Diversity and determinants of the immune response to SARS-CoV-2 in immunocompromised populations

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Frederick National Laboratory Advisory Committee
June 27, 2022

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Frederick National Laboratory for Cancer Research

Serological Sciences Network

Capacity Building Centers

- Arizona State University (Tempe, AZ)
- Feinstein Institute for Medical Research (Manhasset, NY)
- University of Minnesota (Minneapolis, MN)
- Icahn School of Medicine at Mount Sinai (New York, NY)

Centers of Excellence

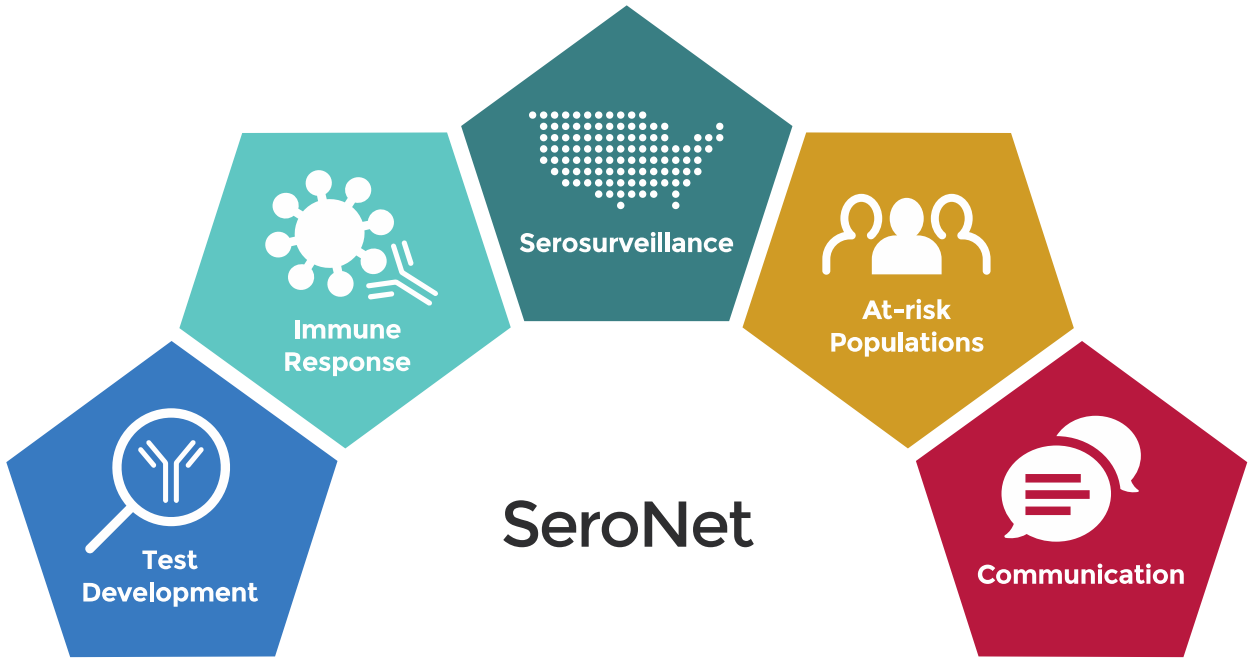
- Ohio State University
- UNC-Chapel Hill
- Cedars-Sinai Medical Center
- Johns Hopkins University
- Tulane University
- Stanford University
- Emory University
- Icahn School of Medicine at Mount Sinai

Research Projects

- Wadsworth Center
- Beth Israel Deaconess Medical Center
- Case Western Reserve University
- Kaiser Foundation Research Institute
- Yale University
- Michigan State University
- University of Arkansas for Medical Sciences
- La Jolla Institute for Immunology
- University of Puerto Rico, Medical Sciences
- University of Alabama at Birmingham
- University of Massachusetts Medical School Worcester
- Harvard School of Public Health

Serological Sciences Network for COVID-19 (SeroNet)

Supports a broad range of serological sciences research to advance our understanding of all aspects of the immune response to SARS-CoV-2



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Figueiredo et al. Open Forum Infect Dis 2022; Karger et al. mSphere 2022

Immunocompromised populations

Individuals with medical conditions or receiving treatments that are associated with altered immune states (~ 7 million)

- Active or recent treatment for solid tumors and hematologic malignancies, receipt of solid-organ or recent hematopoietic stem cell transplant, severe primary immunodeficiency, advanced or untreated HIV, treatment with immunosuppressive or immunomodulatory agents

Higher risk for:

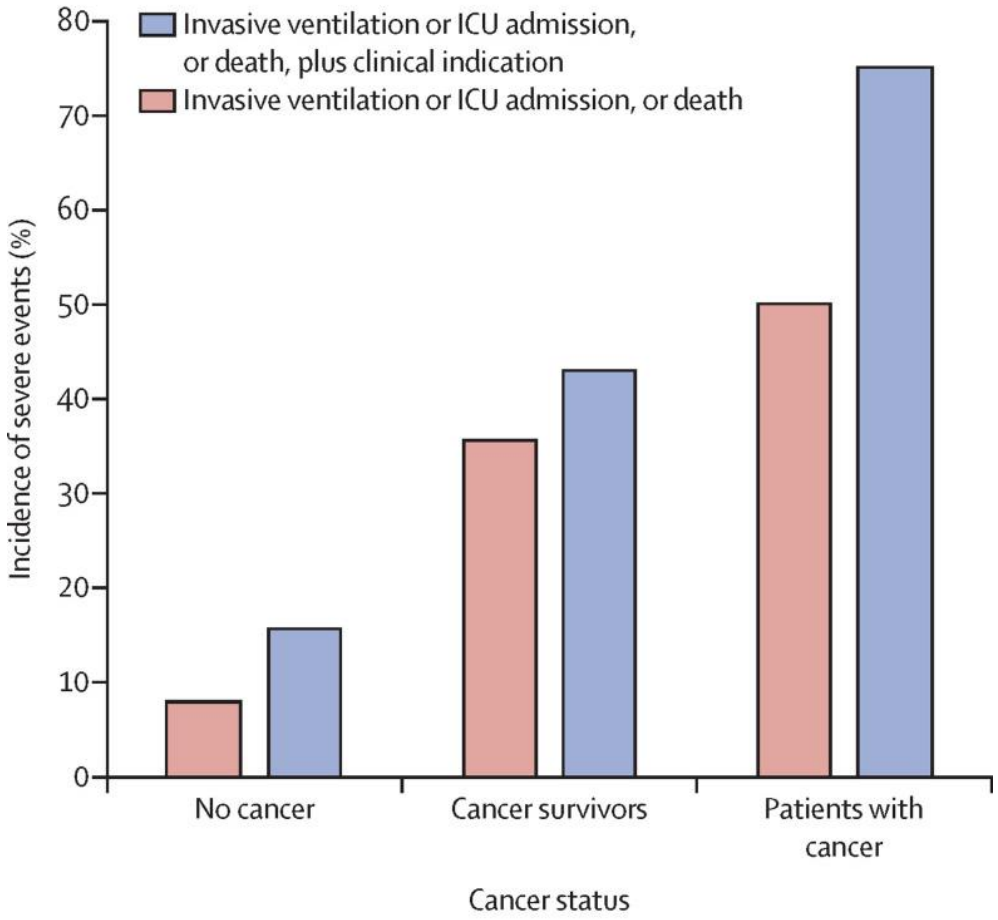
- Prolonged SARS-CoV-2 infection and shedding
- Severe COVID-19 outcomes
- Viral evolution during infection and treatment
- Transmission to household contacts

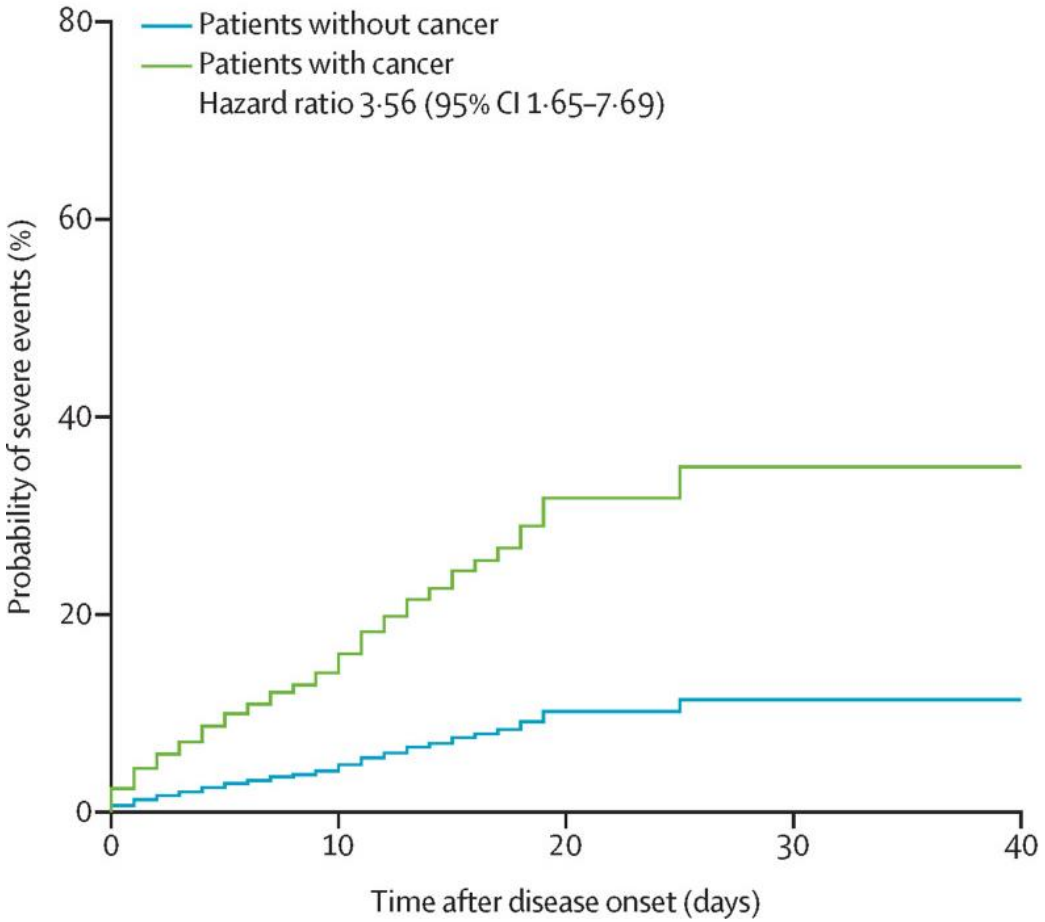
Opportunity to expand knowledge on underlying biology

Remain vulnerable as the pandemic evolves

Williamson et al. Nature 2020; Harpaz et al. JAMA 2016; Baang et al. JID 2021; Lewis et al. CID 2020

Cancer patients and SARS-CoV-2 infection: a nationwide analysis in China





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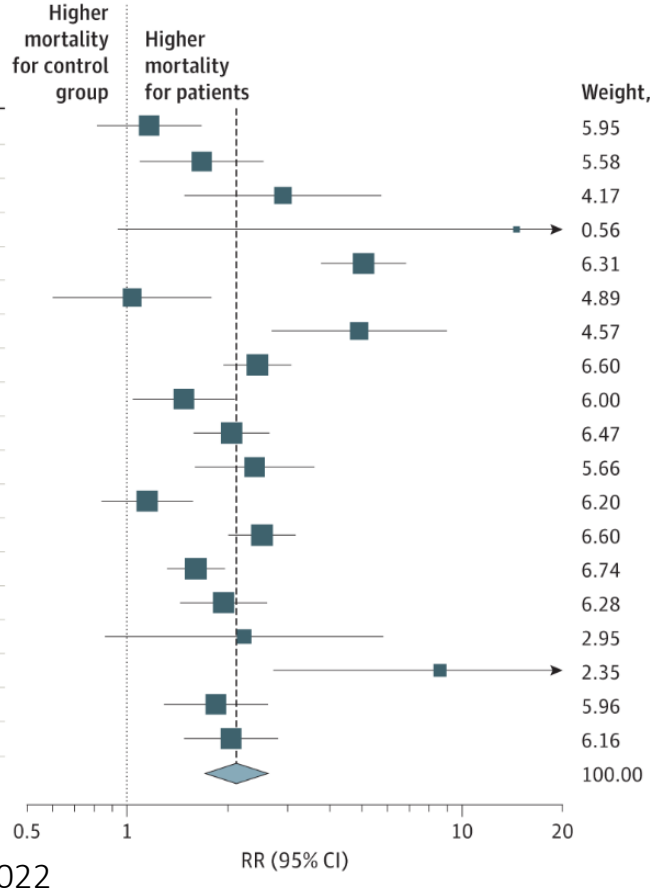
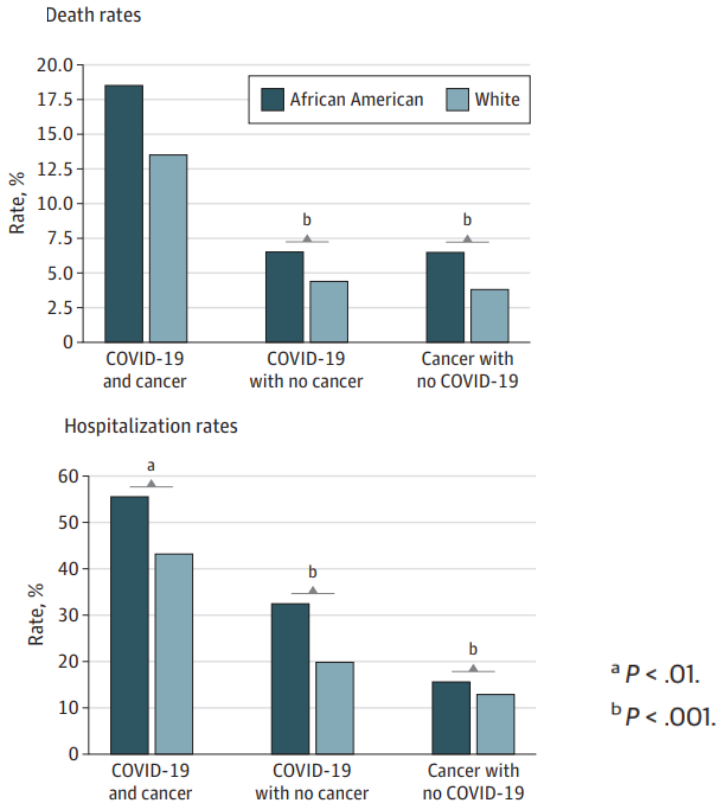
Liang et al. Lancet Oncol. 2020 Mar; 21(3): 335–337

Consistent evidence of greater risk of mortality among cancer patients and ethnic/racial disparities

Study	RR (95% CI)	Weight, %
Brar et al,[19] 2020	1.16 (0.81-1.66)	5.95
Cattaneo et al,[40] 2020	1.67 (1.09-2.55)	5.58
Dai et al,[21] 2020	2.92 (1.48-5.74)	4.17
He et al,[43] 2020	14.57 (0.94-227.02)	0.56
Johannesen et al,[36] 2021	5.08 (3.79-6.81)	6.31
Joharatnam-Hogan et al,[45] 2020	1.03 (0.60-1.78)	4.89
Liang et al,[26] 2020	4.93 (2.70-9.01)	4.57
Lunski et al,[44] 2021	2.45 (1.94-3.09)	6.60
Martínez-López et al,[18] 2020	1.47 (1.04-2.09)	6.00
Mehta et al,[16] 2020	2.05 (1.58-2.65)	6.47
Meng et al,[39] 2020	2.40 (1.59-3.62)	5.66
Miyashita et al,[12] 2020	1.14 (0.84-1.57)	6.20
Montopoli et al,[38] 2020	2.53 (2.00-3.18)	6.60
Rüthrich et al,[37] 2021	1.60 (1.31-1.96)	6.74
Shah et al,[23] 2020	1.94 (1.44-2.61)	6.28
Stroppa et al,[42] 2020	2.23 (0.86-5.82)	2.95
Sun et al,[41] 2021	8.60 (2.73-27.06)	2.35
Tian et al,[14] 2020	1.84 (1.28-2.63)	5.96
Yigenoglu et al,[29] 2021	2.04 (1.48-2.82)	6.16
REML overall (I^2=84.4%)	2.12 (1.71-2.62)	100.00



Khoury et al. JAMA Netw Open 2022



[a] $P < .01$.
[b] $P < .001$.

Wang et al. JAMA Oncol. 2021

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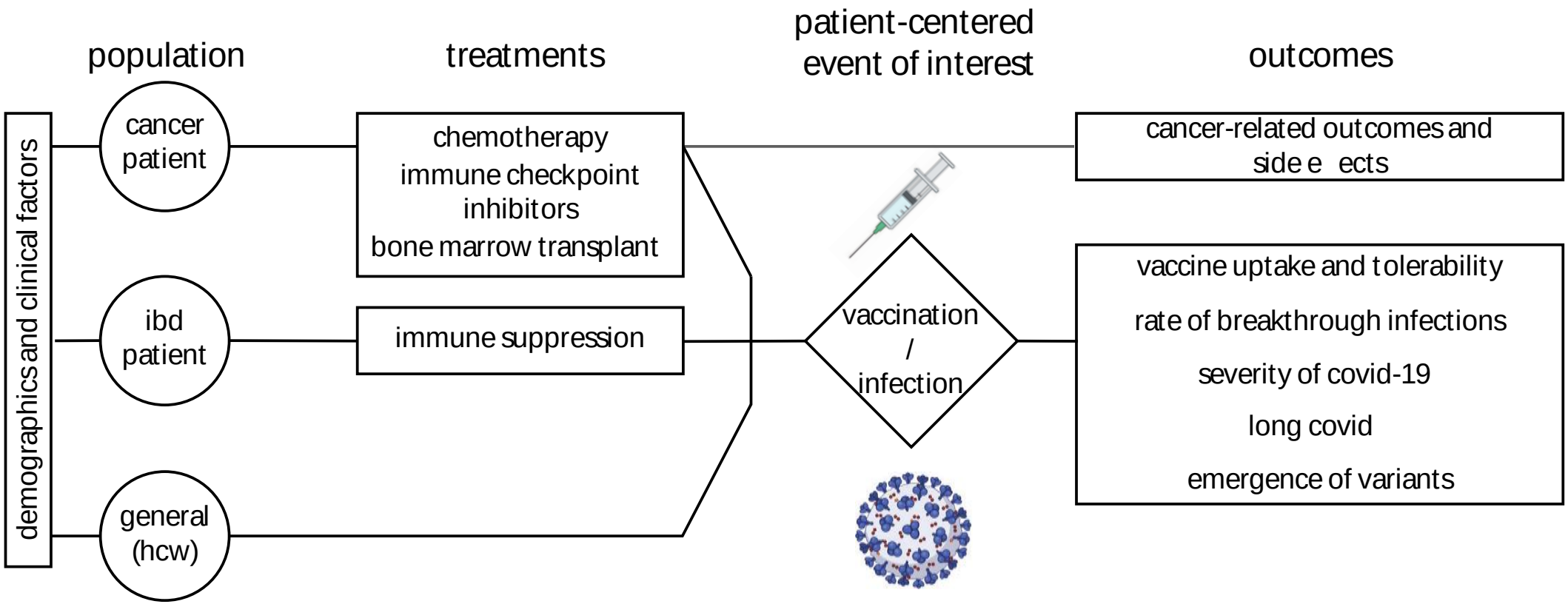
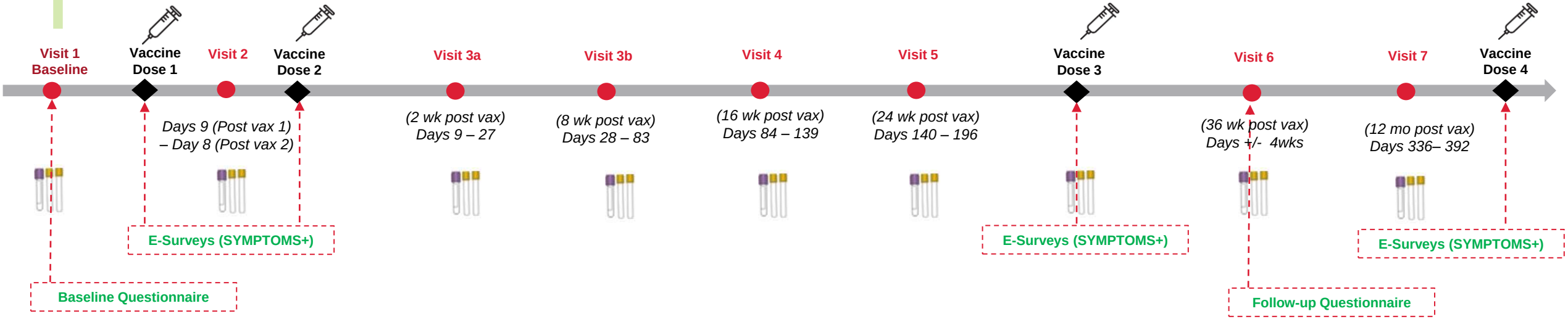
Diversity and Determinants of the Immune-Inflammatory Response to SARS-CoV-2



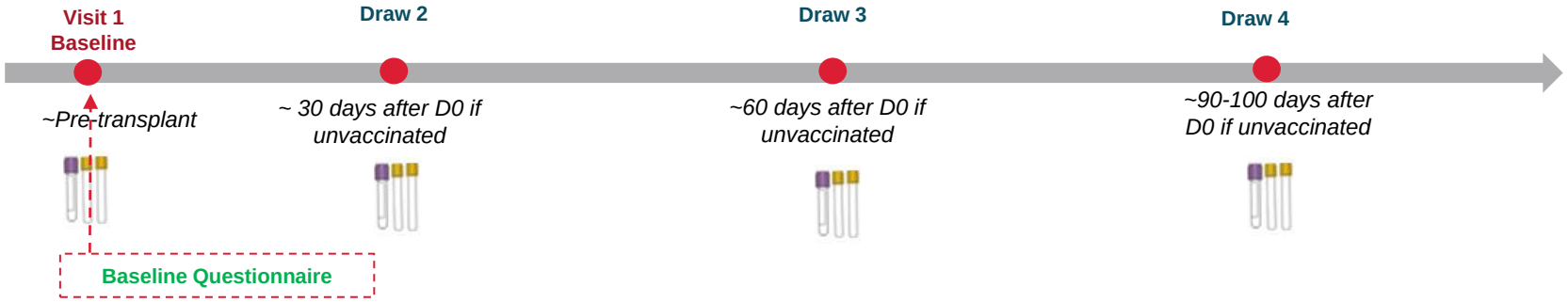
Cancer Cohort

DATA COLLECTION & INTEGRATION

- *ServiceNow, CS-Link, LabVantage, RedCap, OnCore, etc.*
- *Continued EHR surveillance for all health encounters*



HSC Transplant Patients



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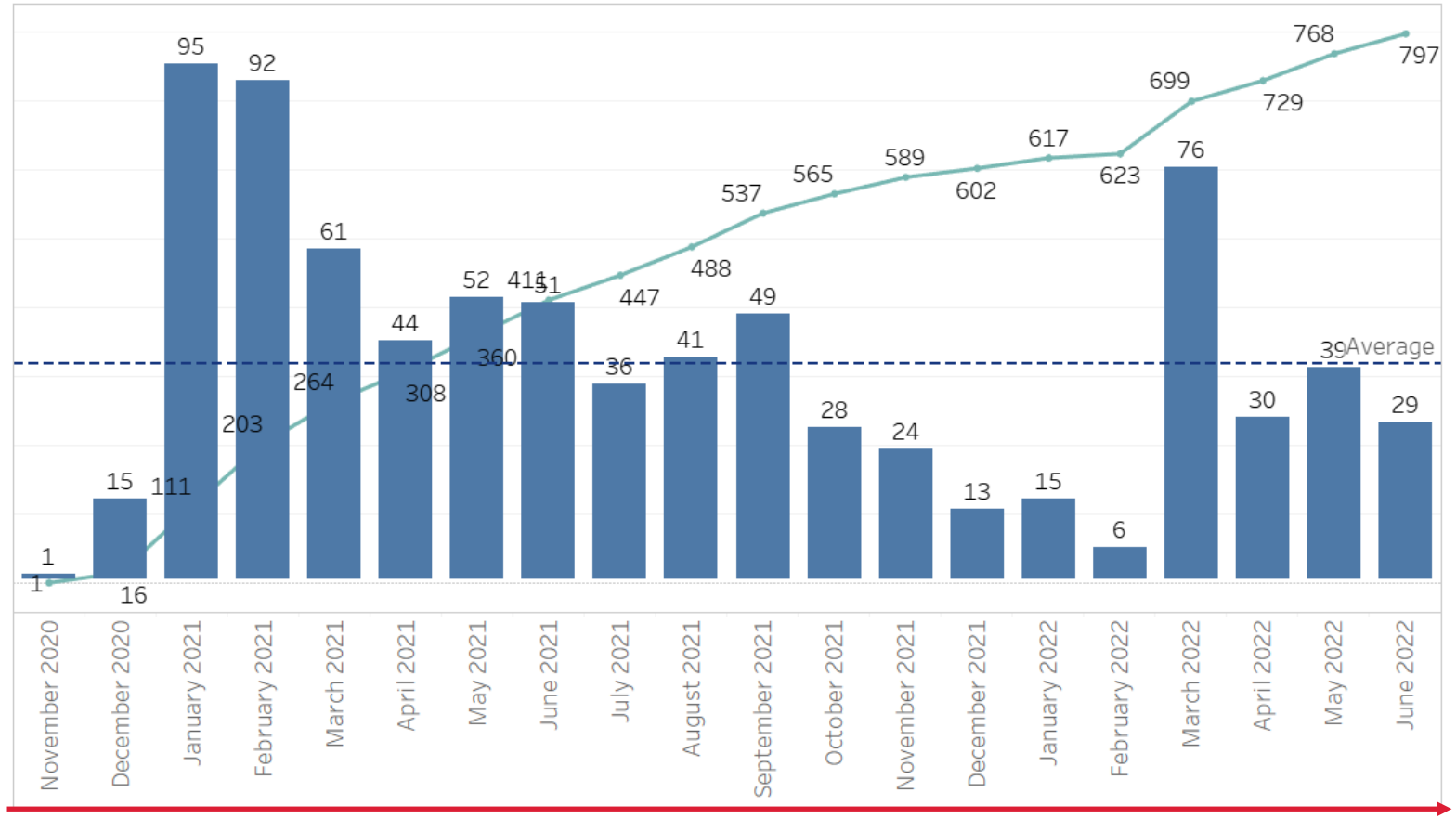
Lavender EDTA, 10 ml ACD tube, 10 ml

SeroNet-CORALE Cohort: Cancer (6-21-22)

Methods:

- Cedars-Sinai Health System
- Patients aged 18 or older
- Recent diagnosis of cancer (largely on active treatment)
- Emphasize on recruitment of:
  - B-cell malignancies
  - Bone marrow transplant recipients
  - Patients with solid tumor on immunotherapies



Samples collected include pre-vaccination and through various surges

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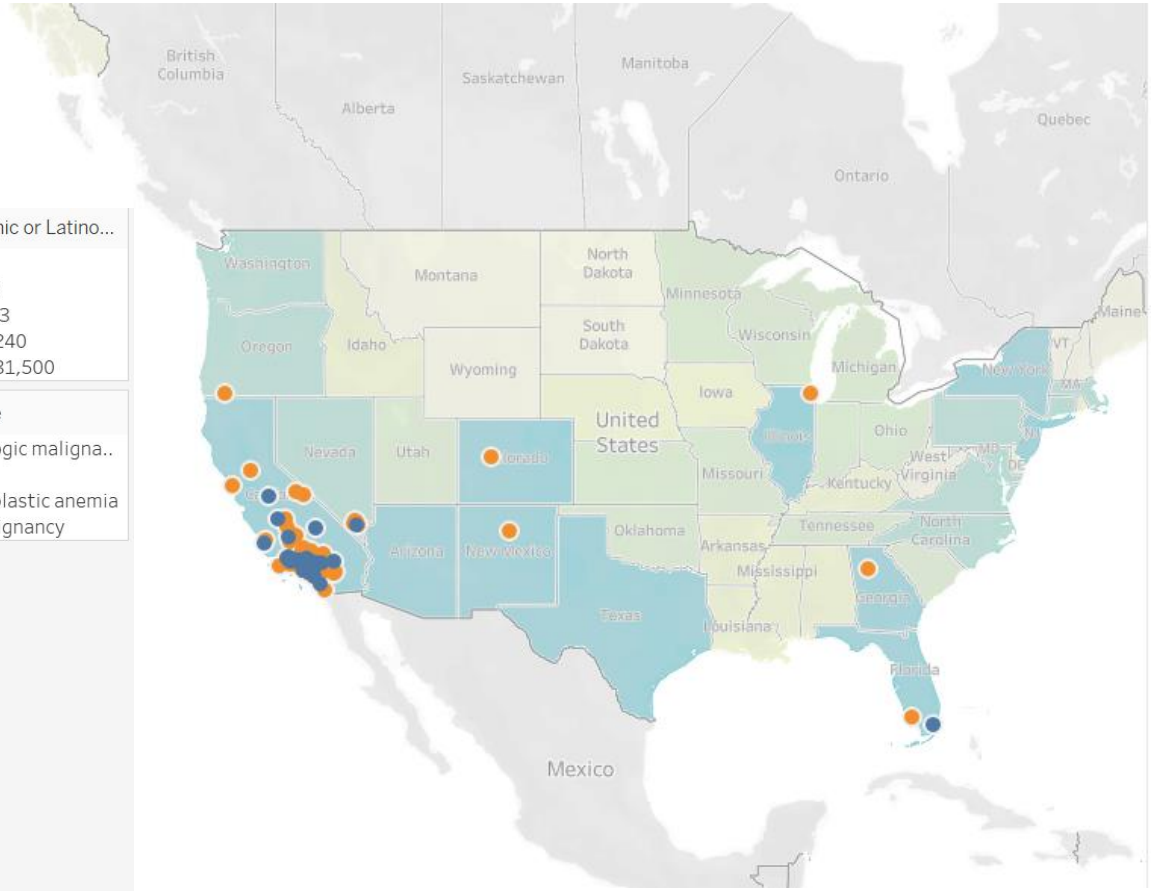
Emphasize on capturing diverse populations across catchment area

The Cedars Sinai Health System is located in the diverse metropolis of Los Angeles, serving a catchment area over 5.7 million (57.6% of the total Los Angeles County population)



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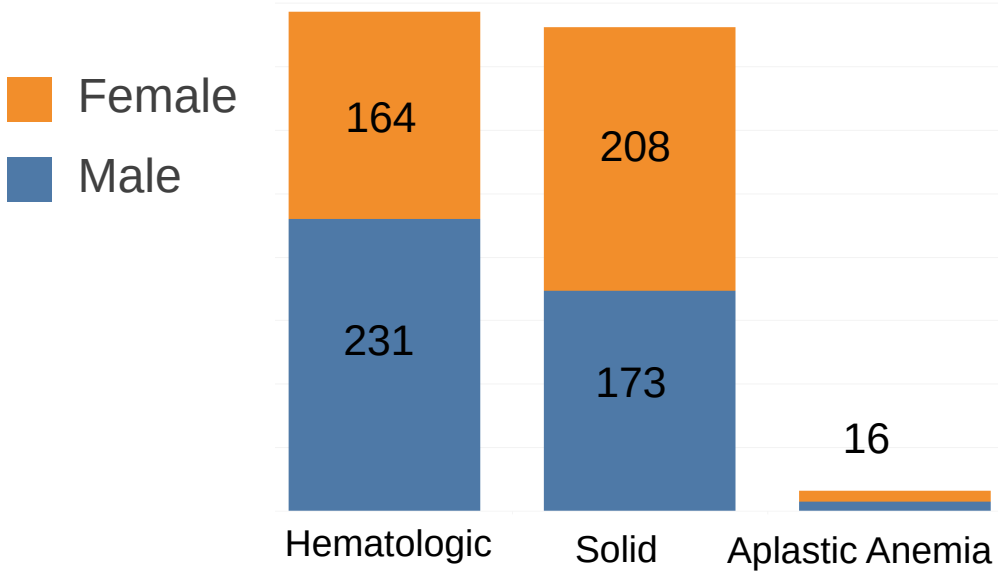
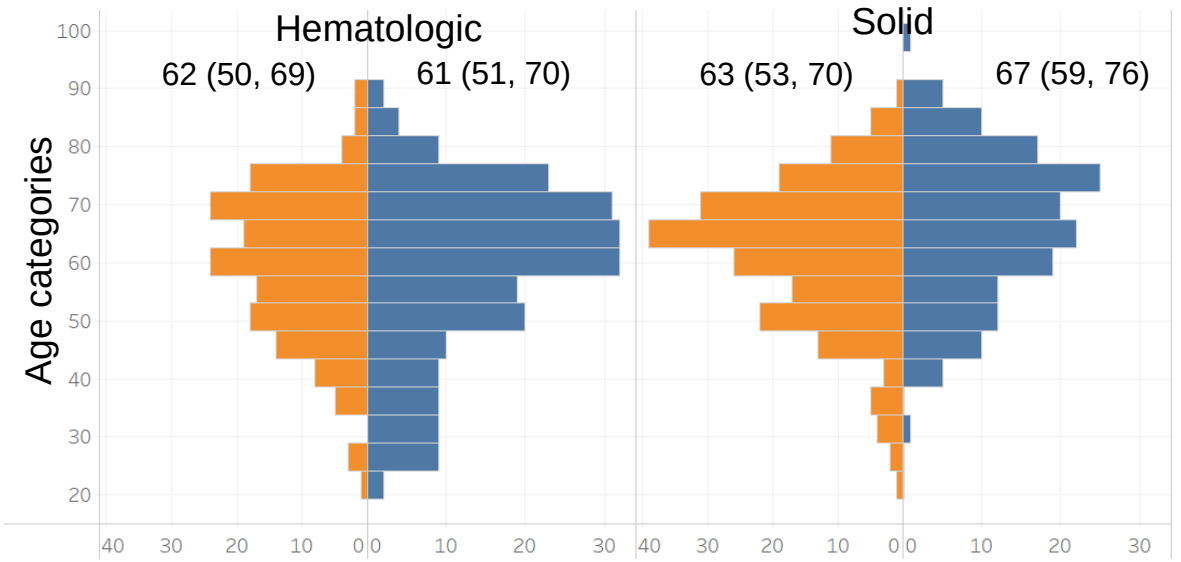
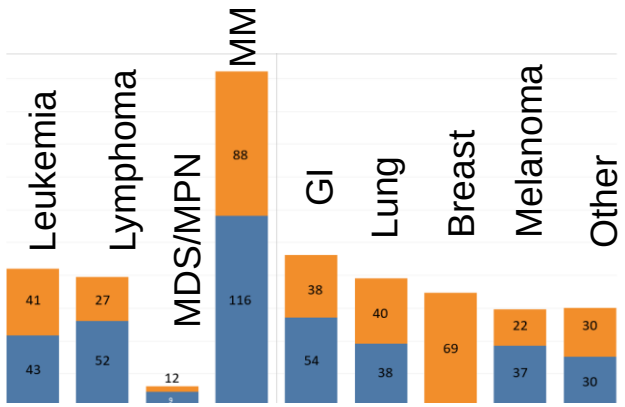
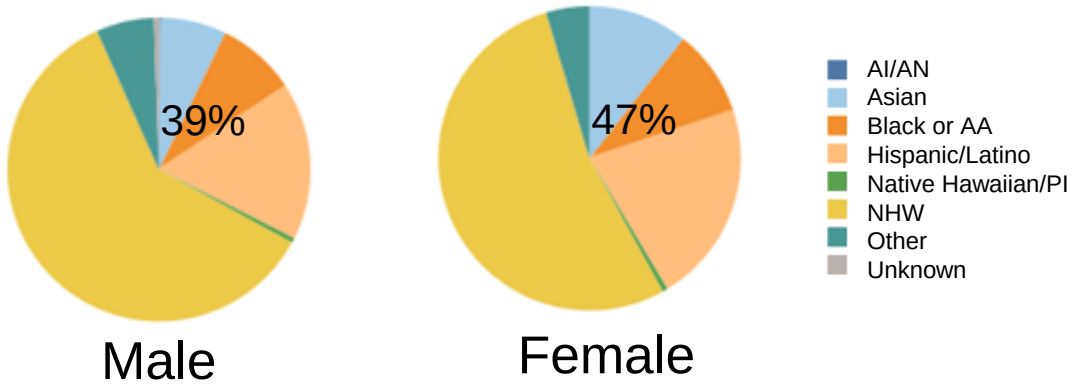
Patient characteristics (6-21-22)









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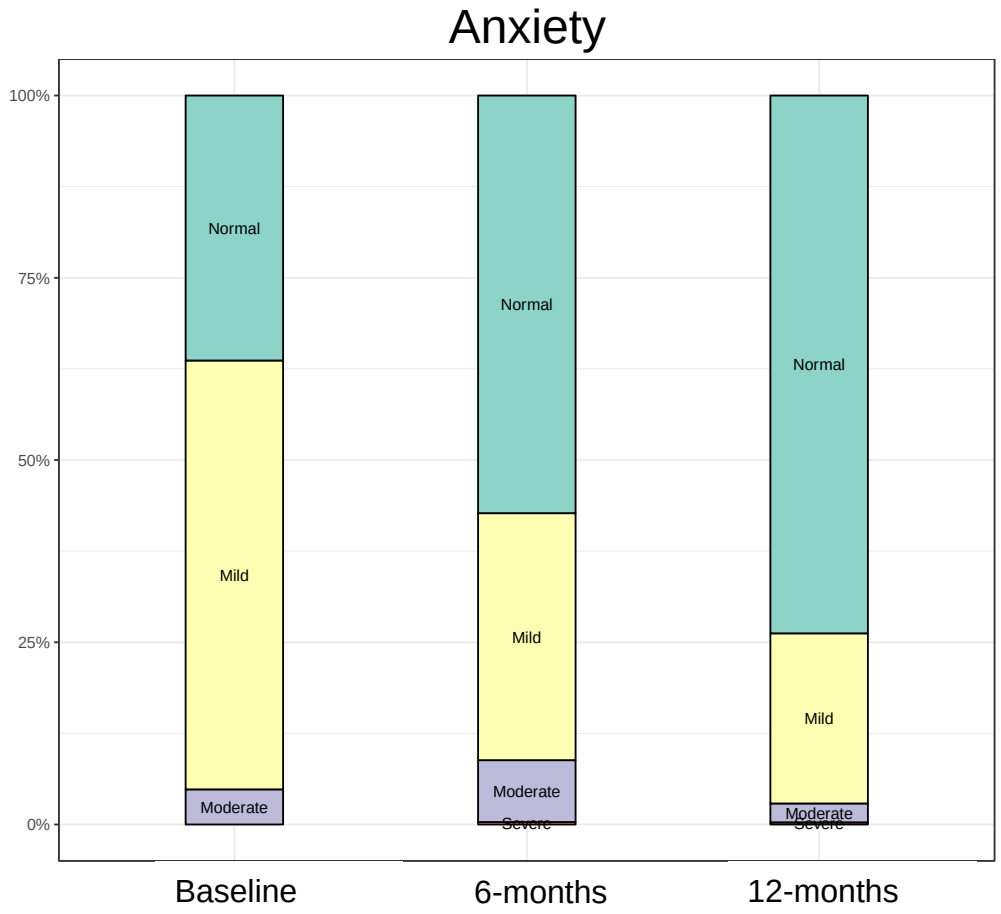
Collection of surveys and assessment of HR-QOL

PROMIS

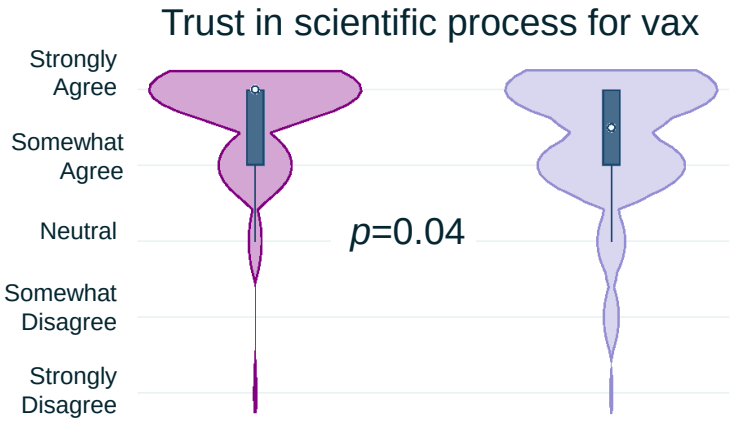
- Anxiety
- Depression
- Fatigue
- Cognitive Function
- Informational Support
- Instrumental Support
- Emotional Support

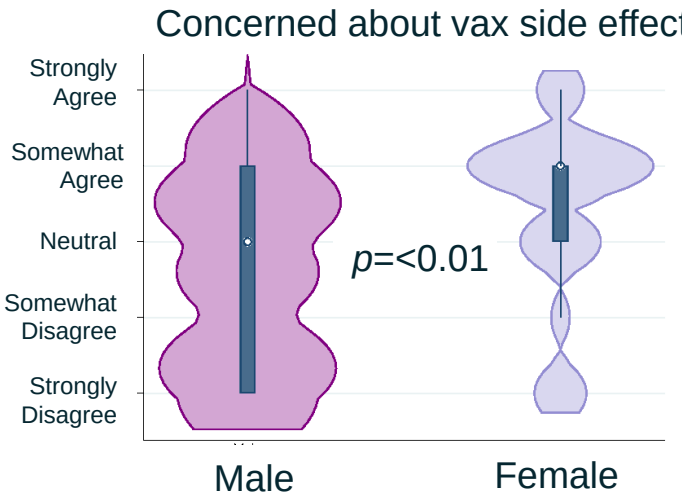


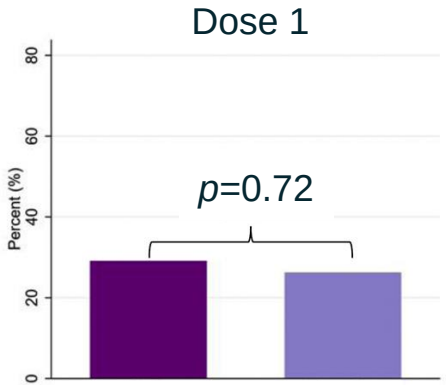
SARS-CoV-2 Vaccine Perspectives

Findings:

- Unvaccinated patients:
  - Women more hesitant than men (35.7% v. 12.9%)
- Common concerns:
  - Fear of adverse reactions (57%)
  - Rushed vaccine development (43%)
  - Insufficient knowledge (64%)







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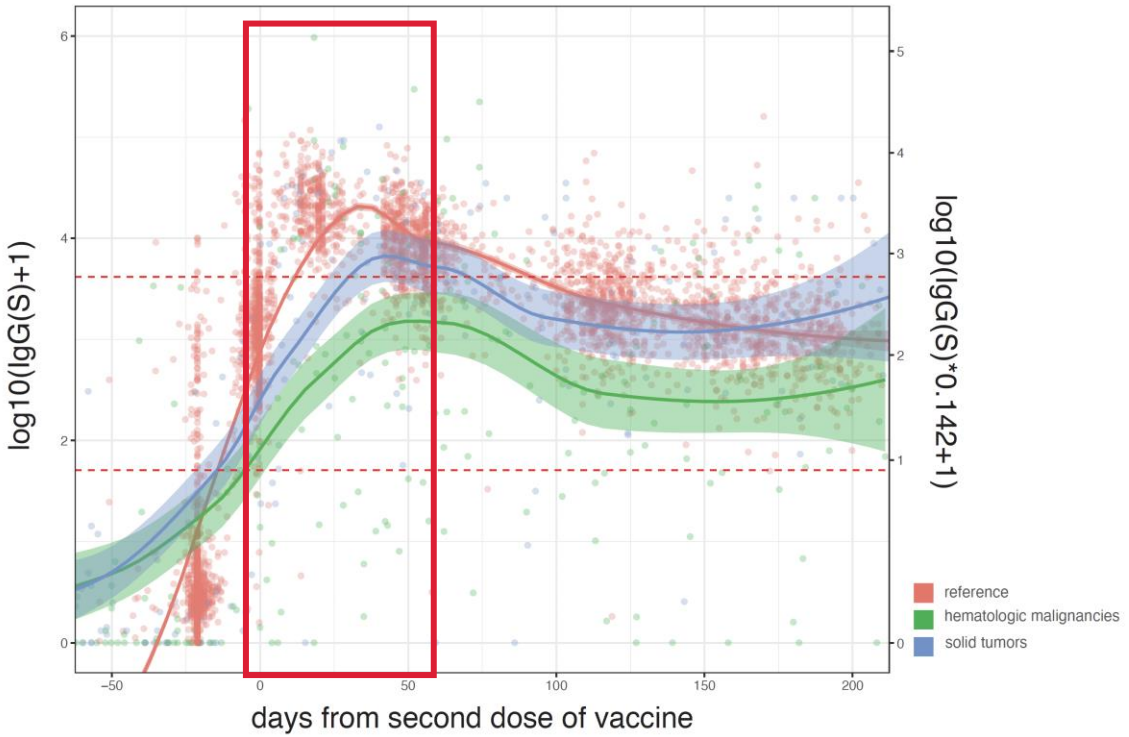
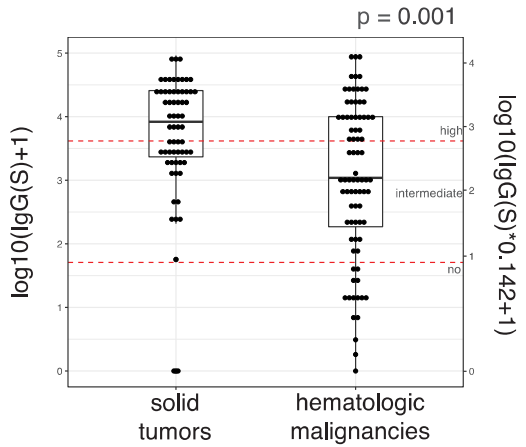
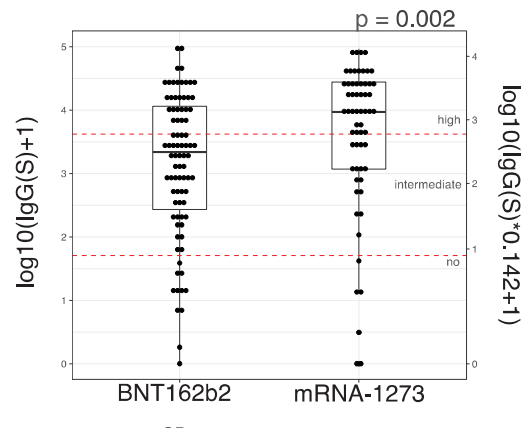
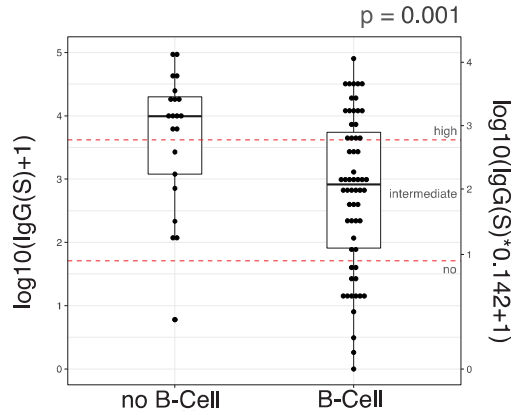
Figueiredo et al. Annals of Oncology 2022

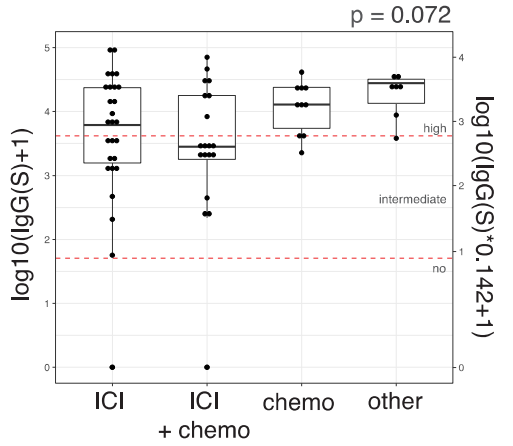
Differences in peak antibody responses by cancer, vaccine and treatment











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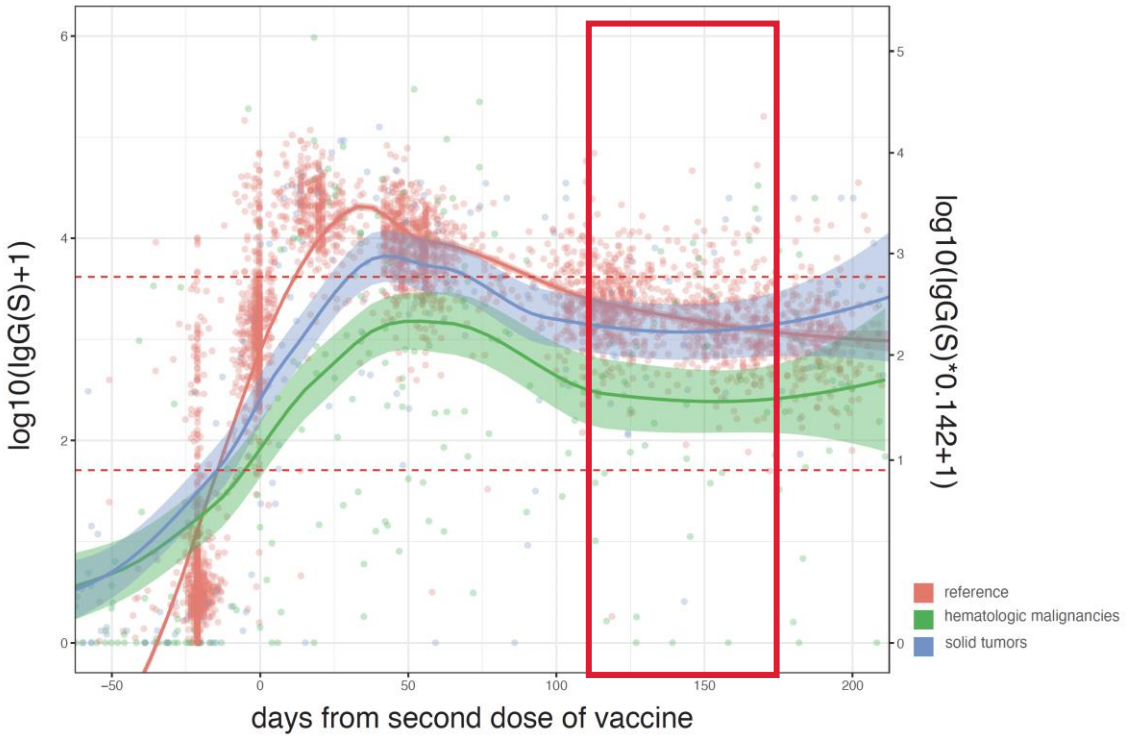
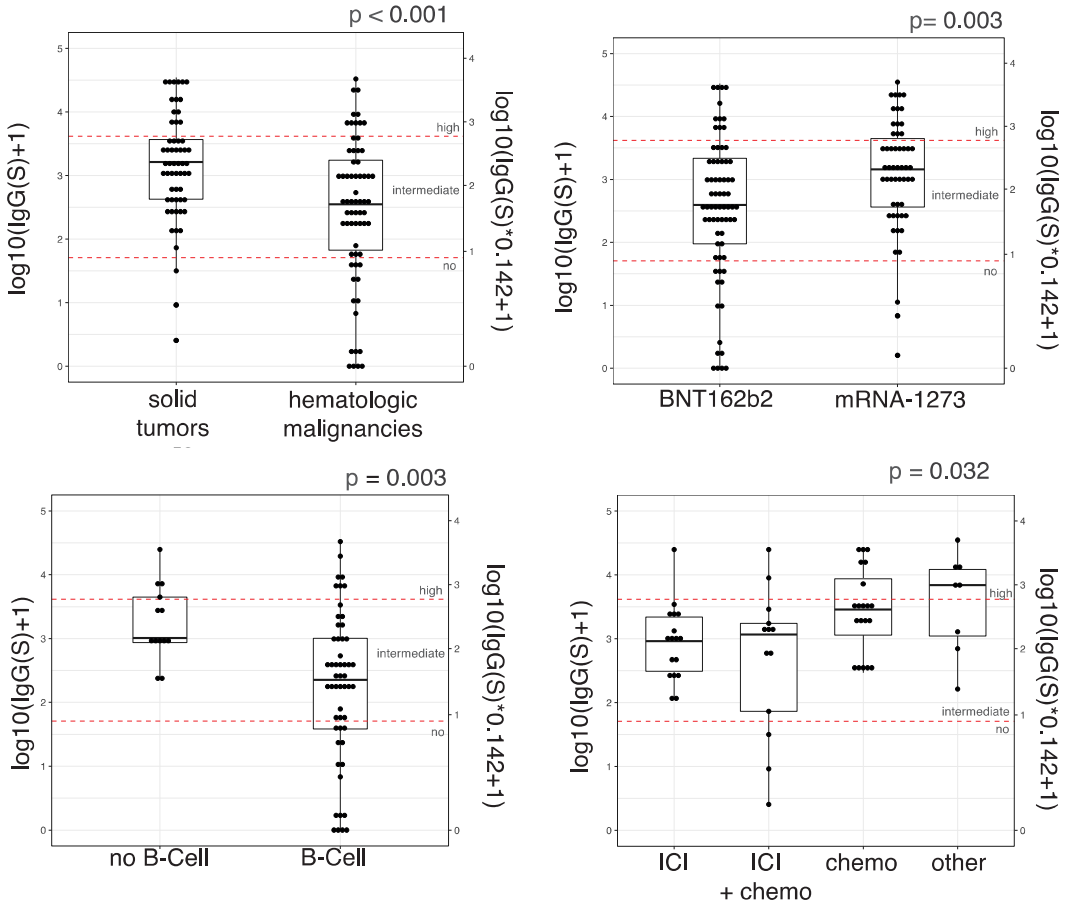
Figueiredo et al. Cancer Res 2021

Differences in sustained antibody responses by cancer, vaccine and treatment





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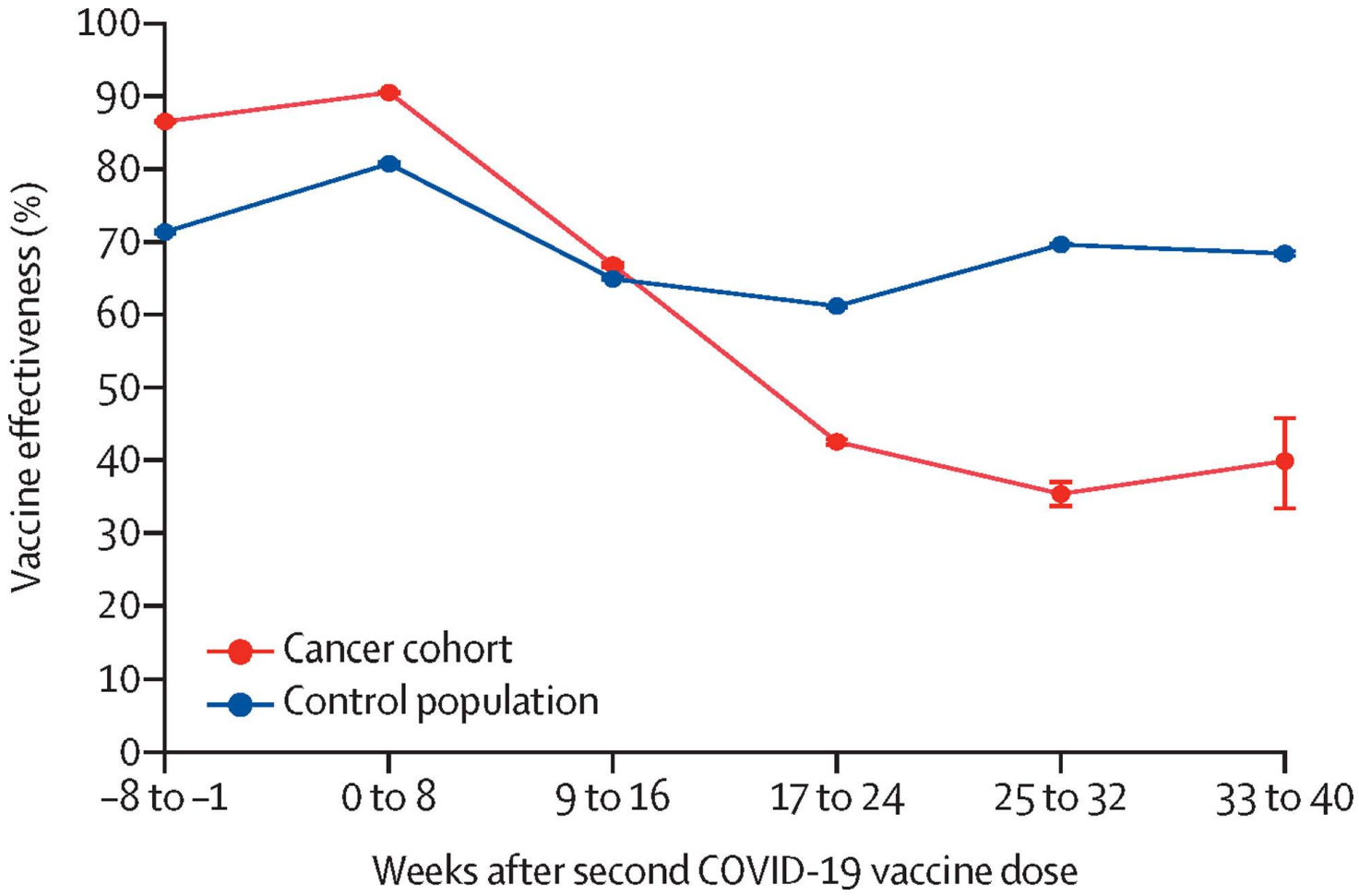
Figueiredo et al. Cancer Res 2021

Vaccine effectiveness lower in patients with cancer: UKCCEP



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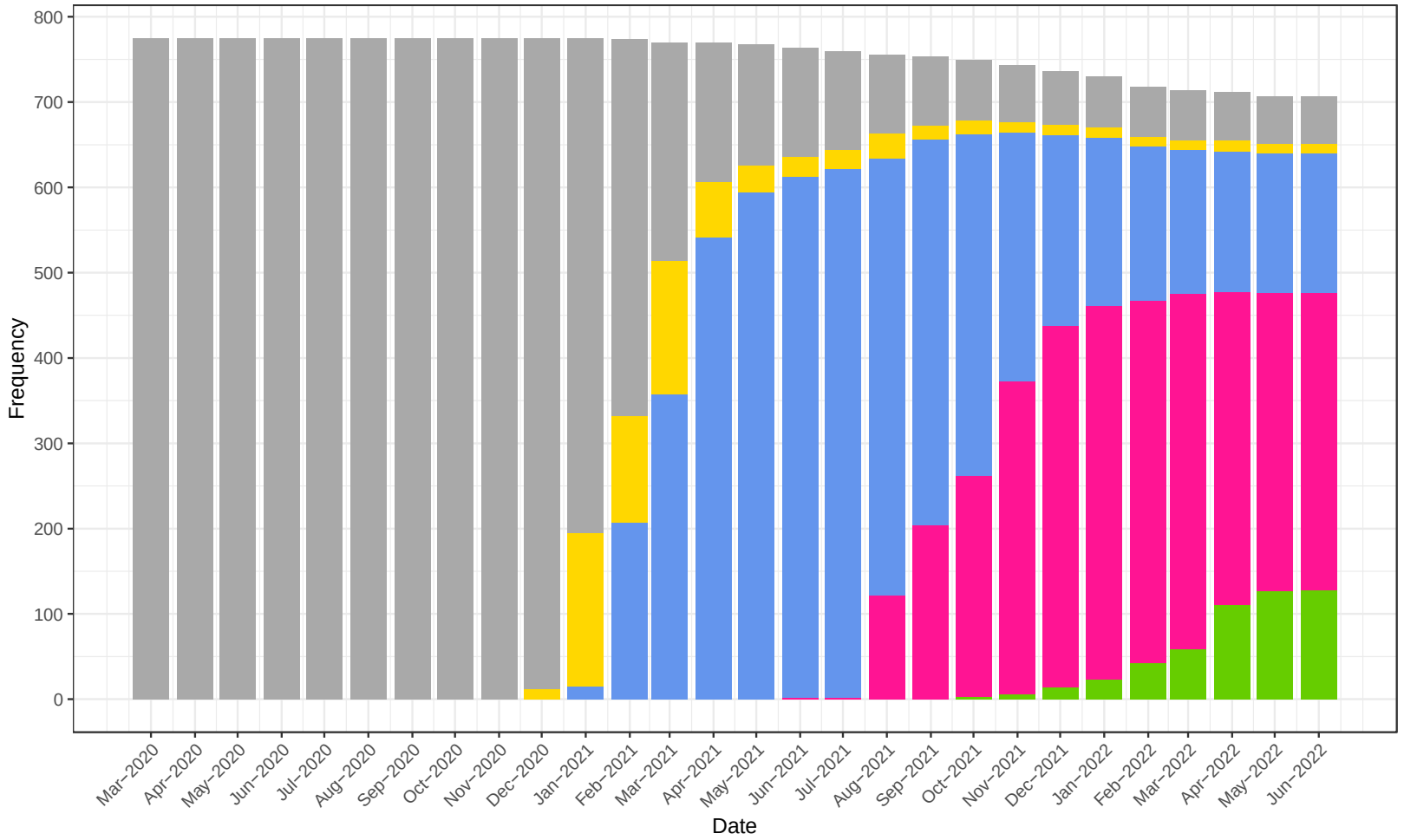
Lee et al. Lancet Oncol 2022

Vaccine uptake in cancer patients



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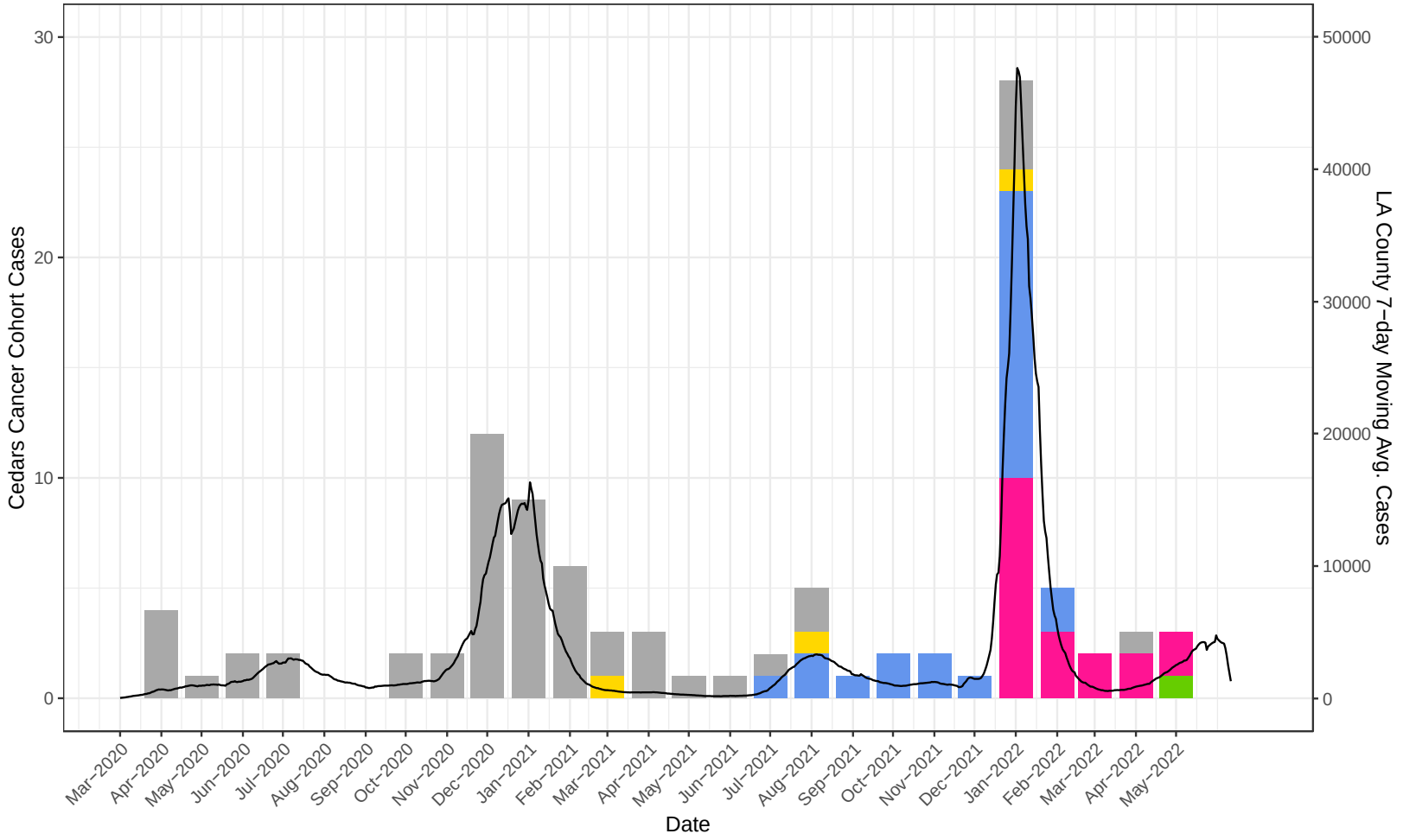
No vaccination | Partial | Complete primary series | Single additional dose | 2+ Additional doses

Breakthrough infections increased after emergence of Omicron



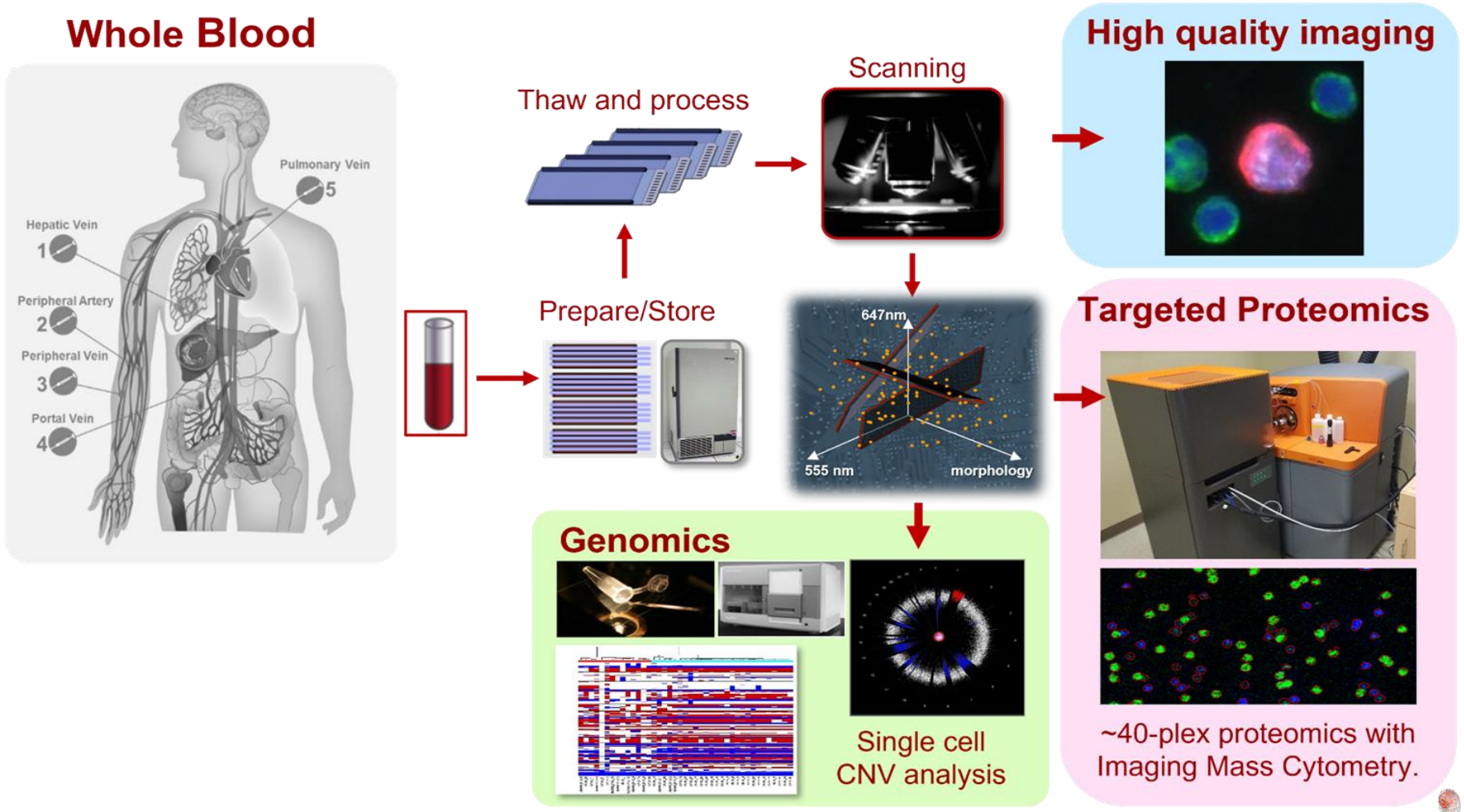
Cedars Sinai

No vaccination | Partial | Complete primary series | Single additional dose | 2+ Additional doses

PASC in Immunocompromised patients

Cohort	Inclusion Criteria
Post-COVID (n=100)	• Adults (≥18 years) AND • Previously infected with SARS-CoV-2
Post-SYMP COVID (n=75)	• Previously hospitalized for COVID-19 disease OR • Previously severely symptomatic for COVID-19 OR • Are symptomatic and being evaluated for PASC
Post-ASYMP COVID (n=25)	• Were asymptomatic for COVID-19
PASC Suspected (n=53)	• Post-SYMP COVID AND • Being evaluated for PASC
PASC Not Suspected (n=22)	• Post-SYMP COVID AND • Not being evaluated for PASC

High-Definition Single Cell Assay (HDSCA): rare event detection in the liquid biopsy



Peter Kuhn, PhD
Elizabeth Qi, PharmD
Stephanie Shishido, PhD

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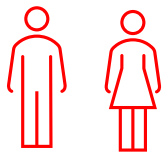
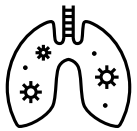
USC Michelson Center
Convergent Science Institute in Cancer

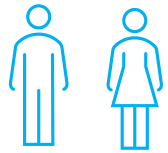
Sequencing and Detecting Antigen-Specific T Cells

IBD + immunomodulation





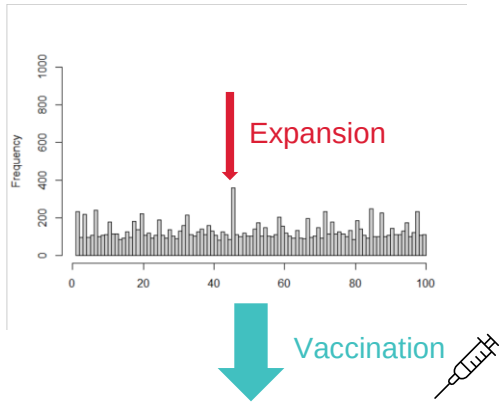
Cancer + B-cell depleted

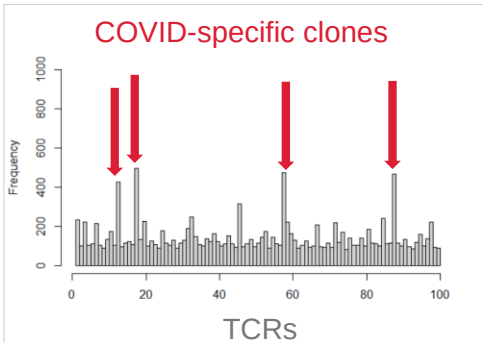


HCW cohort

Adaptive TCR Repertoire Sequencing

ongoing





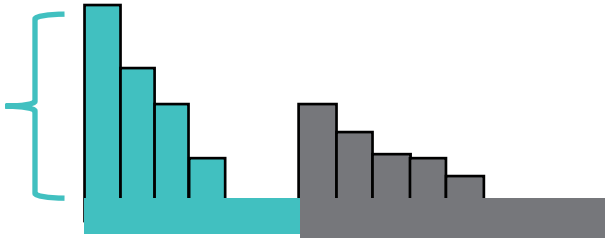
Count # of TCRs encoding each sequence

Each patient has some clonally expanded TCRs

The expanded TCRs change after vaccination

Breadth: How many unique COVID-specific clones are there?

Depth: How expanded are the COVID-specific clones?



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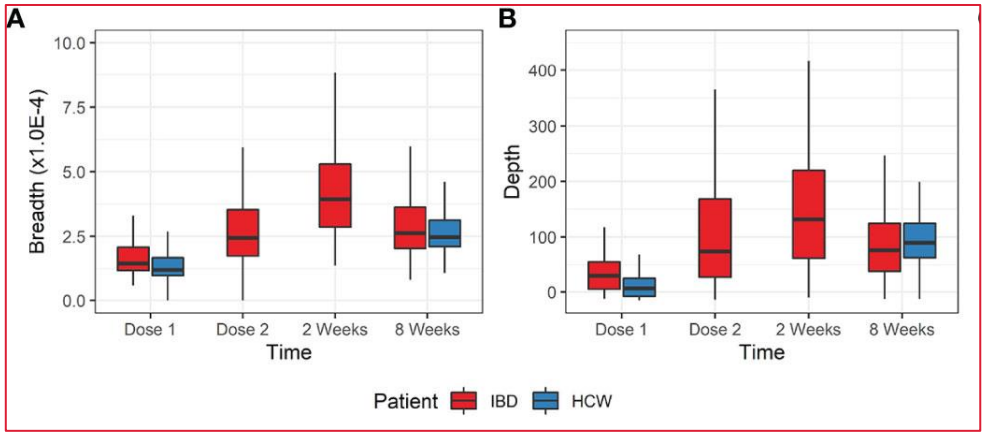
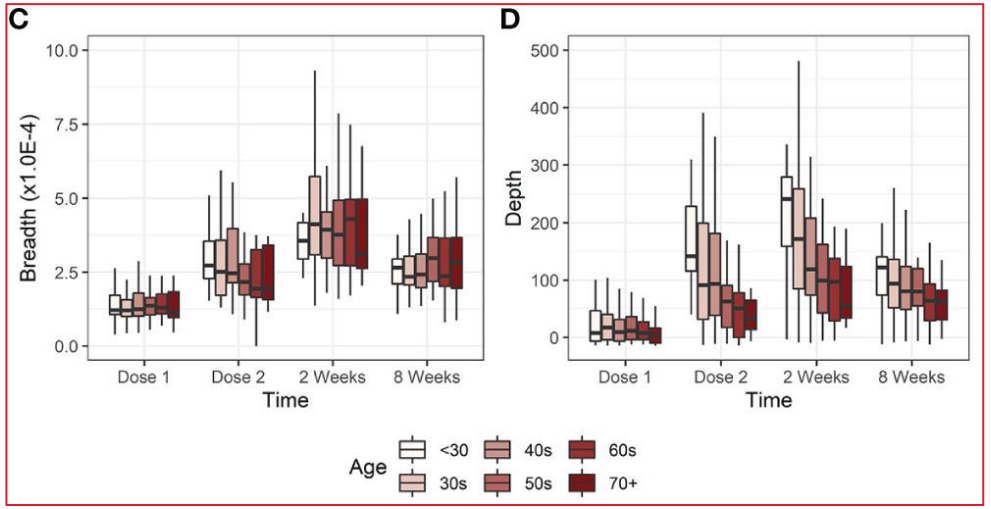
Alex Xu, PhD
Dalin Li, PhD
Jon Braun, MD, PhD
Gil Melmed, MD
Dermot McGovern, MD, PhD
Akil Merchant, MD

Clinical Metrics and T Cell Response:
Study in patients with inflammatory bowel disease (IBD)

IBD ~ HCW over vaccination time course



Depth (but not Breadth) decreases with age



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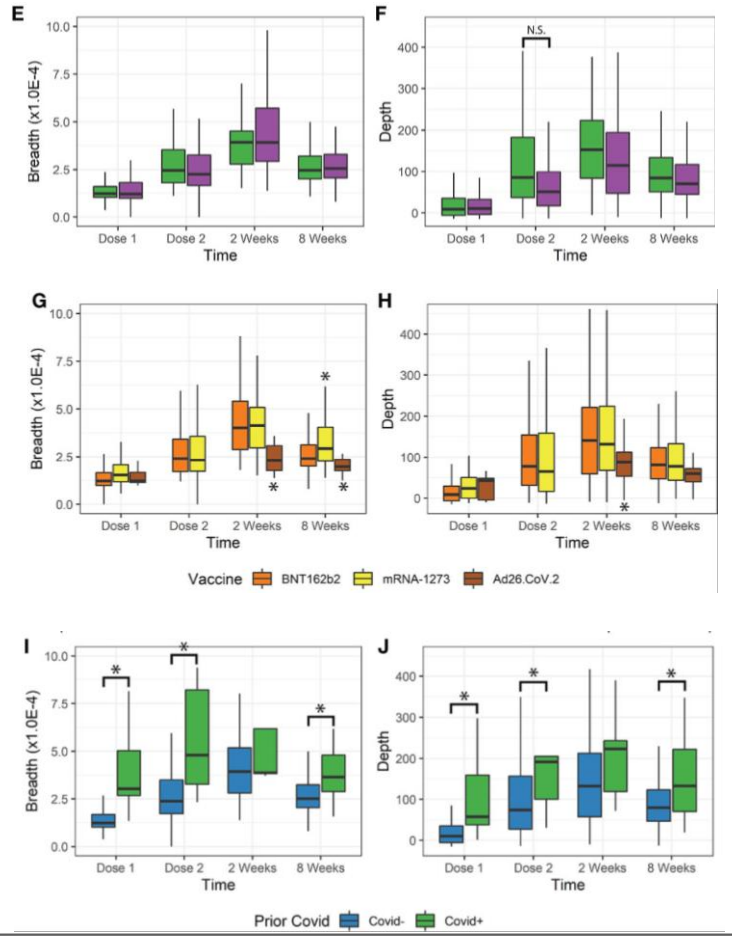
Xu et al. Frontiers Immunol 2022

Clinical Metrics and T Cell Response:
Study in patients with inflammatory bowel disease (IBD)

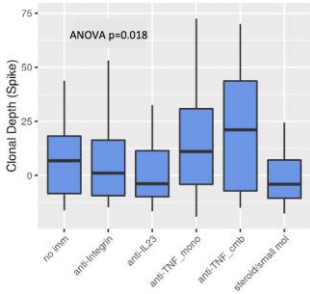
Sex

Vaccine type

Prior COVID infection



Treatment



Xu et al. Frontiers Immunol 2022; Li D and Xu A et al, IBD J 2022 *in press*

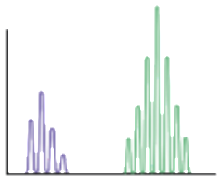
Diversity and Determinants of the Immune-Inflammatory Response to SARS-CoV-2

pre-event of interest assay

pre- and post-event of interest assays

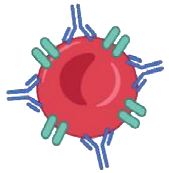
post-event of interest assays

immune phenotyping

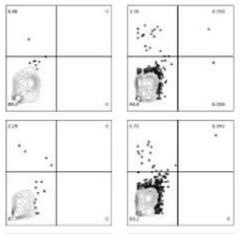


proteomic and metabolomic pro ling

adaptive TCR repertoire

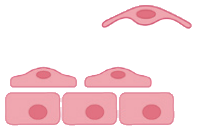


auto antibody



t-cell functional assay

anti-spike titer



circulating endo-cells long covid

viral sequencing

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USC Michelson Center
Convergent Science Institute in Cancer

UCDAVIS
UNIVERSITY OF CALIFORNIA

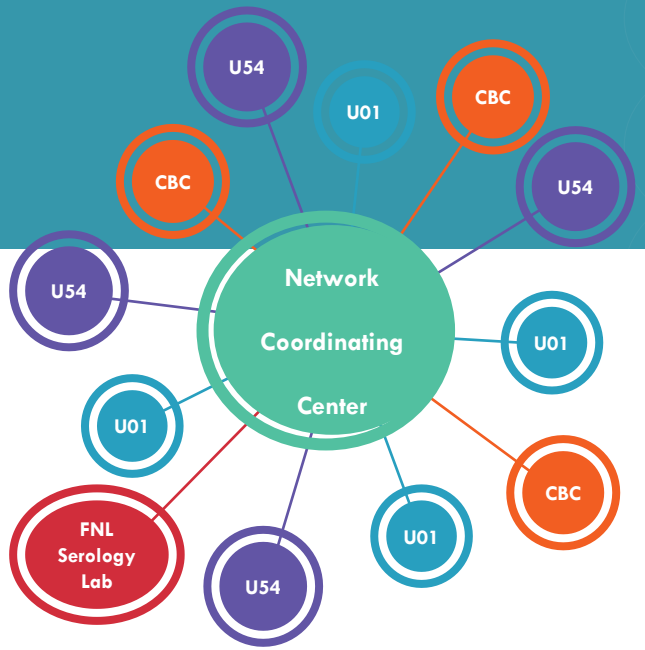
La Jolla Institute
FOR IMMUNOLOGY

UC San Diego

Valuable resource for future research

Samples collected, and data generated by cohort		
Cohort	Sample Type	Total processed
Cancer	EDTA Plasma	4,019
	Buffy Coat	1,185
	PBMC	5,956
	CPT Plasma	917
	ACD Plasma	4,479
HCW	EDTA Plasma	12,636
	Buffy Coat	3,645
IBD	EDTA Plasma	175
	Buffy Coat	175
	PBMC	175
Long COVID	EDTA Plasma	162
	Buffy Coat	54
	PBMC	270

SeroNet Vaccine Response Studies: Immunocompromised patients from CBCs



- Longitudinal studies to study vaccine efficacy
- Focus on immunocompromised subjects along with health controls
- Data and samples being collected by the four Capacity Building Centers
- Large Cohorts

	Cancer	HIV	Organ transplant	Autoimmune Disorders	IBD	Convalescent COVID patients	Healthy Controls
ASU							
UMN							
FIMR							
Mt. Sinai	Multiple myeloma, CLL						

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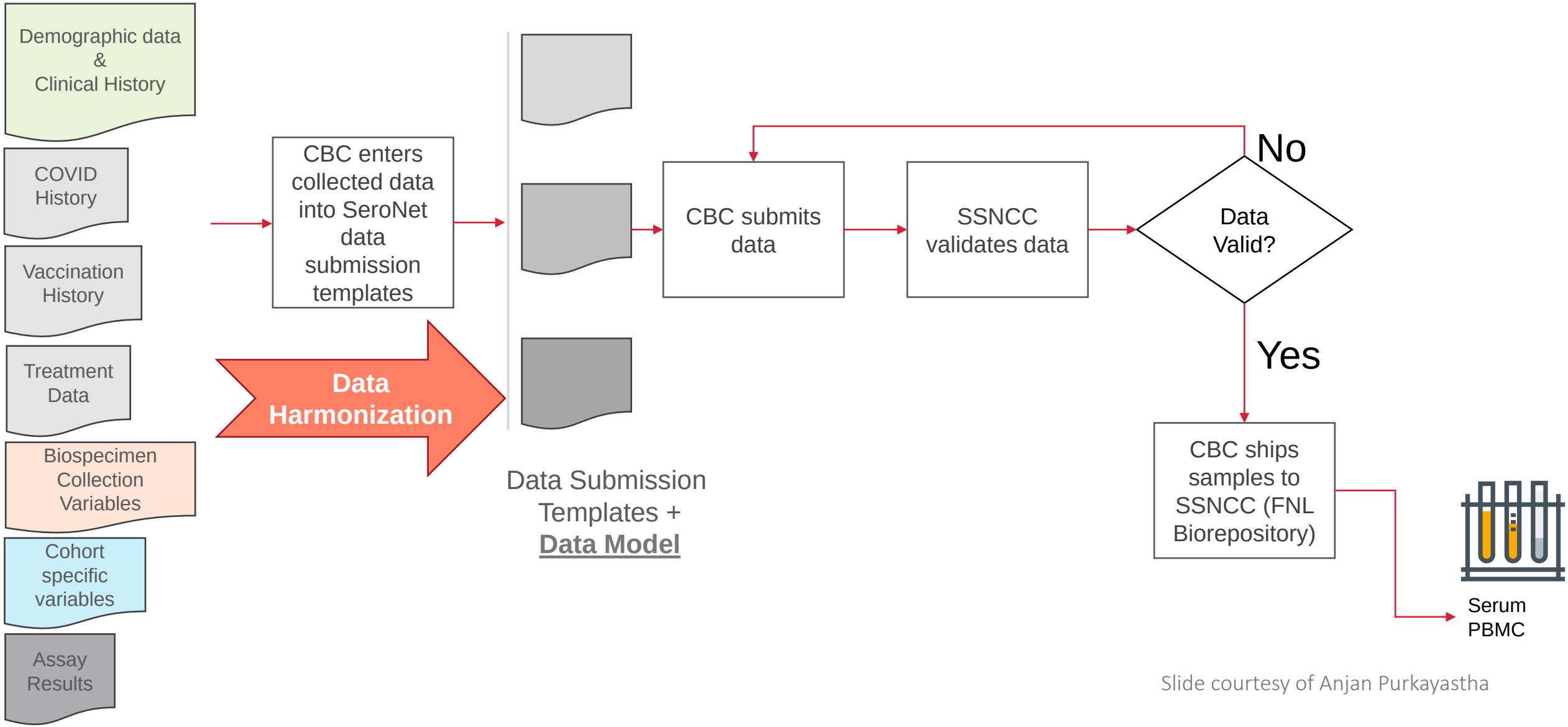
Vaccine Response Studies
Data & Sample Submission to FNL



Slide courtesy of Anjan Purkayastha

Potential for collaborative SeroNet-wide efforts

	Cancer	Solid organ Transplant	Autoimmune
EMR*	~ 200,000	~ 10,000	~ 100,000

	Hematologic	Solid tumor	Solid organ Transplant	Autoimmune
Prospective Cohorts*	~ 1,000	~ 1,000	~ 400	~ 1,000

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* Current estimates (ongoing work from the SeroNet Epidemiology Ops Working Group)

Acknowledgements

We thank all the participants in the SeroNet-CORALE Study, coordinators, staff, and other members of SeroNet

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