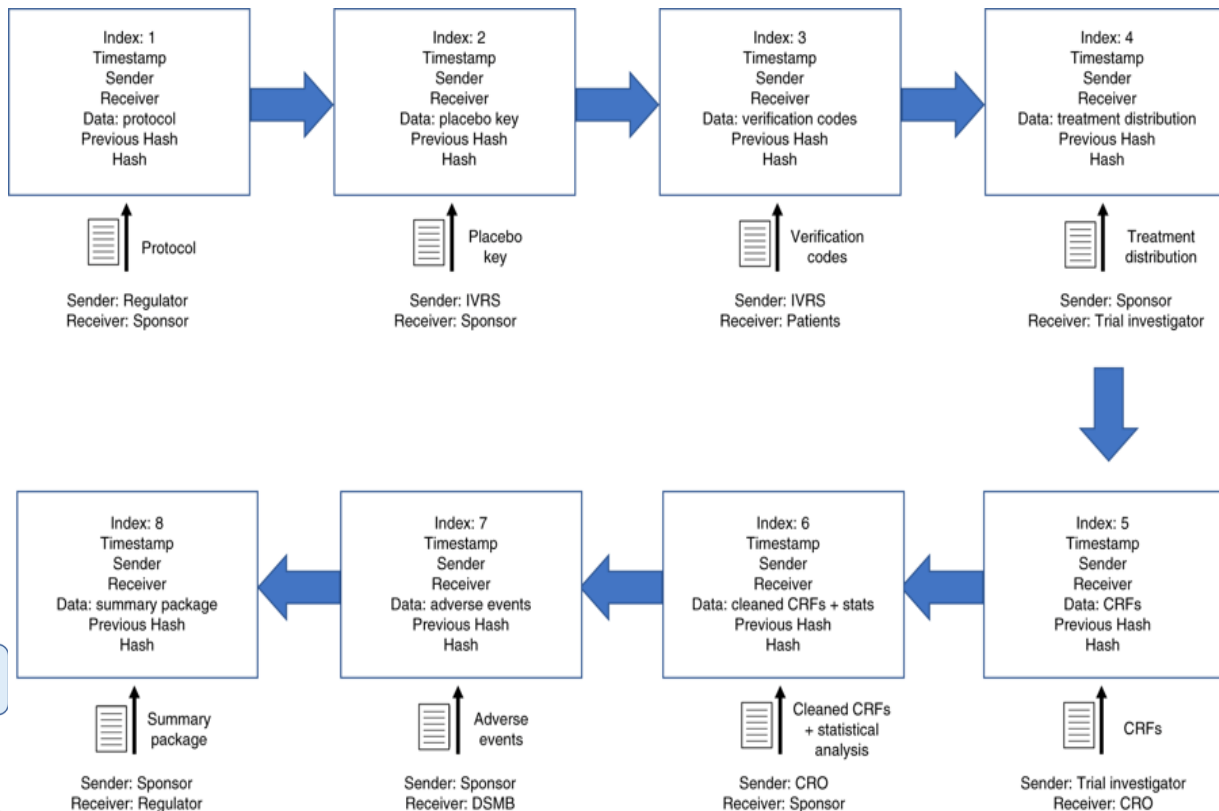
Curated Data





# Prototype of running clinical trials in an untrustworthy environment using blockchain

Daniel R. Wong, Sanchita Bhattacharya & Atul J. Butte



# Take Home Messages

- Holistic approach to analyzing clinical trials data
- Open-access clinical trials are a valuable resource to evaluate new hypotheses, gain novel insights, and inform a better trial design
- Minimum information requirements will be the data format standard for interoperability.
- 10Kimmunomes- reference dataset generated by integrating individual level data from publicly available immunology studies

**Embrace open-access clinical trials!**

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Mazen Nassrallah

Ravi Shankar

## Northrop Grumman Health Solutions

Elizabeth Thomson

Patrick Dunn

Henry Schaefer

John Campbell

Morgan Crafts

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Infectious Diseases (NIAID)

National Institutes of Health (NIH)  
Health and Human Services (HHS)

Contract #: HHSN316201200036W

## Data Providers

Thanks!

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 @sanchitab