COVID-19

Vaccination considerations across the transplant continuum

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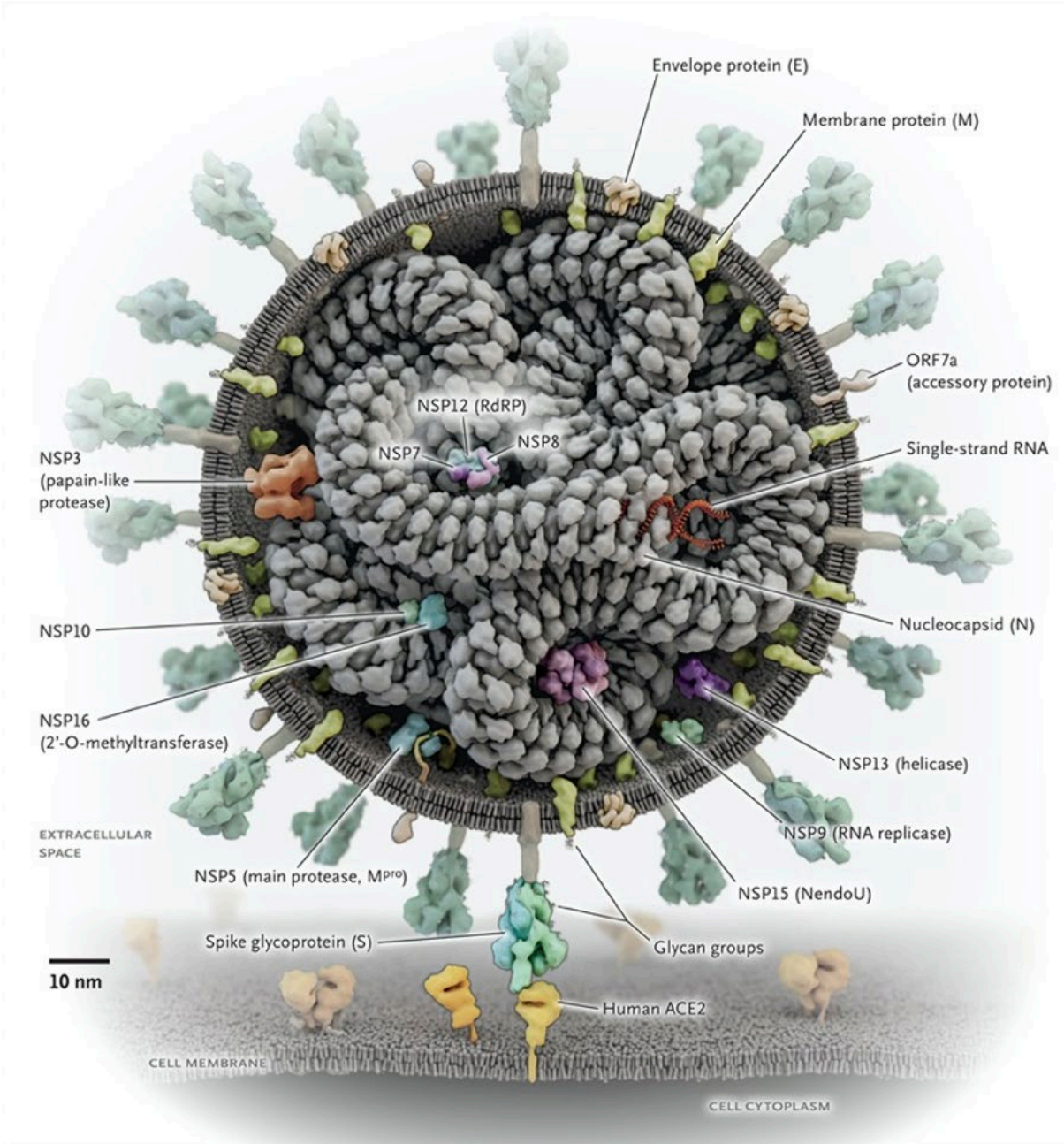
DISCLOSURES:

- DSMB:
  - Janssen – RSV Vaccines
  - Biogen – Covid, SLE therapeutics
  - Atea – Covid therapeutics
  - Adamis – Covid therapeutics
- Advisory Boards:
  - Gilead – Covid therapeutics
  - Adagio – Covid therapeutics
  - Regeneron – Covid therapeutics
  - Synairgen – Covid therapeutics



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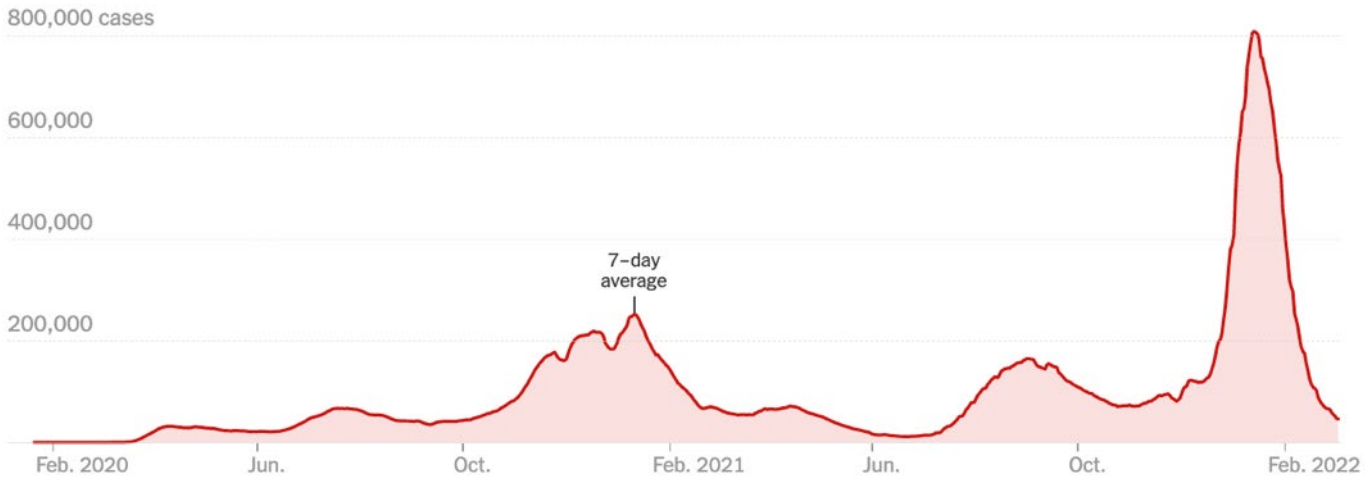
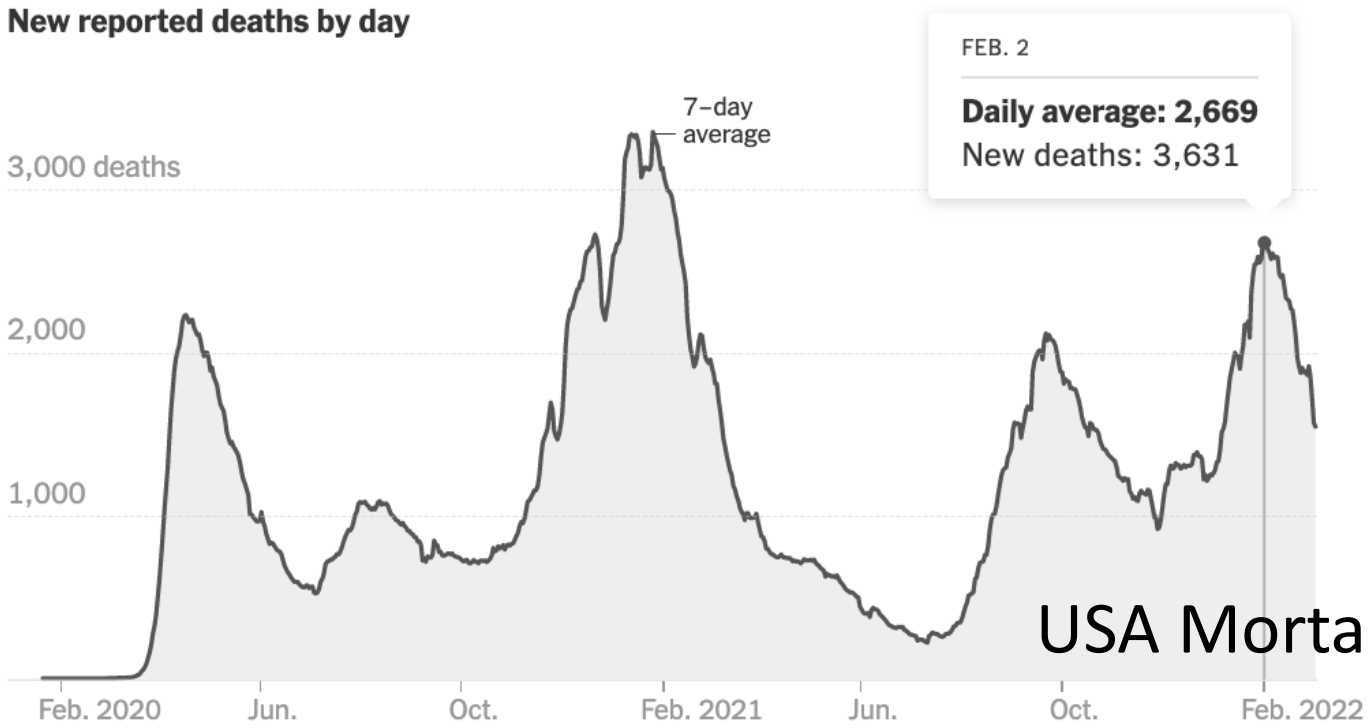
Immunocompromised Host
Infectious Diseases

Epidemiology:





USA Mortality: 957,000

Ourworldindata.org
www.nytimes.com/interactive/2021/us/covid-cases.html
last accessed March 6th, 2022

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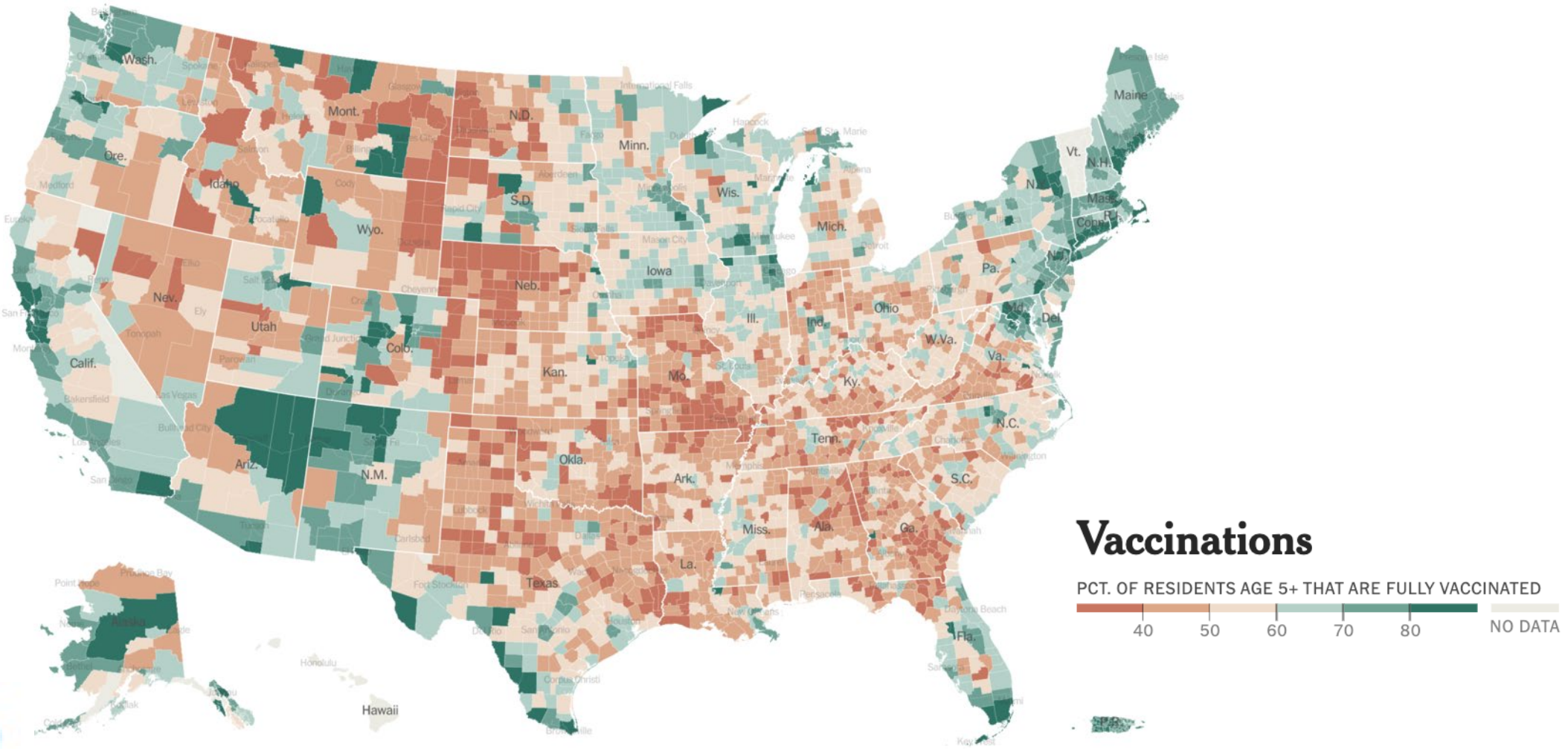

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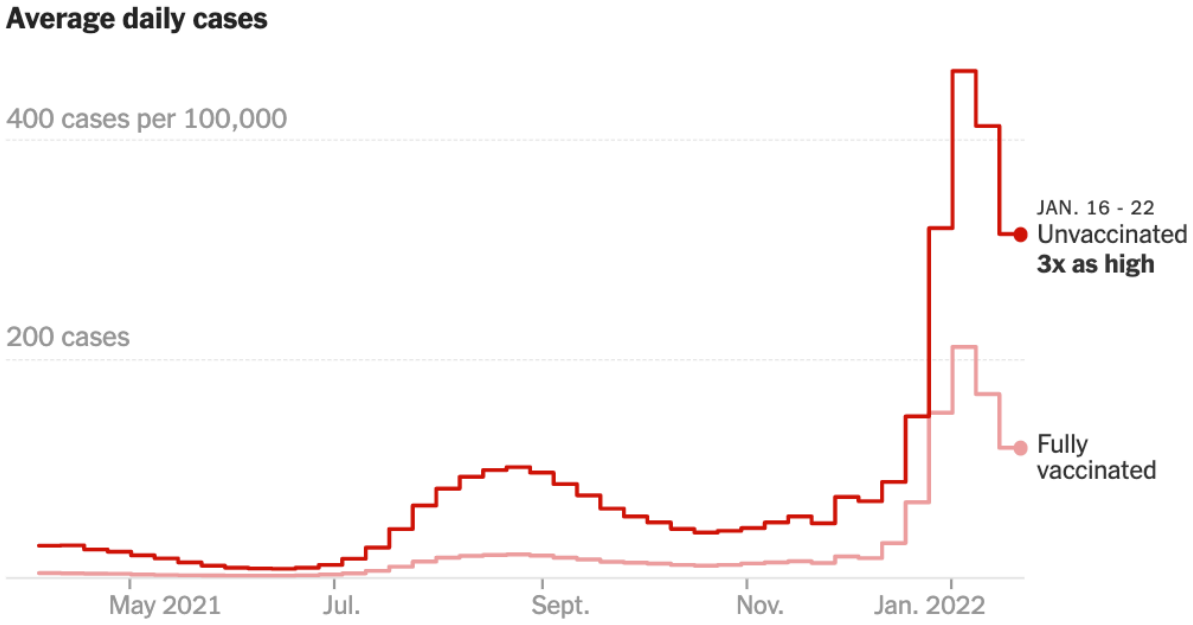

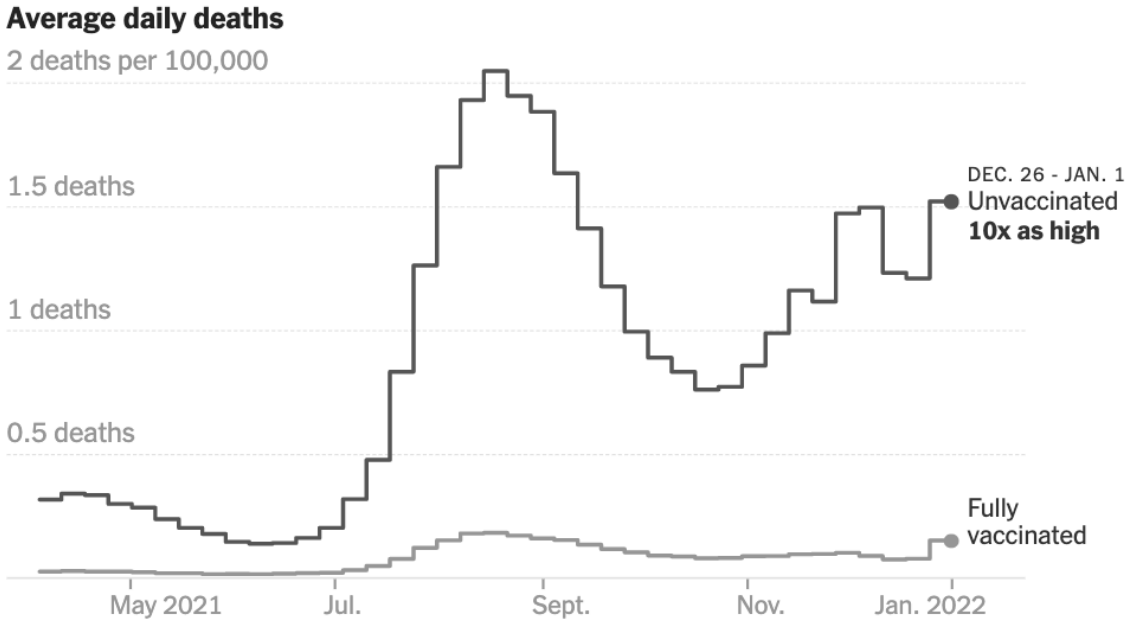

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Where to start?

- Majority of SOT vaccine guidelines are extrapolation of recommendations in healthy persons
- Vaccine efficacy studies are difficult to do in transplantation
  - Most studies rely on immune response
  - Correlates of protection (antibody levels, T-cell responses) are often unknown or may differ in an immunosuppressed population
- Patients are heterogeneous (type of transplant, immunosuppression)
- Adverse event concerns are different than the general population
  - Live vaccines may cause disease
  - Rejection of graft

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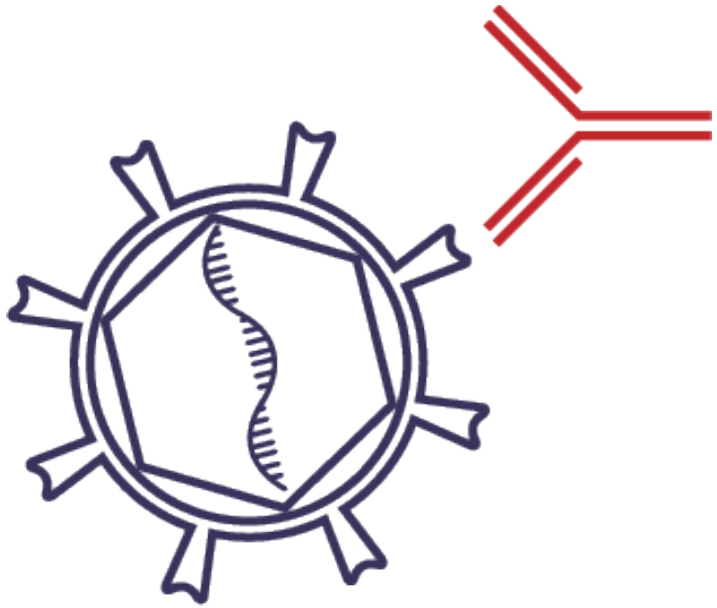
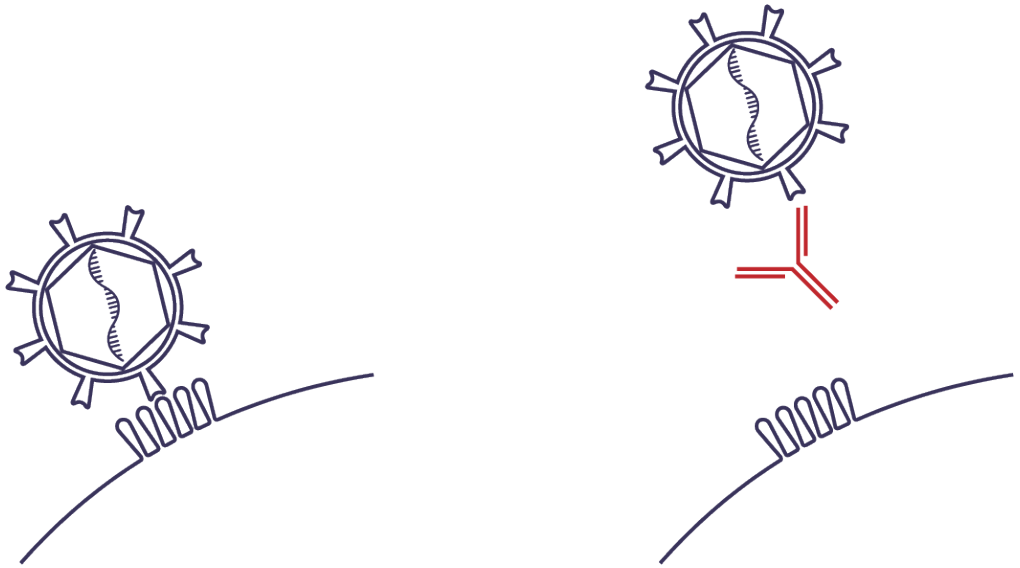
What can we measure?

- **Binding antibodies**
  - Very easy to measure (ELISA, Luminex, MSD)
  - A reasonable measure of an intact immune response (eg, HIP)
  - Do not necessarily reflect functional activity



What can we measure?

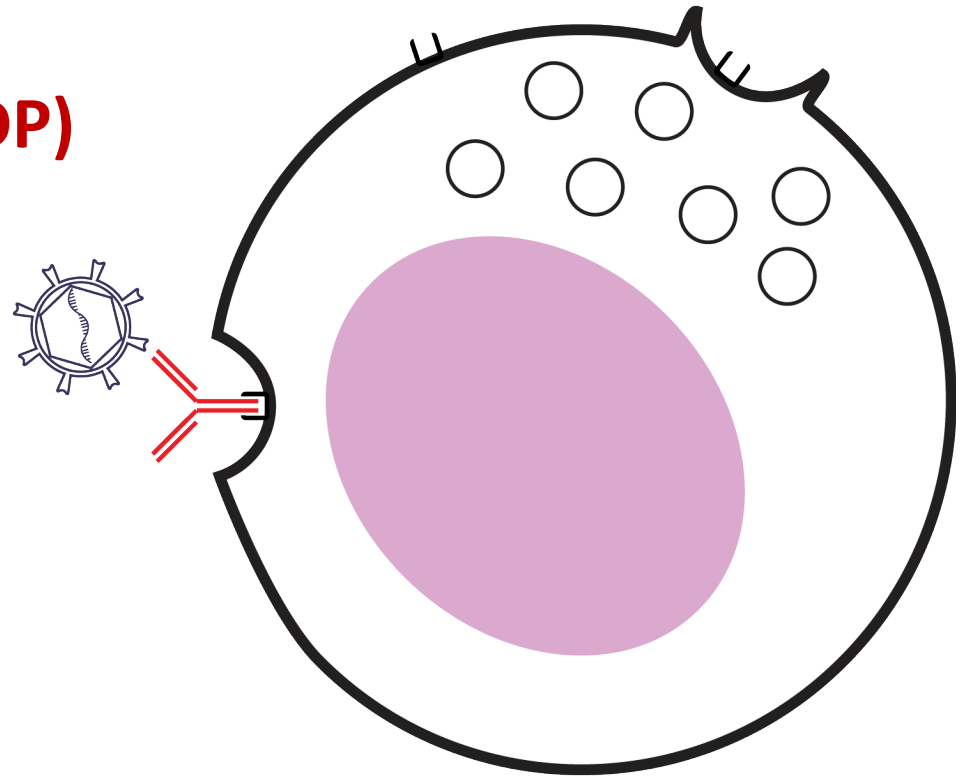
- Binding antibodies
- **Neutralizing antibodies**



- Measure of the ability to block infection
- Can be done with “real” virus or pseudovirus assays
- Neutralizing “real” virus in “real” cells can be challenging, require high BSL
- Pseudovirus neutralizing assays are artificial—may not be the same *in vivo*
- Inhibition of only one part of the virus life cycle

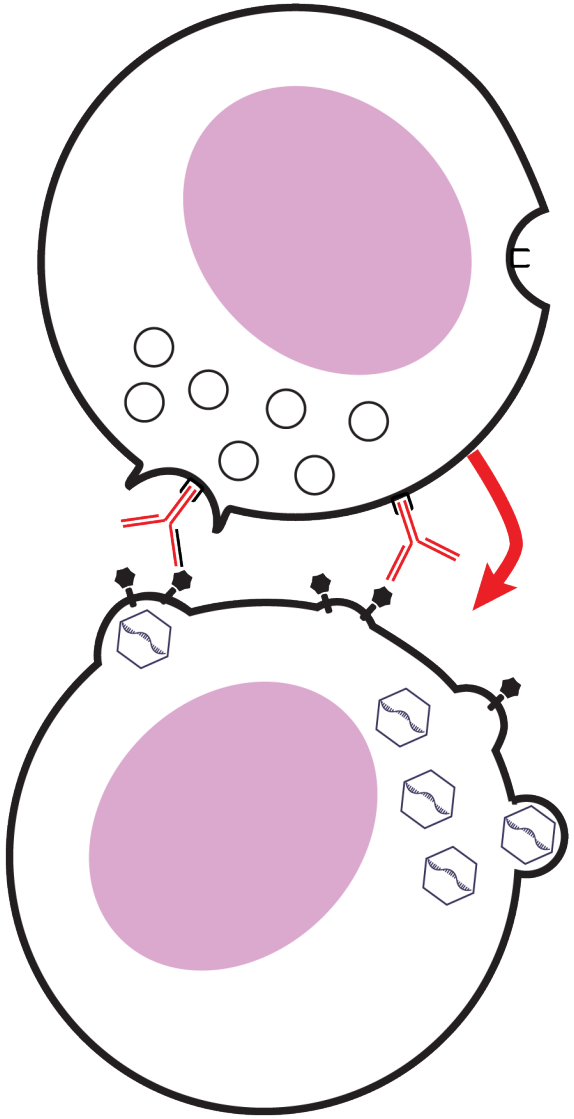
What can we measure?

- Binding antibodies
- Neutralizing antibodies
- **Antibody-dependent phagocytosis (ADP)**
  - Measure the ability of antibodies to promote virus ingestion
  - Virus clearance mechanism
  - Somewhat more complex assay
  - Can be done with model systems (eg, coated beads)



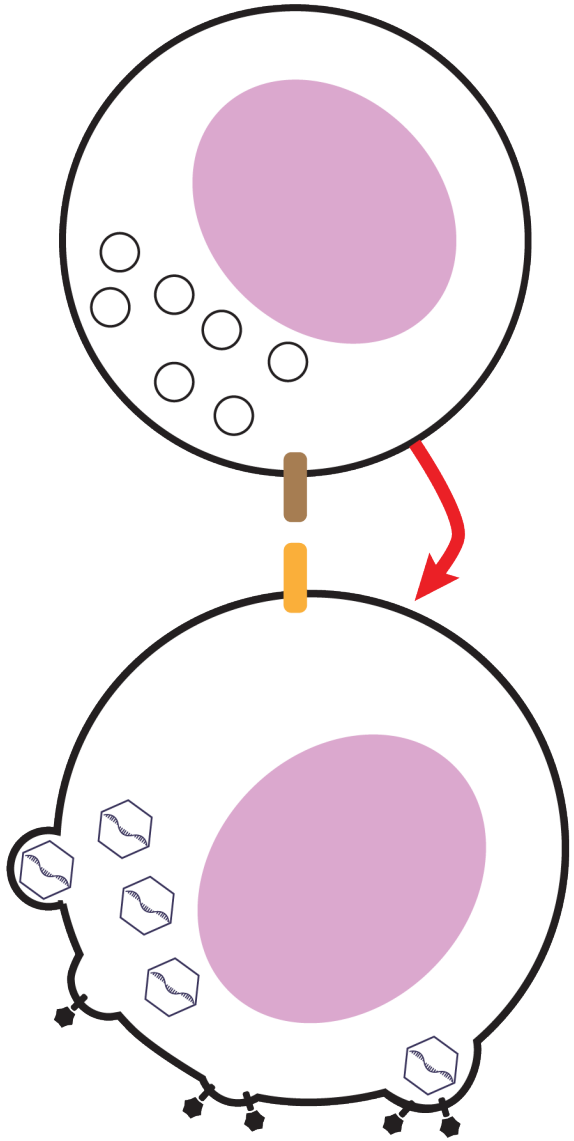
What can we measure?

- Binding antibodies
- Neutralizing antibodies
- Antibody-dependent phagocytosis (ADP)
- **Antibody-dependent cellular cytotoxicity (ADCC)**
  - Measure the ability of antibodies to promote infected cell killing
  - Infected cell clearance mechanism
  - More complex assay to perform
  - Can be done with model systems (eg, coated cells)



What can we measure?

- Binding antibodies
- Neutralizing antibodies
- Antibody-dependent phagocytosis (ADP)
- Antibody-dependent cellular cytotoxicity (ADCC)
- **T cell responses**
  - Measure T cell killing (or help)
  - Infected cell clearance mechanism
  - Complex assay to perform

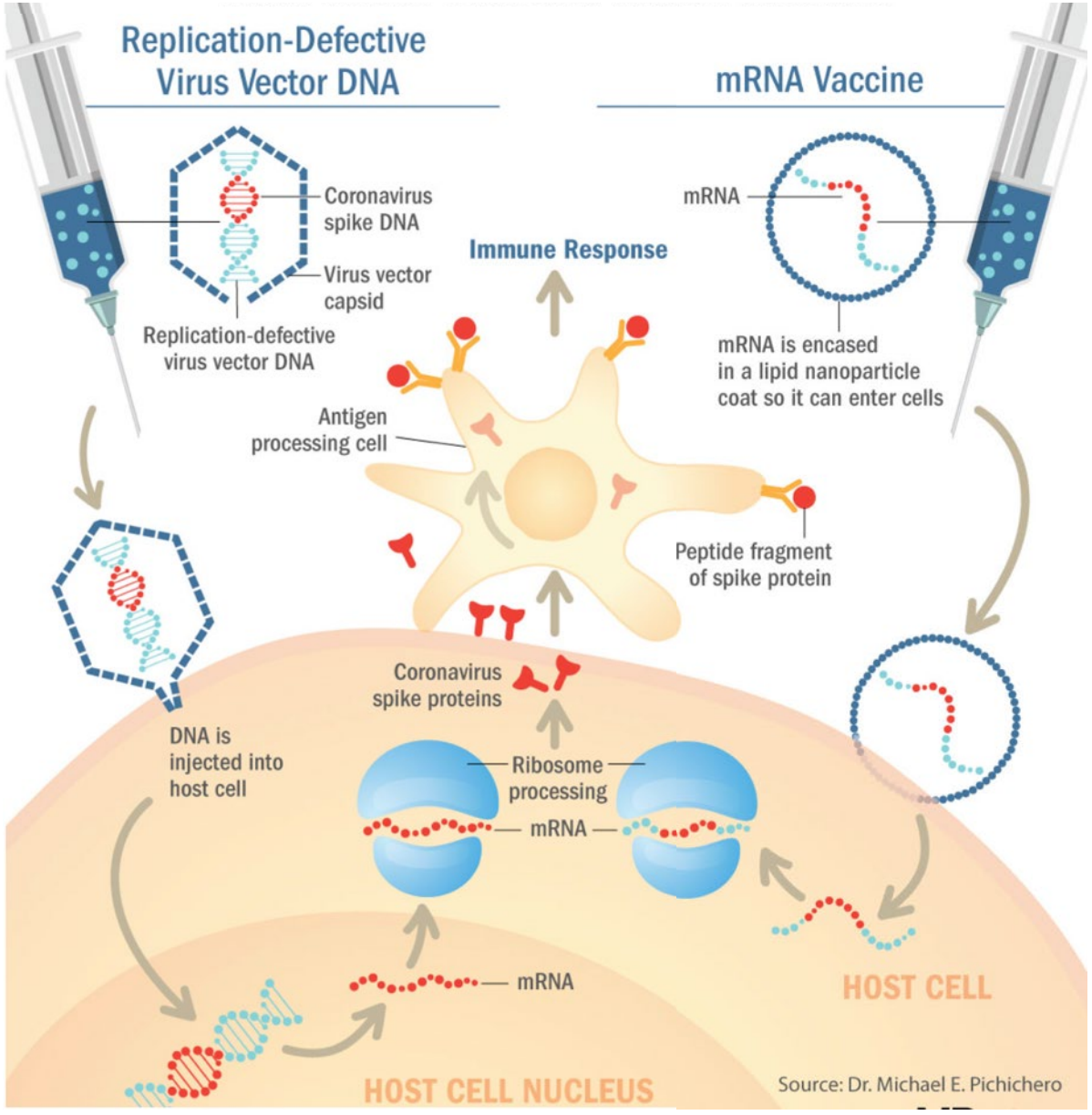


Modern Vaccinology Techniques – Subunit:

Are there other styles of vaccines widely used?

(a) Viral Vector Vaccines
-eg: J&J, Astra-Zeneca Covid

(b) mRNA Vaccines
- Moderna , Pfizer Covid



Lesson #1: Seroconversion is Lower

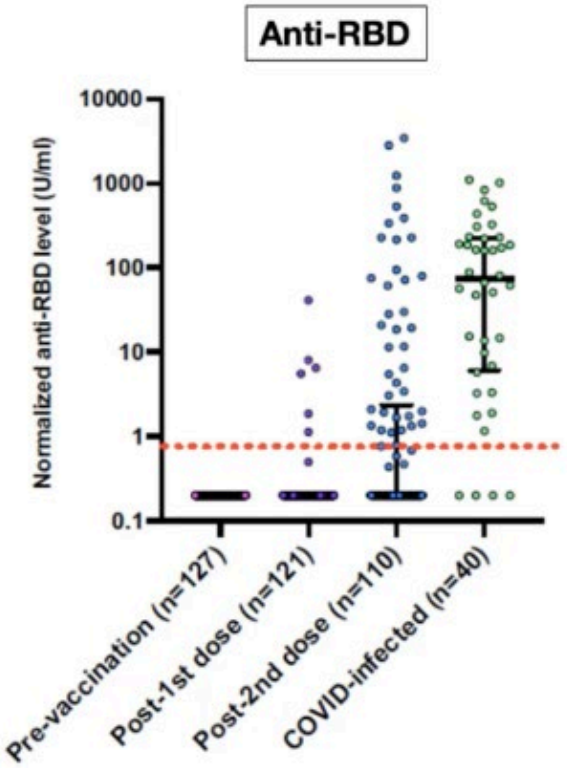
Received: 24 May 2021 | Revised: 25 June 2021 | Accepted: 14 July 2021
DOI: 10.1111/ajt.16766

ORIGINAL ARTICLE

Humoral and cellular immune response and safety of two-dose SARS-CoV-2 mRNA-1273 vaccine in solid organ transplant recipients

Victoria G. Hall[1] | Victor H. Ferreira[1] | Matthew Ierullo[1] | Terrance Ku[1] | Tina Marinelli[1] | Beata Majchrzak-Kita[1] | Anila Yousuf[1] | Vathany Kulasingam[2] | Atul Humar[1] | Deepali Kumar[1]

Key findings



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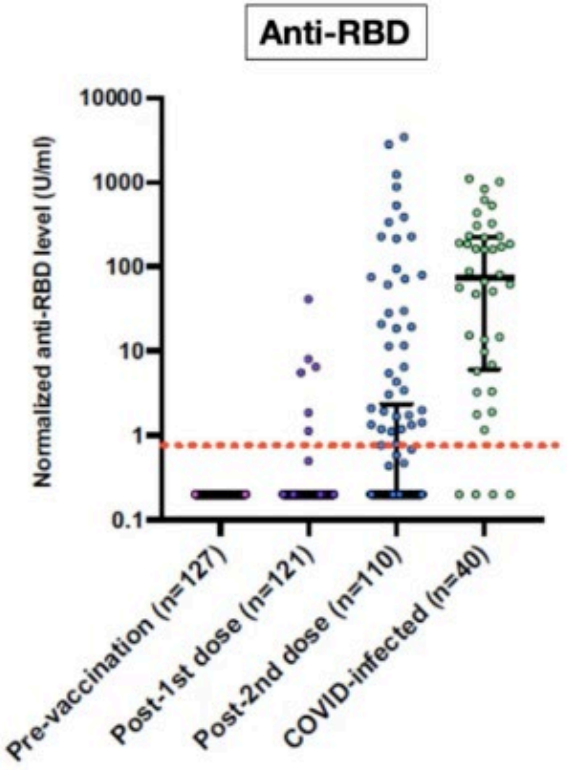

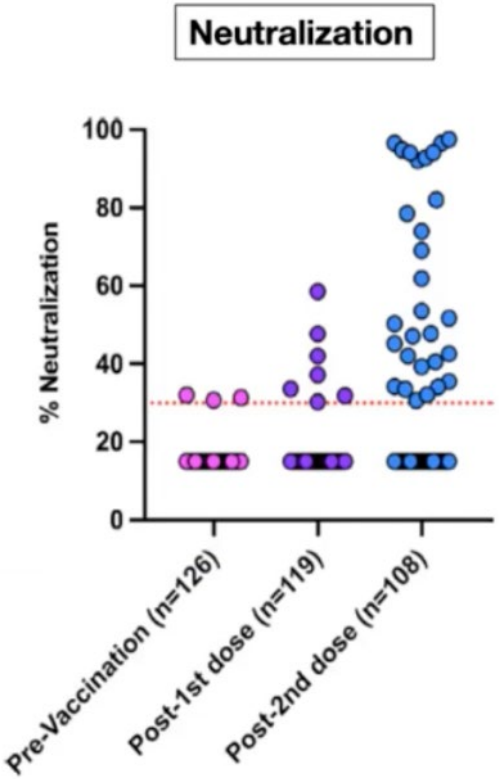

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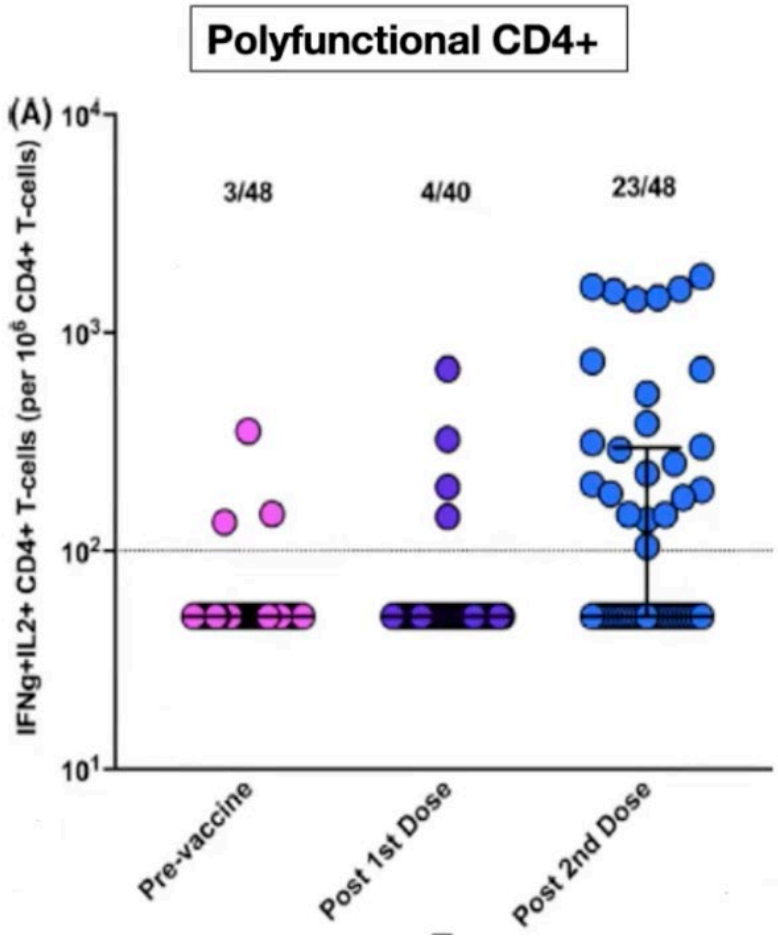

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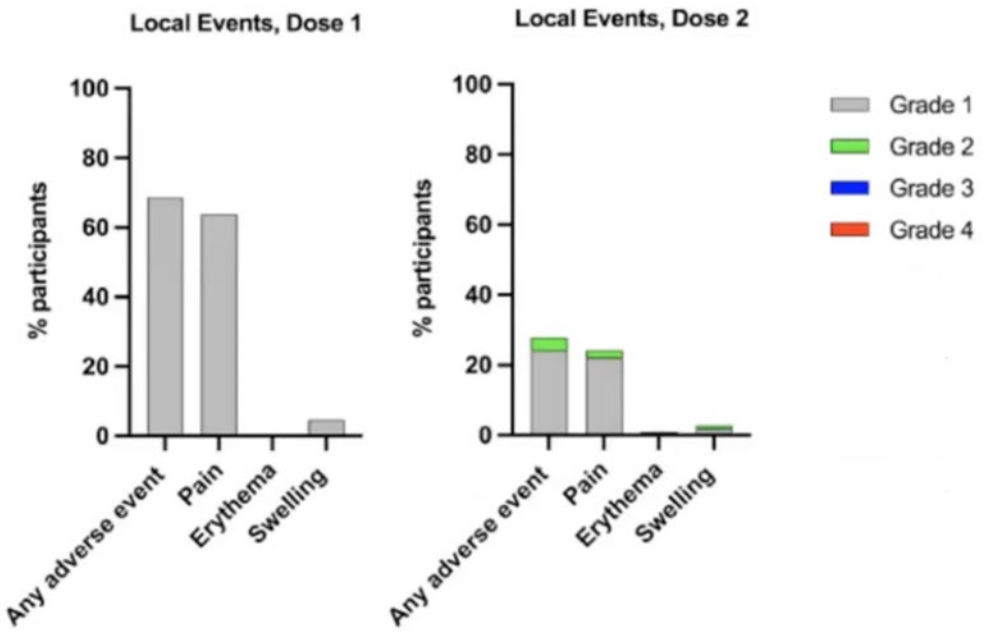

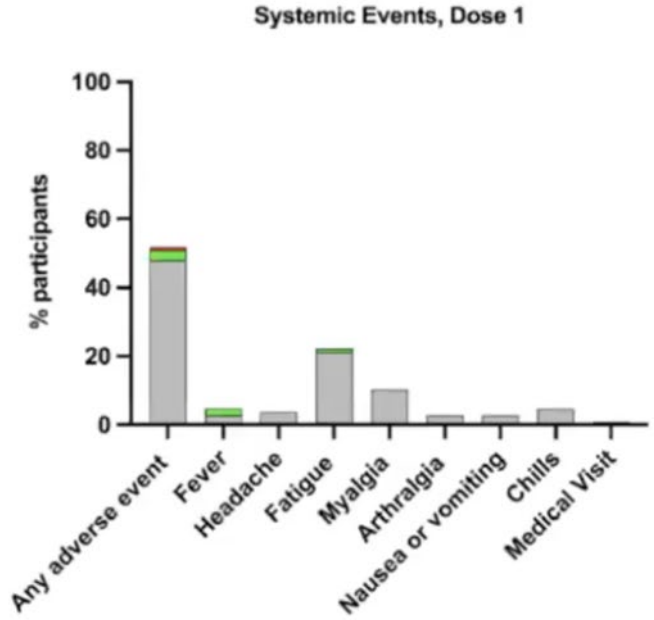

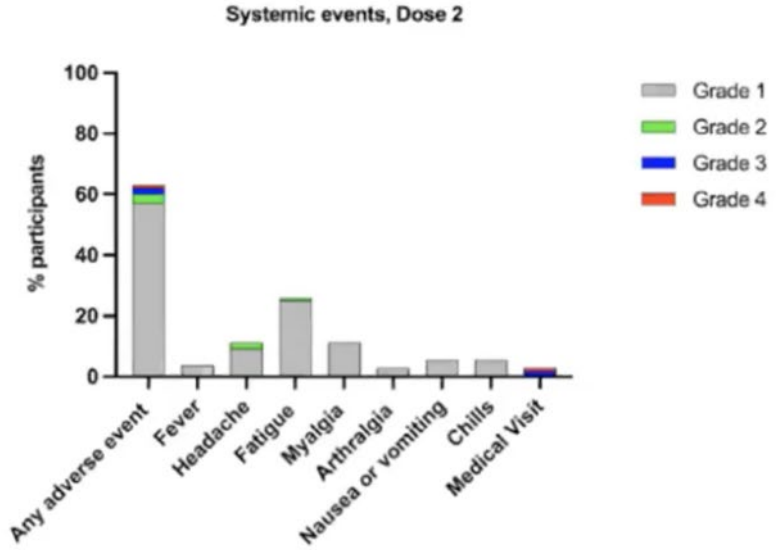

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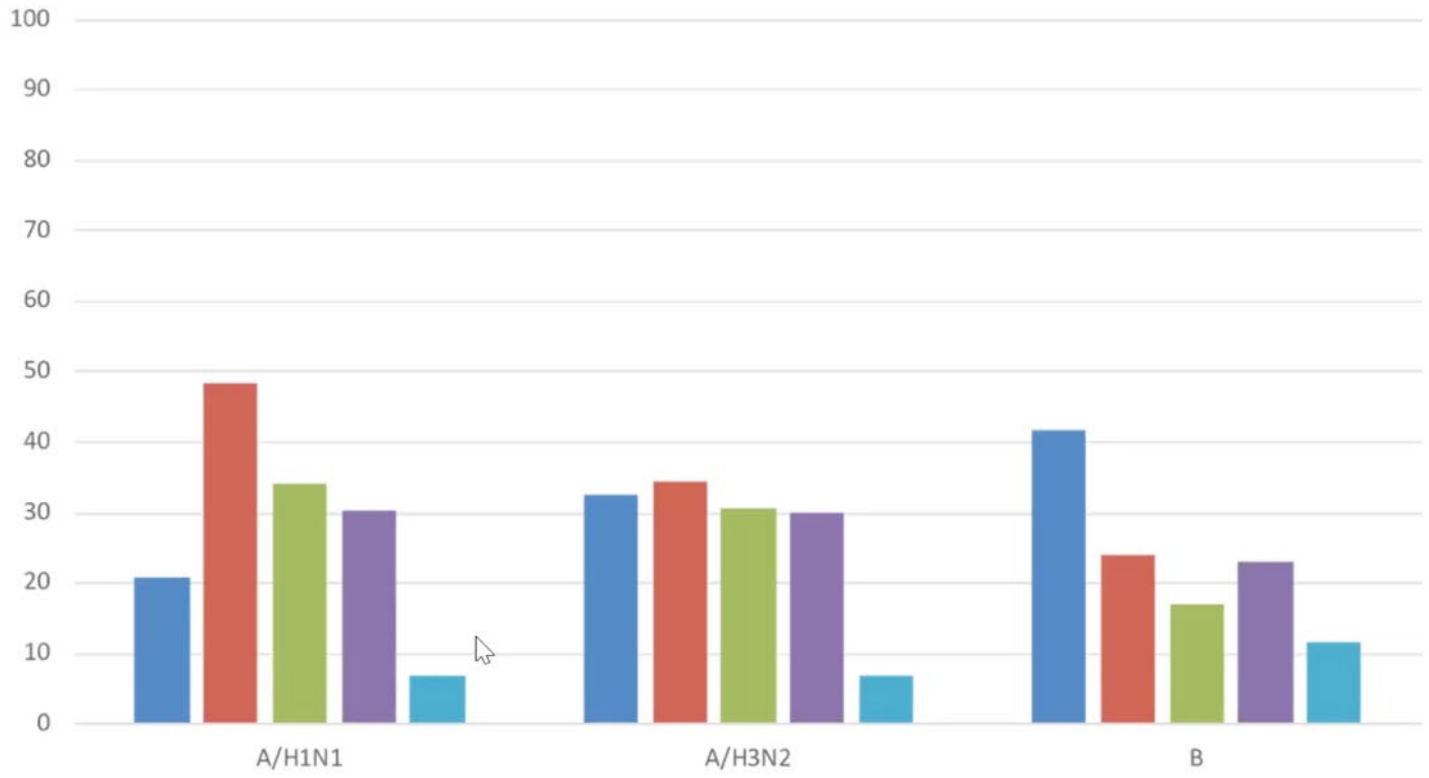
Comparable with Influenza:

Seroconversion rates (%) in influenza vaccine studies of organ transplant recipients are low



Natori, CID 2018; Kumar, Transplantation 2017; Baluch, AJT 2013; Manuel JHLT 2011, Scharpe, AJT 2008

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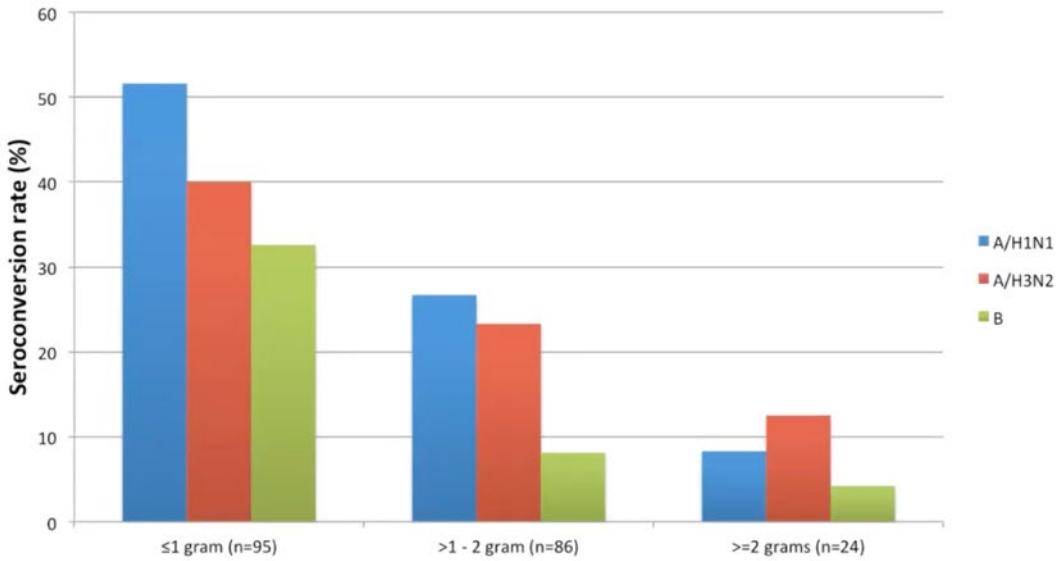
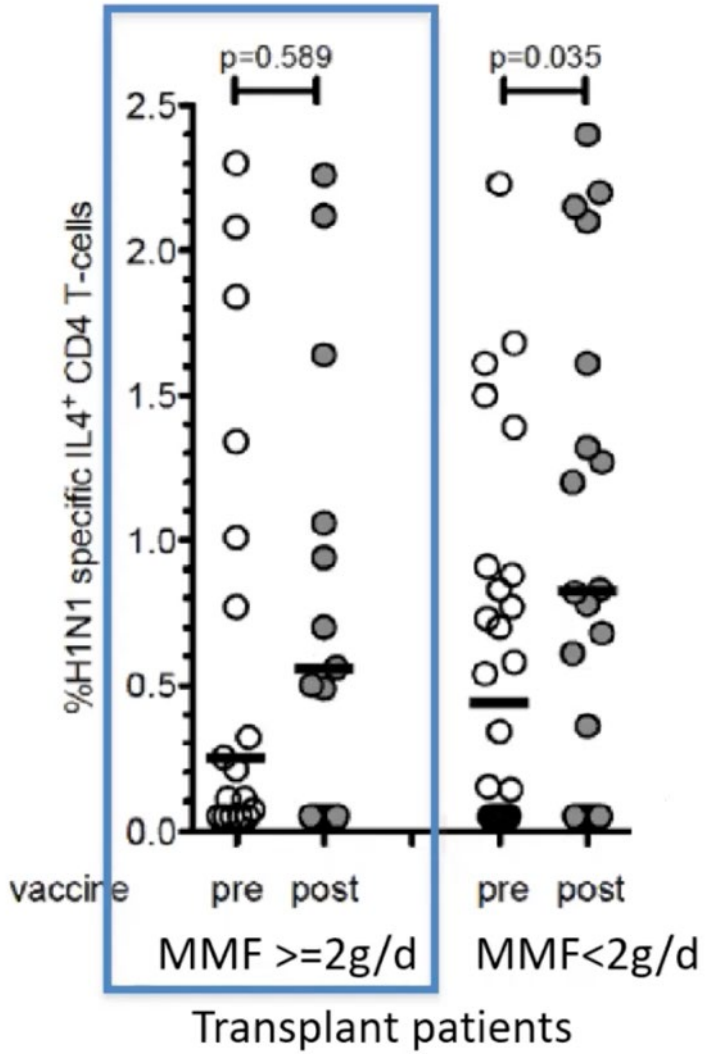
Lesson #2: Not all immunosuppression is the same

Effect of Immunosuppression (Mycophenolate and Influenza Vaccine)

- Several studies have shown that MMF in high doses reduces the immunogenicity of influenza vaccine



Baluch et al, AJT 2013



Egli et al., JID, 2015

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Lesson #2: Not all immunosuppression is the same

Belatacept: Lower Responses

- N=24
- **Post-dose 1**: 0% with detectable anti-spike antibody vs. 14% in matched population (p=0.06)
- **Post-dose 2**: 5% with detectable anti-spike antibody vs. 50% in matched population (p<0.001)
- **Post-dose 3:** only 1/9 boosted (unpublished)

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Ou, Transplantation, May 2021

Lesson #2: Not all immunosuppression is the same

COVID-19 VACCINE ANTIBODY RESPONSE AMONG CLL PATIENTS BY TREATMENT TYPE

Treatment Within Past Two Years	Percent of Patients with No Detectable COVID-19 Antibodies
None	17
Obinutuzumab	90
Rituximab, Acalabrutinib	85
Rituximab, Ibrutinib	77
Multidrug therapy with or without cytotoxic chemotherapy	71
Obinutuzumab, Ibrutinib	70
Obinutuzumab, Acalabrutinib	66
Rituximab	63
Acalabrutinib	55
Ibrutinib	48
Ibrutinib, IVIG	40
IVIG	25

Source: The LLS National Patient Registry. Data collected from 845 patients with chronic lymphocytic leukemia (CLL) who had antibody tests at least 2 weeks after their second dose of Moderna or Pfizer mRNA vaccine. Data collected March 12 to June 12, 2021.

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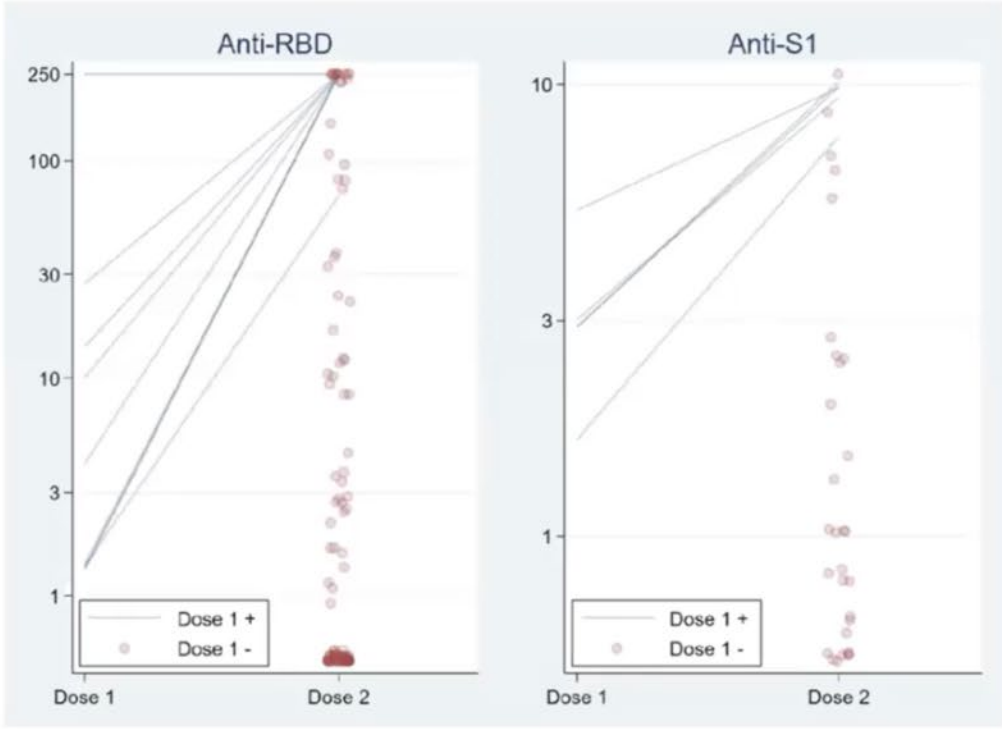
Lesson #2: Not all immunosuppression is the same

Thoracic Transplantation

- Heart (N=90)
  - Neg/Neg, non-responders: **44%**
  - Neg/Pos, weak responders: 47%
  - Pos/Pos, boosted: 9%
- Lung (N=62)
  - Neg/Neg, non-responders: **58%**
  - Neg/Pos, weak responders: 32%
  - Pos/Pos, boosted: 10%



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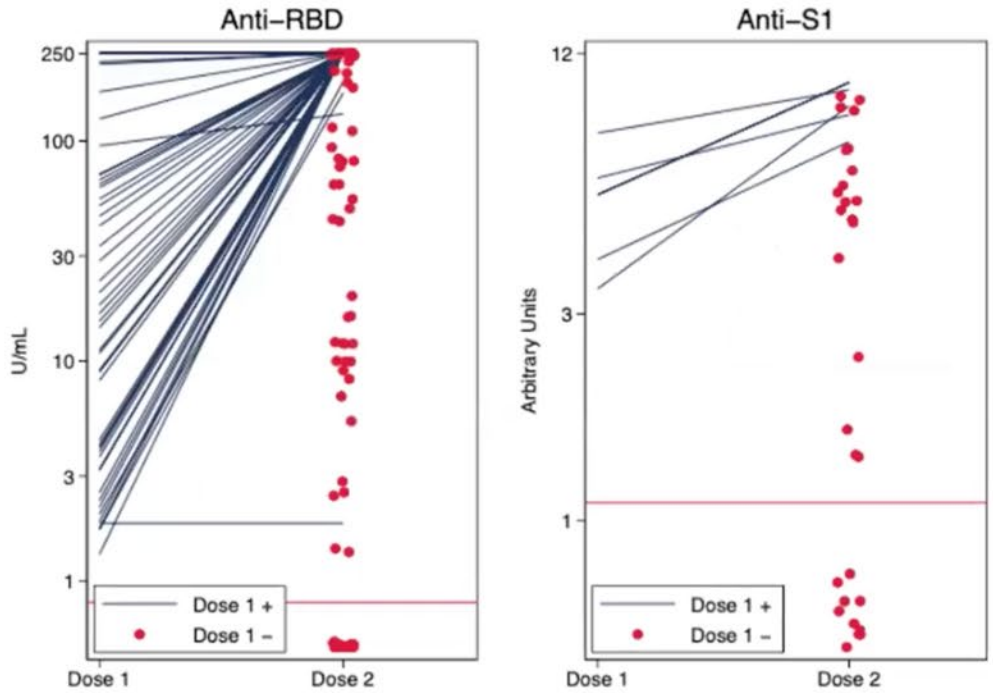
Hallet, JHLT, Aug 2021
Strauss, Liver Transplantation, Aug 2021

Lesson #2: Not all immunosuppression is the same

Liver Transplantation

- N=161
  - Neg/Neg, non-responders: **19%**
  - Neg/Pos, weak responders: 47%
  - Pos/Pos, boosted: 34%



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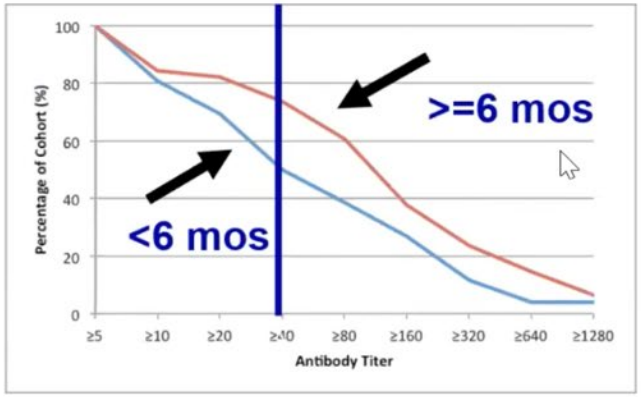
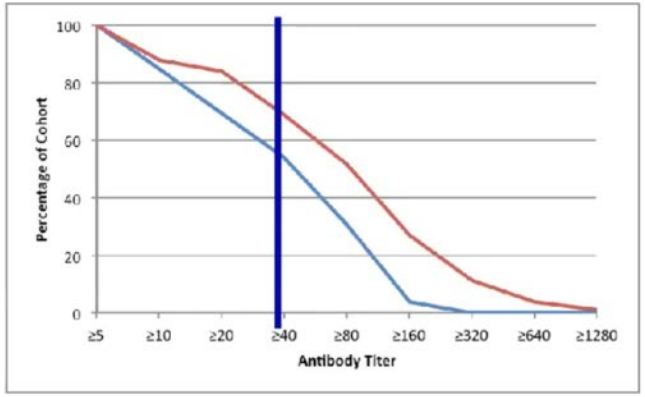
Lesson #3: Timing is Critical

Influenza Vaccine Response: Time from transplant (n=228)

H1N1



H3N2



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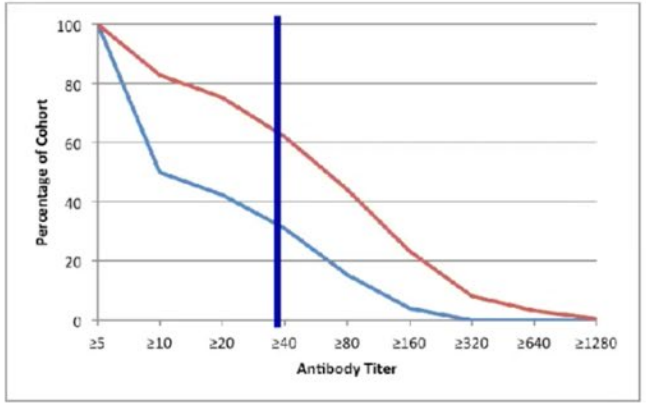

Seroconversion to at least one antigen:
19.2% in those <6 mos from transplant vs. 53.2% in those >6 months, p=0.001

Baluch et al., AJT, 2013

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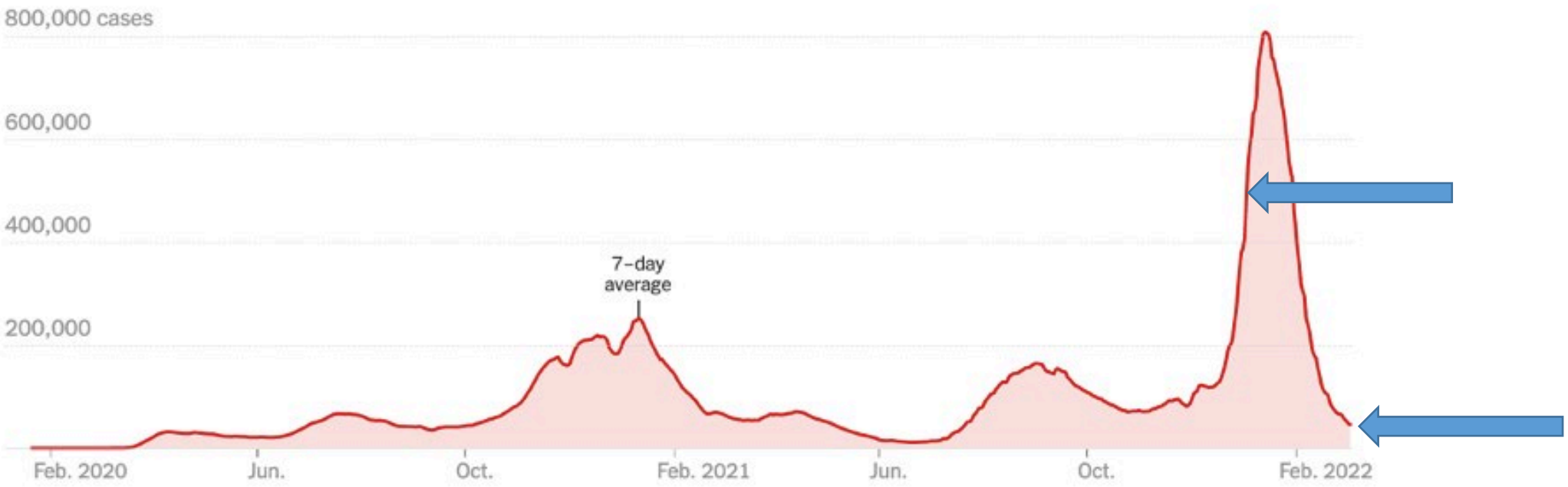
Lesson #3: Timing is Critical



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Lesson #4: Dosing variability can help

Two doses of influenza vaccine

Variable	Single-Dose Vaccination Group (n = 213)	Booster Dose Vaccination Group (n = 211)	OR (95% CI)/ β Coefficient (95% CI)	NNT (ARR, %) With Booster Dose
Short-term seroconversion rate				
A(H1N1)pdm	33 (32.7)	43 (46.7)	**1.81 (1.009–3.24)***	12 (14.1)
A(H3N2)	38 (30.2)	45 (39.1)	1.49 (.87–2.54)	8 (9)
Influenza B	53 (63.9)	63 (75.9)	1.78 (.91–3.50)	9 (12)
Long-term seroconversion rate				
A(H1N1)pdm	20 (19.8)	19 (20.7)	1.05 (.52–2.13)	…
A(H3N2)	57 (45.2)	47 (40.9)	0.84 (.50–1.40)	…
Influenza B	42 (50.6)	53 (63.9)	1.73 (.93–3.21)	…
Short-term seroprotection rate				
A(H1N1)pdm	92 (43.2)	114 (54)	**1.54 (1.05–2.27)***	10 (10.8)
A(H3N2)	97 (45.5)	120 (56.9)	**1.58 (1.08–2.31)***	9 (11.3)
Influenza B	153 (71.8)	176 (83.4)	**1.97 (1.23–3.16)****	9 (11.6)

N=499 adult SOT patients randomized 1:1 to receive single dose or two doses of influenza vaccine 5 wks apart

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Cordero et al., CID, 2017

Lesson #4: Dosing variability can help

CORRESPONDENCE

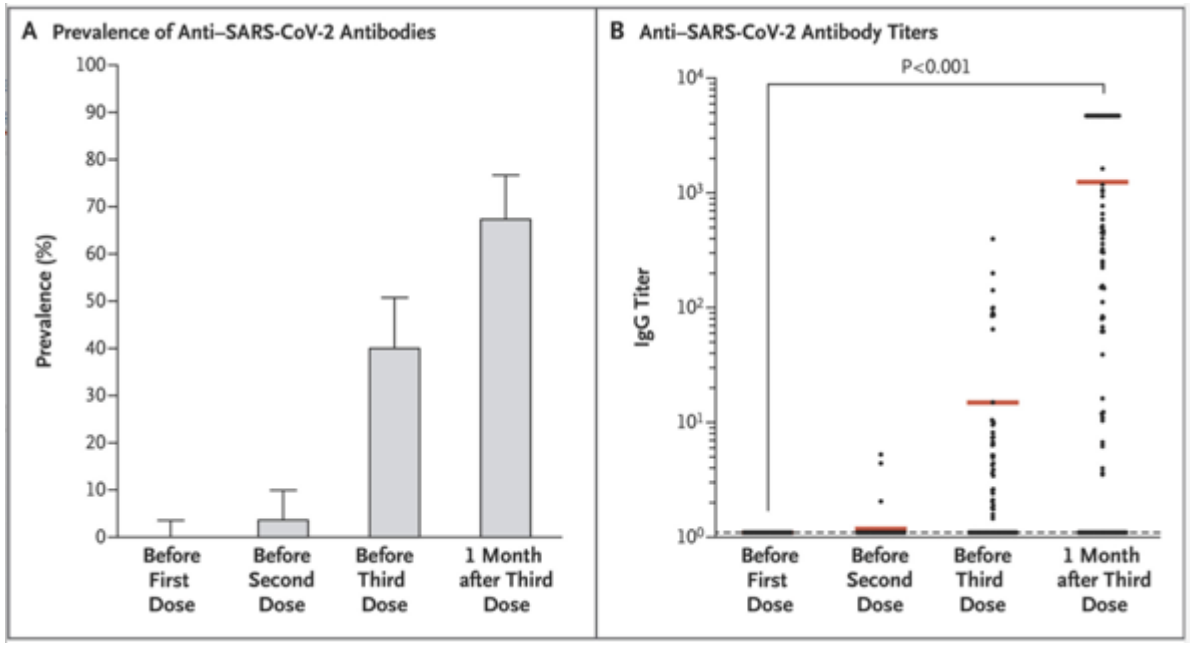
Three Doses of an mRNA Covid-19 Vaccine in Solid-Organ Transplant Recipients

Nassim Kamar, M.D., Ph.D.

Toulouse University Hospital, Toulouse, France

The NEW ENGLAND JOURNAL of MEDICINE

- 101 SOTx French cohort, 3x Pfizer mRNA doses
- 78 kidney, 12 livers, 8 thoracic; median age 58, ~5yrs out



- Of the 59 negative prior to dose 3:
  - Almost half responded
- Of the 40 positive prior to dose 3:
  - Titres went up 36 → 2676

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Lesson #4: Dosing variability can help

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The NEW ENGLAND JOURNAL of MEDICINE

	Anti-SARS-CoV2 positive patients (*N*=67)	Anti-SARS-CoV2 negative patients (*N*=32)	*p*-value
Sex ratio (M/F)	2.2 (46/21)	2.6 (23/9)	0.745
Age (years, mean ±SEM)	54 ±2	65 ±3	**<0.001**
Type of organ transplant, n (%)			0.491
- Kidney	51 (76)	25 (78)	
- Liver	9 (13)	3 (9)	
- Thoracic organs	4 (6)	4 (13)	
- Pancreas	3 (4)	-	
History of rejection in the year preceding vaccination, n (%)	2 (3)	1 (3)	1
Time between vaccine and transplantation (months, mean ±SEM)	99 ±10	94 ±16	0.793
No induction therapy, n (%)	26 (39)	14 (44)	0.667
Induction therapy, n (%)	41 (61)	18 (56)	
- Anti-IL2 receptor blockers	26 (63)	9 (50)	
- Polyclonal antibodies	14 (34)	8 (44)	
- Others	1 (2)	1 (6)	
Type of immunosuppressive regimen, n (%)			
- Calcineurin-inhibitors	55 (82)	23 (72)	0.245
○ Tacrolimus	51 (93)	22 (97)	
○ Ciclosporin A	4 (7)	1 (3)	
- Anti-metabolite	41 (61)	24 (75)	0.176
○ Mycophenolic acid	40 (98)	24	
○ Azathioprine	1 (2)	-	
- mTOR inhibitors	22 (33)	7 (22)	0.262
- Steroids	58 (87)	28 (88)	1
- Belatacept	5 (7)	7 (22)	0.052
Neutrophils count before vaccination (/mm³, mean ±SEM)	5459 ±252	5600 ±664	0.810
Lymphocytes count before vaccination (/mm³, mean ±SEM)	1561 ±123	1173 ±114	**0.049**
CD4+ T-cells count before vaccination (/mm³, mean ±SEM)	n=59 529 ±37	n=30 339 ±38	**0.002**
CD8+ T-cells count before vaccination (/mm³, mean ±SEM)	n=59 440 ±38	n=30 358 ±48	0.201
CD19+ T-cells count before vaccination (/mm³, mean ±SEM)	n=59 182 ±83	n=30 89 ±33	**0.003**
NK cells count before vaccination (/mm³, mean ±SEM)	n=59 235 ±18	n=30 216 ±33	0.582
eGFR before vaccination (mL/min/1.73m²)	60 ±3	45 ±4	**0.005**

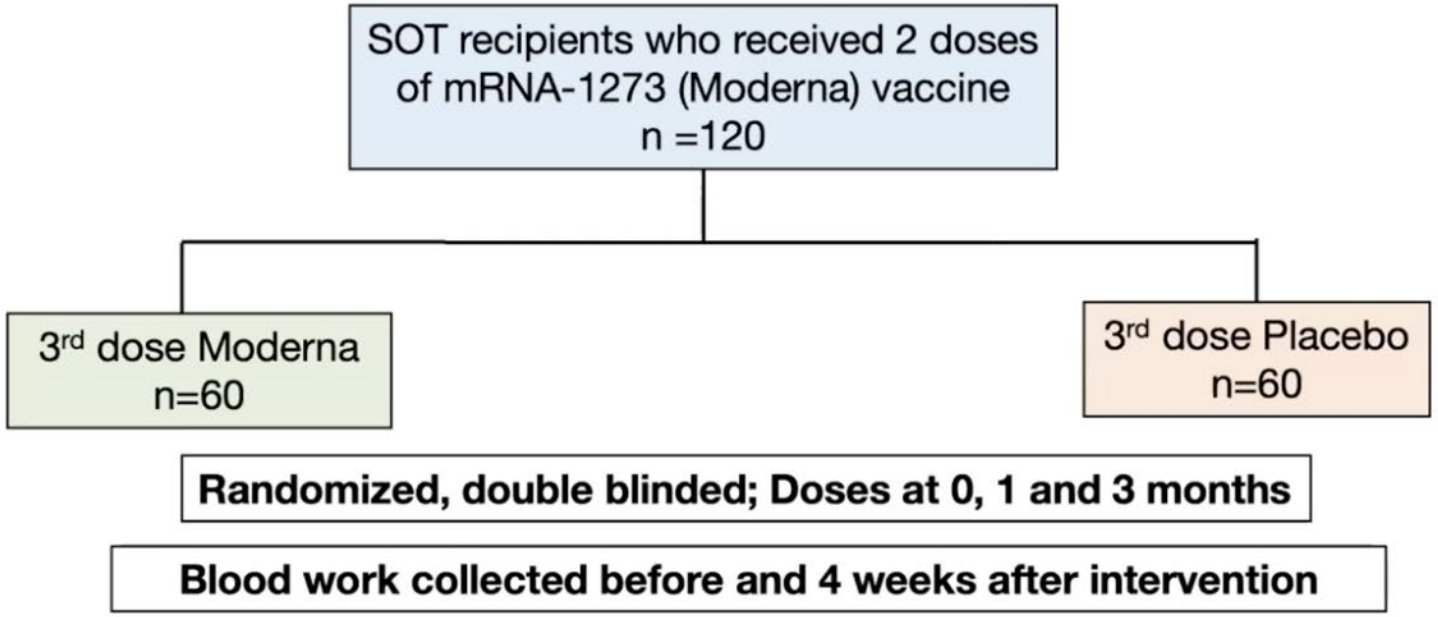
Worse response if you're:

- Older
- T/B cell cytopaenic
- Take More immunosuppression
- Worse renal function

TxID Duke Transplant/ Immunocompromised Host Infectious Diseases

Lesson #4: Dosing variability can help

Methods – study design



Primary outcome: anti-RBD antibody level of ≥ 100 U/ml at month 4

- **Defined prior to start of trial**
- **Based on protective anti-RBD titer in challenge study in non-human primates[20] and corroborated as upper limit of 95% CI for 50% neutralization in a large clinical cohort[21]**

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Characteristic	mRNA-1273 (n=60)	Placebo (n=60)
Age (years), median (IQR)	66.9 (64.0 – 71.8)	65.9 (62.9 – 70.3)
Male sex, n (%)	37 (61.7%)	42 (70.0%)
Time from transplantation to intervention (years), median (IQR)	3.57 (1.99 – 6.75)	2.20 (1.44 – 5.55)
Rejection within the preceding 3 months n (%)	1 (1.7%)	1 (1.7%)
Anti-thymocyte globulin in the preceding 6 months	0	0
Type of transplant (%)		
Thoracic	21 (35.0%)	26 (43.3%)
Lung	11	18
Heart	10	8
Abdominal	39 (65.0%)	34 (56.7%)
Kidney	20	9
Pancreas and Kidney-Pancreas	15	9
Liver	4	16
Immunosuppression		
Prednisone (%)	50 (83.3%)	42 (70.0%)
Prednisone daily dose, mg; median (IQR)	5 (5–5)	5 (5-7.5)
Calcineurin inhibitor (%)	59 (98.3%)	59 (98.3%)
Tacrolimus	47 (78.3%)	46 (76.7%)
Tacrolimus trough level, ng/mL (IQR)	7.6 (5.9 – 9.8)	6.7 (5.3 – 8.6)
Cyclosporine	12 (20.0%)	13 (21.7%)
Mycophenolate mofetil/ mycophenolate sodium (%)	44 (73.3%)	46 (76.7%)
Mycophenolate daily dose; mg, median (IQR)	1080 (720-1440)	720 (585 – 1440)
Azathioprine (%)	8 (13.3%)	4 (6.7%)
Sirolimus (%)	6 (10.0%)	5 (8.3%)

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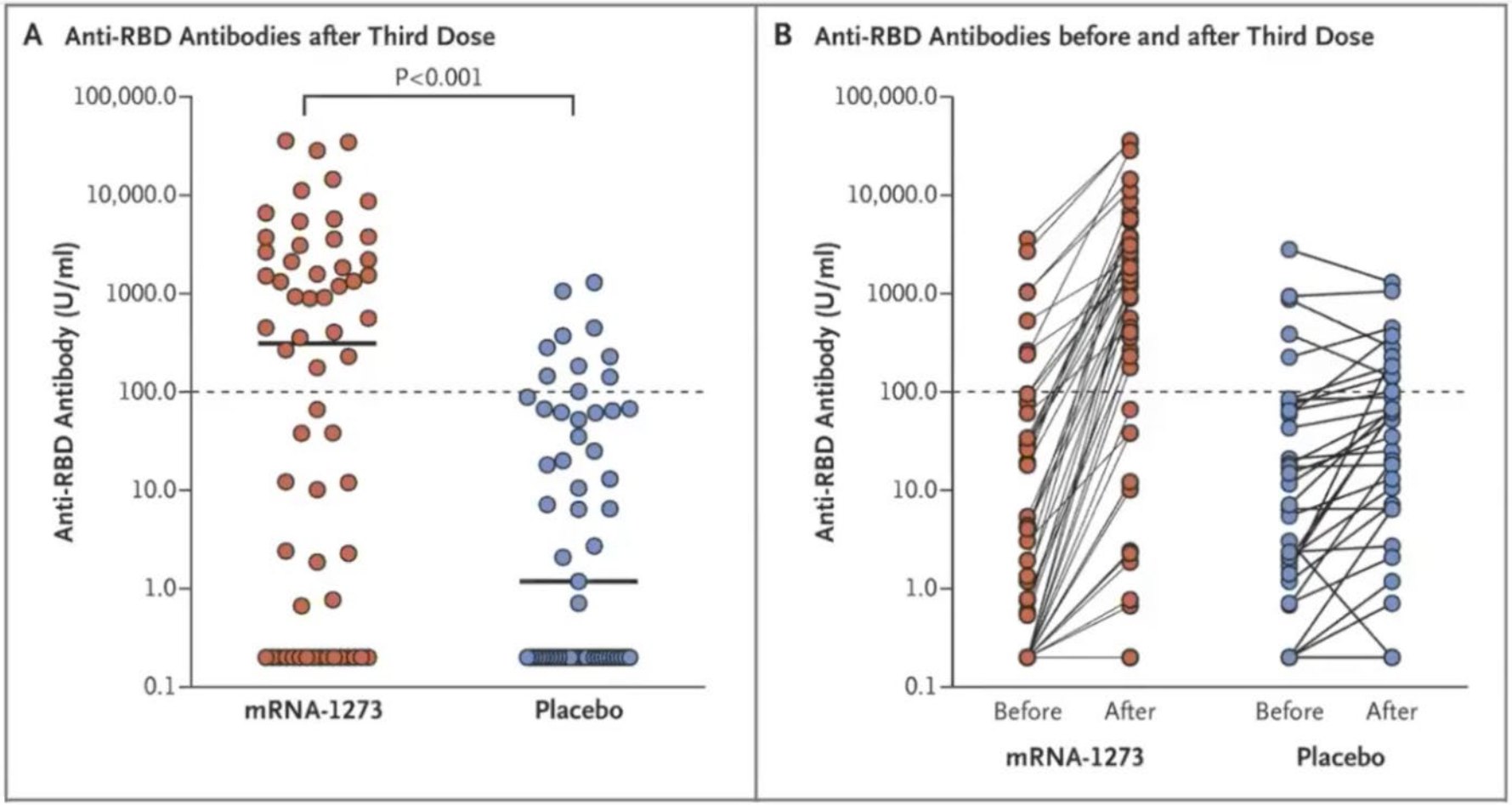
Results



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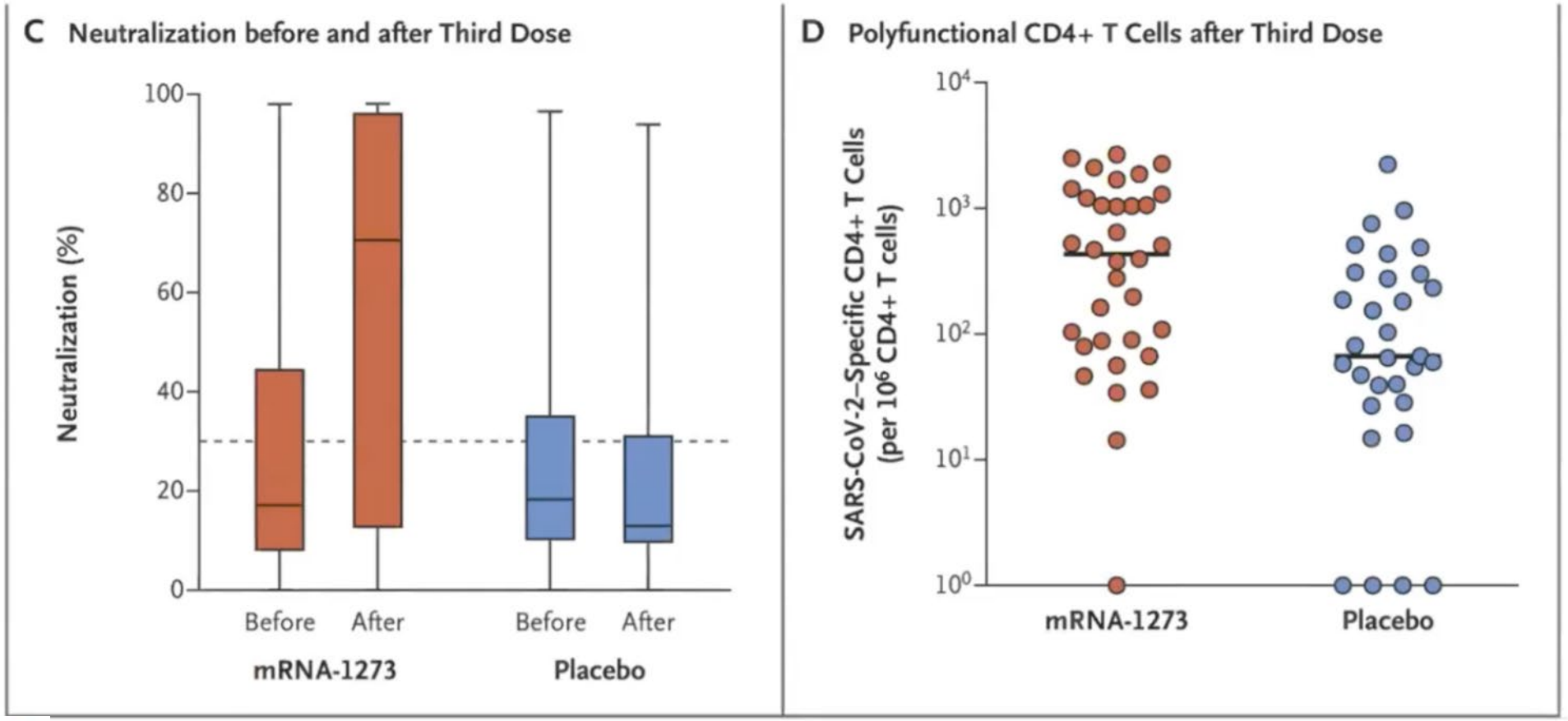
Infectious Diseases

Results



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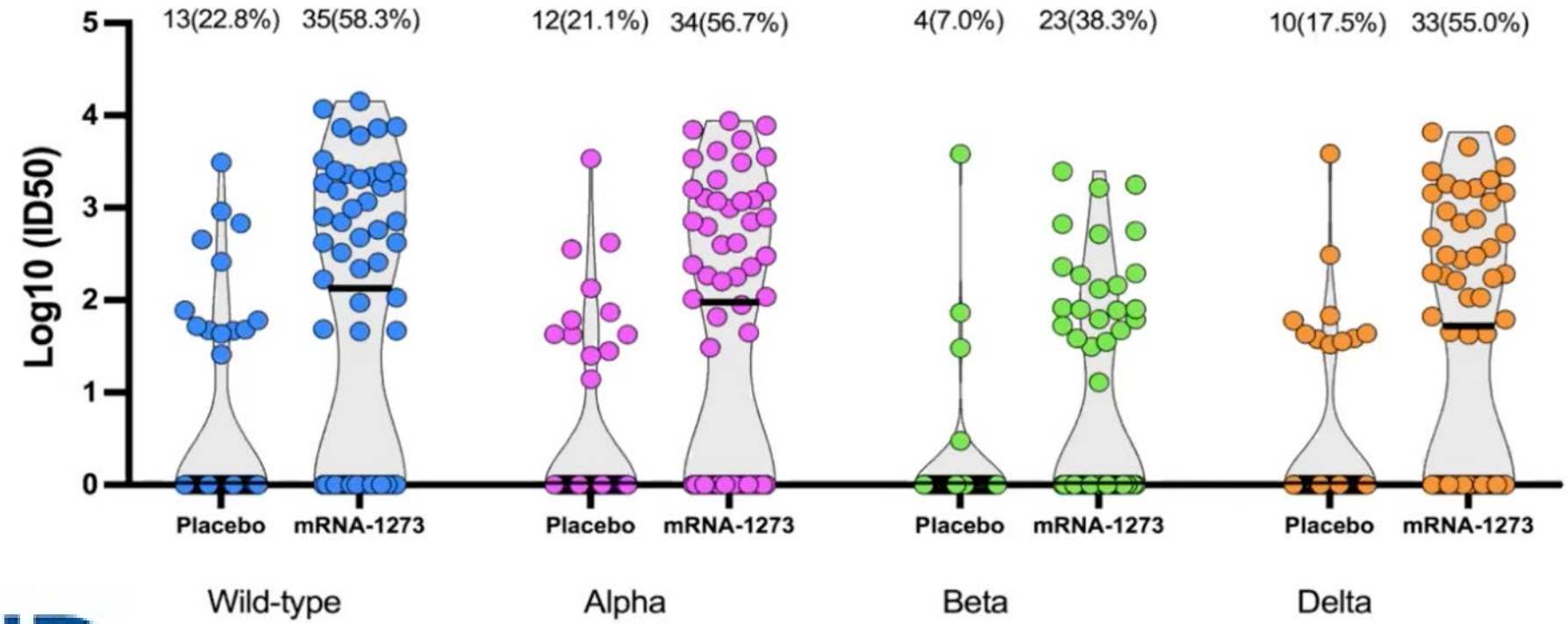
Third dose and neutralization of VOC

Figure 3: Pseudotyped lentivirus neutralization post-3rd dose of placebo or mRNA-1273



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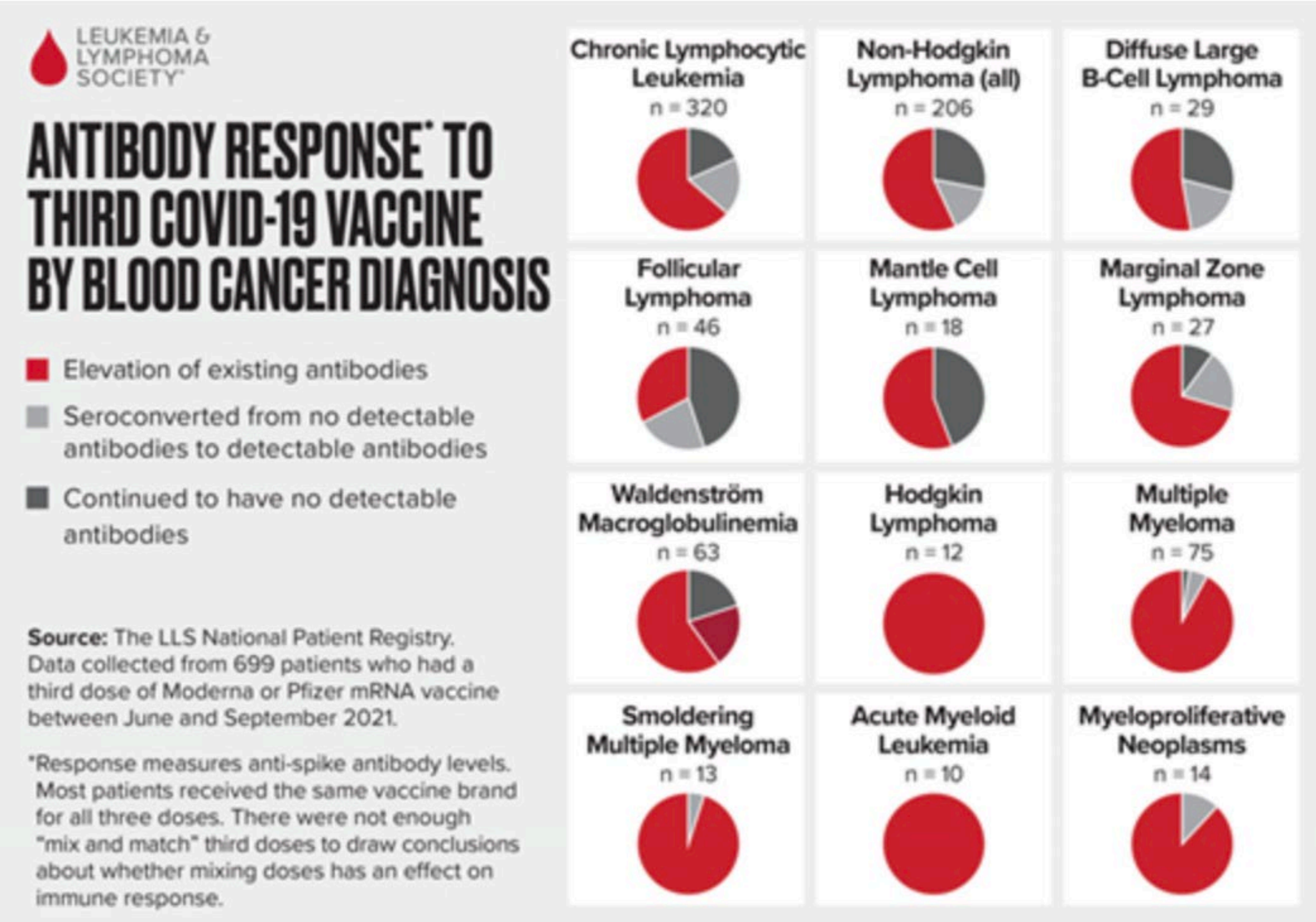
Lesson #4: Dosing variability can help



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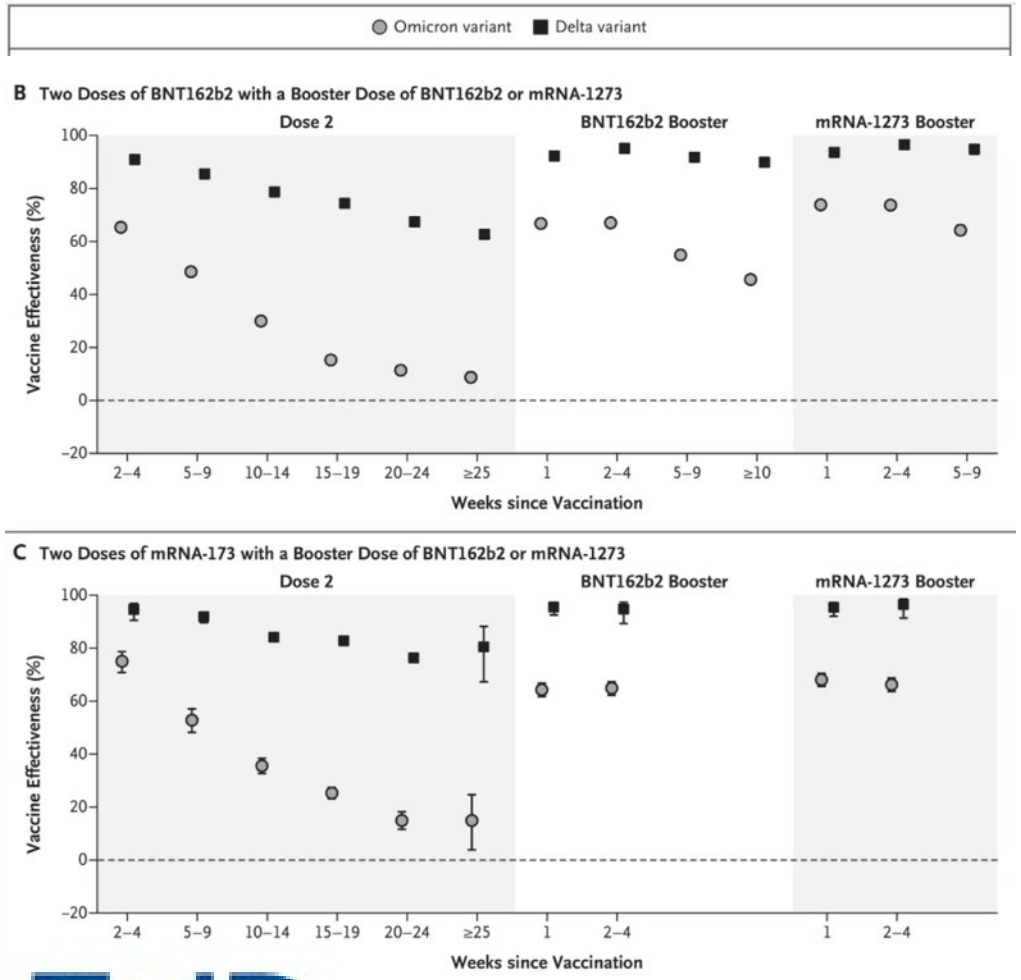
Vaccinations for Omicron:

UK



USA

CDC Centers for Disease Control and Prevention
CDC 24/7: Saving Lives, Protecting People™

Morbidity and Mortality Weekly Report (*MMWR*)

During the Omicron period:

During the 2 months after a third dose:
VE against COVID-19–associated ED/UC visits = 87%
VE against hospitalizations = 91%

By 4 months post third dose:
VE against COVID-19–associated ED/UC visits = 66%
VE against hospitalizations = 78%

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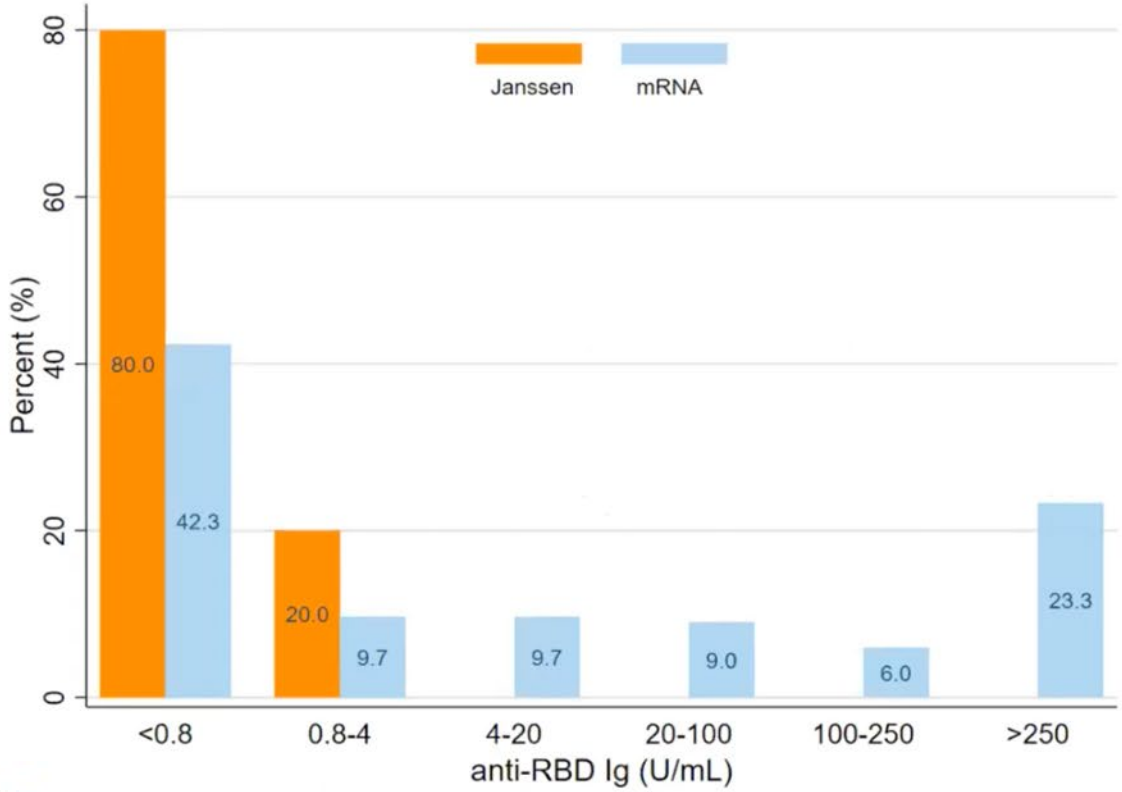
The NEW ENGLAND JOURNAL of MEDICINE

Andrews et al. 2022
Ferdinands et al. 2022

Lesson #5: Not all vaccines equal

Ad26.Cov2.S (Janssen) Vaccine – Lower Responses



- Antibodies: 20% (J&J) vs. 56% (mRNA) p=0.03
  - aOR 0.16 (95% CI 0.03-0.78, p=0.02)
- Median titers 2.39 u/mL (J&J) vs. 106.7 u/mL (mRNA) (p=0.05)

Boyarsky, Transplantation, June 7, 2021

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Lesson #6: Vaccination can attenuate disease despite incomplete seroconversion

Benefits of being vaccinated

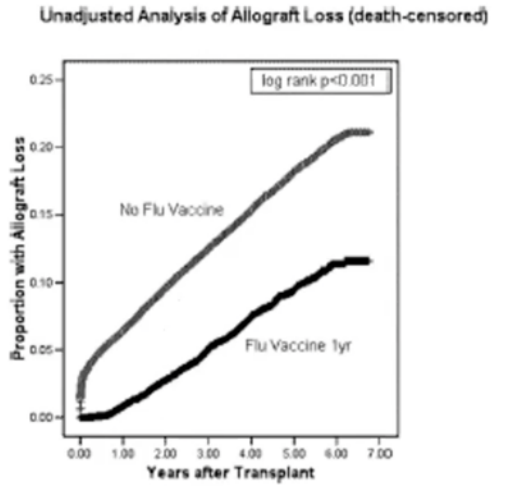
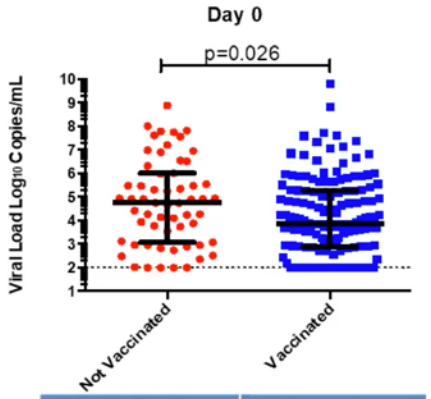


Figure 1. | Time to allograft loss (death-censored) among adult Medicare primary renal transplant recipients who did or did not have Medicare claims for influenza vaccine in the first year post-transplantation.

Hurst et al, Clin J Am Soc Nephrol 2011

N=616 transplant patients with influenza

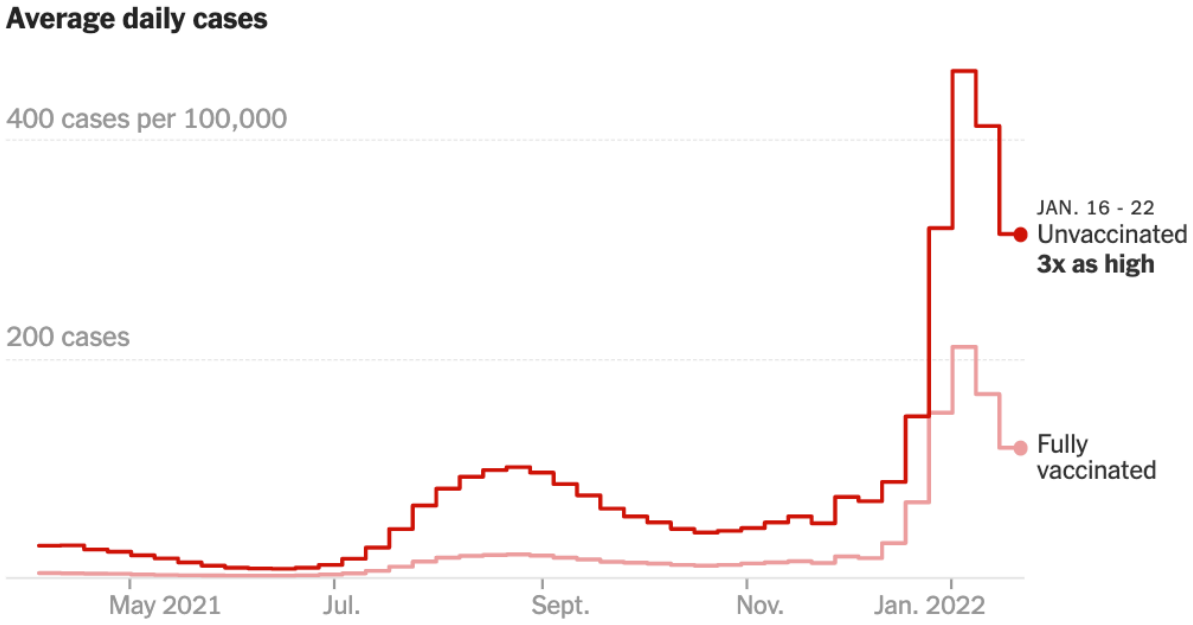


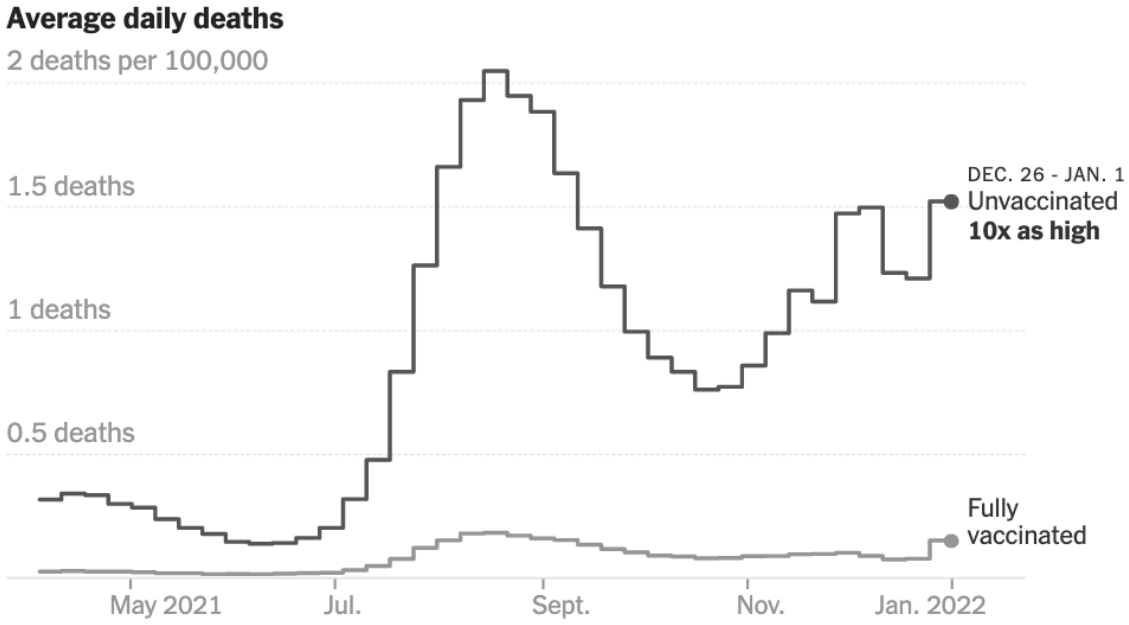
Variable	Odds Ratio for ICU admission (95% CI)
Age*	1.01 (0.99-1.03)
Influenza A vs. B	2.28 (0.93-5.59)
Hospital-acquired influenza	2.46 (0.97-6.25)
Antiviral therapy* Early (<48 hours)	0.41 (0.20-0.84)
Immunization with current season influenza vaccine*	0.40 (0.21-0.78)

*also significantly associated with pneumonia

Kumar et al., Clin Infect Dis, 2018

Lesson #6: Vaccination can attenuate disease despite incomplete seroconversion





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Ourworldindata.org
www.nytimes.com/interactive/2021/us/covid-cases.html
last accessed March 6th, 2022

Knowledge Gaps: Pediatric Vaccinations:

<u>Pfizer-BioNTech vaccine, 3mcg dose</u>

(5-16 get 10mcg; adults get 30mcg)

6-24months met non-inferiority compared to adults
2-5year old population did NOT attain the same immunogenicity as adults

FDA asked Pfizer to add a 3rd dose. Studies ongoing

((additional 5-11yr old 3rd dose studies underway)

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Knowledge Gaps: Second boosters?

nature

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nature › news › article

NEWS | 23 February 2022

Fourth dose of COVID vaccine offers only slight boost against Omicron infection

Israeli trial shows a fourth vaccination raises antibody levels but provides little extra protection against SARS-CoV-2 infection.

<u>Rate of confirmed infection:</u>

Lower in people 12+ days after their fourth dose than among those who received only three doses by factors of 2.0 (95% confidence interval [CI], 2.0 to 2.1).

The rate of severe illness was lower by factors of 4.3 (95% CI, 2.4 to 7.6).

Vaccine efficacy (VE) against infection was"

Pfizer= 30% (95%CI:-9% to 55%)

Moderna = 11% (95%CI:-43% to +43%)

Ie: Breakthroughs remained common, yet mild.

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https://www.medrxiv.org/content/10.1101/2022.02.15.22270948v1

https://www.medrxiv.org/content/10.1101/2022.02.01.22270232v1

COVID Vaccinations:

COVID-19 Vaccination Schedule for People Who Are Moderately or Severely Immunocompromised

Vaccine	0 month	1 month	2 month	3 month	4 month	5 month
Pfizer-BioNTech (ages 5–11 years)	1st dose	2nd dose (3 weeks after 1st dose)	3rd dose (at least 4 weeks after 2nd dose)			
Pfizer-BioNTech (ages 12 years and older)	1st dose	2nd dose (3 weeks after 1st dose)	3rd dose (at least 4 weeks after 2nd dose)		Booster dose* (at least 3 months after 3rd dose)	
Moderna (ages 18 years and older)	1st dose	2nd dose (4 weeks after 1st dose)	3rd dose (at least 4 weeks after 2nd dose)			Booster dose* (at least 3 months after 3rd dose)
Janssen (ages 18 years and older)	1st dose	2nd (additional) dose† using an mRNA COVID-19 vaccine (at least 4 weeks after 1st dose)		Booster dose* (at least 2 months after additional dose)		

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- Required 3rd dose to complete original series, a month after original

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- Required 3rd dose to complete original series, a month after original
- Booster, after original series, now just 3m after completion

Knowledge Gaps:

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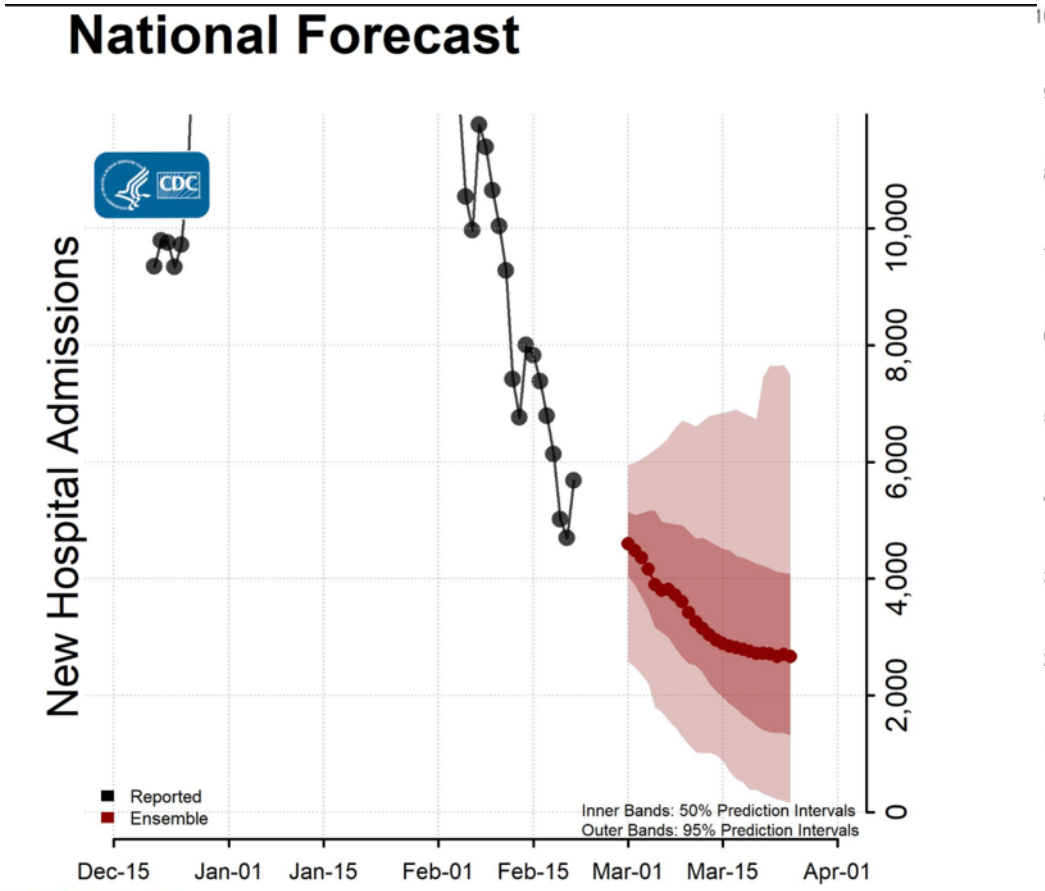
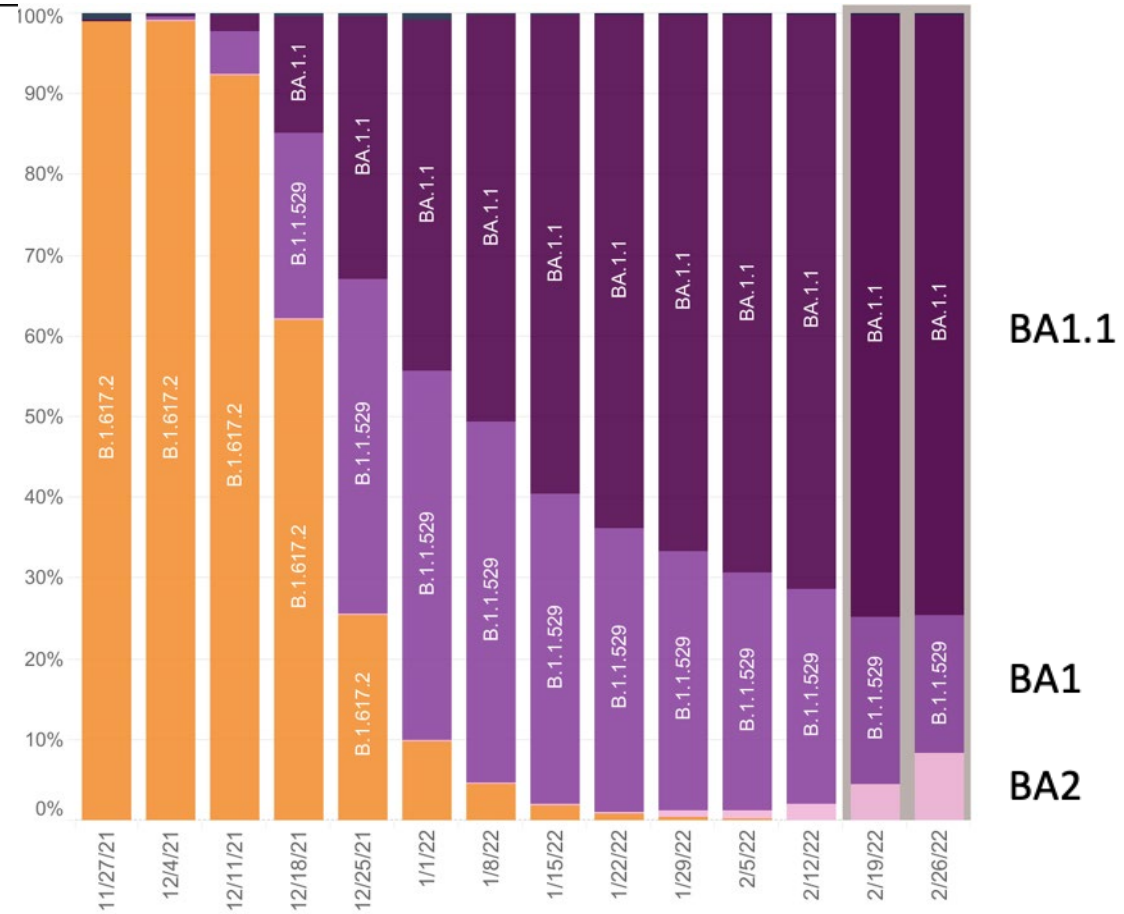
Infectious Diseases

Future Uncertainties?:





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https://covid.cdc.gov/covid-data-tracker/#variant-proportions

Knowledge Gaps:
Countering growing Vaccine Hesitancy

Perceived severity	COVID is not a serious condition in someone like me. COVID is not a serious condition for those around me
Perceived susceptibility	I am not at risk from getting COVID, I stayed safe so far I am not at risk for getting sick with the COVID during this pregnancy.
Perceived benefits	The COVID vaccine is ineffective Vaccination during pregnancy will not protect my baby from COVID complications
Perceived barriers	Cost / access I will experience harmful side effects from the vaccine; it might give me COVID. The vaccine hurt my chances of becoming pregnant I don't have enough information Mixed information from experts

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Freedom of Choice

- Right to choose whether to immunize
- I know what's best for myself
- Belief risks outweigh the benefits of vaccines
- Do not trust organized medicine, public health
- Do not trust government health authorities
- Do not trust pharmaceutical companies
- Ethical, moral or religious reasons

https://www.sciencemag.org/news/2020/06/just-50-americans-plan-get-covid-19-vaccine-here-s-how-win-over-rest

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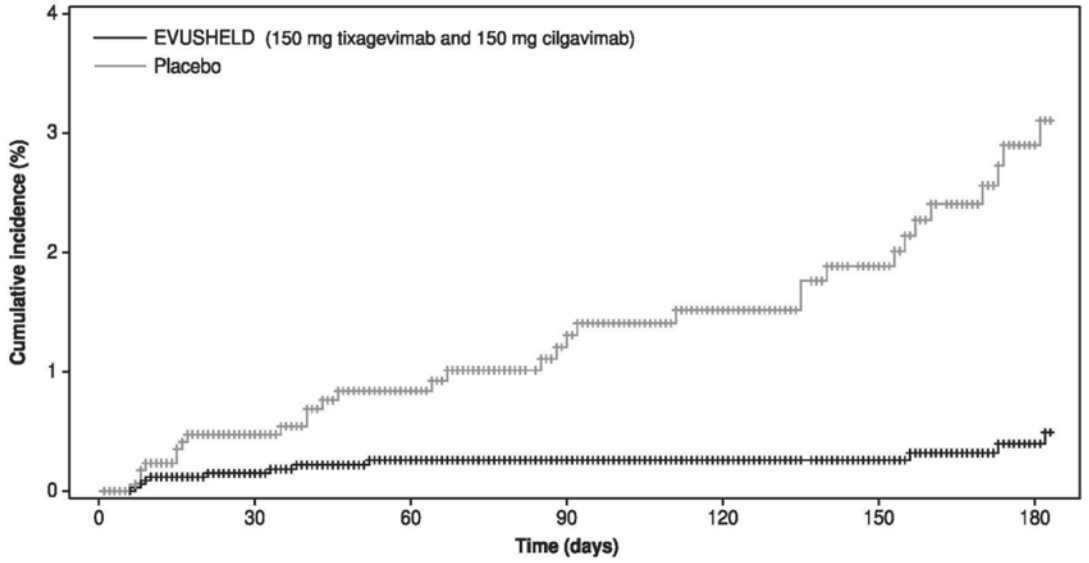
Pediatrics. Volume 138, Number 3, 2016

Tixagevimab / Cilgavimab:

Figure 1 **Kaplan Meier: Cumulative Incidence of Symptomatic COVID-19* (PROVENT)**



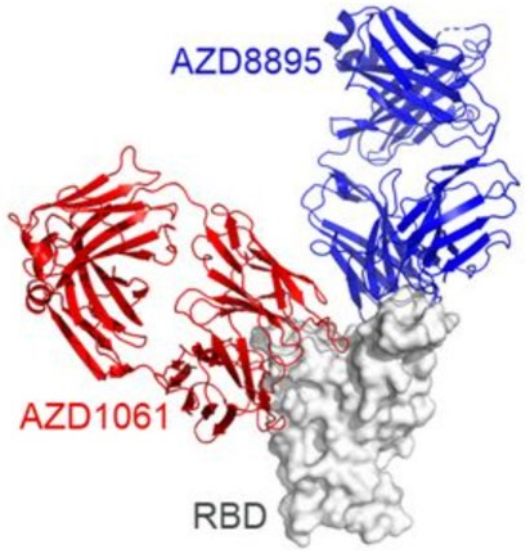
Number of participants at risk

EVUSHELD	3441	2957	2393	2054	1815	1667	1044
Placebo	1731	1483	1177	991	856	774	472

* Subjects who do not experience a primary endpoint event (and had not discontinued) are censored at Day 183. Subjects who were unblinded/vaccinated prior to an event are also censored at the earlier time of unblinding/vaccination.

- >18yrs, 2:1 randomization
- 5197 patients (3460 active arm)
- At 'high-risk' for COVID19
- Endpoints: Symptomatic COVID+ Infection ; Hospitalizations / Mortality

- Demographics:
  - Mean age 57yrs, 36% HTn, 14% DM, 8% CVD



Relative Risk Reduction = 77% for symptomatic illness

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Tixagevimab / Cilgavimab:

Fold change in IC_{50} relative to D614G	RBD mAbs													NTD mAbs					
	Class 1			Class 2				Class 3						Class 4					
	CB6	Brii-196	1-20	REGN 10933	COV2-2196	LY-CoV 555	2-15	REGN 10987	COV2-2130	S309	2-7	Brii-198	LY-CoV 1404	ADG-2	DH1047	10-40	S2X259	4-18	5-7
BA.1	<-428	-298	<-429	<-2201	-306	<-1496	<-2716	<-1716	-83.5	-6.9	-195	2.3	1.4	-11.0	-14.2	-21.1	-13.7	<-26.7	-4.1
BA.1 + R346K	<-428	-135	<-429	-415	-187	<-1496	<-2716	<-1716	<-687	-4.5	-82.1	<-22	1.5	-15.7	-7.9	-20.5	-7.5	<-26.7	-5.5
BA.2	<-428	-322	<-429	<-2201	-680	<-1496	<-2716	-253	-1.9	-27.0	-7.3	-10.5	1.1	<-555	<-58.0	<-114	<-96	<-26.7	<-171
T19I	-3.1	-4.9	-5.3	-3.7	[illegible]	-2.2	-2.0	-2.1	[illegible]	-1.8	-5.1	-1.6	-1.7	-1.7	-1.5	-2.7	-2.9	-6.1	-3.3
L24S	-2.9	-4.0	-4.6	-3.2	[illegible]	-2.4	-2.8	-4.2	[illegible]	-1.5	-2.6	-2.2	-1.6	-1.3	-1.1	-2.4	-2.0	-3.1	-1.1
Del25-27	-1.2	-2.6	-2.0	-1.3	[illegible]	-1.4	-1.2	-1.3	[illegible]	-1.3	-2.8	2.0	-1.2	1.1	1.6	-1.8	1.1	-23.1	-16.8
V213G	-2.5	-3.1	-3.0	-3.1	[illegible]	-1.1	-1.6	-2.2	[illegible]	-1.2	-3.2	-1.1	-1.5	1.1	1.0	-2.0	-1.7	1.9	-2.8
S371F	-143	-126	-95.1	-27.9	[illegible]	-5.1	-6.3	-86.6	[illegible]	-20.5	-30.6	<-22	-2.4	-43.0	-60.9	<-114	-77.5	7.8	2.3
T376A	-1.9	-3.1	-2.5	-2.1	[illegible]	-1.7	-1.3	-1.9	[illegible]	1.0	-2.7	2.0	-1.7	1.1	1.1	-1.5	-2.3	1.3	-1.3
D405N	-25.6	-2.3	-2.9	-2.8	[illegible]	-1.9	-1.7	-1.6	[illegible]	1.5	-3.1	-1.6	1.3	3.3	-1.2	-3.9	-2.2	5.6	1.5
R408S	1.4	-1.1	-1.3	-1.1	[illegible]	-1.6	-1.3	1.2	[illegible]	1.0	1.2	1.4	-1.4	-1.6	-2.1	-1.2	-3.6	1.1	-1.3

>3	<-3	<-10	<-100

TxID
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Dispensing:

Proposed Prioritization Tiers:

1) Received B-cell depleting therapies (e.g. rituximab, obinutuzumab, ocrelizumab, alemtuzumab) within last 6 months & age > 65

2) Received B-cell depleting therapies , within the last 6 months, and age < 65yrs. Any ongoing use of BTK inhibitors (ibrutinib, acalabrutinib)

3) Received allogeneic HCT or CAR-T therapy within the past 6-12 months

4) Lung transplants, other SOT recipients on continual belatacept therapy, or multiple myeloma (actively receiving treatment);

5) Autologous HCT, or other solid organ transplants age > 65 yrs and within 6 months of transplant

6) Other actively treated hematologic malignancies or severe congenital immunodeficiency syndromes; patients receiving high-dose cyclophosphamide or similarly immunosuppressive regimens

7) Solid tumor malignancies or inflammatory syndromes on immunomodulatory chemotherapy (eg: high-dose cyclophosphamide); advanced AIDS

8) Other groups not previously mentioned.

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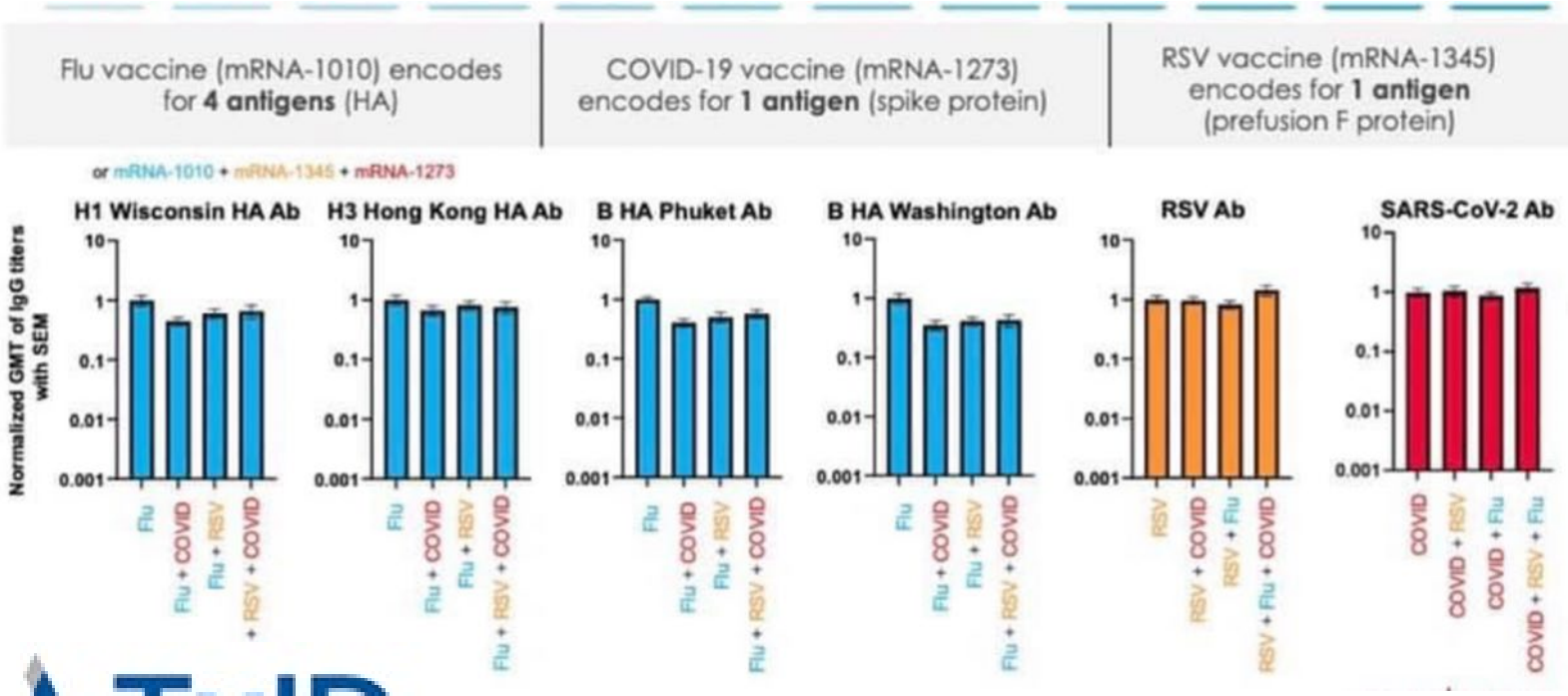
So where are vaccines headed?

1. Combination mRNA vaccines

FluA + RSV + Covid combined



2. Universal influenza vaccines

Computer-generated image of nanoparticle influenza vaccine. *NIAID*

TxID
Duke Transplant/ Immunocompromised Host Infectious Diseases

Review:

1. Seroconversion is lower in SOT and Heme malignancy patients
2. Not all immunosuppression is the same
3. Timing is critical
4. Dosing variability can help
5. No all vaccines created equal
6. Vaccination attenuates disease even with incomplete seroconversion

7. … Much still to learn… !!

TxID
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Infectious Diseases

Questions?

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Infectious Diseases