

COVID-19 serology

October 29, 2020

5.1.2e

5.1.2e

5.1.2e

IIV COVID-19 meetings

- IMM-IMS-KIM joined meeting
 - Birds-eye view
- Subsequent meetings
 - More details / in-dept
 - Discussion
 - Aims
 - content
 - Connection to other COVID-19 projects
- For now, 2 more scheduled, topics pending

Acknowledgements

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- Study participants
- Volunteers
- IIV sidekicks
- PiCo study team
- FFX study team

Serology for SARS-CoV-2

- Identification of infection (in addition to PCR)
- Serosurveillance at population level
- Cost-effective
- Highly quantitative

- Develop a multiplex bead-based immunoassay to
 - Study seroprevalence
 - Investigate host immune responses

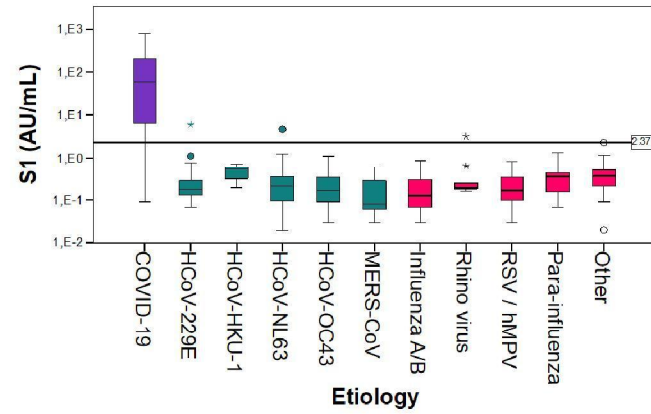
- Approach
 - Nucleoprotein, Spike subunits S1 and RBD

Program today

- Seroprevalence in the Pienter-Corona study
- Extension of the assay: IgM, IgA, avidity
- Longevity of antibody responses
- Antibodies in relation to symptoms
- Spike S1 versus Trimeric Spike and D614G

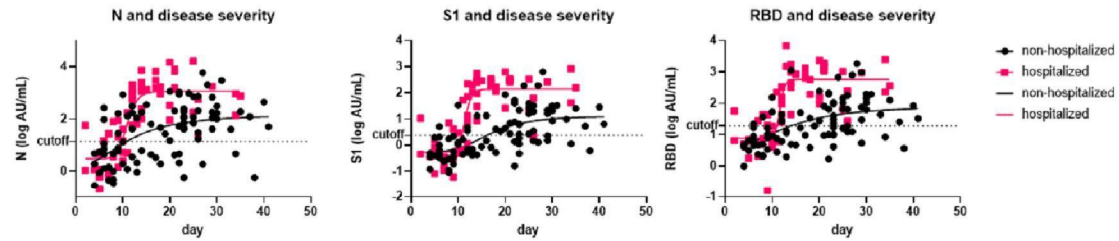
Ability to discriminate samples with different etiology

1
(1)





Severity of symptoms



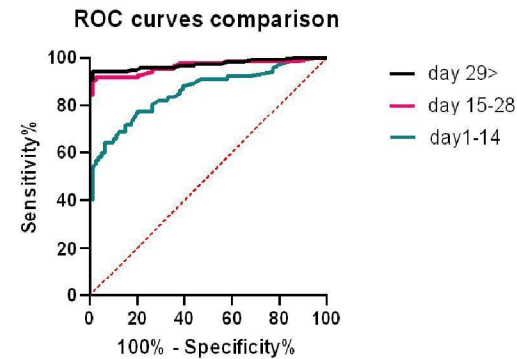
N	Hospitalized	
	No	Yes
Slope	2.95	8.43
R square	0.284	0.705
P-value	<0,0001	

S1	Hospitalized	
	No	Yes
Slope	3.64	51.1
R square	0.293	0.753
P-value	<0,0001	

RBD	Hospitalized	
	No	Yes
Slope	2.36	17.7
R square	0.192	0.707
P-value	<0,0001	

Sample selection ~ Assay performance

- Clinical background, time since infection
- Assay sensitivity and specificity
- True seroprevalence



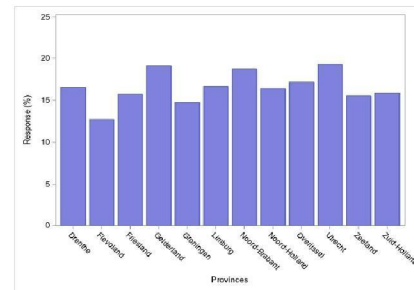
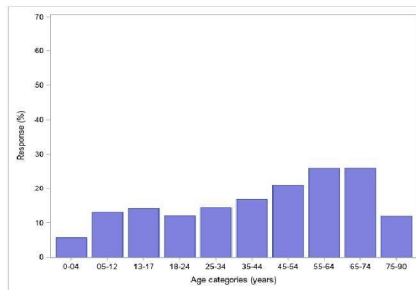
	Cutoff	Sensitivity%	Specificity%	Likelihood ratio	Area	SE	z	P
Day 1-14	> 0.5614	53,73	98,73	42,45	0,858	0,0318	reference	
Day 15-28	> 0.6618	90,48	98,73	71,48	0,964	0,0151	3,023	0,0025
Day >29	> 0.6350	94,21	98,73	74,43	0,973	0,0114	3,404	0,0007

The PiCo study

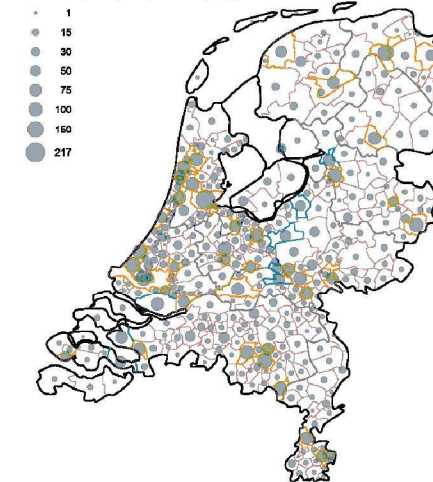
- Pienter 3 – 2016/2017
 - Municipality-based
 - PiCo1 – April – N ~ 3400
 - Within P3
 - PiCo2 – June – N ~ 7400
 - PiCo1 + additional random sample
 - PiCo3 – October – N > 6500
-
- Extensive questionnaire

PICO2 – June, 2020

- **Longitudinal measures:**
 - PICO2-NS sample: n=> 2,300
 - PICO2-LVC sample: approx. 500
- An additional sample to enhance the geographical spread (sampling across the NL and all ages)
PICO2-PLUS: extra n=> 4,600



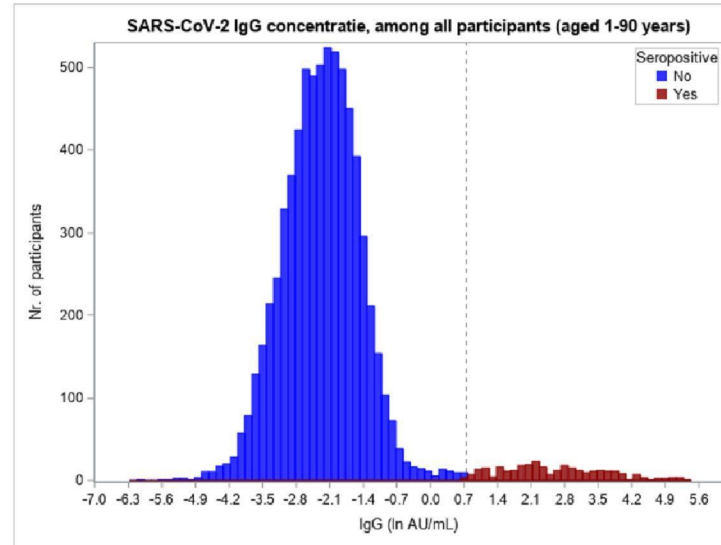
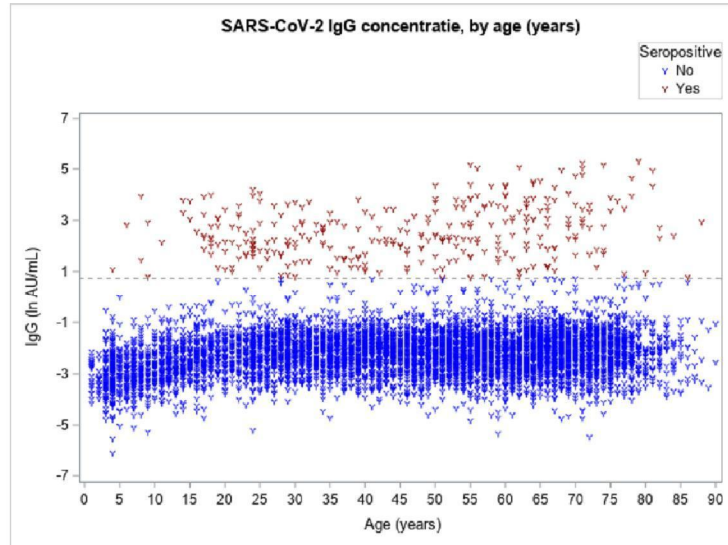
Number of participants per municipality, PICO2



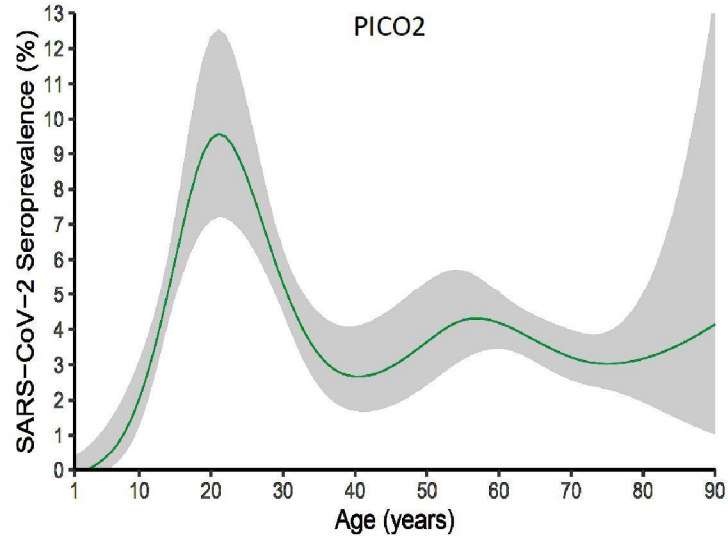
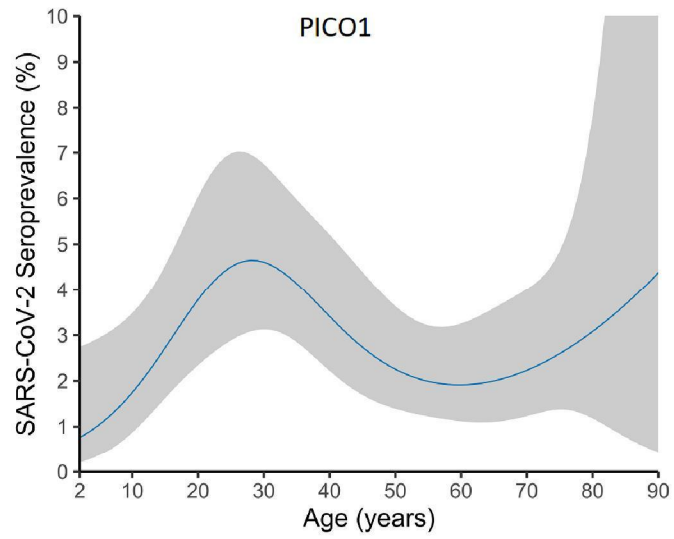


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Ministry of Health, Welfare and Sport

SARS-CoV-2 IgG concentration (S1, ln AU/mL), PICO2

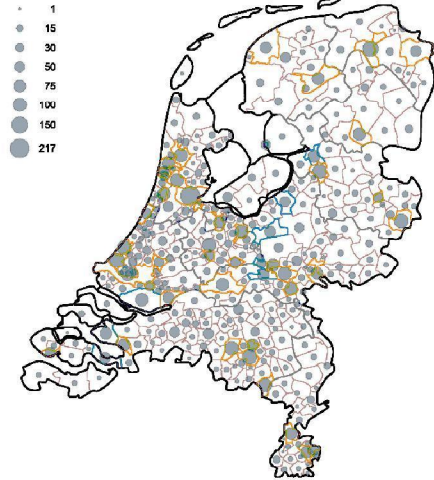


April versus June 2020

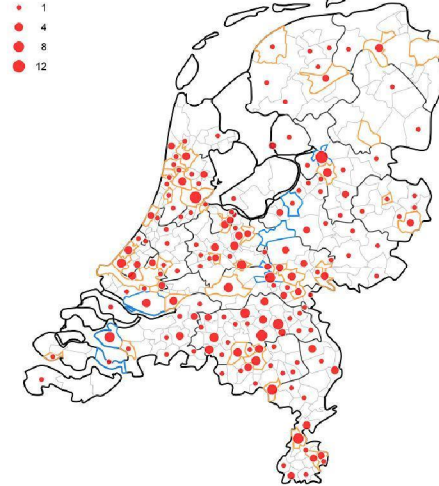


Seroprevalence – NL, by geo spread

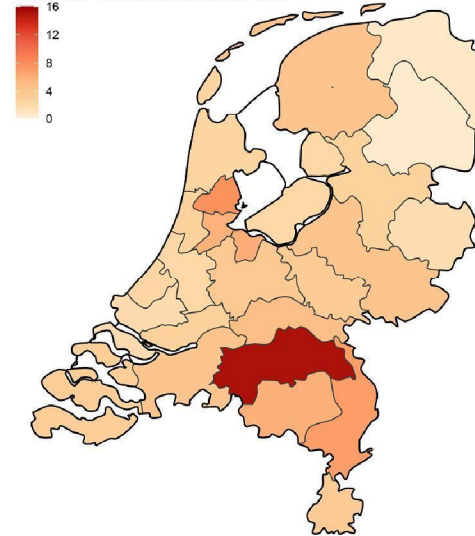
Number of participants per municipality, PICO2



Number of SARS-CoV-2 seropositive participants per municipality



SARS-CoV-2 seroprevalence (%), PICO2



Ongoing analyses (PiCo2, PiCo3)

- Risk factors
 - Contact patterns
- Symptoms
- Age-specific risk factors?
- Ig concentrations
 - Time
 - symptoms



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CNN health Food Fitness Wellness Parenting Vital Signs **EN**

British study shows evidence of waning immunity to Covid-19

By **Jan Christensen**, CNN
Updated 03:59 GMT (11:59 HKT) October 27, 2020

CNN health Food Fitness Wellness Parenting Vital Signs **EN**

New reports show coronavirus immunity can last for months

By **Maggie Fox**, CNN
Updated 11:55 GMT (10:55 HKT) October 14, 2020

The New York Times

The Coronavirus Outbreak > **LIVE** Latest Updates Maps and Cases Vaccine Tracker Spike in Hospitalizations Answers to Your Questions

Why You Shouldn't Worry About Studies Showing Waning Coronavirus Antibodies

Experts say it's normal for levels of antibodies to drop after clearing an infection, and that they represent just one arm of the immune response against a virus.

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Health | Coronavirus

Coronavirus immunity: Can you catch it twice?

By **James Gallagher**
Health and science correspondent

26 August

Coronavirus pandemic

Sanquin Blood donations Blood groups Over Blood Over Sanquin Over words **NL**

Persbericht

Corona-antistoffen bij donors landelijk gedaald

15 juli 2020

Deel dit bericht

What causes the confusing flow of news

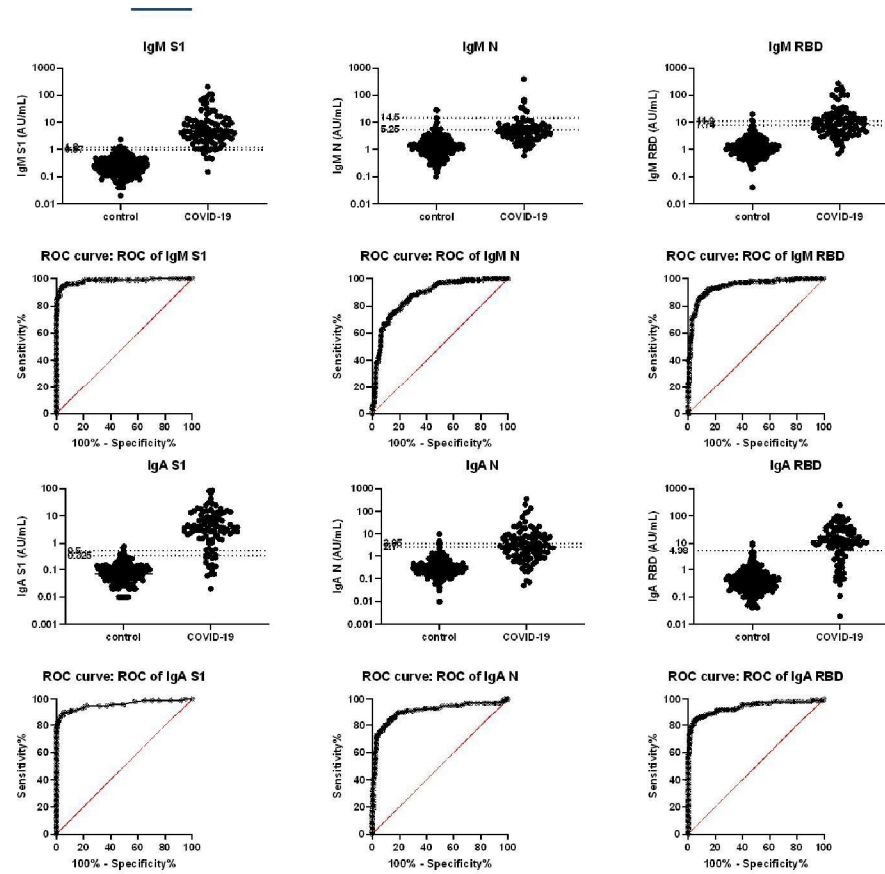
- A lot at stake
- Researchers with different backgrounds involved
- Sampling strategy
 - Representative / corrected?
 - Independent samples / Longitudinal?
- Assay
 - Performance
 - Antigen
 - Which Ig
- Interpretation and communication..

What we do

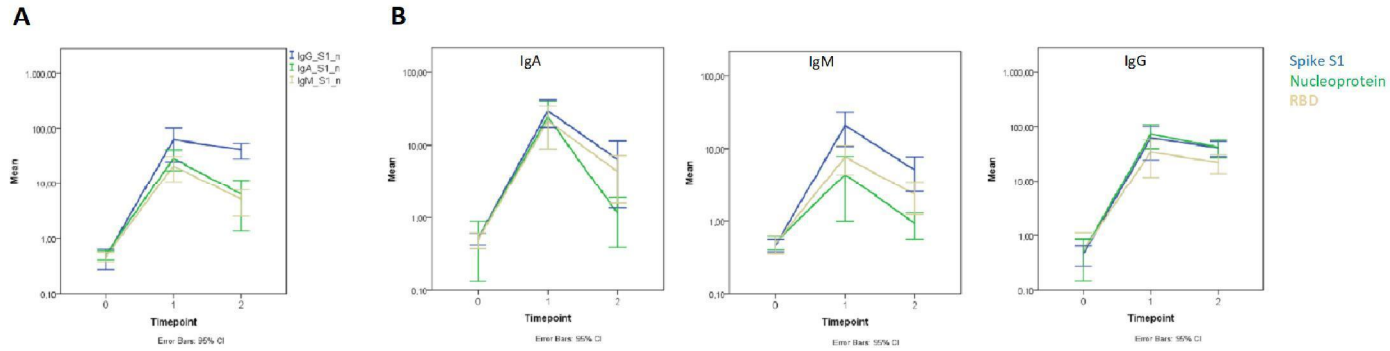
- PiCo
 - Include N and Spike
 - Measure IgM, IgA, IgG separately
 - Longitudinal
-
- Disseminate

IgM, IgA

- Less separation
 - N
 - RBD
- IgG superior for classification of samples

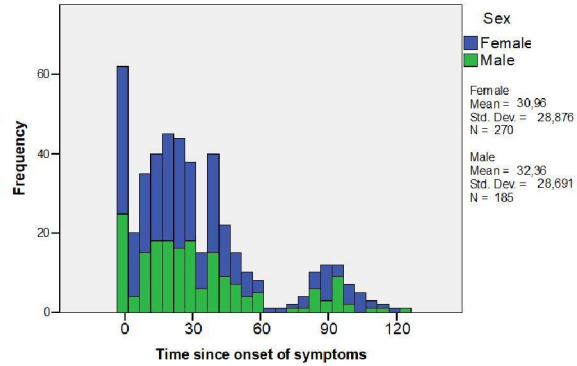
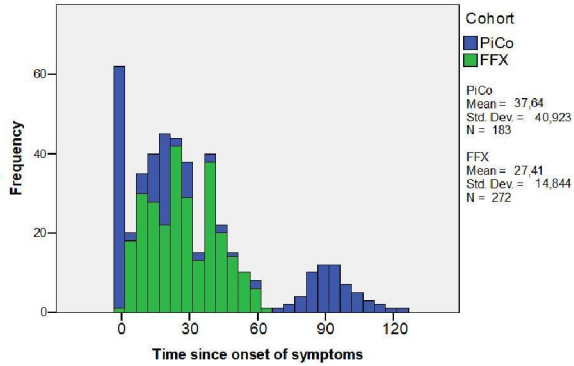
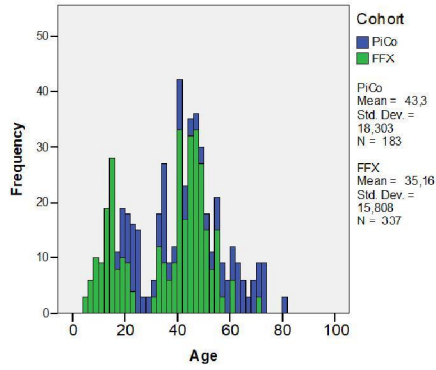


Ig kinetics vary between isotype and specificity (PiCo)

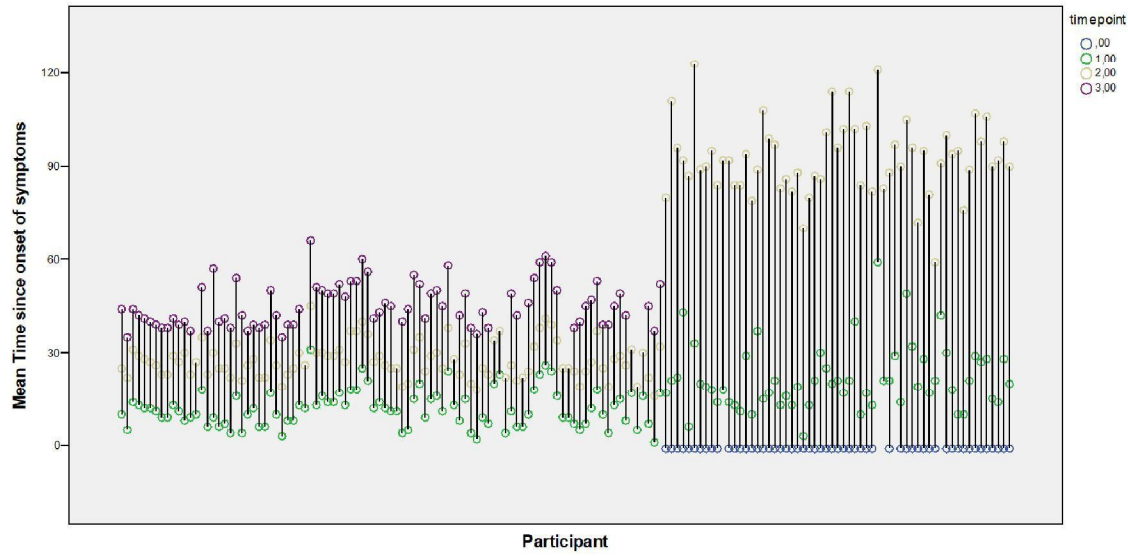


FFX versus PiCo

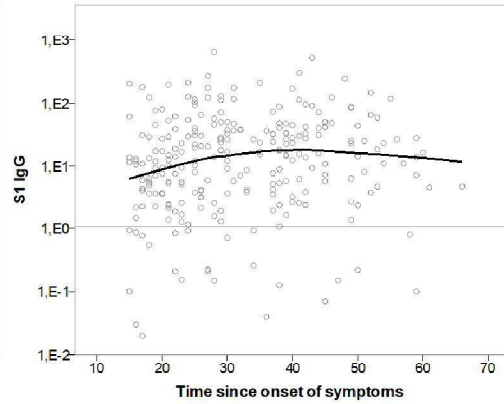
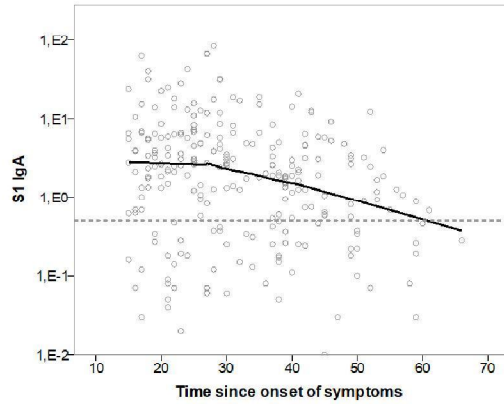
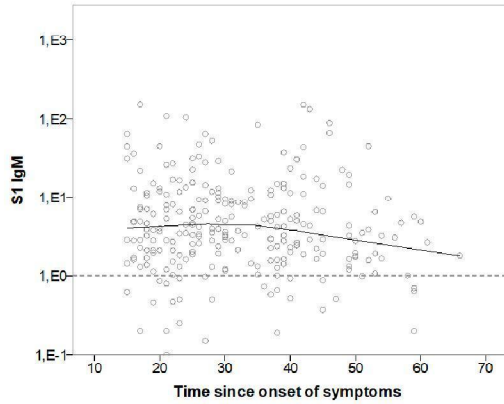
- Fundamentally different study design
- Similar data collected
 - Questionnaire
 - Humoral data
- Could datasets be merged?
 - More samples
 - Better distribution of (early) time points
 - If 2 independent studies show the same result...
- Restriction: no epi conclusions



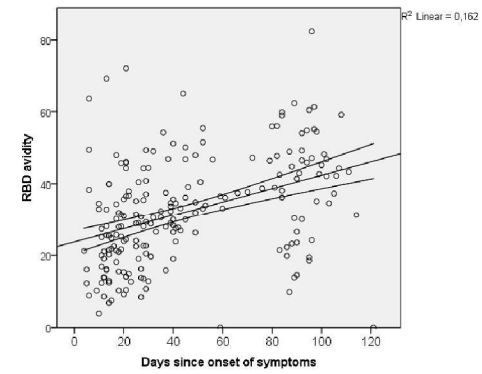
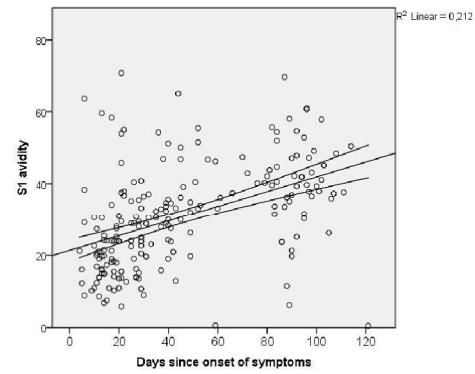
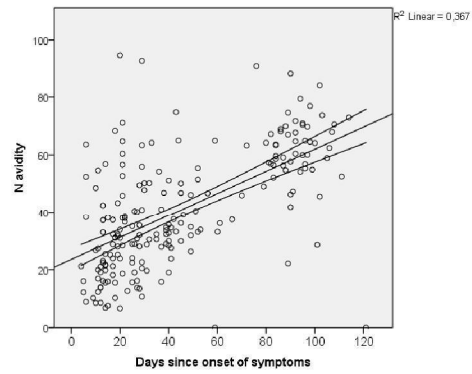
Longitudinal samples FFX & PiCo (P3, Pico1,2)



Spike S1-specific antibody kinetics

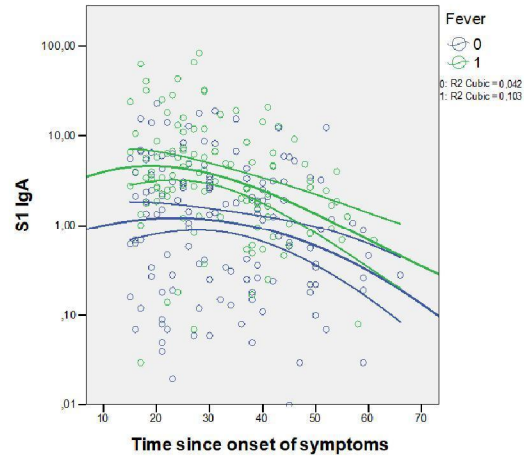
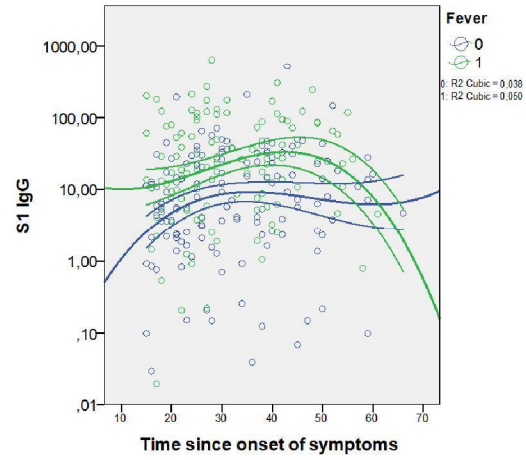


IgG avidity

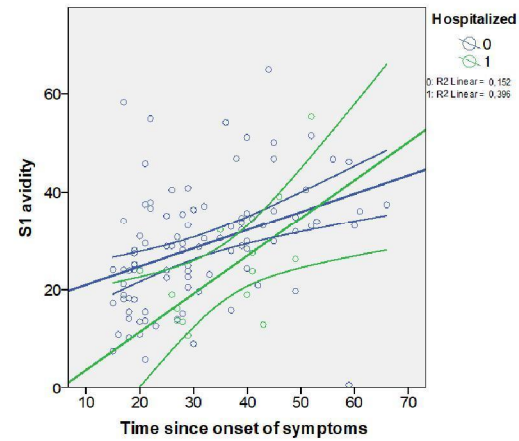
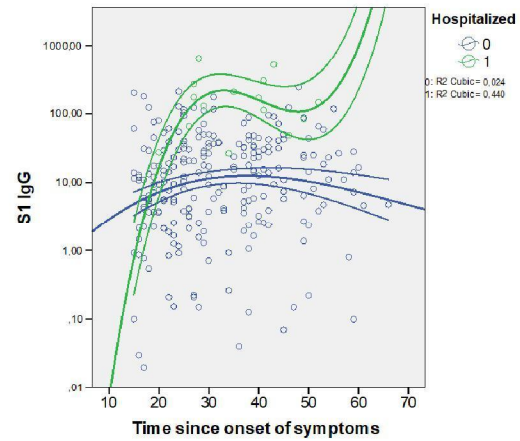


Preliminary statistical results

	IgG	IgA
Fever	,000	,000
Fatigue	,015	,007
Coughing	,003	,001
Runny nose	,051	
Diarrhea	,015	,016
Hospital	,000	,000
Time	-	--



IgG avidity & hospitalization

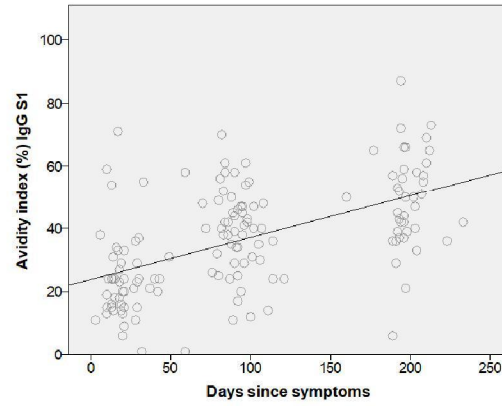
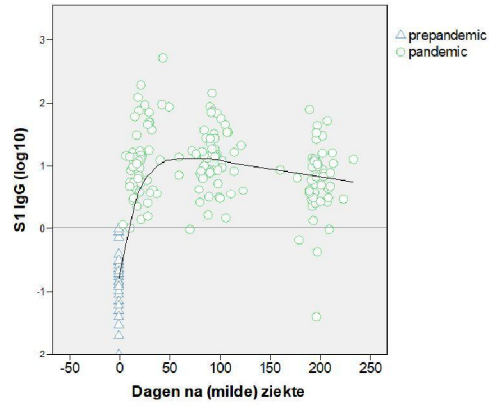


Preliminary results PiCo3

Table 2: Numbers and % of participants with antibodies to SARS-CoV-2 Spike S1 in the PiCo study rounds

		S1_IgG	S1_IgA	S1_IgM	Day Median (95% CI)
PiCo 1	N tot	59	59	59	19
	N pos	59	49	51	(17-21)
	%	100	83,1	86,4	
PiCo 2	N tot	59	59	59	92
	N pos	58	31	33	(90-97)
	%	98,3	52,5	55,9	
PiCo 3	N tot	50	50	50	197
	N pos	47	26	22	(196-203)
	%	94	52	44	

IgG



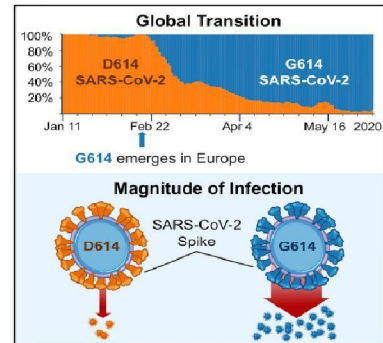
Are we still assessing abs to the right target?

Cell

Article

Tracking Changes in SARS-CoV-2 Spike: Evidence that D614G Increases Infectivity of the COVID-19 Virus

Graphical Abstract



Authors

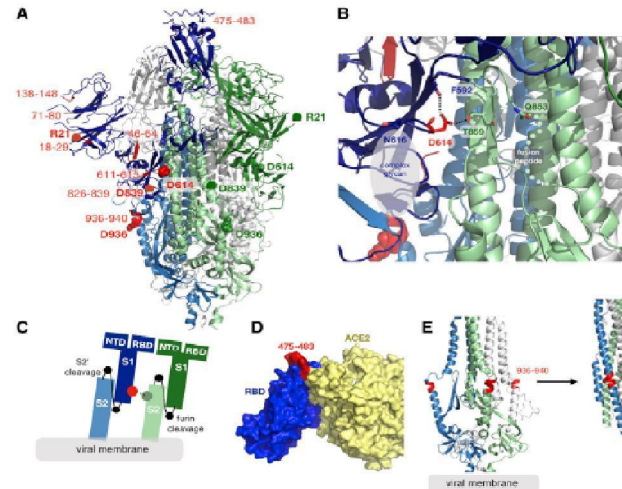
Bette Korber, Will M. Fischer,
Sandrasegaram Gnanakaran, ...,
Celia C. LaBranche, Erica O. Saphire,
David C. Montefiori

Correspondence

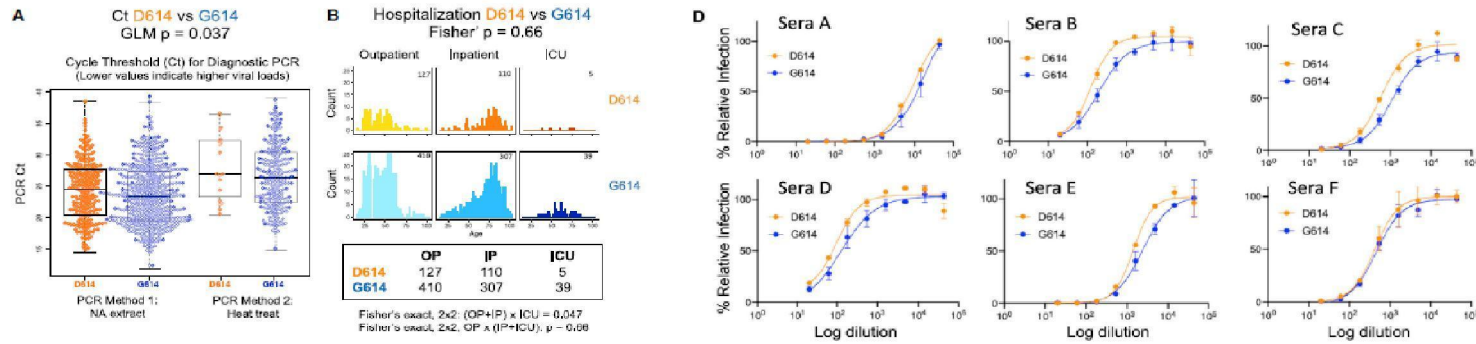
btk@lanl.gov

In Brief

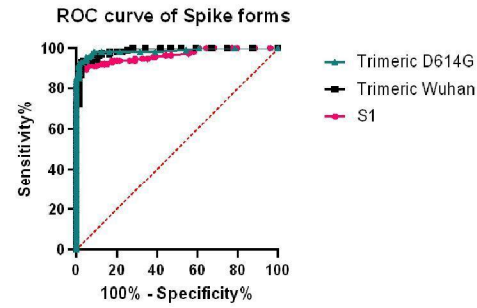
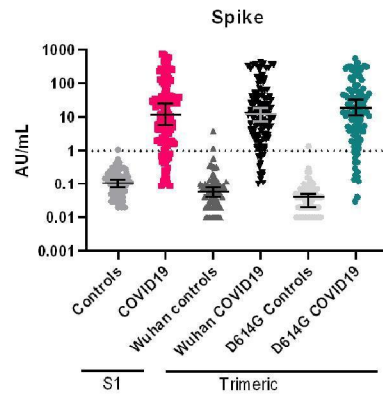
Korber et al. present evidence that there are now more SARS-CoV-2 viruses circulating in the human population globally that have the G614 form of the Spike protein versus the D614 form that was originally identified from the first human cases in Wuhan, China. Follow-up studies show that patients infected with G614 shed more viral nucleic acid compared with those with D614, and G614-bearing viruses show significantly higher infectious titers *in vitro* than their D614 counterparts.



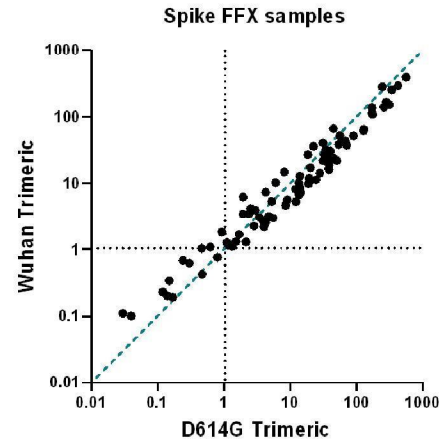
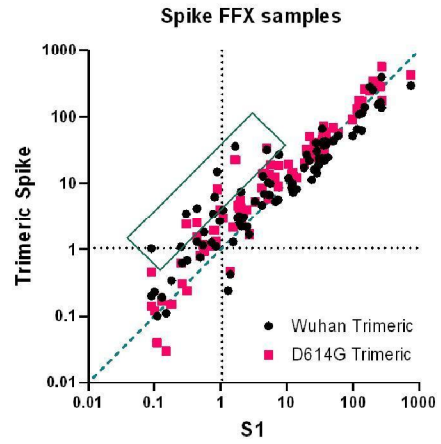
Implications of the D614G mutation



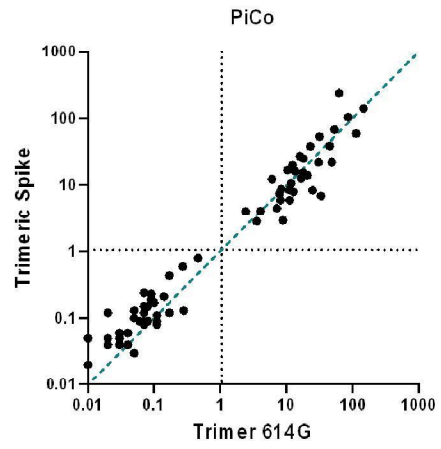
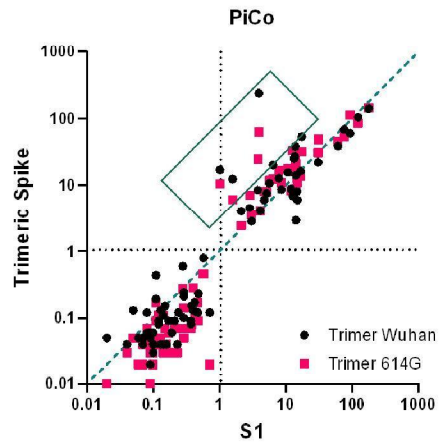
S1 v trimeric Spike RIVM MIA



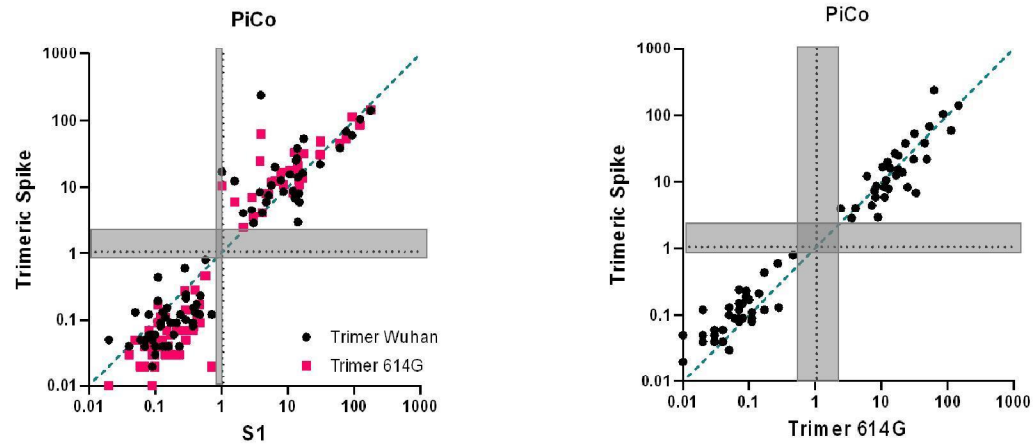
FFX



PiCo



Superior separation by trimeric spike?



Conclusions

- A reproducible, quantitative multiplex assay
- Characterized and evaluated for accurate seroprevalence studies

- Used to assess seroprevalence (few μL), longitudinal (PiCo)
- Able to precisely study kinetics (PiCo, FFX)
 - IgG, IgA, IgM, Avidity
- Decay of IgA, persistence of IgG, specificity dependent
- Increasing IgG avidity
- Concentrations associate with symptoms
- Trimeric Spike may enhance assay performance
 - no evidence for altered binding due to D614G

Ongoing projects

- Gene expression profiling of SARS-CoV-2 infected innate cells: a role for epigenetic reprogramming
- SARS-CoV-2-specific T cell responses in COVID-19: characterization, cross-reactivity and longevity
- Immunity induced by different SARS-CoV-2 vaccine concepts and correlation with protection in the ferret model
- SARS-CoV-2 epithelial infection model and antibody Fc-functionality
- Serology
 - In-dept and functional serology
 - Big data analyses
 - Support for PiCo

Connect to..

- Connection seroprevalence and immunity study
 - Ig functionality
- B cell cloning
- T cells
- Innate
- Mucosal response (FFX saliva)