



Seattle Children's®
HOSPITAL • RESEARCH • FOUNDATION

PLUGS®

Patient-centered Laboratory
Utilization Guidance Services

WEBINAR SERIES

Brought to you by



www.medtraining.org

LabTalk: Covid-19: Laboratory Testing, Laboratory Experiences

Participants:

Mike Astion, MD, PhD – Medical Director, Department of Laboratories Seattle Children's Hospital, Clinical Professor, Univ Washington (UW) Department of Laboratory Medicine; Co-founder of PLUGS

Jane Dickerson, PhD, DABCC – Chemistry Medical Director, Department of Laboratories Seattle Children's Hospital, Clinical Assoc. Professor, Univ Washington (UW) Department of Laboratory Medicine; Co-founder of PLUGS

Mark Wener, MD, - Director UW Medical Center Clinical Laboratories; Director Clinical Immunology Laboratory and Professor, UW Department of Laboratory Medicine

Elise Occhipinti, MD - Chair of Pathology, Ochsner Medical Center, New Orleans, LA

Tips for Managing a Laboratory During the Covid-19 Pandemic....

- Avoid extreme thinking
- The vast majority of lab workers come to work to do a great job. They can handle the stressful work associated with this pandemic.
- It is easy to be “right”, it is hard to be “effective”. Choose being effective.
- Forgive yourself.
- Consider putting out a FAQ and lab strategy document.
- Thank hospital leaders for removing some of the administrative burdens that were previously present, and now removed.

Questions from our audience about the use of antibody tests....

- Why is it useful to know the prevalence of antibodies in a population, e.g., in New Orleans?
- If the false positive rate of a test is 1%, can you measure the prevalence of antibody positivity if the prevalence is low (e.g. 1%).
- Why are there so many crummy tests out there?
- Could Ab testing be useful for people going onto aircraft carriers, fishing vessels, oil drilling platforms, jail, or other constrained living environments?
- Is it useful to know in a person who has to take care of the elderly?
- How useful is it in patients who did not get PCR testing, but likely had Covid-19?
- What is the evidence that immunity is protective?
- Do titers matter? Would a high titer be more likely to suggest immunity?
- Will these same assays be used after a vaccine is developed?

COVID19 Serology at University of Washington Lab MTS

April 30, 2020
Mark Wener, MD

COVID19 Serology

UWMMC Immunology Lab

> Virology Lab

April 30, 2020

Mark Wener, MD

Abbott Architect

- Automated
- High throughput
- Platform on hand
- Sensitivity after 14 days of symptoms 100%
- Specificity 99.6%
- Local UW confirmation of stats

Positive Agreement by Days Post-Symptom Onset

Days Post-Symptom Onset	n	Positive	Negative	PPA (95% CI)
< 3	5	0	5	0.00% (0.00, 52.18)
3 - 7	10	5	5	50.00% (18.71, 81.29)
8 - 13	34	31	3	91.18% (76.32, 98.14)
≥ 14	73	73	0	100.00% (95.07, 100.00)

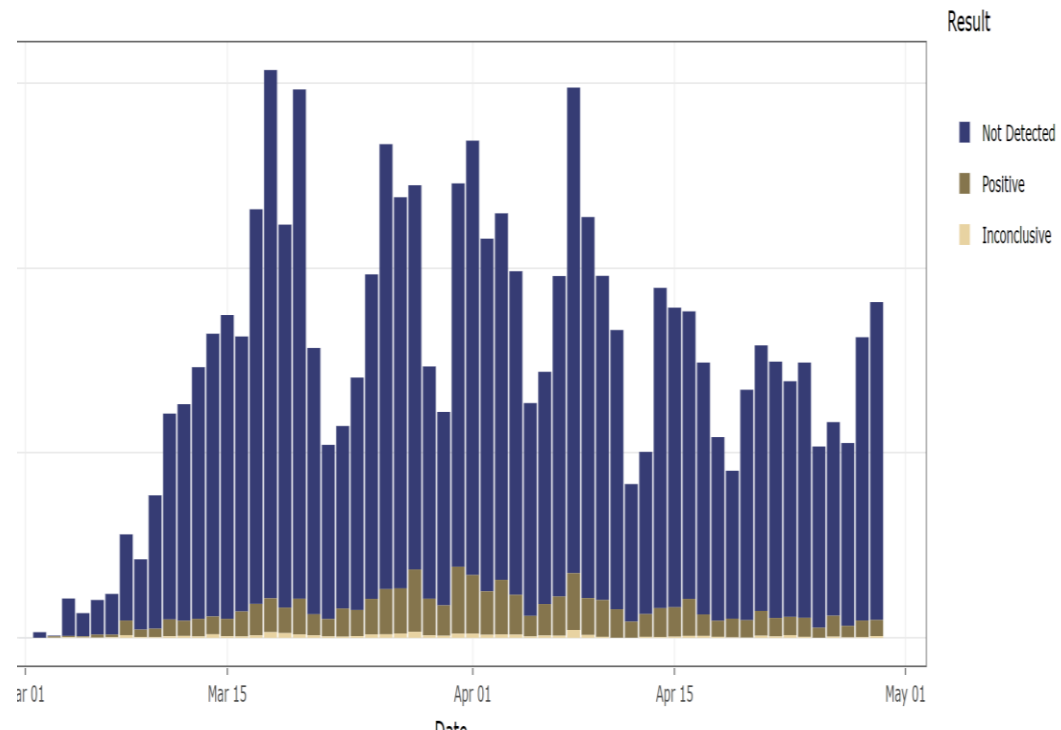
Negative Agreement by Category

Category	n	Positive	Negative	NPA (95% CI)
Pre-COVID-19 Outbreak	997	4	993	99.60% (98.98, 99.89)
Other Respiratory Illness	73	0	73	100.00% (95.07, 100.00)
Total	1070	4	1066	99.63% (99.05, 99.90)

SARS-CoV-2 Testing Volumes

**rtPCR: initial exponential, max 3000/d,
now about 1000-1500/d**

As of date:	Total (distinct) positive/inconclusive patients:	Overall patient positivity rate:
	8,036	9.5%
As of on 2020-04-29:	Daily positive/inconclusive samples on 2020-04-29:	Sample positivity rate on 2020-04-29:
	96	5.3%

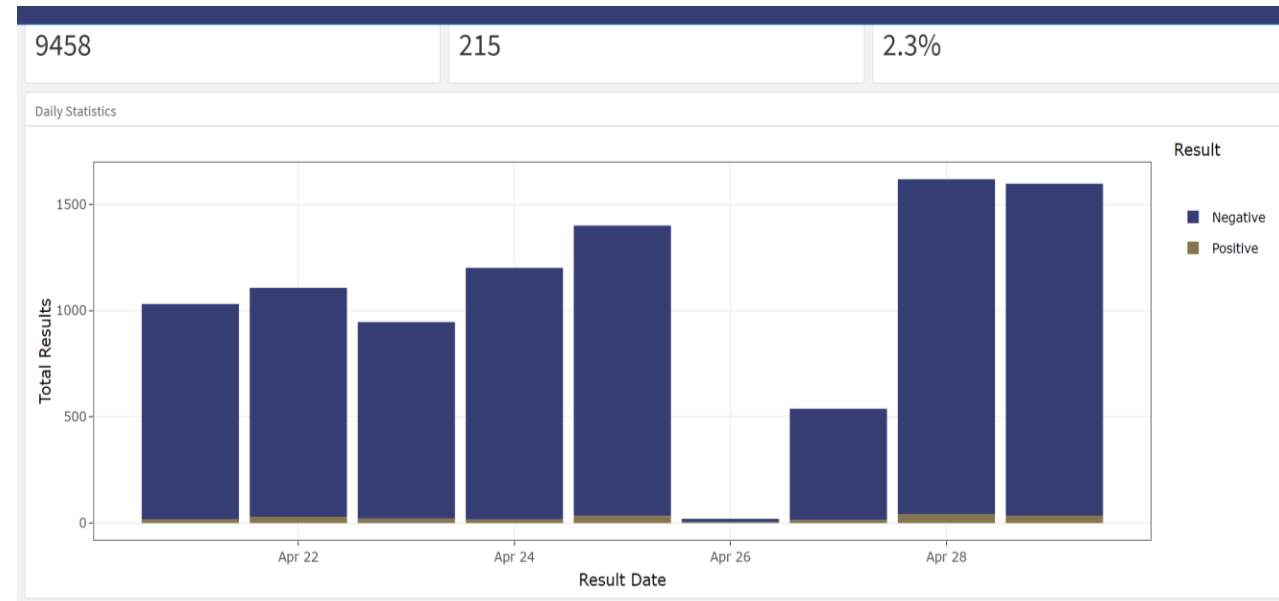


Serology: About 1000 - 1500/d

Few clinical orders

Mostly from employer groups.

Seropositive about 2-2.5%

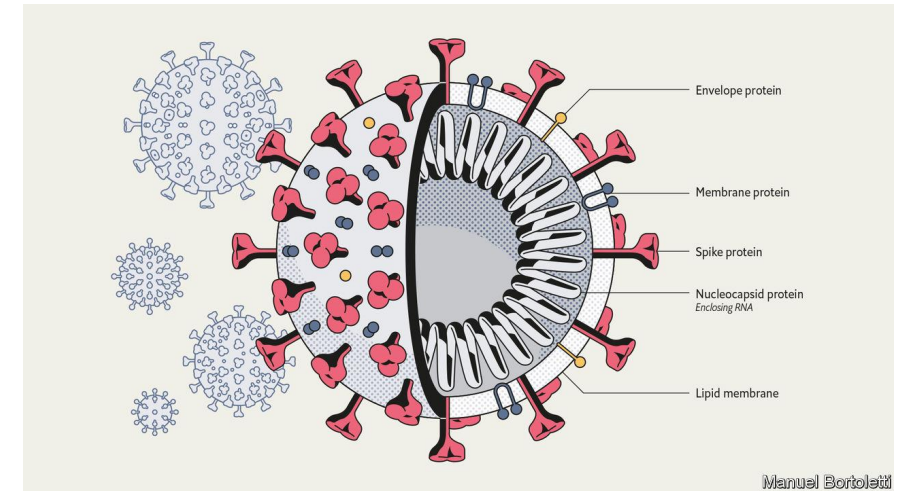


Analytical Options/Choices

- What should the antigen be? What are the possible targets?
- What antibody? IgG, IgM, IgA? Separately or combined?
- Platform?
- How to determine sensitivity and specificity?
 - How to determine cross-reactivity?
- Do any tests equate with immunity?
 - 'Back to work'? 'Immunity passport?' 'Risk-free certificate?'

SARS-CoV-2

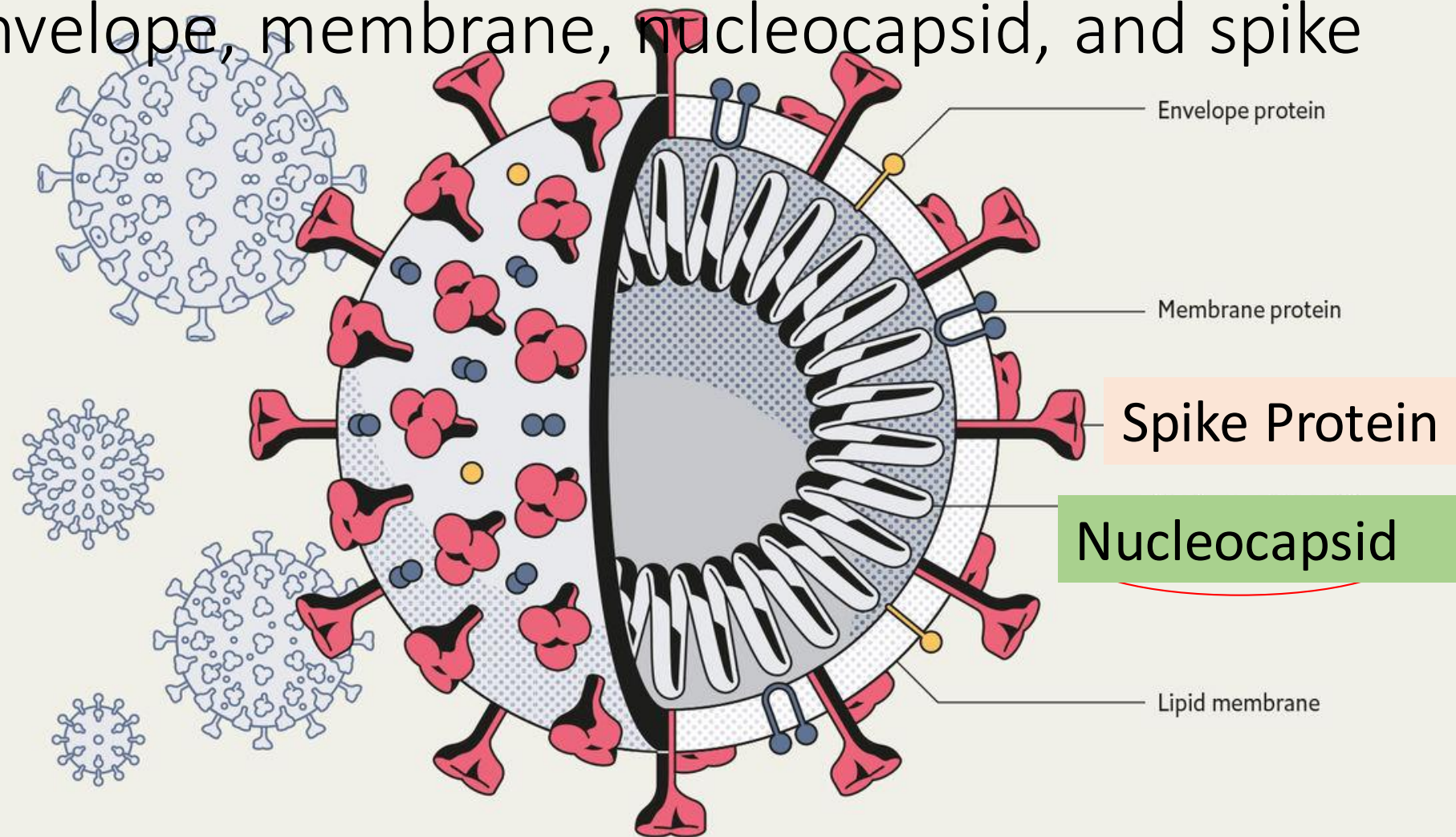
- "Severe acute respiratory syndrome coronavirus 2"
- Single-stranded, enveloped RNA virus
 - Family = Coronaviridae
 - Genus = Betacoronavirus
 - Betacoronavirus contains 4 different lineages
 - SARS-CoV and SARS-CoV-2 belong to the B lineage
 - MERS-CoV belongs to the C lineage
- Comprised of 29,891 nucleotides
- Mature SARS-CoV-2 virion has 4 structural proteins: envelope, membrane, nucleocapsid, and spike



Dilcher, L et al. (2020) SARS-CoV-2: a novel deadly virus in a globalised world

Courtesy of Marie Hensley, Resident

SARS-CoV-2: Mature SARS-CoV-2 virion has 4 structural proteins: envelope, membrane, nucleocapsid, and spike

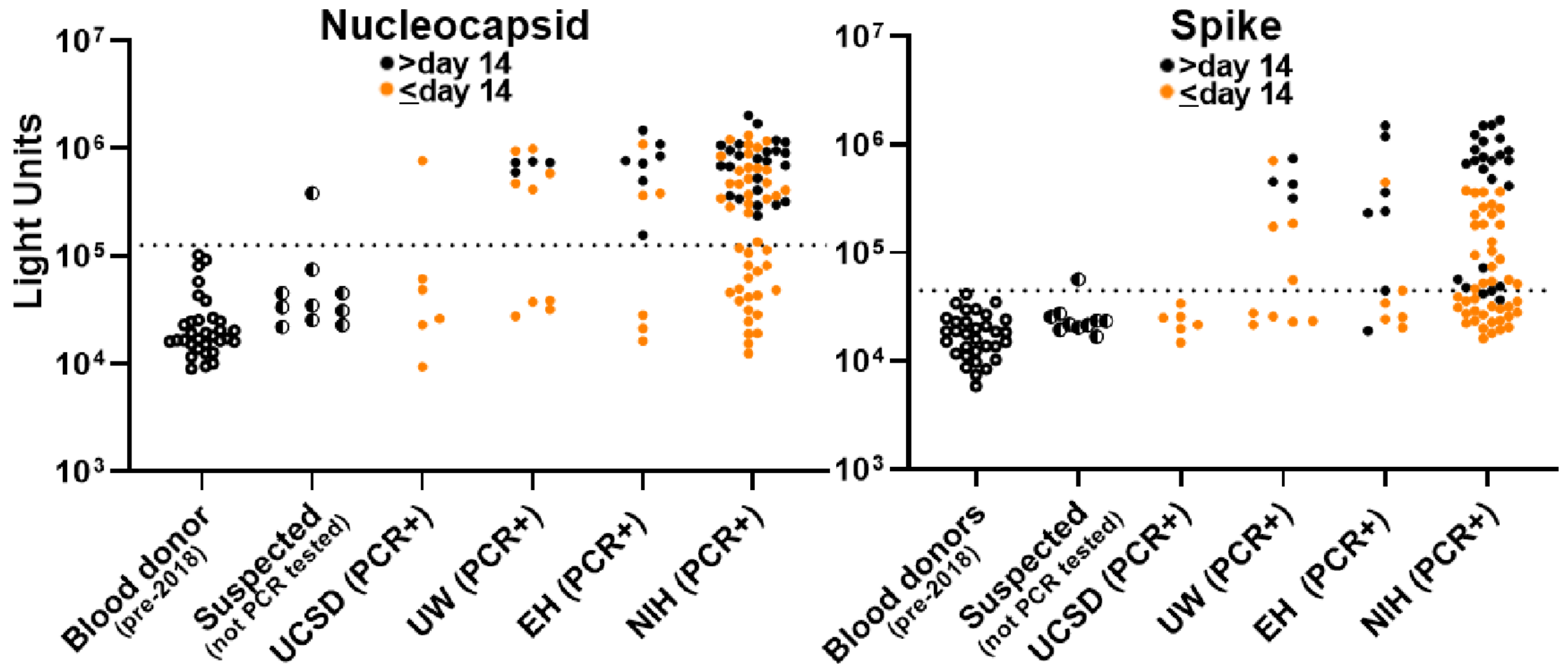


Manuel Bortoletti

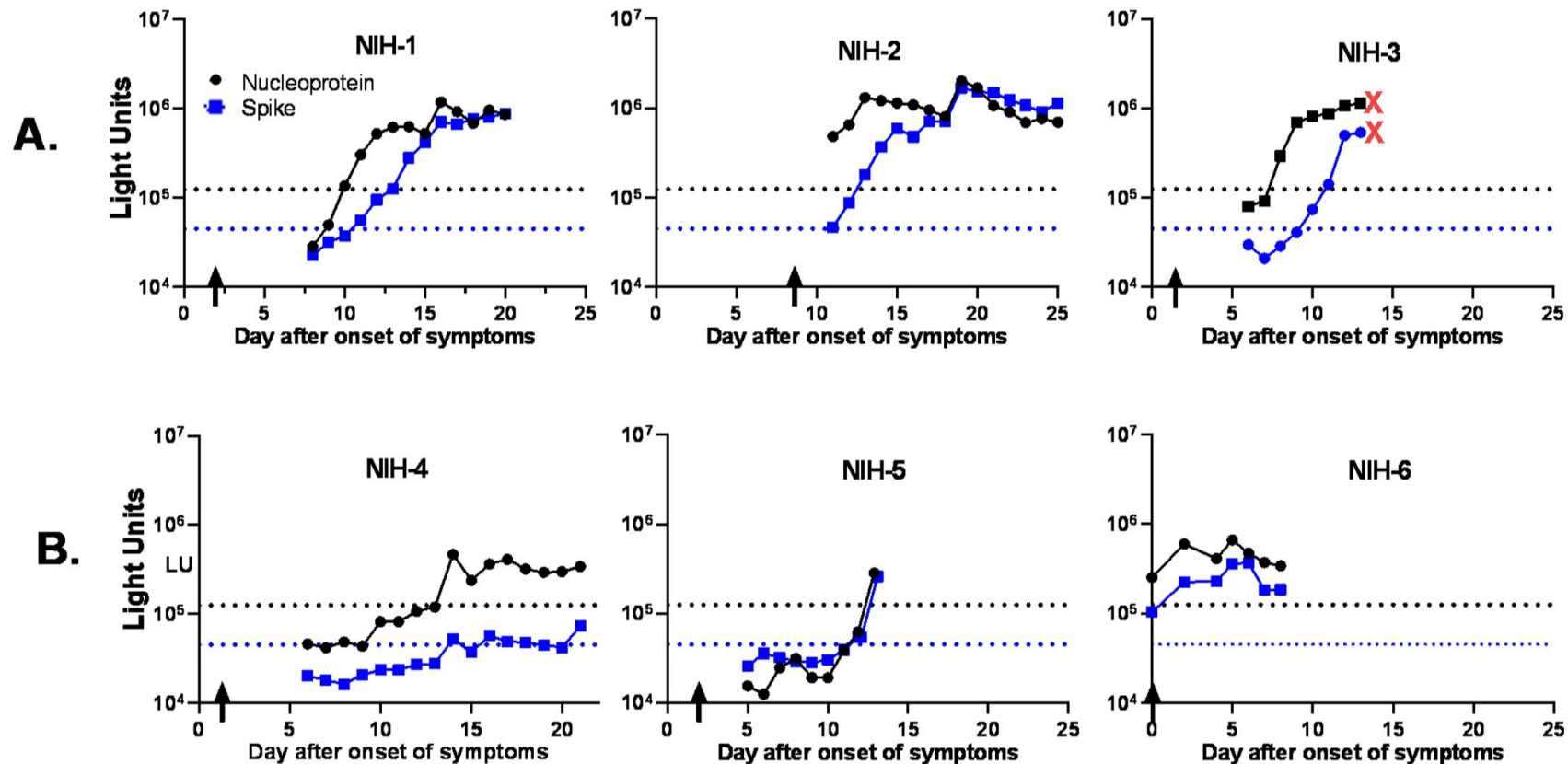
Dilcher, L et al. (2020) SARS-CoV-2: a novel deadly virus in a globalised world

Courtesy of Marie Hensley, Resident

Nucleocapsid More Sensitive Than Spike D>14



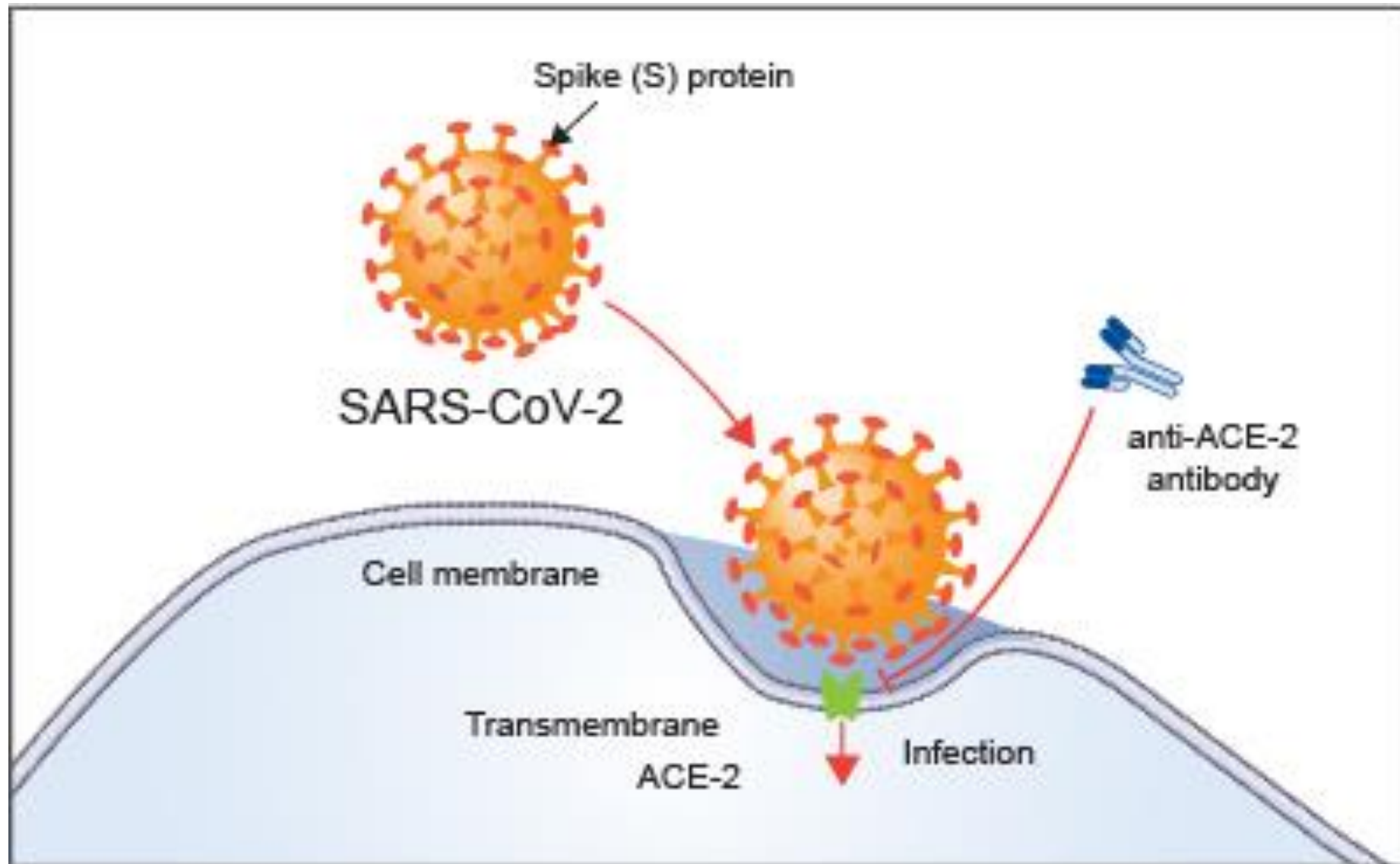
Nucleocapsid Slightly Earlier Than Spike



Nucleocapsid Better than Spike as Target for Seroprevalence and Early Diagnosis (?)

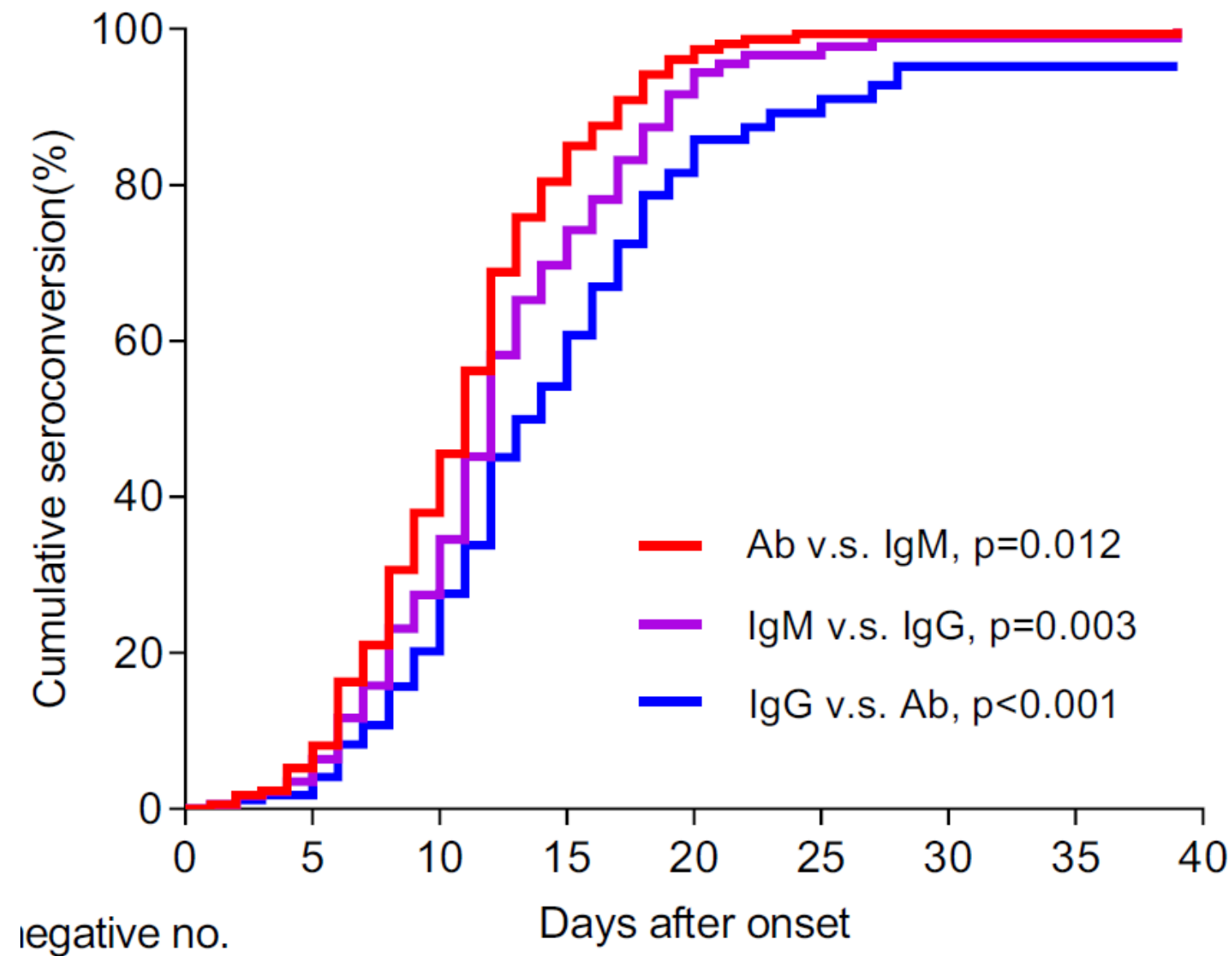
- To maximize sensitivity and early seroprevalence:
- NC more sensitive than S protein antigen

Why Measure Spike Antibodies?



What Class of Antibody? IgG, IgA, IgM, all?

- Answer: IgG, or all.
- Too many false positives with IgA and IgM (?)

A

Time of
Seroconversion,
Guandong

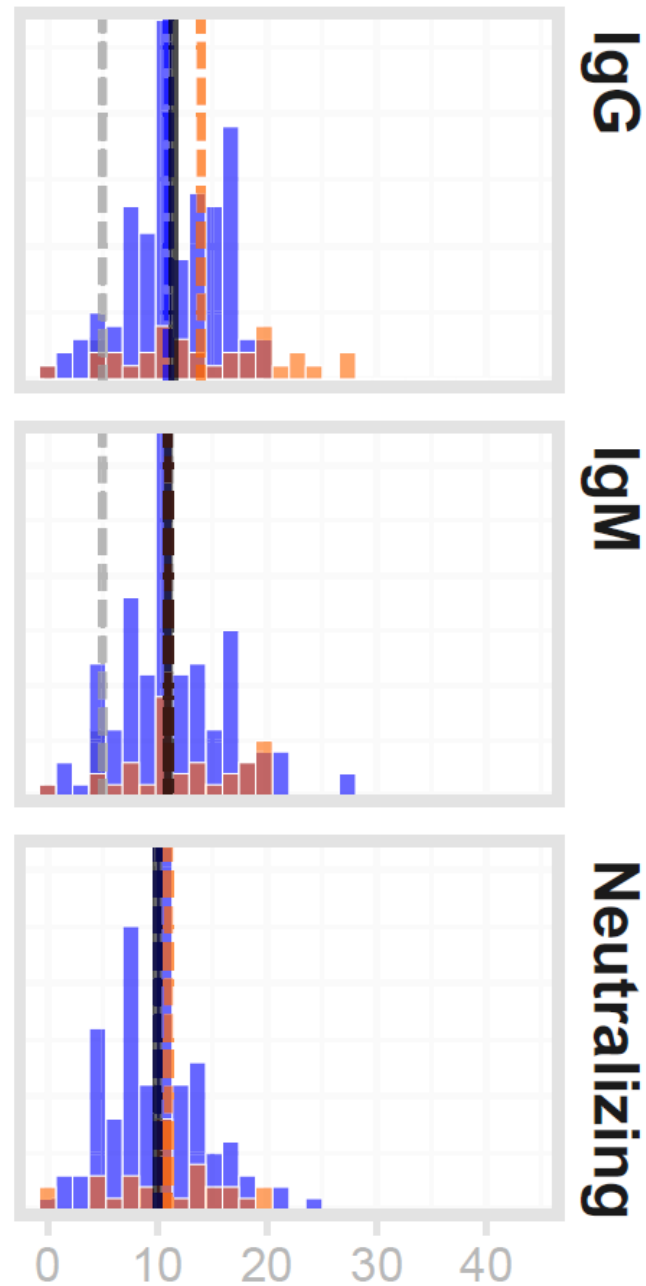
Authors: Junhui Zhao¹, Qian Yuan², Haiyan Wang¹, Wei Liu², Xuejiao Zhao¹

Brief Title: Antibody responses in COVID-19 patients
disease 2019

Title: Antibody responses to SARS-CoV-2 in patients of novel coronavirus

IgG, IgM, &
Neutralizing
Antibodies Nearly
Simultaneously

SARS-CoV-2



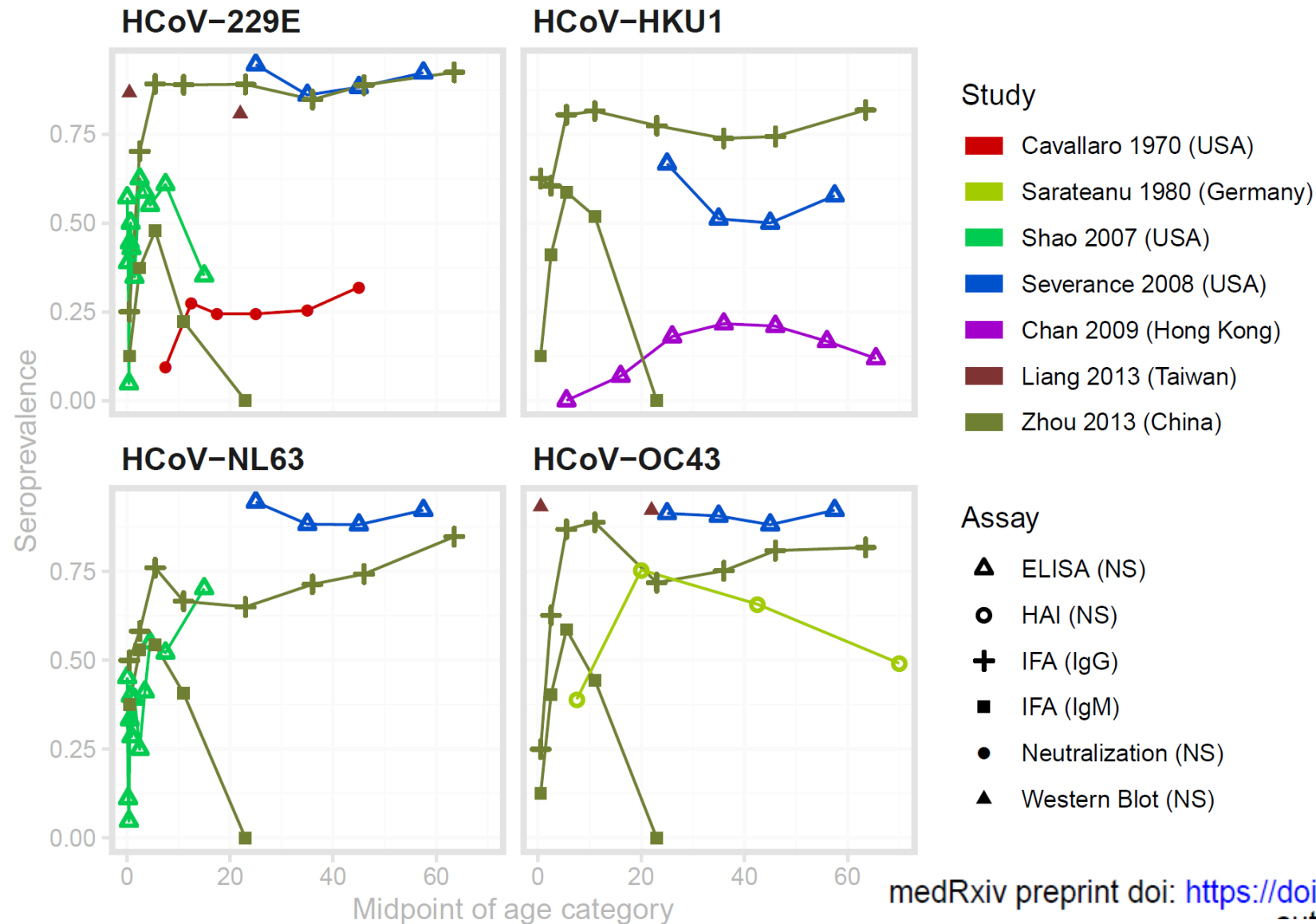
Cross-Reactivity?

- All EUA assays have warnings about lack of specificity and potential for false positives.
 - My experience: Lack of specificity seen for IgA and IgM assays, not much for IgG 'professional' assays.
 - Lateral flow: most IgM-only sera are false-positives
 - Rheumatoid factor positive sera frequently false-positives.
 - Neither sensitive nor specific as visual test. Maybe ok for IgG as quantitative test (??)
 - What about other corona viruses?

Likely cross-reactive with SARS (original SARS).
Theoretical concern with seasonal cold Coronaviruses, but not seen.

Caveat: not many proven positive sera to test

Seasonal 'Cold' Coronavirus Seroprevalence



Why Do Serology Tests (1)?

- Public health planning
 - Seroprevalence allows determination of who has been infected
 - Determination of population groups at high or low risk of infection
 - Selection of groups to test for efficacy in immunization trials
 - In low risk groups, harder to ascertain vaccine efficacy
- Clinical indications – Uncommon now
 - Suspected infectious or post-infectious complication, without positive pcr. (NOT replacement for pcr acutely)
 - ? Interstitial lung disease
 - ? Cardiac (? Kawasaki disease-like condition in children)
 - ? Neurologic, ? Thrombotic, ? Cutaneous, ? Other

Seattle Times, 04/30/20, 6 am

'Frostbite' toes, other peculiar rashes may be signs of virus

By ARIANA EUNJUNG CHA
The Washington Post

As a dermatologist at Massachusetts General Hospital in Boston, Esther Freeman was prepared for things to be a bit quieter during the coronavirus pandemic lockdown. But not too long after it began, she started getting urgent calls about odd frostbite-like patches showing up on people's toes.

The rash itself was rather harmless.

While some complained of a burning sensation, the inflammation usually disappeared on its own in two to three weeks without treat-

ment. What was striking is that many of those patients had tested positive for the coronavirus that causes the COVID-19 illness.

"My inbox and my telemedicine clinic are full of just toes. It's all about toes. I have never seen so many toes," Freeman said.

The phenomenon has also caught the interest of researchers in hot zones such as France, Italy and China. But the reports had been mostly limited to individual case studies and first-person observations, making it difficult to determine what these rashes mean, why they are occurring and how they

are linked to the virus.

A U.S.-based group is preparing to publish the first in-depth look at the virus' dermatologic effects, based on a registry of nearly 300 patients confirmed or suspected of having the virus. The report offers some tantalizing clues about the pathogen and its wildly different effects on different people.

Four months into the battle with the novel coronavirus, the paper is part of a flood of scientific evidence that is challenging early assumptions that the virus primarily affects the lungs. While the majority of cases

turn out to be mild and may involve no symptoms at all, we now know infection can sometimes result in devastating injury to the kidneys, heart and other major organs.

In the same way the first sign of infection for some may be loss of smell and taste — those are among the six new coronavirus symptoms the Centers for Disease Control and Prevention added to its list Monday — the toe rashes may be an early marker of exposure, or possibly one that it has resolved and passed.

One of the clearest findings of the new paper is that

most patients with "COVID toes" were asymptomatic or had only mild symptoms. Another is their age. Nearly all were children or adults in their 20s and 30s, a group that as a whole tends to have a less severe response to the disease than its older counterparts.

Freeman, a Harvard Medical School researcher who led the analysis in collaboration with the American Academy of Dermatology, said the information should be comforting to those who have seen the lesions on themselves or loved ones.

"Most of the patients were young, healthy and had a

benign clinical course," she said.

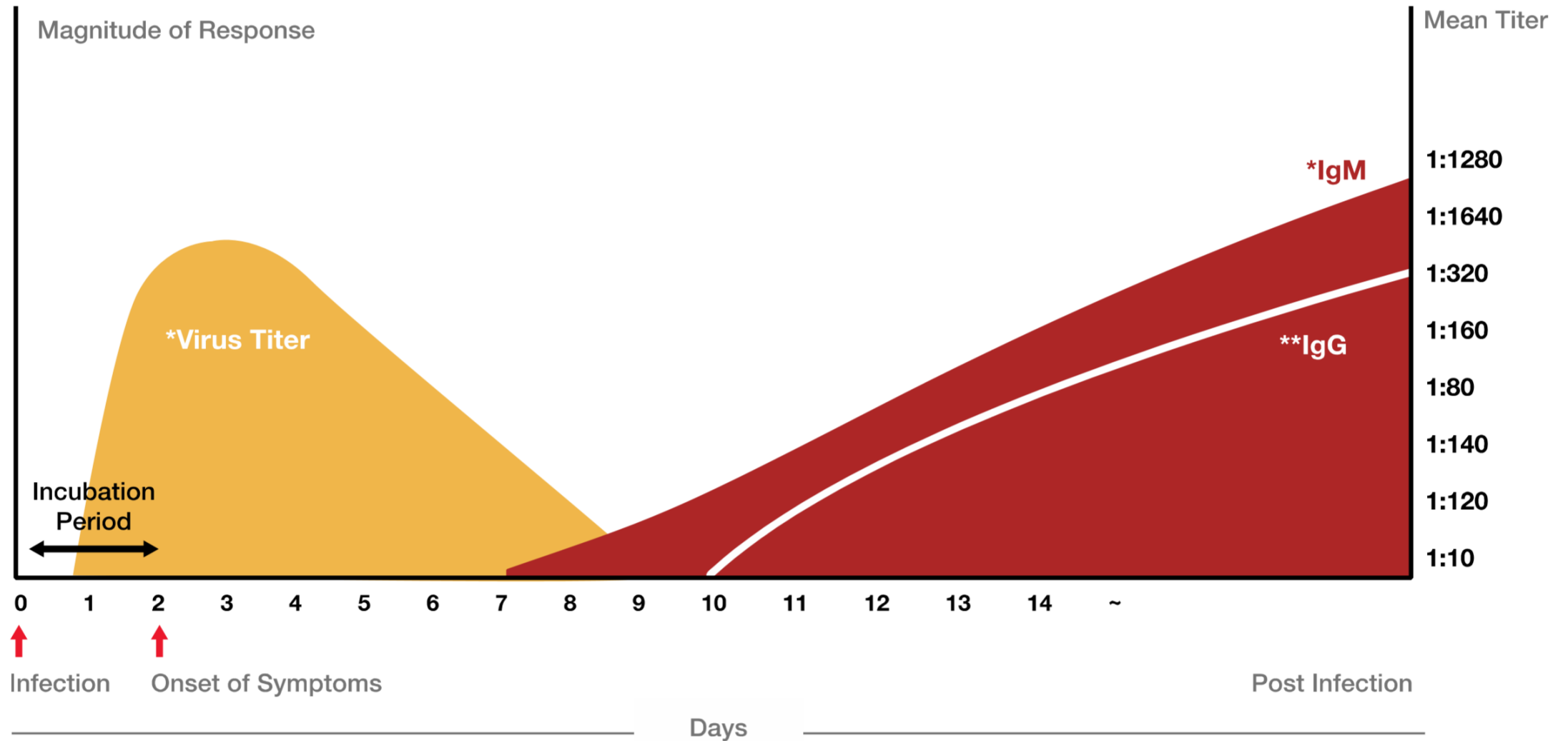
Viral rashes are not unusual. But the location of the rash on the toes, and sometimes fingers too, has puzzled researchers.

This type of rash, called pernio or chilblains, usually occurs in winter because of exposure to cold, such as when a person is slogging in freezing rain in wet socks. But virus patients are getting it in springtime. Doctors also typically see the rash in people who work as florists or in warehouses that are not temperature-controlled — not in children, as is happening now.

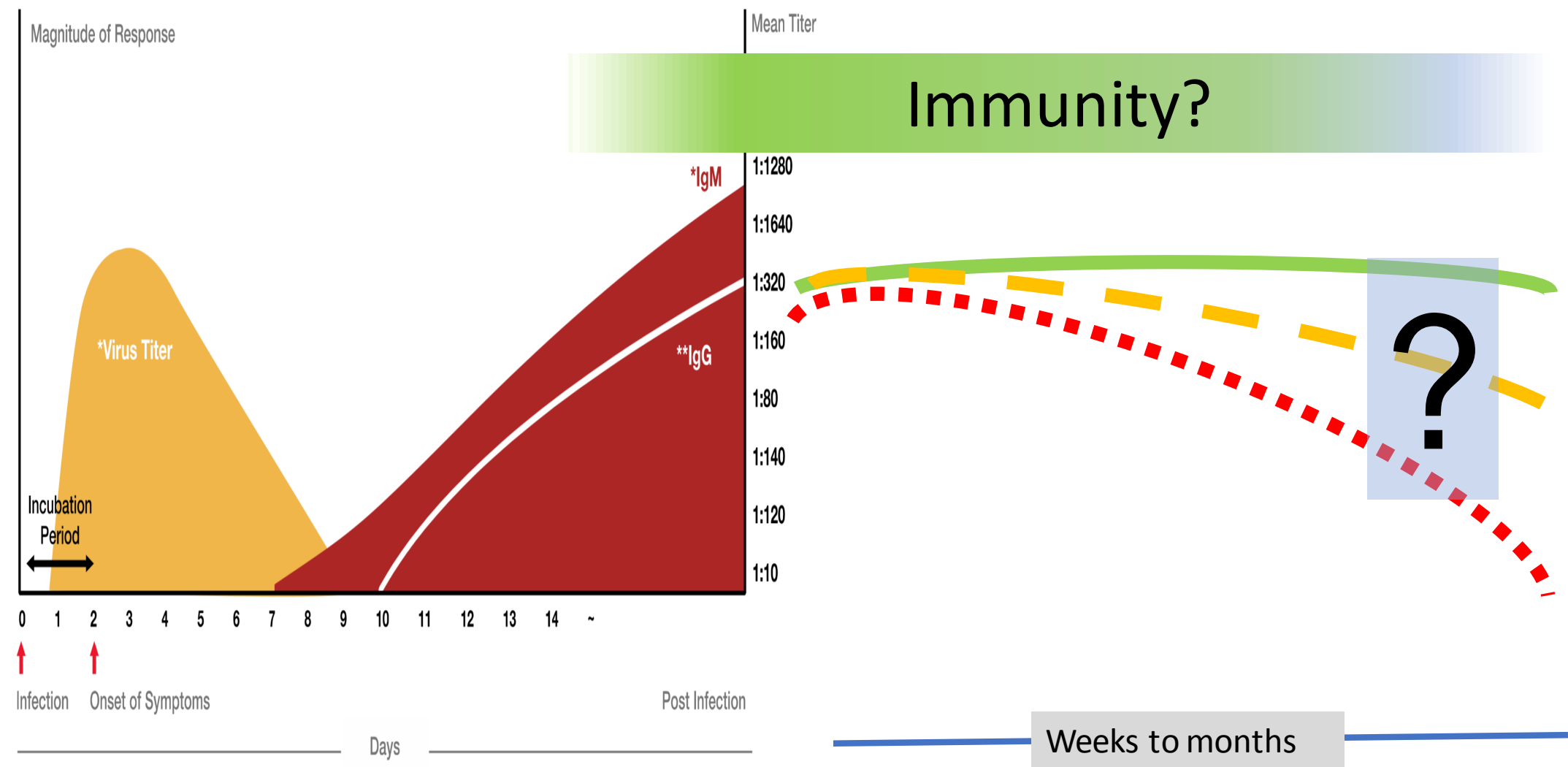
Why Do Serology Tests (2)?

- Clinical trials: Selection of convalescent plasma donors (UW)
- Return to work ascertainment ???
 - Unclear if antibodies = immunity (prevent future infection)
 - Based on experience with other virus infections, expect past infection indicates lower risk for infection or lower risk of severe infection
 - Exception: some evidence of antibody-enhanced infection in Dengue, SARS1, Zika, MERS,
- Curiosity/public requests
 - “I want to know about that infection/sore throat/runny nose/muscle ache...”
 - “ I want to know if I can go back to work safely”

Course of Epidemic: Virology, Serology



Course of COVID-19: Virology, Serology of Individuals



Adapted from Royal College of Pathology of Australia. <https://www.rcpa.edu.au/getattachment/bf9c7996-6467-44e6-81f2-e2e0cd71a4c7/COVID19-IgG-IgM-RAPID-POCT-TESTS.aspx>

THANK YOU!!

Ochsner Health System Coronavirus Lab Response

Elise A. Occhipinti, M.D.

Department of Pathology and Laboratory Medicine (OMC NOLA)

April 30, 2020

Coronavirus in Louisiana: 27,286 cases | 1,758 dead | 1,666 in hospital | 17,303 recovered

Ochsner Timeline:

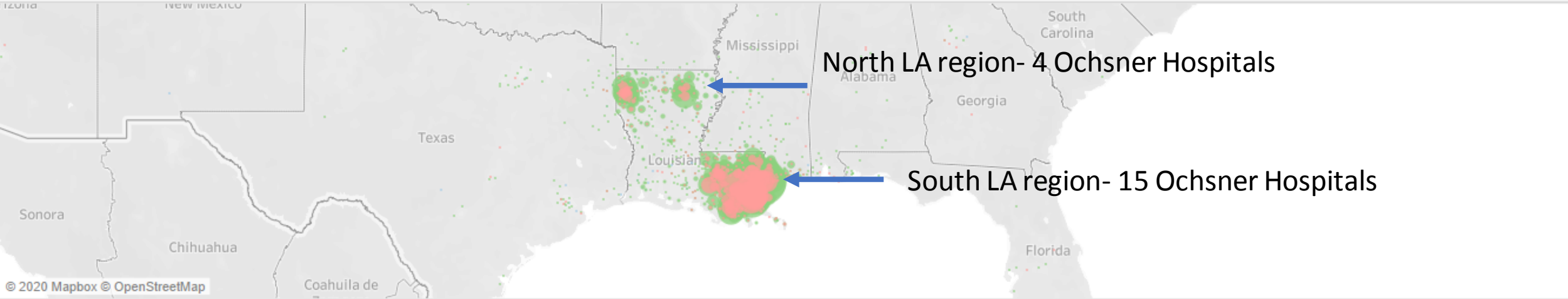
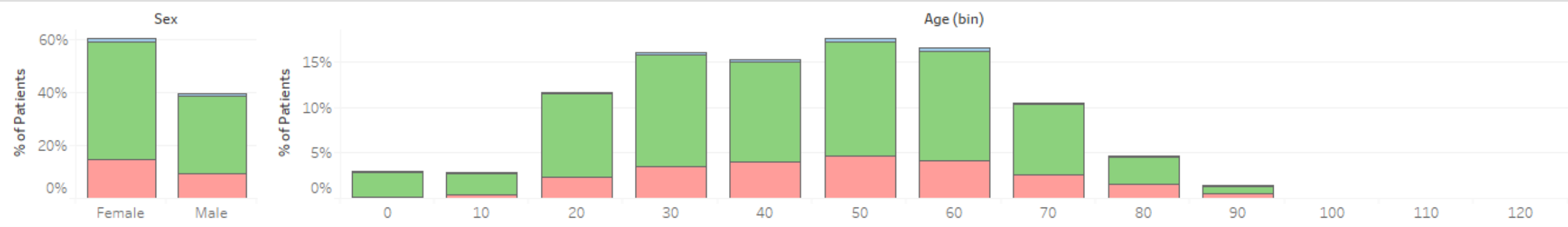
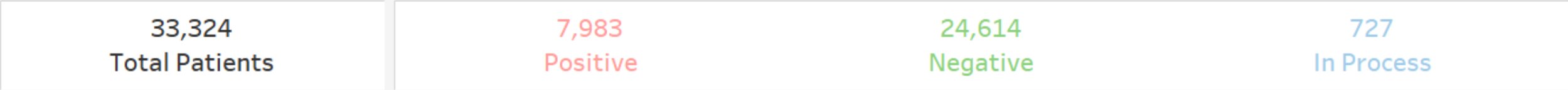
- Mardi Gras: Feb 25
- 13 days later: March 9- First case in LA (New Orleans)
- March 20: Began in house PCR testing (Abbott m2000)
- March 27: Added Cepheid platform
- April 2: ID NOW(s) validated and deployed to ED and L&D areas
- April 22: Began in house antibody testing (Abbott i2000)

Patient Population Overview

PCR Testing- Overall positivity rate approx. 25% (50% at peak)

This dashboard displays the count of patients that have one or more resulted or in process (pending) orders for COVID-19 since testing has begun. The COVID-19 Label Source can be toggled to change the test type(s) included. This is extracted from the Epic reporting database (Clarity) each night.

Patient Labels:
Positive = 1+ Positive Results
Negative = 0 Positive Results and 1+ Negative Results
In Process = 0 Positive Results, 0 Negative Results, and 1+ In Process Results



PCR strategy

- Goal- maximize testing, provide turn around time that fits need of population and navigate kit/reagent/swab allocation

M2000 (routine)

Clinic outpatients
Drive through collections
Urgent Care
In patients not yet tested
Post acute care discharges
Pre-op (location dependent)
Rad onc/Heme onc (location dependent)

Cepheid (expedited)

Transfers not yet tested
Health care providers
Organ donation
Urgent Pre-op
Urgent infusion

IDNOW (STAT)

ED patients with symptoms
All admits from ED
All admits from L&D
NICU
Emergent procedures (Cath, endo)
Direct admits

COVID-19 Collected Specimen Orders (Antibody)

Collection Date
3/1/2020 12:00:00 AM to ..

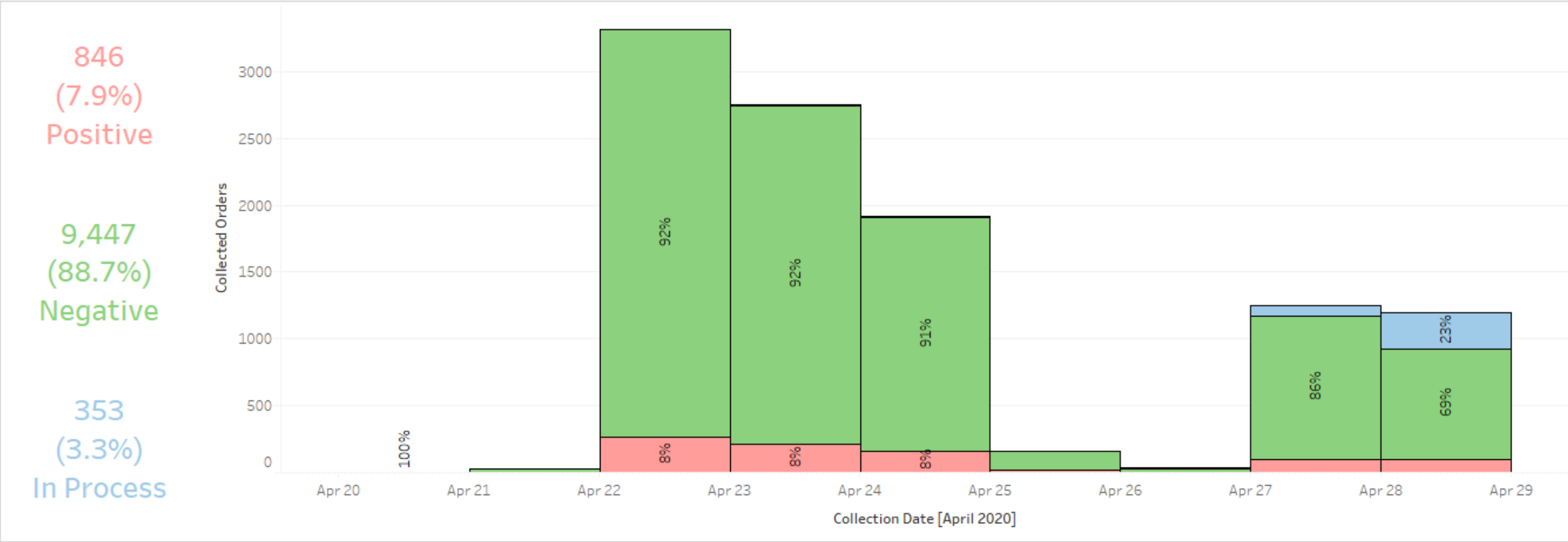
Test
All

Resulting Lab
All

Ordering Location
All

This dashboard displays the count of collected COVID-19 antibody orders by the collection date. The counts are broken out by positive final result, negative final result, and in process (pending result). This is extracted from the Epic reporting database (Clarity) each night. If you are looking for numbers more reflective of current state and not as of last night, Ochsner SOFT reports would be more appropriate.

It is important to note that this is a total count of orders and can represent a single patient more than once. It is also a count of the orders placed inside of Epic and will not reflect orders placed incorrectly outside of Epic.



	Total	4/20	4/21	4/22	4/23	4/24	4/25	4/26	4/27	4/28
Grand Total	10,646	1	26	3,317	2,754	1,916	162	31	1,246	1,193
In Process	353				2	5		1	73	272
Negative	9,447	1	24	3,055	2,541	1,751	147	28	1,072	828
Positive	846		2	262	211	160	15	2	101	93

Thank you for attending

SAVE THE DATE

Lessons Learned from COVID19 regarding Digital Health Resources –
Considerations for Genetics and Beyond

Date: May 12, 2020

Time: 11:00 AM PT

Presenter: Ellen T. Matloff, MS, CGC – My Gene Counsel

If you have any ideas for topics or speakers
we would love to hear them!

Send us your ideas to
PLUGS@seattlechildrens.org