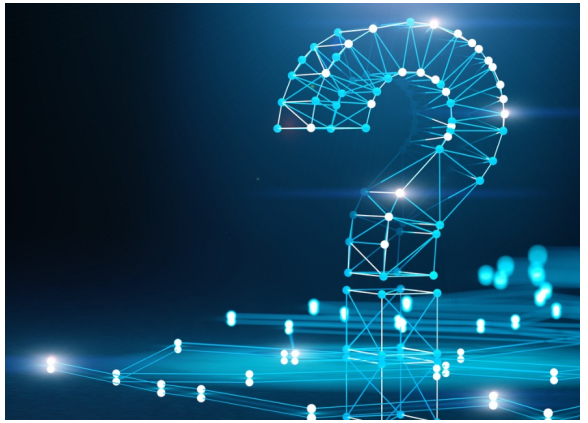
Sarcoidosis, Immunosuppressive Treatments, and the COVID-19 Vaccine

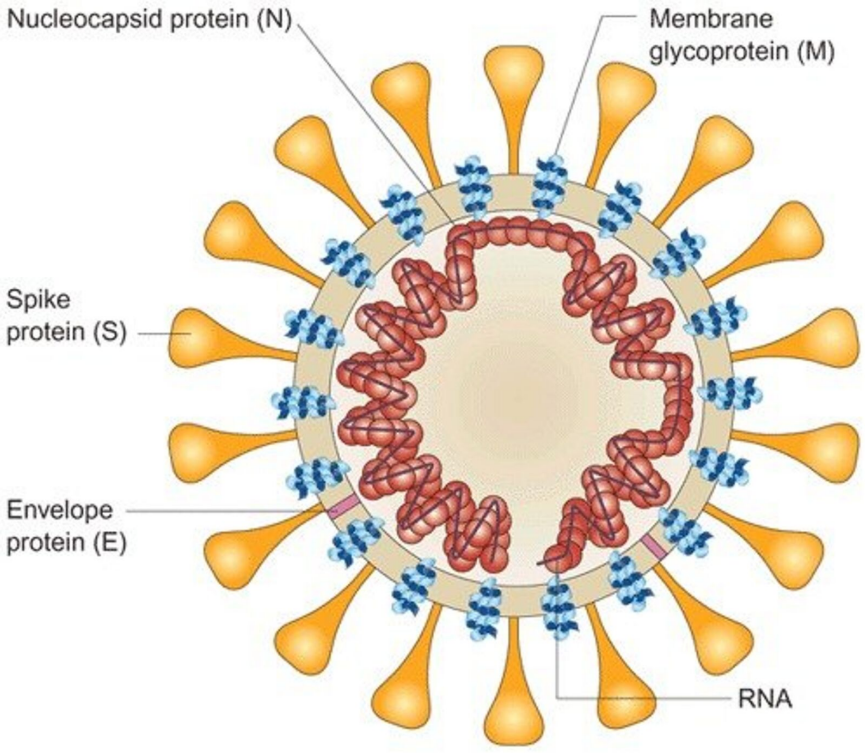
Matthew C. Baker, M.D., M.S.
Clinical Chief, Division of Immunology and Rheumatology
Co-Director, Stanford Multidisciplinary Sarcoidosis Program
Department of Medicine, Stanford University

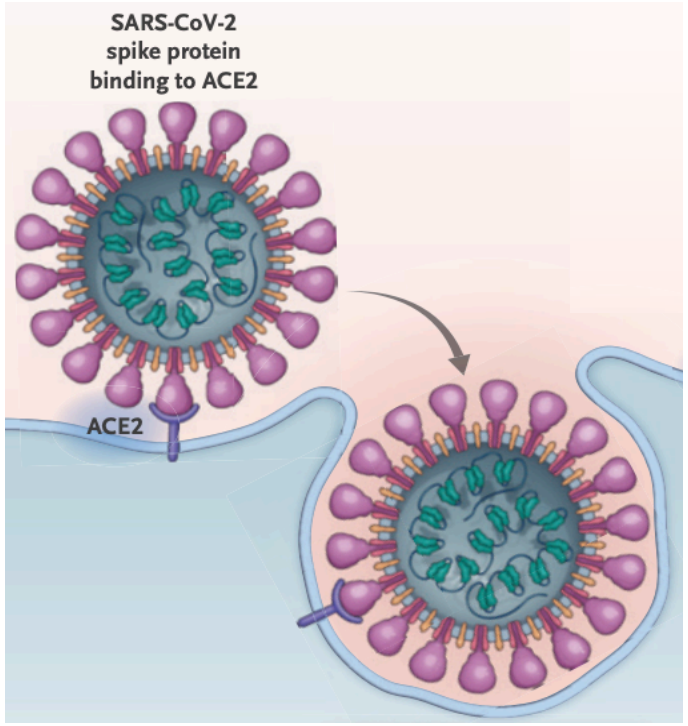
Agenda

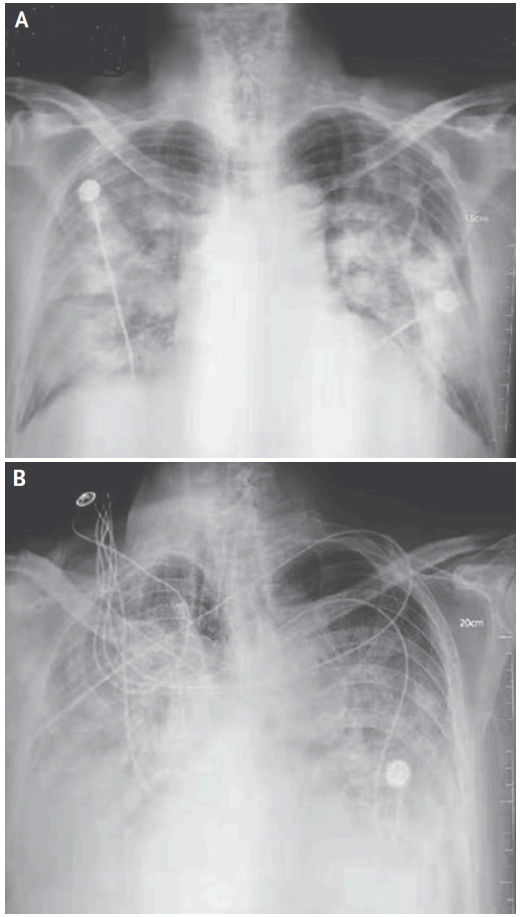
- Presentation (30 minutes)
  - SARS-CoV-2
  - COVID-19 and sarcoidosis
  - COVID-19 vaccines
  - Assessing immunity after vaccination
  - Current recommendations
- Q & A (20 minutes)



SARS-CoV-2 and COVID-19







https://www.lubio.ch/blog/neutralizing-antibodies
Vaduganathan M, et al. Renin-Angiotensin-Aldosterone System Inhibitors in Patients with Covid-19. N Engl J Med. 2020;382(17):1653-9.
Zhu N, et al. A Novel Coronavirus from Patients with Pneumonia in China, 2019. N Engl J Med. 2020;382(8):727-33.

COVID-19

- All ages susceptible to SARS-CoV-2 infection
- Increased risk for severe COVID-19 or death
  - Men > 60 years with comorbidities
  - Black, Hispanic, and South Asian individuals in the U.S.
  - Patients with **underlying lung disease** and **immunocompromised** states
- Very little sarcoidosis-specific data
  - Knowledge extrapolated from other immune-mediated diseases

Hu B, et al. Characteristics of SARS-CoV-2 and COVID-19. Nat Rev Microbiol. 2021;19(3):141-54.

Are Sarcoidosis Patients More Likely to Contract COVID-19?

- Self-reported questionnaire study from April to July 2020
  - Rate of COVID-19 amongst sarcoidosis patients was 2.23% (22,308 per million)
  - USA rate was 0.106% (1,060 per million) at the time
  - Subset analysis of same locality and time period = similar rate of infection
- In another cohort study, the rate of COVID-19 was 2.1% (5 out of 238 sarcoidosis patients) from March to April 2020
- There is no current evidence that sarcoidosis patients are inherently more susceptible to COVID-19

Baughman RP, et al. Risk and outcome of COVID-19 infection in sarcoidosis patients: results of a self-reporting questionnaire. Sarcoidosis Vasc Diffuse Lung Dis. 2020;37(4):e2020009.
Manansala M, et al. Case Series: COVID-19 in African American Patients With Sarcoidosis. Front Med (Lausanne). 2020;7:588527.
Manansala M, et al. COVID-19 and Sarcoidosis, Readiness for Vaccination: Challenges and Opportunities. Front Med (Lausanne). 2021;8:672028.

Do Sarcoidosis Patients Get More Severe COVID-19?

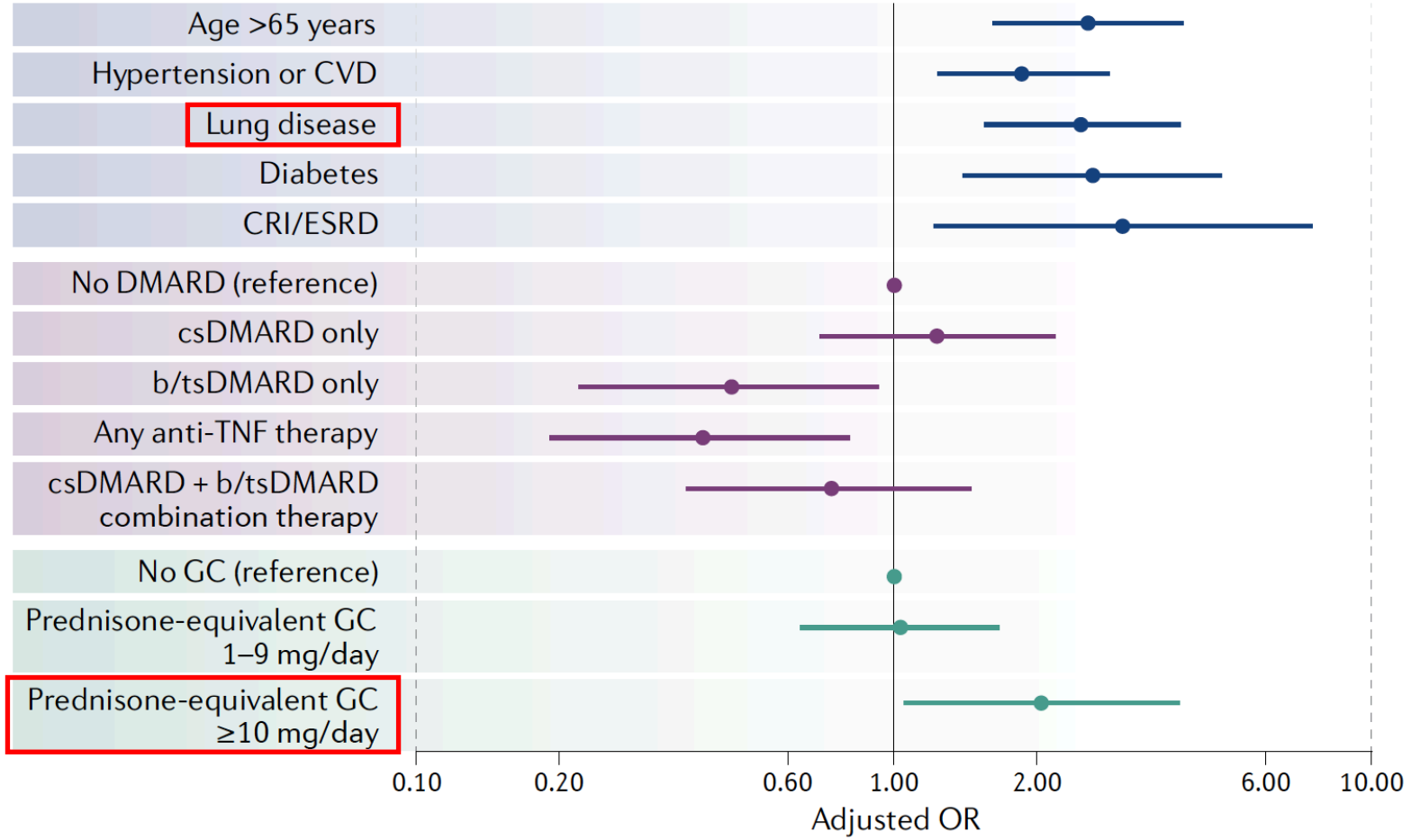
Factors Associated with COVID-19 Hospitalization in Patients with Immune-Mediated Disease

Table 1 Demographic and clinical characteristics of patients with rheumatic disease with COVID-19 (n=600)

	N (%)
Region	
Region of the Americas: North	340 (57)
Region of the Americas: South	16 (3)
European region	218 (36)
African region	<5 (<1)
Eastern Mediterranean region	11 (2)
South-East Asian region	<5 (<1)
Western Pacific region	13 (2)
Female	423 (71)
Age (years)	
18–29	32 (5)
30–49	169 (28)
50–65	229 (38)
>65	170 (28)
Median (IQR)	56 (45–67)
Most common rheumatic disease diagnoses*	
Rheumatoid arthritis	230 (38)
Systemic lupus erythematosus	85 (14)
Psoriatic arthritis	74 (12)
Axial spondyloarthritis or other spondyloarthritis	48 (8)
Vasculitis	44 (7)
Sjögren's syndrome	28 (5)
Other inflammatory arthritis	21 (4)
Inflammatory myopathy	20 (3)
Gout	19 (3)
Systemic sclerosis	16 (3)
Polymyalgia rheumatica	12 (2)
Sarcoidosis	10 (2)
Other	28 (5)
Most common comorbidities	
Hypertension	199 (33)
Lung disease†	127 (21)
Diabetes	69 (12)
Cardiovascular disease	63 (11)
Chronic renal insufficiency/end-stage renal disease	40 (7)

Gianfrancesco M, et al. Characteristics associated with hospitalisation for COVID-19 in people with rheumatic disease: data from the COVID-19 Global Rheumatology Alliance physician-reported registry. Ann Rheum Dis. 2020;79(7):859-66.

Factors Associated with COVID-19 Hospitalization in Patients with Immune-Mediated Disease



Hyrich KL, et al. Rheumatic disease and COVID-19: epidemiology and outcomes. Nat Rev Rheumatol. 2021;17(2):71-2.

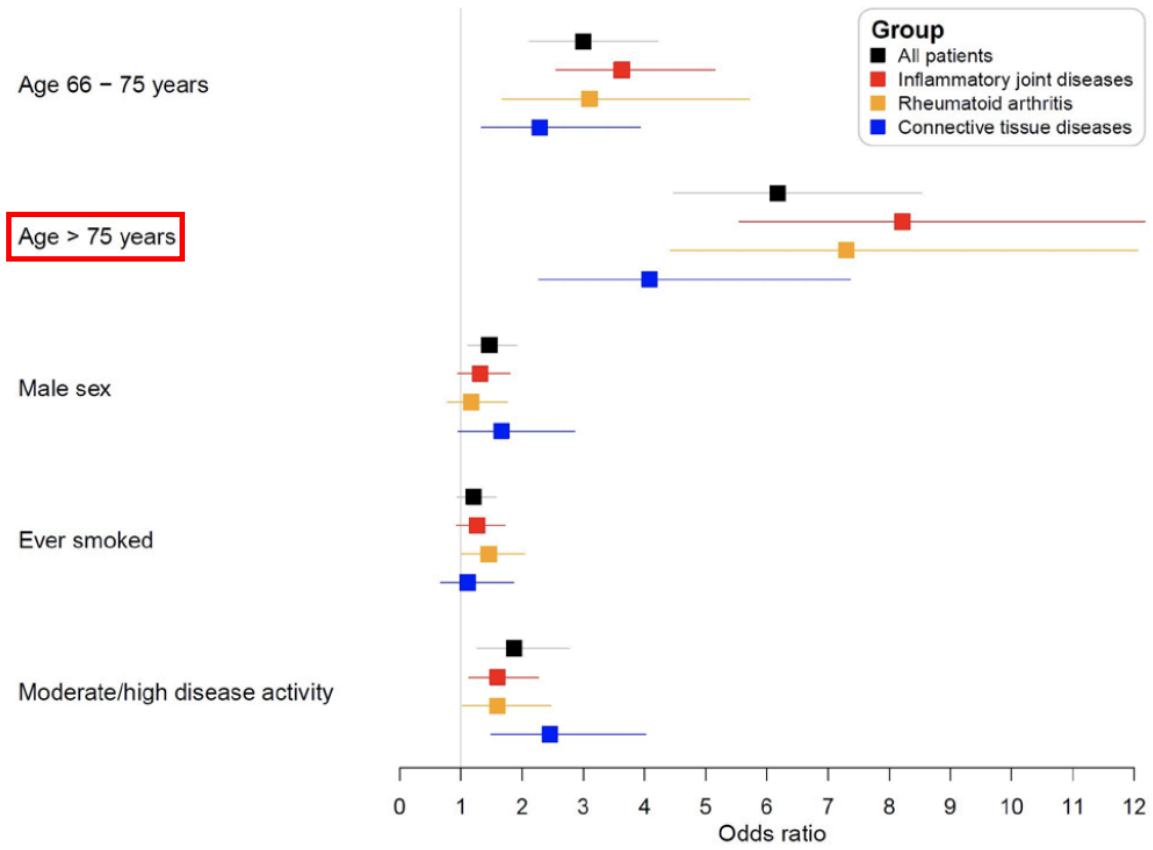
Factors Associated with COVID-19 Death in Patients with Immune-Mediated Disease

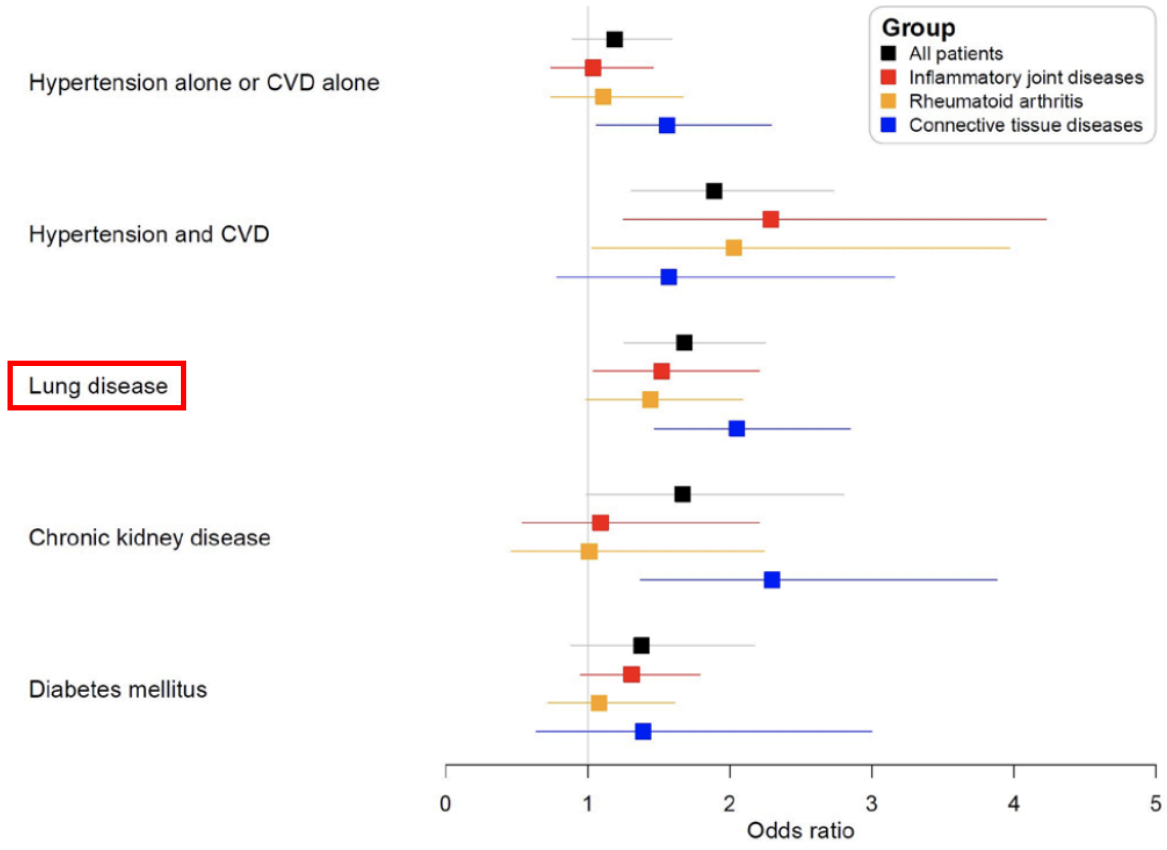
Table 1 Patient demographic and clinical characteristics

Parameter	Not deceased	Deceased	Total
N	**3339**	**390**	**3729**
General			
Age (years)	55.5 (15.2)	69.7 (14.6)	57.0 (15.7)
≤30	197 (5.9)	9 (2.3)	206 (5.5)
31–50	1012 (30.3)	31 (7.9)	1043 (28)
51–65	1255 (37.6)	82 (21)	1337 (35.9)
66–75	536 (16.1)	109 (27.9)	645 (17.3)
>75	339 (10.2)	159 (40.8)	498 (13.4)
Male sex	1031 (30.9)	164 (42.1)	1195 (32)
Inflammatory joint diseases			
Rheumatoid arthritis	1224 (36.7)	170 (43.6)	1394 (37.4)
Spondyloarthritis	416 (12.5)	15 (3.8)	431 (11.6)
Psoriatic arthritis	420 (12.6)	20 (5.1)	440 (11.8)
Juvenile idiopathic arthritis (poly, oligo, not systemic)	21 (0.6)	4 (1)	25 (0.7)
Other inflammatory arthritis	90 (2.7)	8 (2.1)	98 (2.6)
Total Inflammatory joint diseases	2158 (64.6)	215 (55.1)	2373 (63.6)
Connective tissue diseases/Vasculitis			
Systemic lupus erythematosus	355 (10.6)	36 (9.2)	391 (10.5)
Connective tissue diseases (other than SLE)	473 (14.2)	60 (15.4)	533 (14.3)
Vasculitis	258 (7.7)	68 (17.4)	326 (8.7)
Total CTD	1035 (31)	158 (40.5)	1193 (32.0)
Other RMDs			
Total	306 (9.2)	50 (12.8)	356 (9.5)

Strangfeld A, et al. Factors associated with COVID-19-related death in people with rheumatic diseases: results from the COVID-19 Global Rheumatology Alliance physician-reported registry. Ann Rheum Dis. 2021.

Factors Associated with COVID-19 Death in Patients with Immune-Mediated Disease





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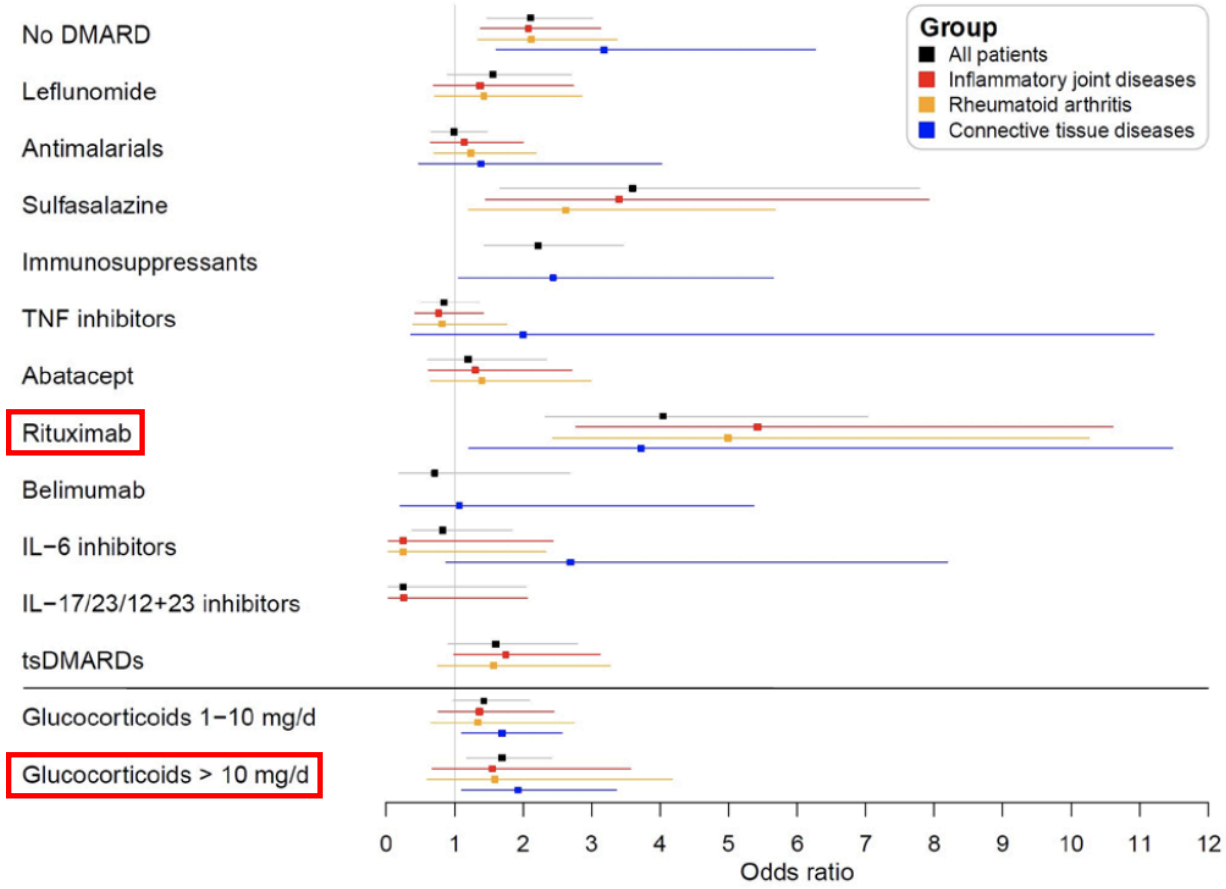
Factors Associated with COVID-19 Death in Patients with Immune-Mediated Disease



Strangfeld A, et al. Factors associated with COVID-19-related death in people with rheumatic diseases: results from the COVID-19 Global Rheumatology Alliance physician-reported registry. Ann Rheum Dis. 2021.

Factors Associated with COVID-19 Severity in Patients with Rheumatoid Arthritis

Table 1 Baseline characteristics according to use of biologic or targeted synthetic disease-modifying antirheumatic drugs for rheumatoid arthritis at the time of COVID-19 onset

	Overall N=2869	Abatacept n=237	Rituximab n=364	IL-6 inhibitors n=317	JAK inhibitors n=563	TNF inhibitors n=1388
Demographics						
Mean age (years), SD	56.7 (13.4)	61.4 (14.0)	58.0 (12.9)	56.4 (12.0)	58.0 (12.3)	55.2 (14.0)
Female	2316 (80.8)	188 (79.3)	299 (82.1)	257 (81.3)	470 (83.5)	1102 (79.4)
Race/ethnicity						
White	1670 (69.0)	78 (69.5)	187 (64.5)	169 (67.9)	360 (73.2)	829 (69.3)
Black	113 (4.7)	5 (3.2)	14 (4.8)	11 (4.4)	22 (4.5)	60 (5.0)
Hispanic	472 (19.5)	32 (20.8)	66 (22.8)	46 (18.5)	79 (16.1)	233 (19.5)
East Asian	81 (3.3)	8 (5.2)	10 (3.4)	12 (4.8)	10 (2.0)	37 (3.1)
Other	85 (3.3)	2 (1.3)	13 (4.5)	11 (4.4)	21 (4.3)	38 (3.2)

Sparks JA, et al. Associations of baseline use of biologic or targeted synthetic DMARDs with COVID-19 severity in rheumatoid arthritis: Results from the COVID-19 Global Rheumatology Alliance physician registry. Ann Rheum Dis. 2021.

Factors Associated with COVID-19 Severity in Patients with Rheumatoid Arthritis

Table 4 Multivariable* OR of biologic or targeted synthetic disease-modifying antirheumatic drugs at each binary level of the COVID-19 severity scale (N=2869)

	Abatacept		Rituximab		IL-6 inhibitors		JAK inhibitors		
COVID-19 outcome	OR (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)	P value	TNF inhibitors
Hospitalised	1.18 (0.76 to 1.82)	0.47	4.53 (3.32 to 6.18)	<0.01	0.84 (0.53 to 1.33)	0.45	2.40 (1.78 to 3.24)	<0.01	Ref
Hospitalised with oxygenation/ventilation or death	1.12 (0.70 to 1.81)	0.63	2.87 (2.03 to 4.06)	<0.01	0.72 (0.43 to 1.20)	0.20	1.55 (1.04 to 2.18)	0.01	Ref
Death	1.46 (0.72 to 2.89)	0.30	4.57 (3.32 to 9.01)	<0.01	1.13 (0.50 to 2.59)	0.77	2.04 (1.58 to 2.65)	<0.01	Ref
Mechanical ventilation (restricted to only hospitalised patients, n=613)	1.41 (0.94 to 2.10)	0.09	4.05 (3.08 to 5.33)	<0.01	0.75 (0.51 to 1.10)	0.14	2.03 (1.56 to 2.62)	<0.01	Ref
Mechanical ventilation or death	1.14 (0.78 to 1.66)	0.50	4.44 (3.39 to 5.82)	<0.01	0.74 (0.50 to 1.09)	0.12	2.02 (1.56 to 2.61)	<0.01	Ref

*Adjusted for age, sex, region, calendar time, obesity, smoking, concomitant csDMARD use, glucocorticoid use/dose, comorbidity count, hypertension/cardiovascular disease, interstitial lung disease, cancer and rheumatoid arthritis disease activity.
csDMARD, conventional synthetic disease-modifying antirheumatic drug; IL-6, interleukin 6; JAK, Janus kinase; Ref, reference; TNF, tumour necrosis factor.

Sparks JA, et al. Associations of baseline use of biologic or targeted synthetic DMARDs with COVID-19 severity in rheumatoid arthritis: Results from the COVID-19 Global Rheumatology Alliance physician registry. Ann Rheum Dis. 2021.

Factors Associated with COVID-19 Severity in Patients with Lung Disease

- Between Jan 24 - April 30, 2020 this study included 8,256,161 people in England
- 14,479 (0·2%) were admitted to hospital with COVID-19, 1,542 (<0·1%) were admitted to the ICU, and 5,956 (0·1%) died

	Number of patients with outcome (n [%]/N)	Unadjusted HR (95% CI)*	HR (95% CI) adjusted for age and sex	HR (95% CI) also adjusted for other demographic factors†	HR (95% CI) also adjusted for comorbidities‡
Hospitalisation					
COPD	1555 (0·8%)/193 520	5·09 (4·83–5·36)	1·85 (1·75–1·95)	1·79 (1·70–1·90)	1·54 (1·45–1·63)
Asthma	2266 (0·2%)/1 090 028	1·22 (1·17–1·28)	1·39 (1·33–1·46)	1·32 (1·26–1·38)	1·18 (1·13–1·24)
Active asthma	1720 (0·3%)/535 126	1·95 (1·85– 2·05)	1·56 (1·48–1·64)	1·43 (1·35–1·50)	1·26 (1·20–1·33)
Severe asthma	1369 (0·4%)/385 702	2·14 (2·02–2·26)	1·65 (1·56–1·75)	1·47 (1·39–1·55)	1·29 (1·22–1·37)
Bronchiectasis	319 (0·8%)/41 271	4·53 (4·06–5·07)	1·70 (1·52–1·90)	1·67 (1·49–1·87)	1·34 (1·20–1·50)
Cystic fibrosis	5 (0·2%)/2081	1·37 (0·57–3·30)	1·62 (0·67–3·89)	1·78 (0·74–4·28)	1·55 (0·65–3·73)
Sarcoidosis	84 (0·5%)/17 624	2·74 (2·21–3·39)	1·74 (1·40–2·15)	1·53 (1·23–1·90)	1·36 (1·10–1·68)
Extrinsic allergic alveolitis	16 (0·7%)/2331	3·97 (2·43–6·48)	1·75 (1·07–2·85)	1·86 (1·14–3·03)	1·35 (0·82–2·21)
Idiopathic pulmonary fibrosis	110 (1·5%)/7454	8·80 (7·29–10·62)	2·40 (1·99–2·89)	2·28 (1·89–2·75)	1·59 (1·30–1·95)
Other interstitial lung diseases	73 (1·3%)/5677	7·57 (6·02–9·53)	2·54 (2·02–3·20)	2·43 (1·93–3·05)	1·66 (1·30–2·12)
Lung cancer	139 (1·3%)/10 792	7·92 (6·70–9·36)	2·73 (2·31–3·23)	2·63 (2·22–3·11)	2·24 (1·89–2·65)

Aveyard P, et al. Association between pre-existing respiratory disease and its treatment, and severe COVID-19: a population cohort study. The Lancet Respiratory Medicine.

Factors Associated with COVID-19 Severity in Patients with Lung Disease

	Number of patients with outcome (n [%]/N)	Unadjusted HR (95% CI)*	HR (95% CI) adjusted for age and sex	HR (95% CI) also adjusted for other demographic factors†	HR (95% CI) also adjusted for comorbidities‡
ICU admission§					
COPD	59 (<0·1%)/193 520	1·68 (1·29–2·18)	0·85 (0·65–1·11)	0·92 (0·70–1·20)	0·89 (0·68–1·17)
Asthma	213 (<0·1%)/1 090 028	1·05 (0·91–1·22)	1·18 (1·02–1·36)	1·09 (0·95–1·27)	1·08 (0·93–1·25)
Active asthma	165 (<0·1%)/535 126	1·73 (1·47–2·03)	1·62 (1·37–1·90)	1·36 (1·16–1·61)	1·34 (1·14–1·58)
Severe asthma	124 (<0·1%)/385 702	1·79 (1·49–2·15)	1·64 (1·37–1·98)	1·33 (1·10–1·60)	1·30 (1·08–1·58)
Bronchiectasis	18 (<0·1%)/41 271	2·37 (1·49–3·78)	1·36 (0·85–2·17)	1·46 (0·91–2·33)	1·47 (0·91–2·36)
Sarcoidosis	10 (0·1%)/17 624	3·06 (1·64–5·70)	2·22 (1·19–4·14)	1·65 (0·89–3·08)	1·51 (0·81–2·81)
Idiopathic pulmonary fibrosis	6 (0·1%)/7454	4·48 (2·01–9·99)	1·87 (0·84–4·18)	1·88 (0·84–4·19)	1·97 (0·85–4·55)
Death¶					
COPD	811 (0·4%)/193 520	6·66 (6·19–7·18)	1·82 (1·69–1·96)	1·64 (1·51–1·77)	1·54 (1·42–1·67)
Asthma	762 (0·1%)/1 090 028	0·96 (0·89–1·04)	1·19 (1·1–1·28)	1·12 (1·04–1·21)	0·99 (0·91–1·07)
Active asthma	602 (0·1%)/535 126	1·62 (1·49–1·77)	1·28 (1·18–1·39)	1·18 (1·09–1·29)	1·05 (0·96–1·15)
Severe asthma	476 (0·1%)/385 702	1·78 (1·62–1·95)	1·35 (1·23–1·48)	1·21 (1·11–1·34)	1·08 (0·98–1·19)
Bronchiectasis	138 (0·3%)/41 271	4·77 (4·03–5·65)	1·35 (1·14–1·60)	1·29 (1·09–1·52)	1·12 (0·94–1·33)
Sarcoidosis	32 (0·2%)/17 624	2·53 (1·79–3·58)	1·63 (1·15–2·31)	1·58 (1·11–2·23)	1·41 (0·99–1·99)
Extrinsic allergic alveolitis	8 (0·3%)/2331	4·82 (2·41–9·65)	1·75 (0·87–3·50)	2·02 (1·01–4·03)	1·56 (0·78–3·13)
Idiopathic pulmonary fibrosis	62 (0·8%)/7454	12·09(9·42–15·53)	2·14 (1·66–2·74)	2·04 (1·58–2·62)	1·47 (1·12–1·92)
Other interstitial lung diseases	45 (0·8%)/5677	11·37 (8·48–15·25)	2·7 (2·01–3·62)	2·71 (2·02–3·63)	2·05 (1·49–2·81)
Lung cancer	60 (0·6%)/10 792	8·33 (6·46–10·74)	2·18 (1·69–2·81)	1·95 (1·51–2·51)	1·77 (1·37–2·29)

Aveyard P, et al. Association between pre-existing respiratory disease and its treatment, and severe COVID-19: a population cohort study. The Lancet Respiratory Medicine.

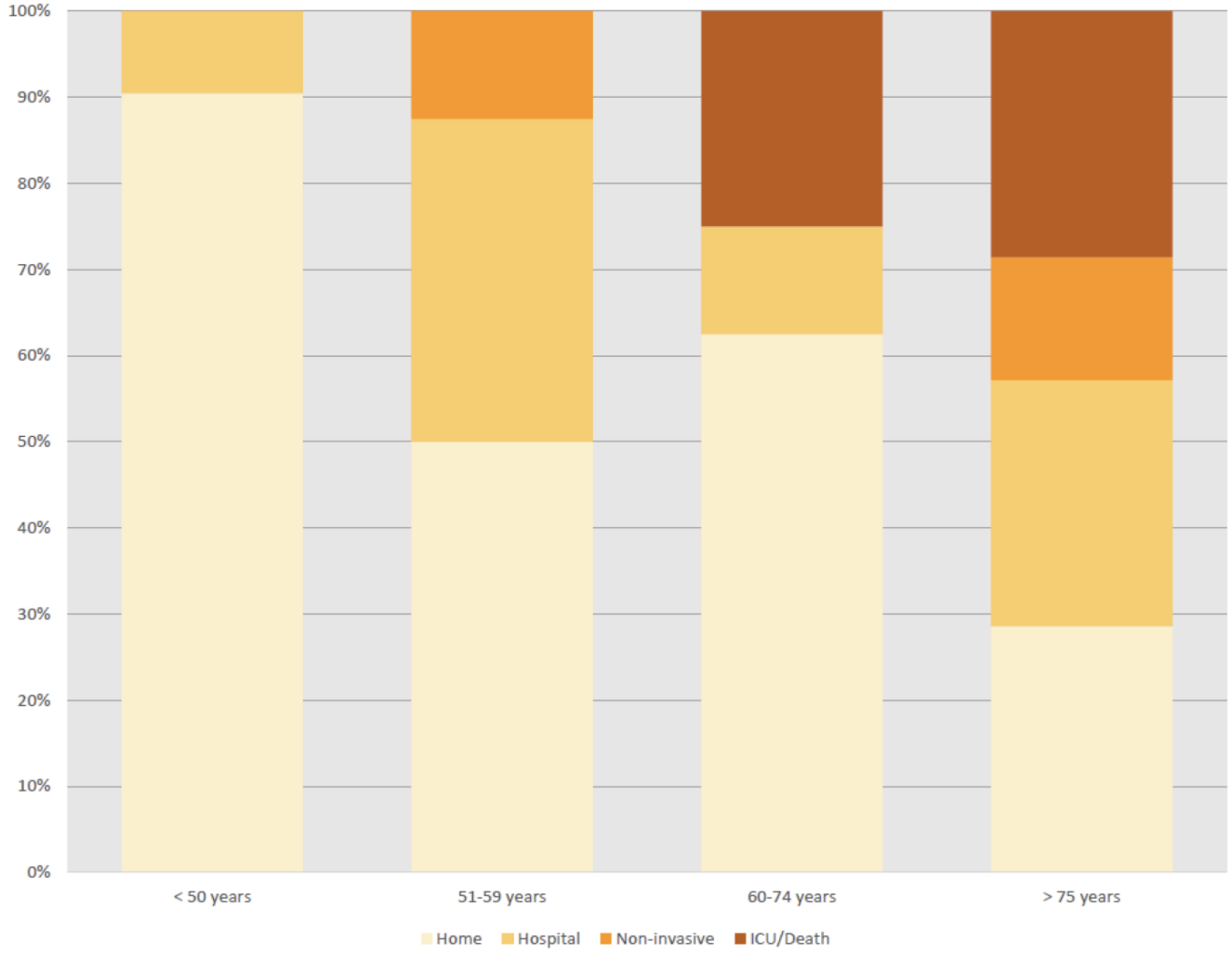
COVID-19 Outcomes in Sarcoidosis Patients

- 45 sarcoidosis patients with SARS-CoV-2 infection were identified in Southern Europe
- 36 patients presented a symptomatic SARS-CoV-2 infection and 14 were hospitalized
  - 12 required supplemental oxygen, 2 intensive care unit admission and 1 mechanical ventilation, 4 patients died due to progressive respiratory failure

		Patients	Frequency
Age, Years (Mean, Range)	55.4 (31–89)	(*n*/N)	(%)
Sex	Male	17/45	37.8
	Female	28/45	62.2
Comorbidities	Any comorbidity	23/45	54.1
	Hypertension	15/45	33.3
	Diabetes mellitus	10/45	22.2
	Chronic pulmonary disease	8/45	17.8
	Cardiovascular disease	5/45	11.1
	Chronic renal/liver disease	5/45	11.1
Active therapies for sarcoidosis	Any	28/45	62.2
	Corticosteroids	15/45	33.3
	Immunosuppressant agents	7/45	15.6
	Biological therapies	0/45	0.0

Brito-Zeron P, et al. Characterization and Outcomes of SARS-CoV-2 Infection in Patients with Sarcoidosis. Viruses. 2021;13(6).

COVID-19 Outcomes in Sarcoidosis Patients



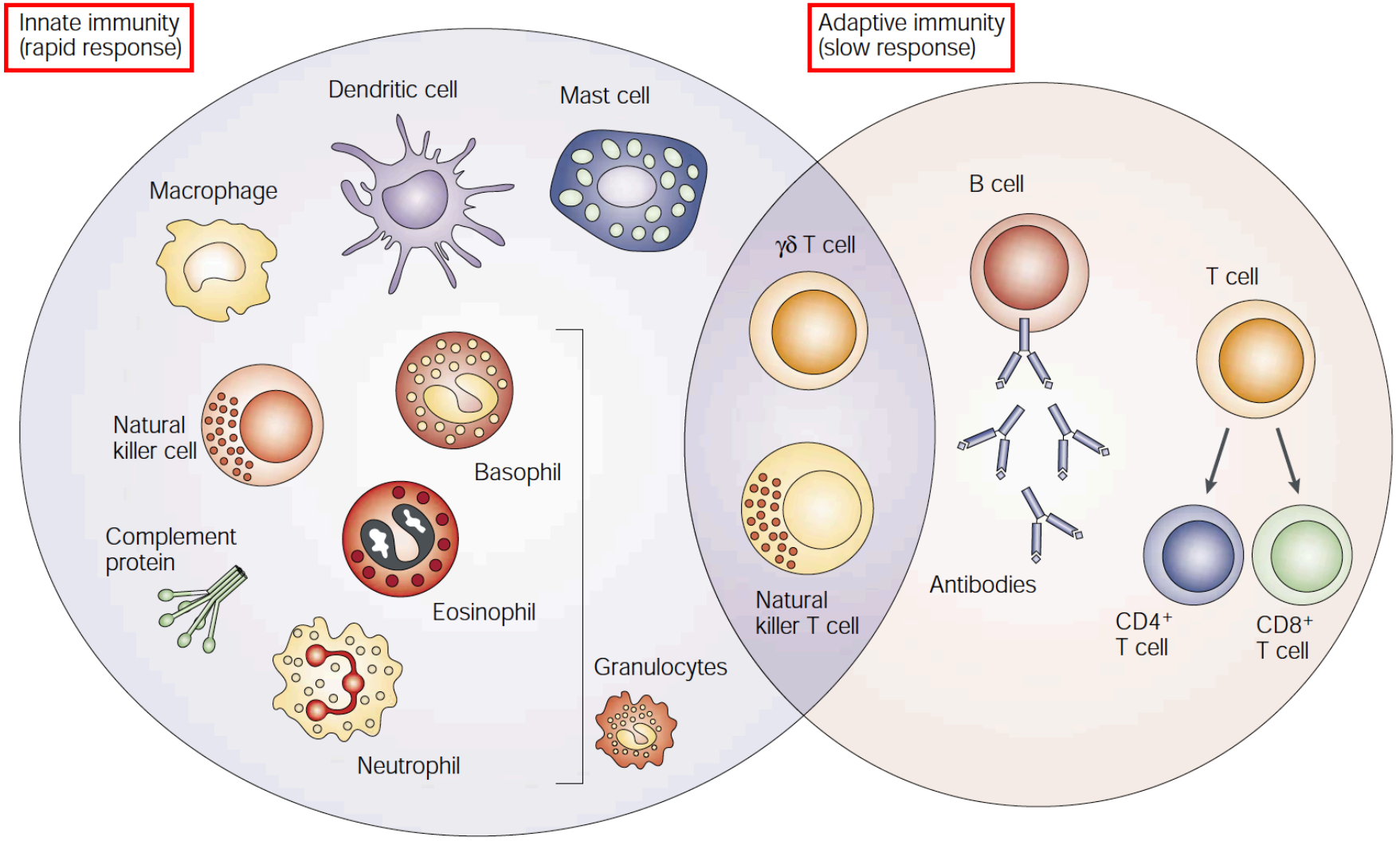
Brito-Zeron P, et al. Characterization and Outcomes of SARS-CoV-2 Infection in Patients with Sarcoidosis. Viruses. 2021;13(6).

Do Sarcoidosis Patients Get More Severe COVID-19?

- Likely an increased risk of more severe COVID-19
  - There is a spectrum depending on the individual patient
- Risk factors that are meaningful for sarcoidosis patients:
  - Older age
  - Comorbidities
    - Hypertension, cardiovascular disease, diabetes
  - Underlying lung involvement
  - Immunosuppression
    - Rituximab
    - Glucocorticoids
- Methotrexate and TNF inhibitors are not likely major risk factors

Should Sarcoidosis Patients Get The COVID-19 Vaccine?

Understanding Vaccines: The Immune System

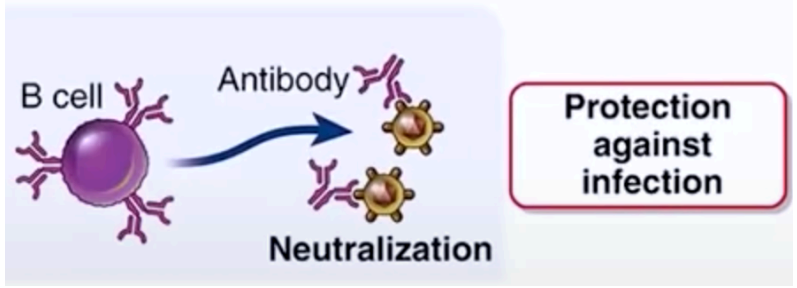


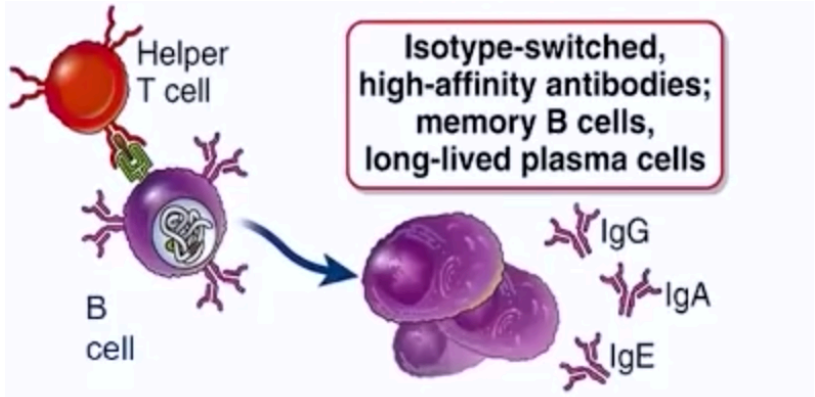
Dranoff G. Cytokines in cancer pathogenesis and cancer therapy. Nat Rev Cancer. 2004;4(1):11-22.

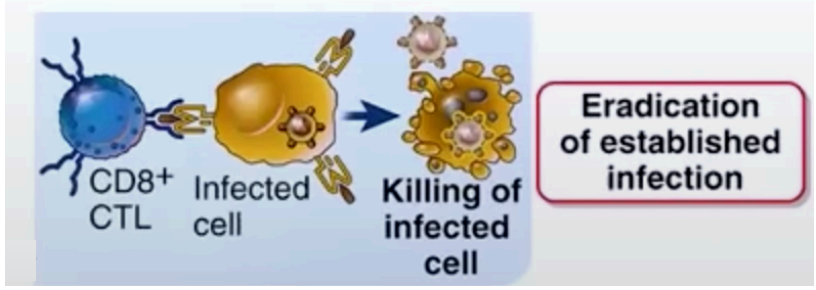
Understanding Vaccines: The Immune System

- Innate Immune System
  - Dendritic cells and macrophages
    - Antigen presenting cells
    - Critical in the immediate response but do not provide specific memory

- Adaptive Immune System
  - B cells
    - Make antibodies
  - T cells
    - Help B cells
    - Directly kill infected cells







Abbas, Lichtman, and Pillai. Cellular and Molecular Immunology. 9th edition.

Different Types of Vaccines

There are three main approaches to making a vaccine:

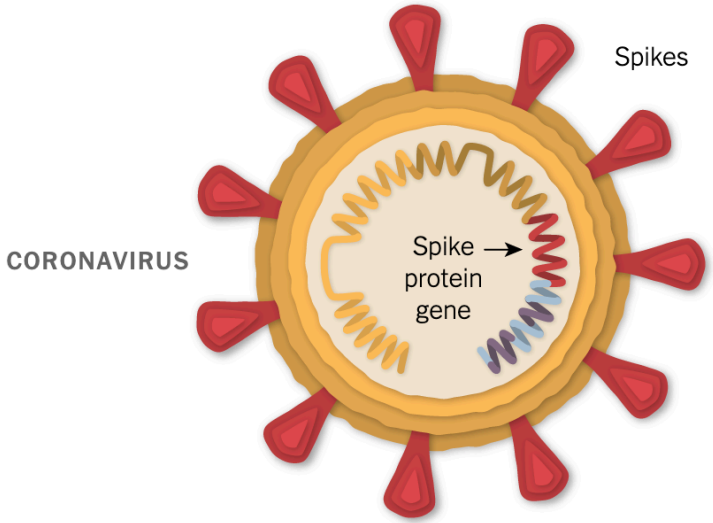
Using a whole virus or bacterium

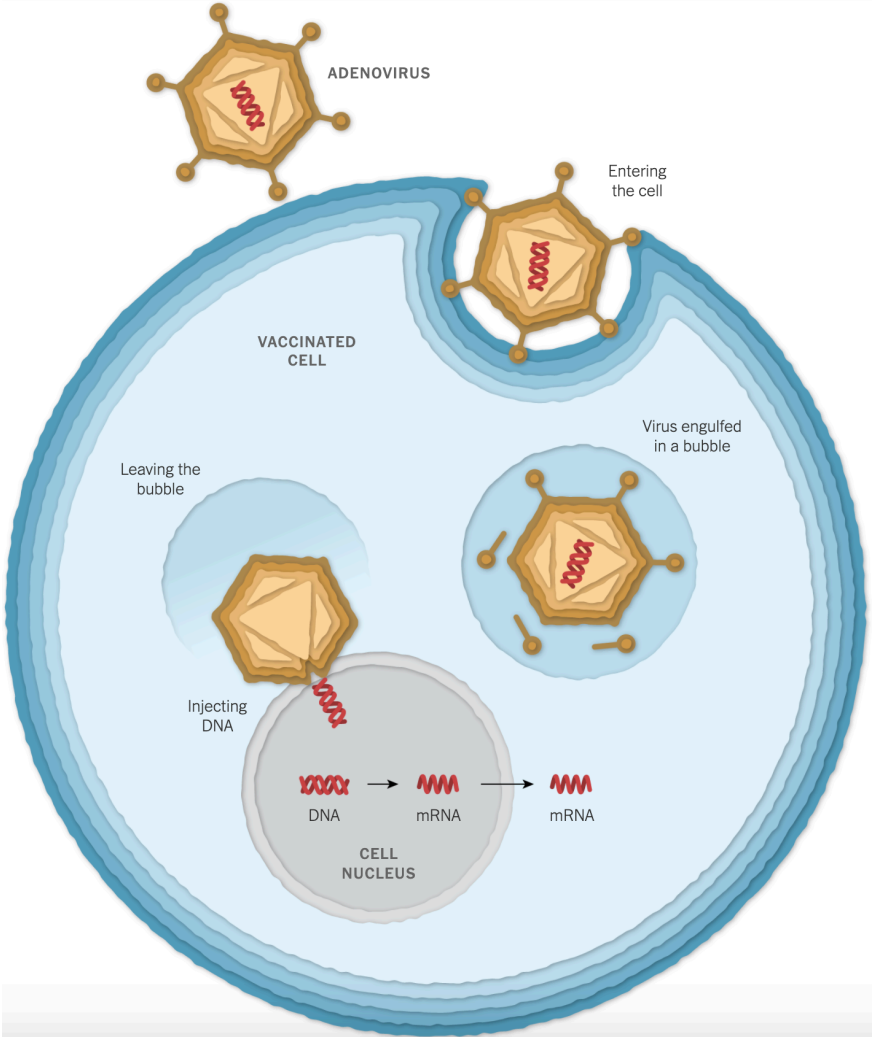
Parts that trigger the immune system

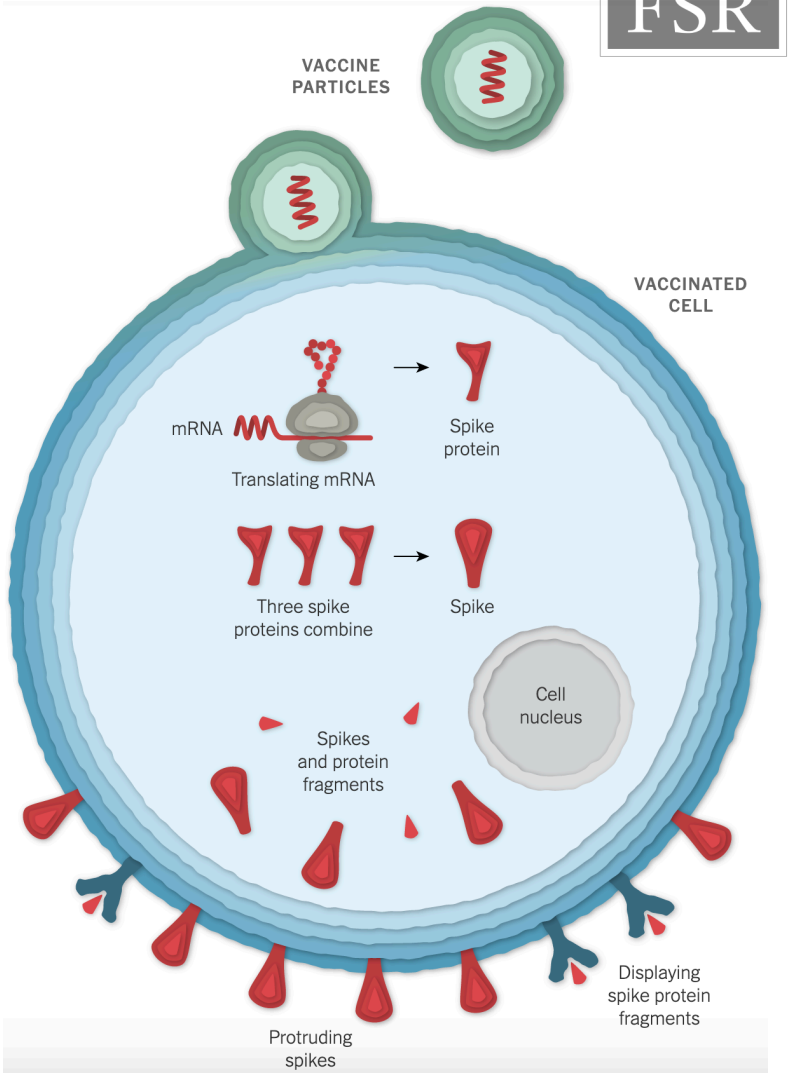
Just the genetic material

https://www.who.int/news-room/feature-stories/detail/the-race-for-a-covid-19-vaccine-explained

Authorized COVID-19 Vaccines in the U.S.

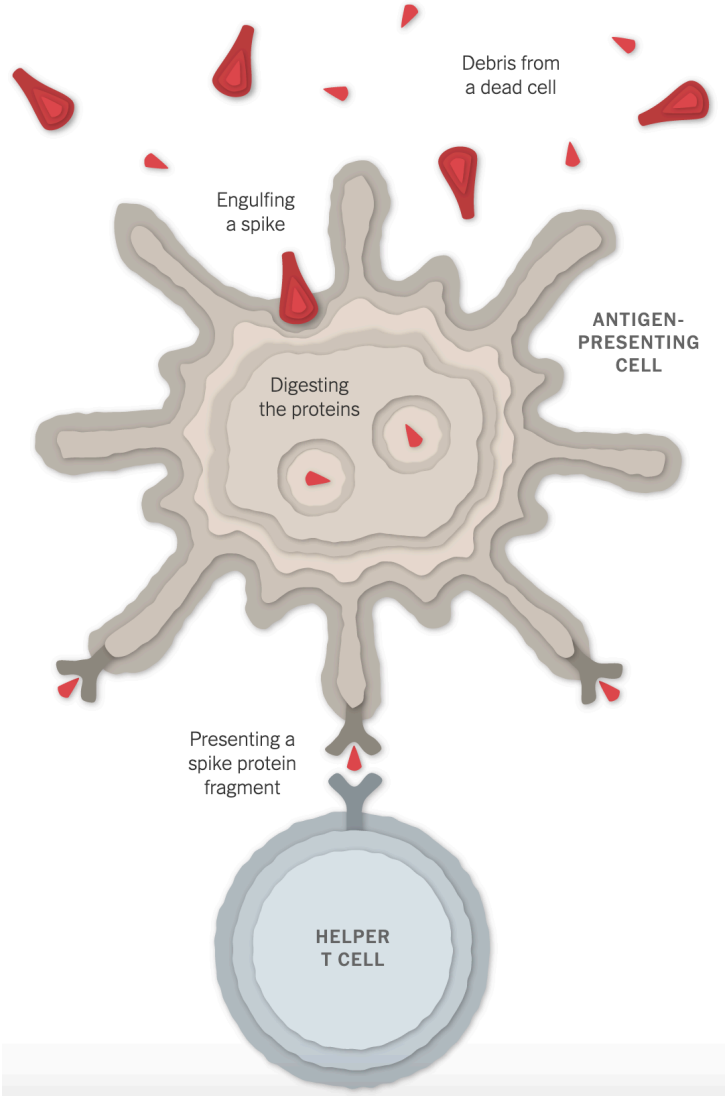


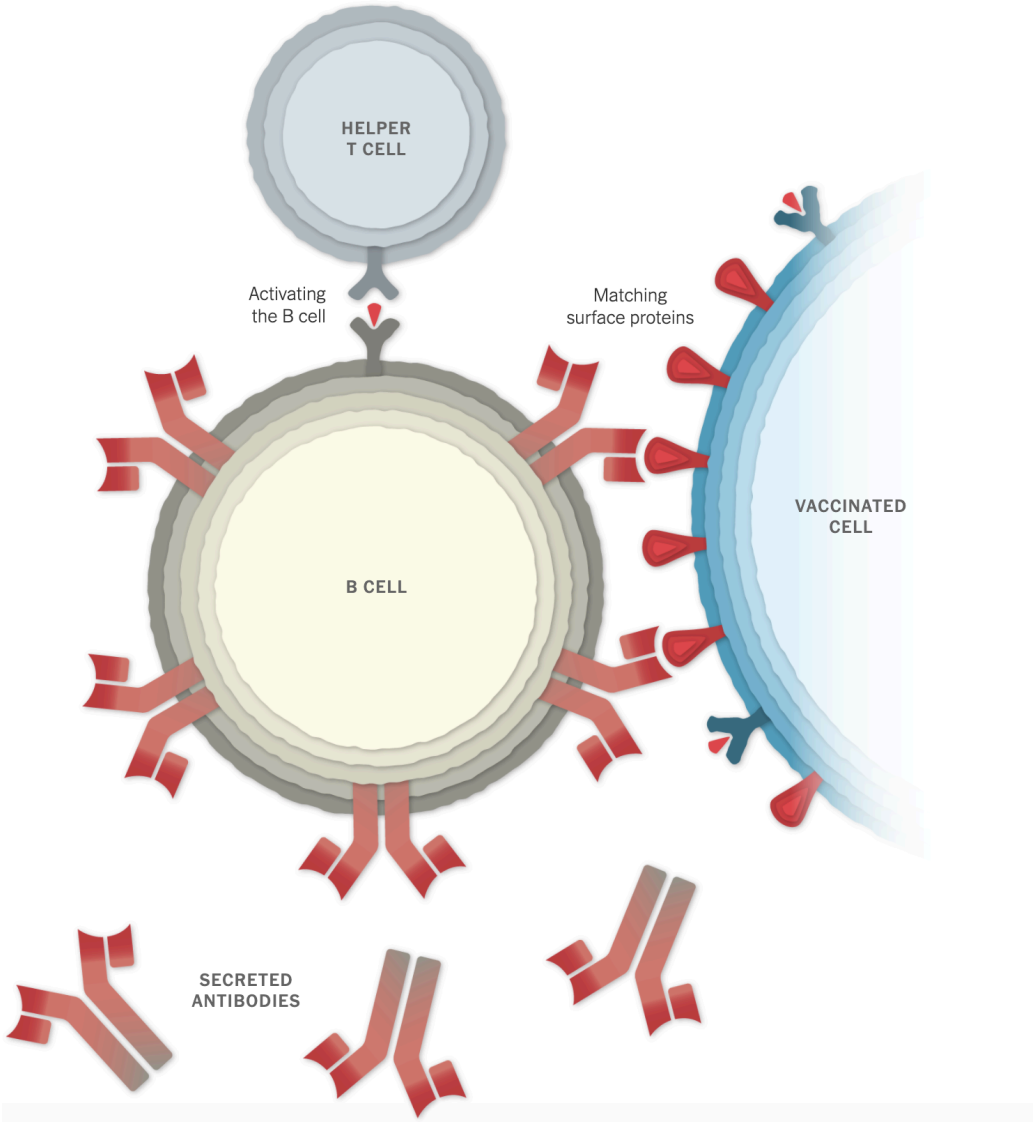




https://www.nytimes.com/interactive/2020/health/moderna-covid-19-vaccine.html?login=smartlock&auth=login-smartlock
https://www.nytimes.com/interactive/2020/health/johnson-johnson-covid-19-vaccine.html?searchResultPosition=1

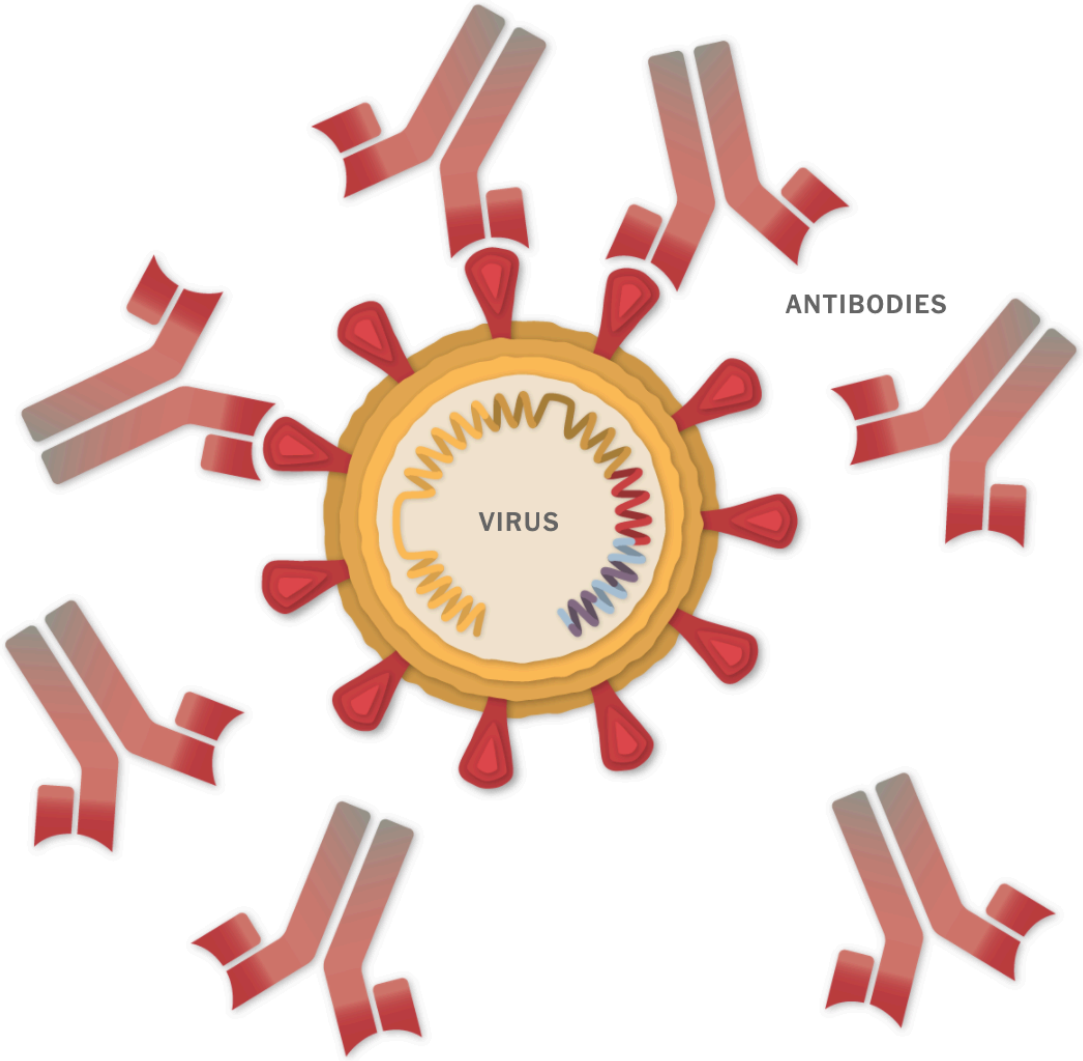
Making Antibodies

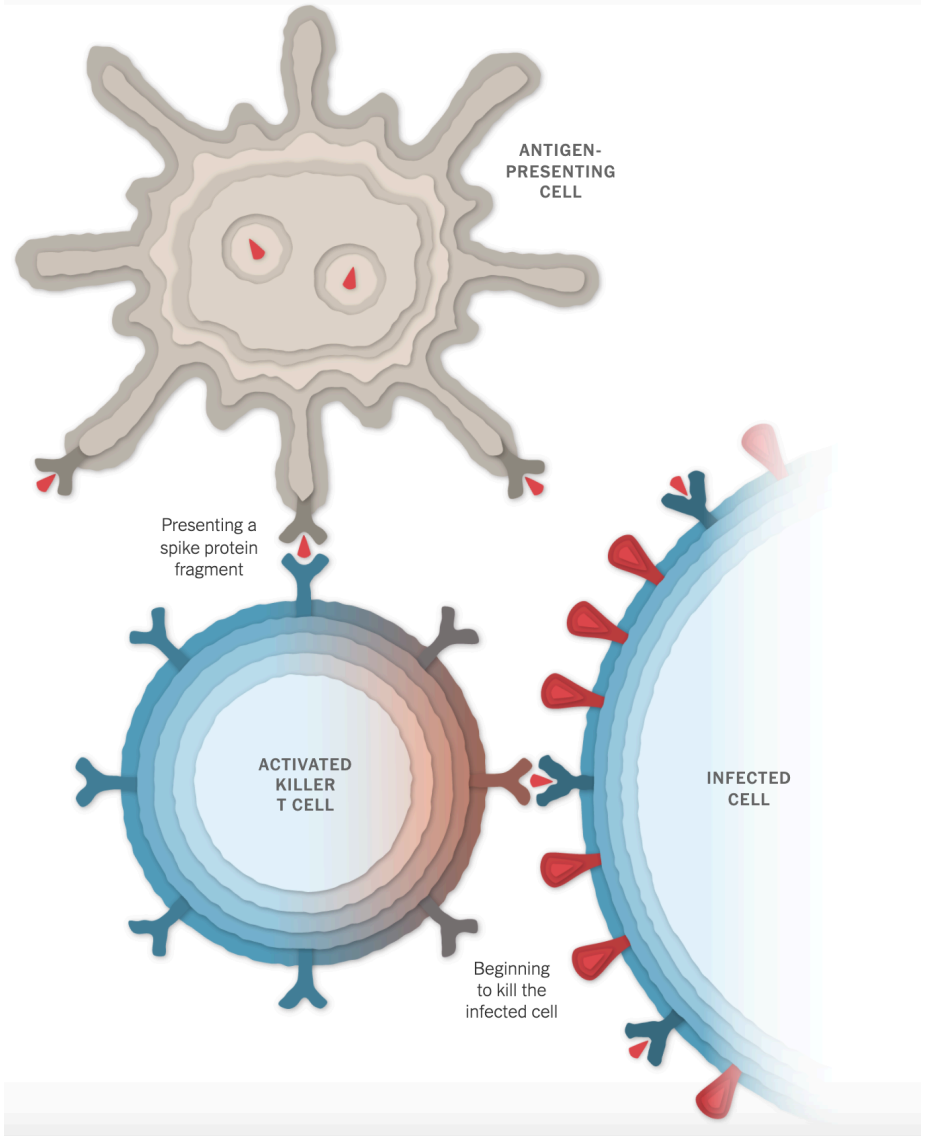




https://www.nytimes.com/interactive/2020/health/moderna-covid-19-vaccine.html?login=smartlock&auth=login-smartlock

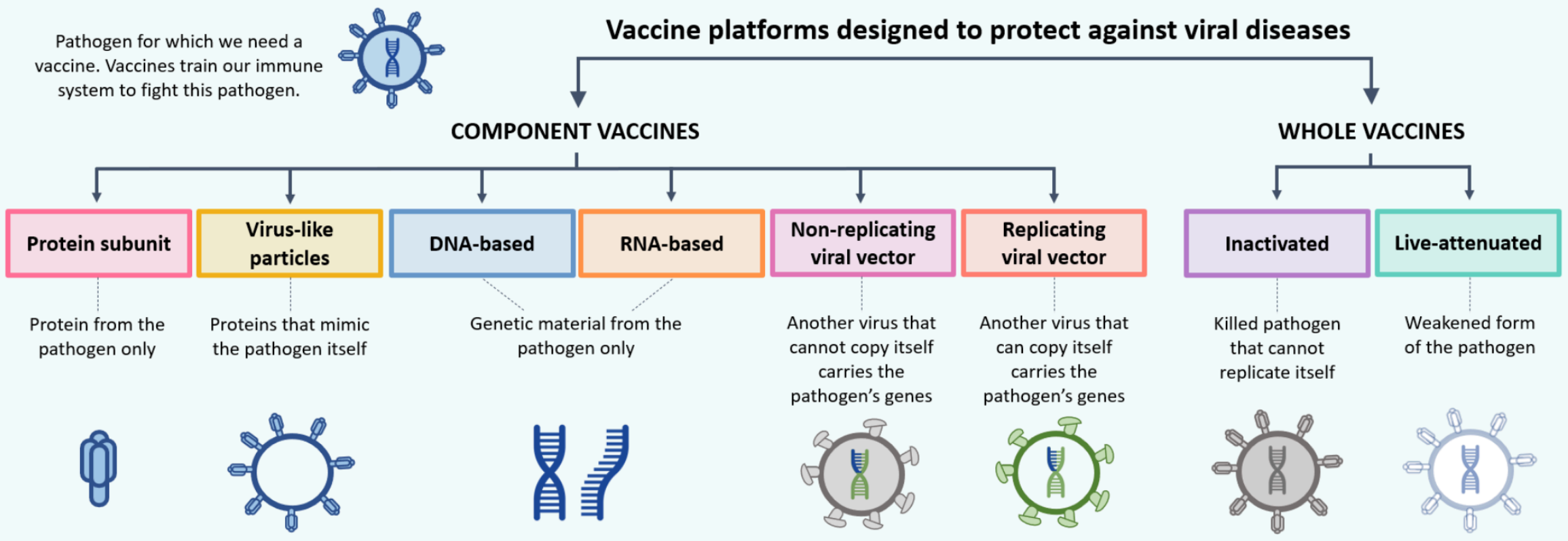
Providing Protection





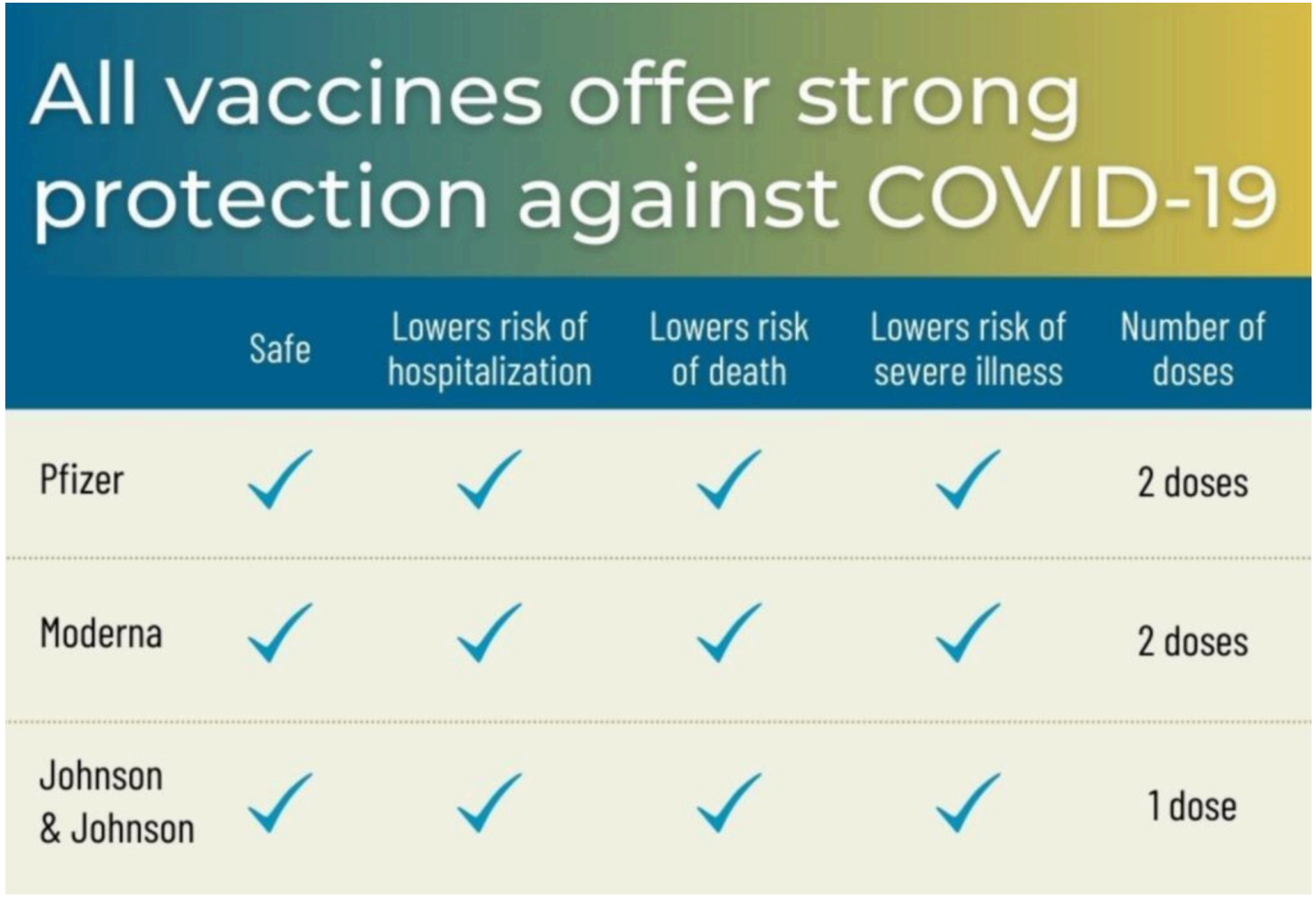
https://www.nytimes.com/interactive/2020/health/moderna-covid-19-vaccine.html?login=smartlock&auth=login-smartlock

Different Types of Vaccines



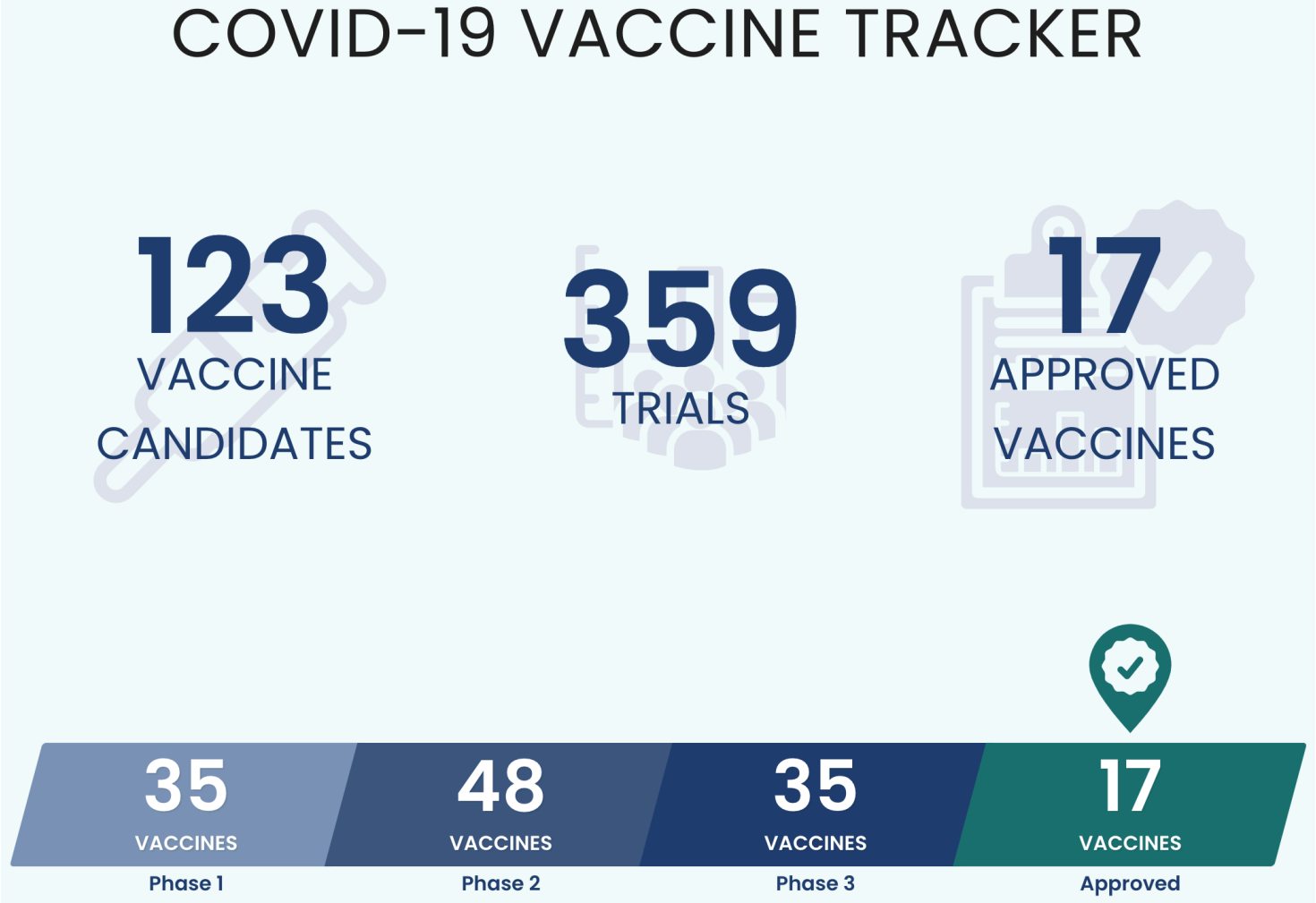
https://covid19.trackvaccines.org/how-do-vaccines-work/#types

Three COVID-19 Vaccines Currently Authorized for Emergency Use in the U.S.



https://communicarehc.org/wp-content/uploads/2021/03/vaccine-comparison-chart-1024x859.jpg

COVID-19 Vaccines Worldwide



https://covid19.trackvaccines.org/vaccines/

Some of the Available COVID-19 Vaccines

RNA

Pfizer/BioNTech
BNT162b2

Approved in 85 countries

26 trials in 15 countries

RNA

Moderna
mRNA-1273

Approved in 49 countries

21 trials in 4 countries

Non Replicating Viral Vector

Janssen (Johnson & Johnson)
Ad26.COV2.S

Approved in 44 countries

11 trials in 17 countries

Non Replicating Viral Vector

Oxford/AstraZeneca
AZD1222

Approved in 102 countries

32 trials in 19 countries

Non Replicating Viral Vector

Gamaleya
Sputnik V

Approved in 68 countries

19 trials in 6 countries

Non Replicating Viral Vector

Serum Institute of India
Covishield

Approved in 40 countries

2 trials in 1 country

Inactivated

Sinopharm (Beijing)
BBIBP-CorV

Approved in 47 countries

6 trials in 7 countries

Inactivated

Bharat Biotech
Covaxin

Approved in 9 countries

5 trials in 1 country

Inactivated

Sinovac
CoronaVac

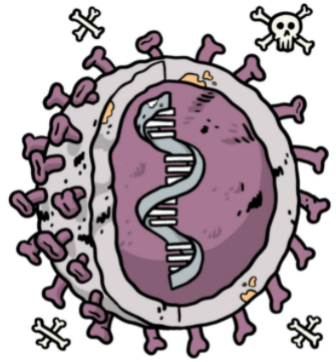
Approved in 26 countries

15 trials in 7 countries

https://covid19.trackvaccines.org/vaccines/

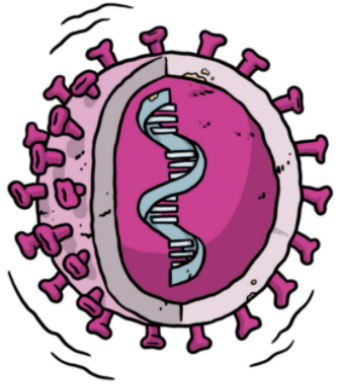
Currently Available COVID-19 Vaccines are Safe for Immunocompromised Patients

- **Inactivated vaccines are safe**
  - Use the killed version of the germ that causes a disease
  - Inactivated vaccines are not alive and cannot replicate
  - Cannot cause disease even in people with severely weakened immune systems



Inactivated vaccine

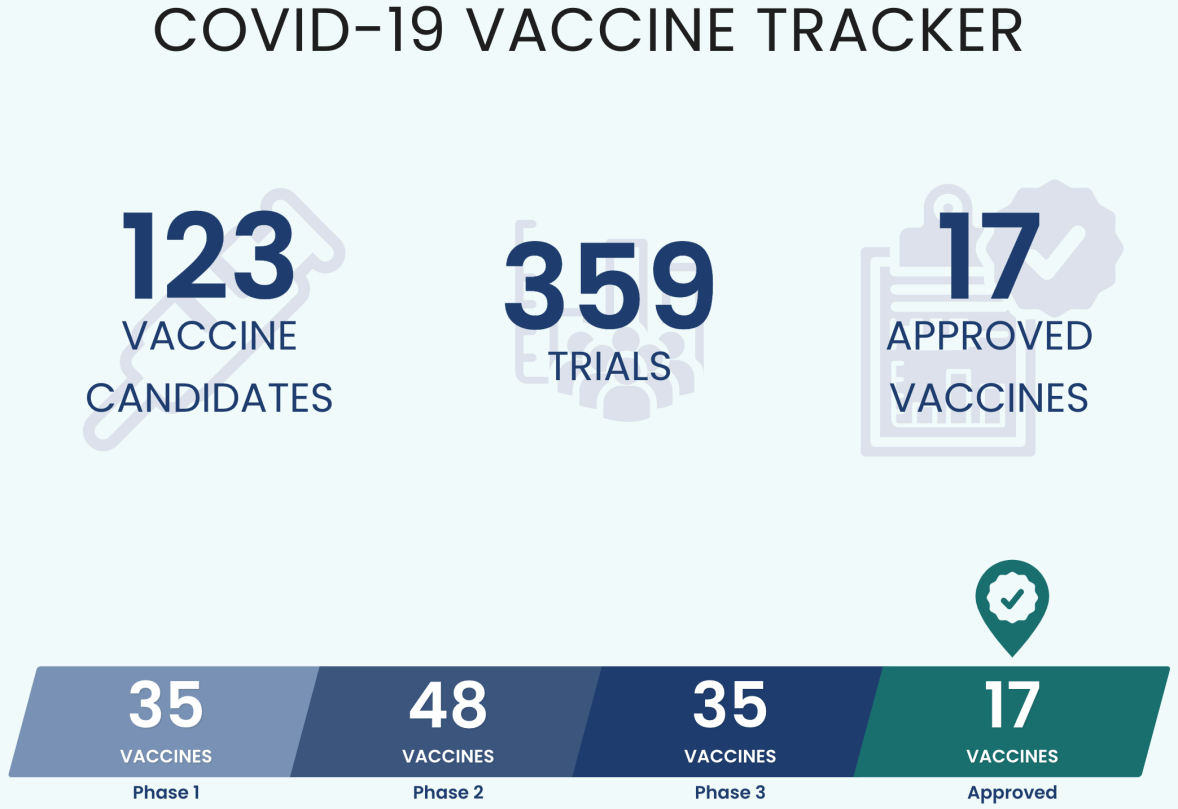
- **Live-attenuated vaccines should be avoided**
  - Use a weakened form of the virus that causes the disease
  - Must replicate in the vaccinated person, usually causing no or mild disease
  - Uncontrolled replication and severe disease can occur in immunocompromised individuals

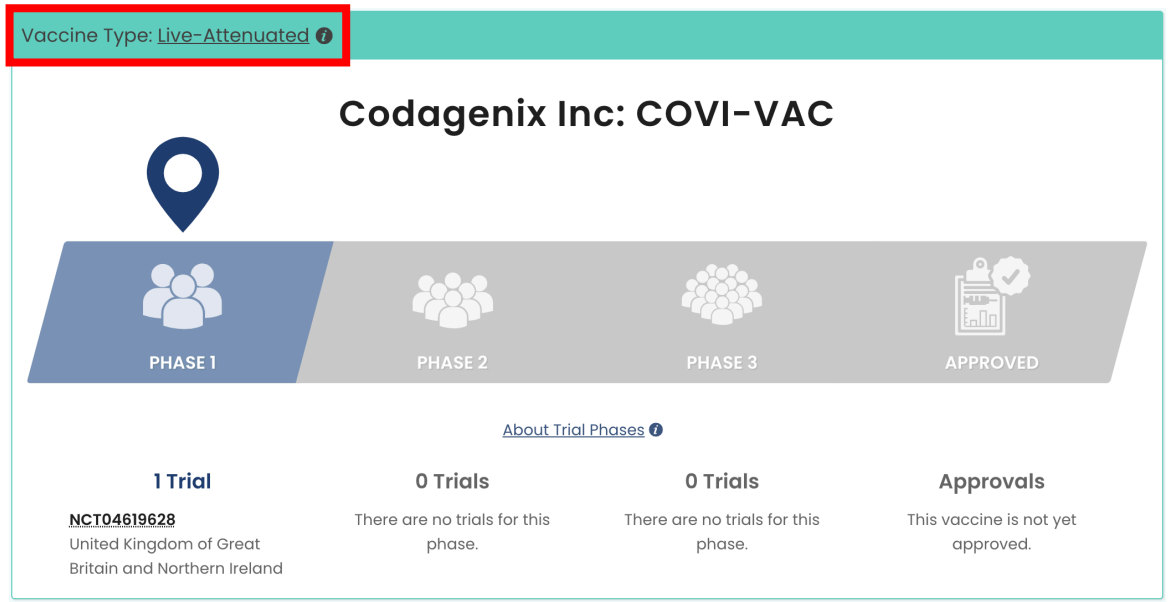


Live-attenuated vaccine

https://www.cdc.gov/vaccines/pubs/pinkbook/downloads/prinvac.pdf
https://www.who.int/news-room/feature-stories/detail/the-race-for-a-covid-19-vaccine-explained

Only One Live-Attenuated COVID-19 Vaccine in Development

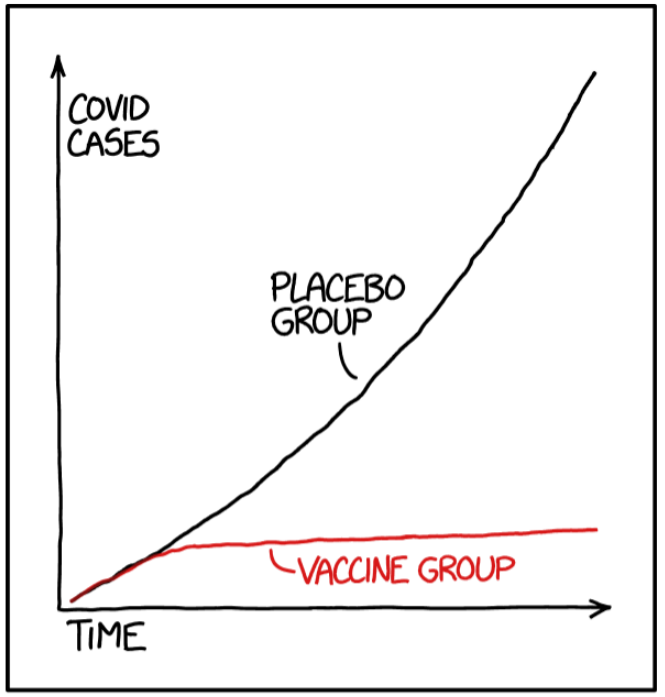




https://covid19.trackvaccines.org/vaccines/

COVID-19 Vaccines are Highly Effective

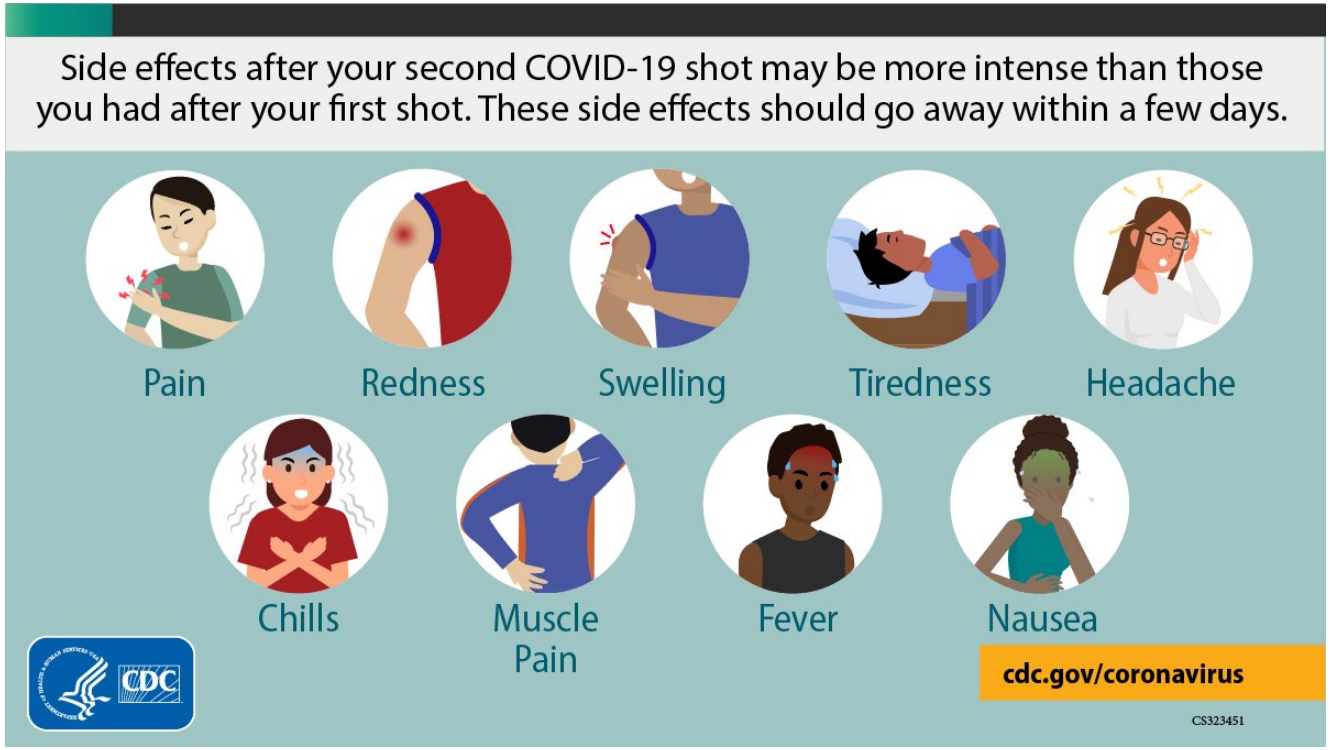
- Pfizer and Moderna mRNA vaccines
  - Enrolled tens of thousands of patients
  - 95% reduction in COVID-19 compared with placebo injections
  - Prevented severe disease and death
  - Two weeks after second shot for full protection
- Johnson & Johnson adenovirus vaccine
  - 40,000 participants globally
  - 66% reduction in moderate-severe Covid-19
  - Prevented severe disease and death
  - Two weeks after one and only shot



STATISTICS TIP: ALWAYS TRY TO GET DATA THAT'S GOOD ENOUGH THAT YOU DON'T NEED TO DO STATISTICS ON IT

https://xkcd.com/2400/

COVID-19 Vaccines Side Effects are Generally Mild and Expected

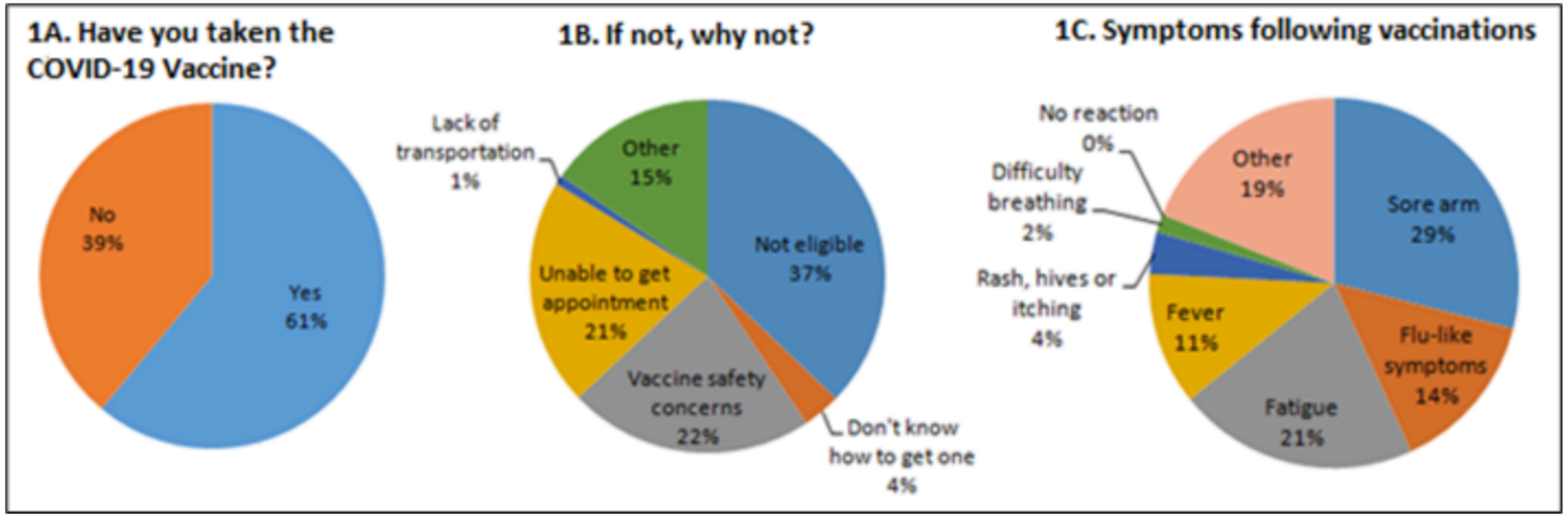


- In the U.S. rare reports of:
  - Anaphylaxis: 2-5 people per million vaccinated
  - Thrombosis with thrombocytopenia syndrome (blood clots): 35 confirmed reports after 11.2 million doses of J&J vaccine
  - Myocarditis: 268 confirmed reports, most among people ages 30 and younger
  - Death: 5,208 reports of death (0.0017%) with no causal link to COVID-19 vaccines established

https://twitter.com/CDCgov/status/1380181175474393091/photo/1
https://www.cdc.gov/coronavirus/2019-ncov/vaccines/safety/adverse-events.html

Sarcoidosis Patients and the COVID-19 Vaccine

- 292 respondents out of 5,000 surveyed
- Data as of February 2021

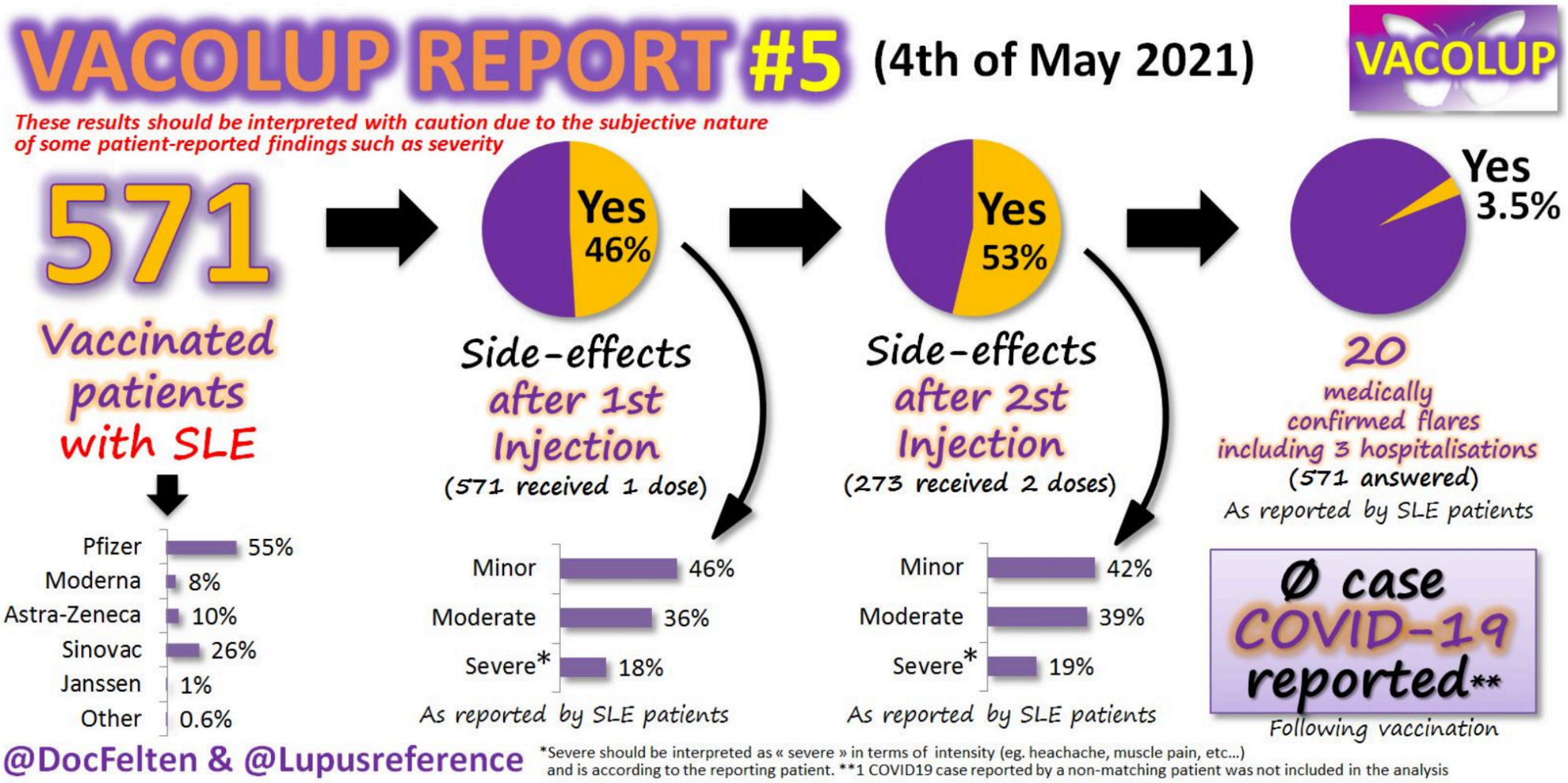


https://www.stopsarcoidosis.org/covid-19-vaccine-and-sarcoidosis-a-survey-of-vaccination-rate-tolerance-and-barriers/#:~:text=Thus%2C%20the%20results%20of%20the,following%20the%20COVID%2D19%20vaccines.

Should Sarcoidosis Patients Get The COVID-19 Vaccine?

- Are patients with sarcoidosis recommended to receive the vaccine? YES
- Is there a significant concern that patients with sarcoidosis will flare after receiving the vaccine? NO
- Is there a concern that patients with sarcoidosis will not have a strong response to the vaccine? MAYBE

Vaccine Related Flares in Lupus are Rare



https://maladie-autoimmune.fr/vacolup/

Do COVID-19 Vaccines Provide Strong Protection in Patients with Sarcoidosis?

Immunosuppressed Patients and Response to Vaccines

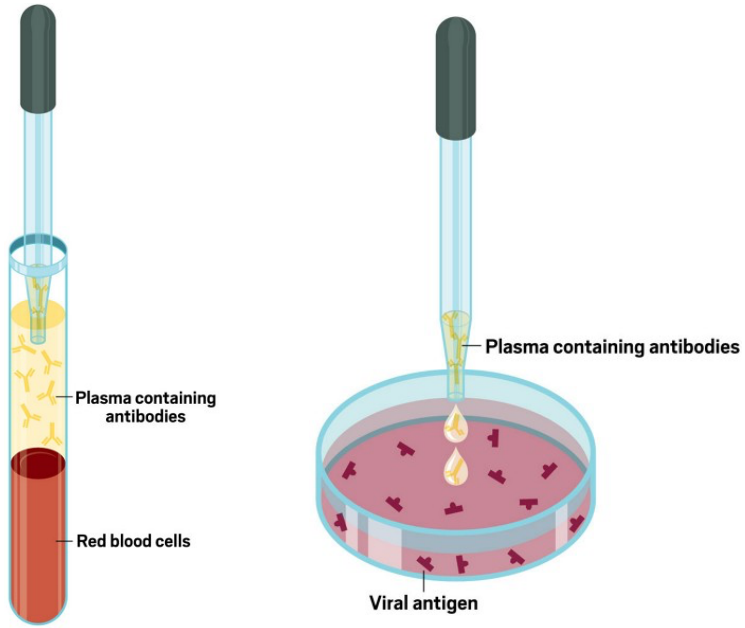
- There are no studies measuring the vaccine immune response in sarcoidosis patients specifically

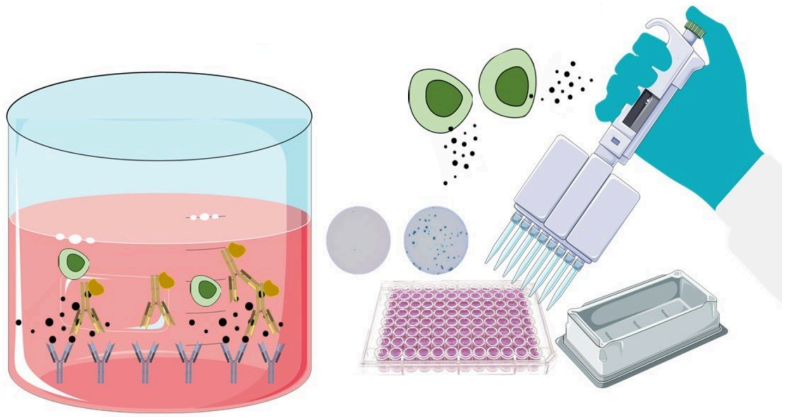
- Data is extrapolated from other patients with immunocompromised states or immune-mediated diseases:
  - Patients with cancer
  - Patients with organ transplants
  - Patients with other immune-mediated diseases

How Is Vaccine Response Measured?

- Antibody tests
  - Many different types
  - Relatively easy to measure
  - Binding or neutralizing tests
  - No clinically meaningful antibody titer cutoffs established

- T cell tests
  - Challenging to conduct
  - Often not clinically available
  - Most done in the research setting

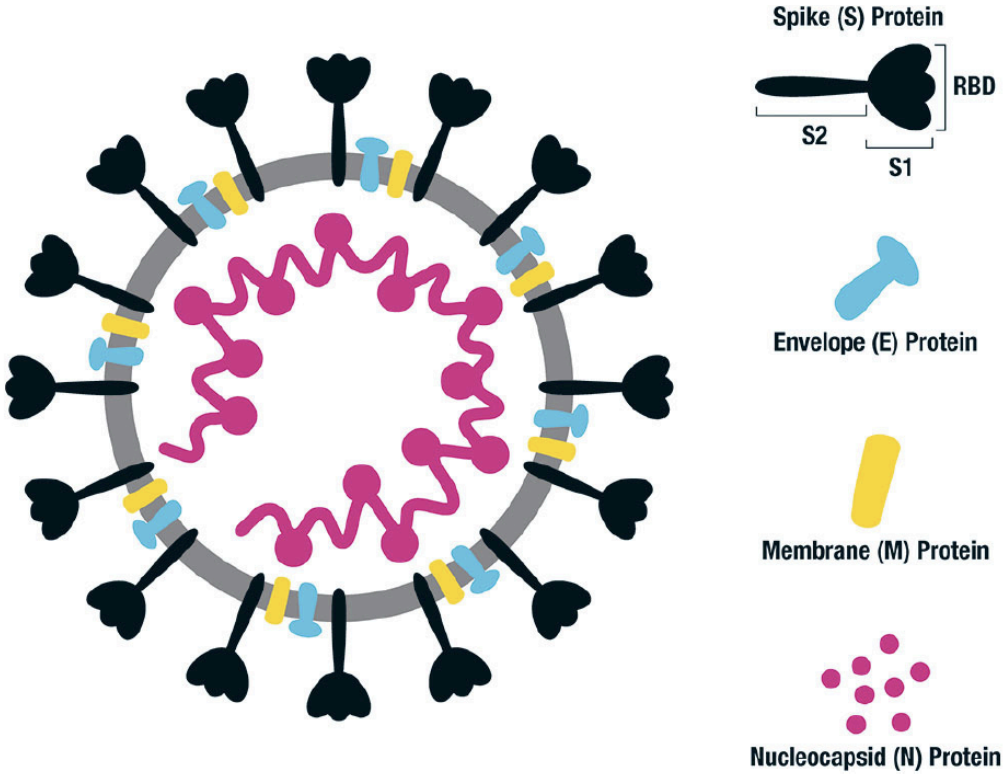




https://cen.acs.org/analytical-chemistry/diagnostics/COVID-19-antibody-tests-are-raising-as-many-questions-as-they-answer/98/i22
https://www.youtube.com/watch?v=7MBcUOUy-ug

Understanding SARS-CoV-2 Antibodies

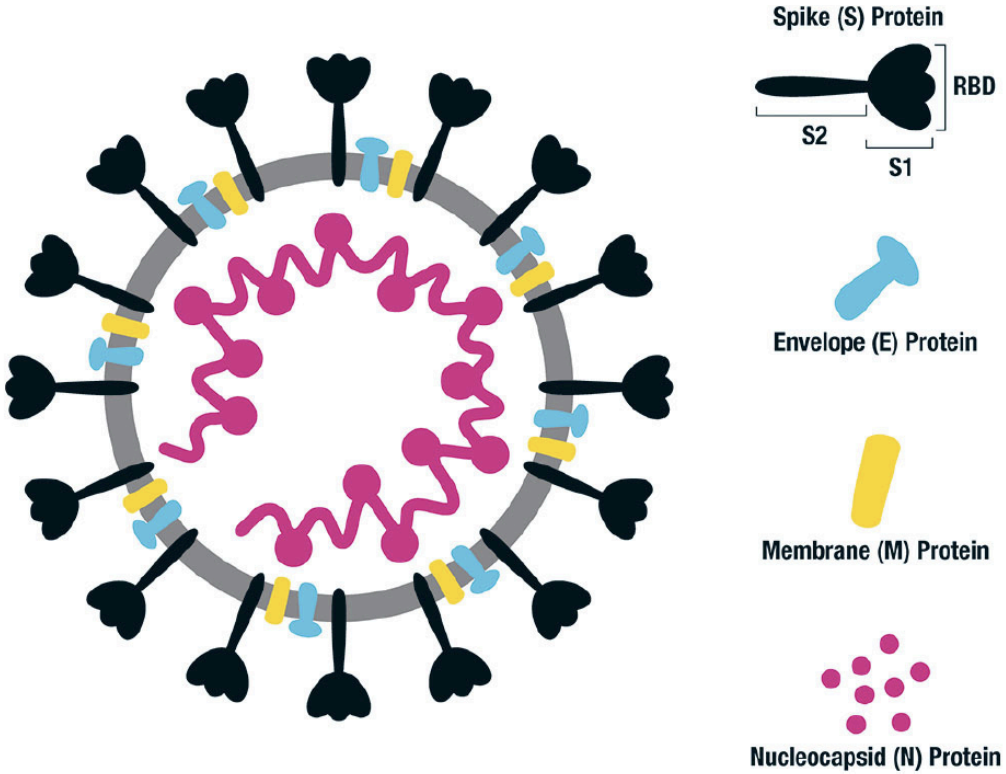
- Anti-nucleocapsid antibodies (N protein) develop after natural infection
  - Will not arise after many of the current vaccines
  - Not helpful to assess response to most vaccines or immunity to SARS-CoV-2
- Anti-spike antibodies (S protein) can develop after both natural infection and after vaccination
  - Multiple forms of S protein
  - Full-length (S1+S2)
  - Partial (S1 domain or RBD)



Flanagan KL, et al. Progress and Pitfalls in the Quest for Effective SARS-CoV-2 (COVID-19) Vaccines. Front Immunol. 2020;11:579250.

Antibody Binding Versus Neutralization

- Binding tests
  - Can use any antigen from the virus
  - Not all tests uses antigens related to the vaccine
  - Do not assess function of antibody
- Neutralizing tests
  - Determine the functional ability of antibodies to prevent infection by virus or pseudovirus *in vitro*
  - Monitor inhibition of viral growth in cell culture
  - Monitor interaction of RBD with the ACE-2 receptor by ELISA



https://www.cdc.gov/coronavirus/2019-ncov/lab/resources/antibody-tests-guidelines.html

Flanagan KL, et al. Progress and Pitfalls in the Quest for Effective SARS-CoV-2 (COVID-19) Vaccines. Front Immunol. 2020;11:579250.

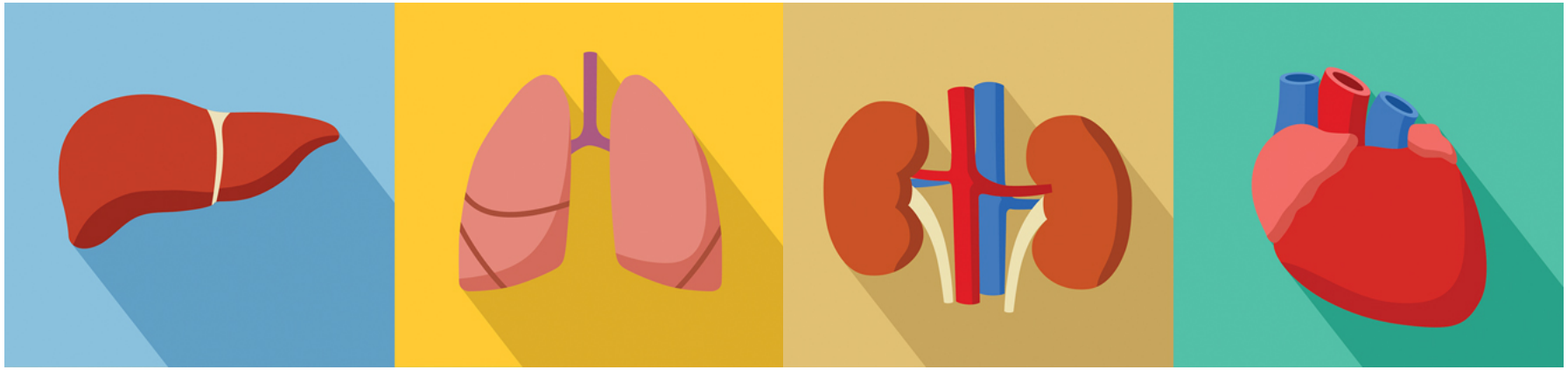
Vaccine Response in Patients with Solid Tumors

	First-dose immunogenicity at week 3 (95% CI)	Immunogenicity at week 5 (95% CI)	
		No boost	Day 21 boost
Anti-SARS-CoV-2 IgG response			
Health-care workers	32/34; 94% (81–98)	18/21; 86% (65–95)	12/12; 100% (76–100)
Solid cancer cohort	21/56; 38% (26–51)	10/33; 30% (17–47)	18/19; 95% (75–99)
Haematological cancer cohort	8/44; 18% (10–32)	4/36; 11% (4–25)	3/5*; 60% (23–88)
T-cell vaccine response			
Health-care workers	14/17; 82% (59–94)	9/13; 69% (42–87)	3/3*; 100% (44–100)
Solid cancer cohort	22/31; 71% (53–84)	8/15; 53% (30–75)	14/16; 88% (64–97)
Haematological cancer cohort	9/18; 50% (29–71)	6/18; 33% (16–56)	3/4*; 75% (40–95)

Monin L, et al. Safety and immunogenicity of one versus two doses of the COVID-19 vaccine BNT162b2 for patients with cancer: interim analysis of a prospective observational study. Lancet Oncol. 2021;22(6):765-78.

Vaccine Response in Patients with Solid Organ Transplantation

- 658 transplant recipients who received 2 doses of an mRNA vaccine
- Majority (72%) treated with mycophenolate mofetil (Cellcept)
- Dose 1 -> 21 days -> antibody detectable in 98 participants (15%)
- Dose 2 -> 29 days -> antibody detectable in 357 participants (54%)



Boyarsky BJ, et al. Antibody Response to 2-Dose SARS-CoV-2 mRNA Vaccine Series in Solid Organ Transplant Recipients. JAMA. 2021;325(21):2204-6.
https://www.cedars-sinai.org/blog/myths-about-organ-donation.html

Vaccine Response in Patients with CLL

Characteristic	Proportion, unless otherwise specified
Baseline characteristics	
Age at vaccination, median (range)	71 years (37–89)
Male	23/44 (52%)
CLL treatment history	
Never treated	18/44 (41%)
Prior CLL-directed therapy	26/44 (59%)
Current CLL-directed therapy	18/44 (41%)
BTK inhibitor	14/44 (32%)
Venetoclax	7/44 (16%)
Anti-CD20 monoclonal antibody within 1 year	14/44 (32%)

Anti-SARS-CoV-2 S1/S2 antibody		
Positive	23/44 (52%)	
Negative	21/44 (48%)	
Predictors of positive antibody response	Odds ratio	95% confidence interval, p value
Age <70 vs. ≥ 70	12.0	2.9–50.5, $p = 0.001$
Never treated vs. prior-CLL directed therapy	56.7	6.2–518, $p < 0.001$
Active observation vs. current therapy	16.7	3.6–77.7, $p < 0.001$
BTKi at time of vaccination	0.14	0.031–0.60, $p = 0.009$
Anti-CD20 monoclonal antibody within 1 year	0.071	0.013–0.39, $p = 0.002$

Herishanu Y, et al. Efficacy of the BNT162b2 mRNA COVID-19 vaccine in patients with chronic lymphocytic leukemia. Blood. 2021;137(23):3165-73.

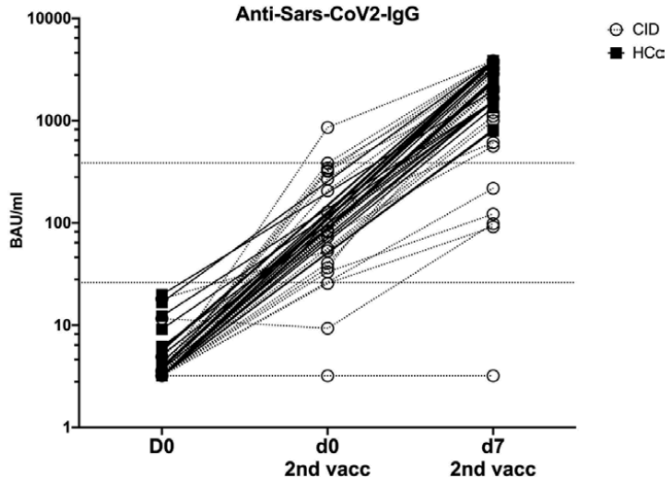
Vaccine Response in 26 Patients with Immune-Mediated Disease

Table 1 Demographics and clinical characteristics of the included patients

Sex	Age (years)	Inflammatory disease	Biological DMARD	Conventional DMARD	Steroids
F	44	Psoriatic arthritis	Golimumab	Leflunomide	5 mg prednisolone
F	35	Psoriatic arthritis	Certolizumab pegol	–	–
F	43	Rheumatoid arthritis	Certolizumab pegol	–	5 mg prednisolone
M	46	MCTD	–	Hydroxychloroquine	–
F	39	Rheumatoid arthritis	Etanercept	Leflunomide	–
F	51	Rheumatoid arthritis	–	Sulfasalazine	–
F	65	Spondyloarthropathy	Infliximab	–	–
M	38	Spondyloarthropathy	Etanercept	–	–
F	45	Sarcoidosis	Infliximab	–	15 mg prednisolone
F	33	Rheumatoid arthritis	Certolizumab pegol	–	–
M	84	Giant cell vasculitis	Tocilizumab	–	5 mg prednisolone
F	47	Psoriasis	Ixekizumab	–	–
M	83	Rheumatoid arthritis	Etanercept	–	2.5 mg prednisolone
M	38	Crohn's disease	Vedolizumab	–	–
F	53	Rheumatoid arthritis	–	Leflunomide	7 mg prednisolone
F	24	Systemic lupus erythematosus	–	Hydroxychloroquine	–
M	42	Psoriasis	Adalimumab	–	–
F	54	Rheumatoid arthritis	Adalimumab	–	–
M	58	Spondyloarthropathy	Secukinumab	–	–
F	51	Psoriasis	Secukinumab	–	–
F	53	Crohn's disease	Infliximab	–	–
M	61	Psoriasis	Ustekinumab	–	–
M	36	Systemic lupus erythematosus	Belimumab	Hydroxychloroquine	–
F	89	Myositis	–	–	2.5 mg prednisolone
F	49	Multiple sclerosis/Crohn's disease	–	Azathioprine	–
F	54	Rheumatoid arthritis	Adalimumab	–	–

Boyarsky BJ, et al. Antibody Response to 2-Dose SARS-CoV-2 mRNA Vaccine Series in Solid Organ Transplant Recipients. JAMA. 2021;325(21):2204-6.

Vaccine Response in 26 Patients with Immune-Mediated Disease



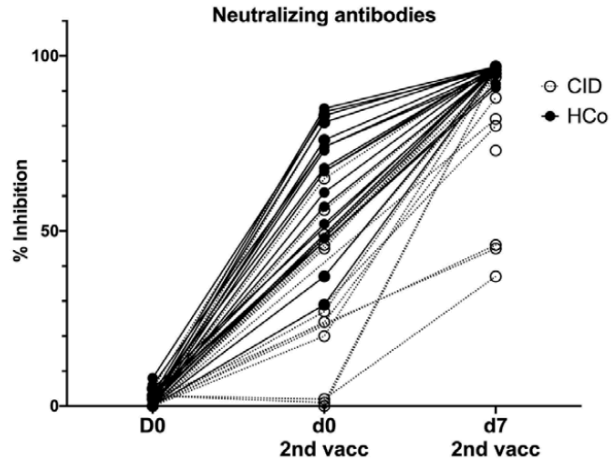


Table 2 Side effects after secondary immunisation in healthy controls and patients with CID as documented 7 days after the vaccination

	Healthy donors n=38/42 (%)		Patients n=26/26 (%)	
Symptoms	**N**	**%**	**N**	**%**
Local pain at injection side	25	65.8	17	65.4
Local reddening	2	5.6	2	7.7
Local swelling	4	11.1	4	15.4
Fatigue	16	43.2	14	53.8
Headache	13	35.1	10	38.5
Fever >38°C	5	13.5	0	0
Fever >40°C	0	0	0	0
Lymph node swelling	4	10.8	3	11.5
Chills	8	21.6	1	3.8
Arthralgia	6	16.2	4	15.4
Myalgia	12	31.6	11	42.3
Other side effects	7	18.4	5	19.2
Need for NSAIDs	10	26.3	9	34.6

No disease flares

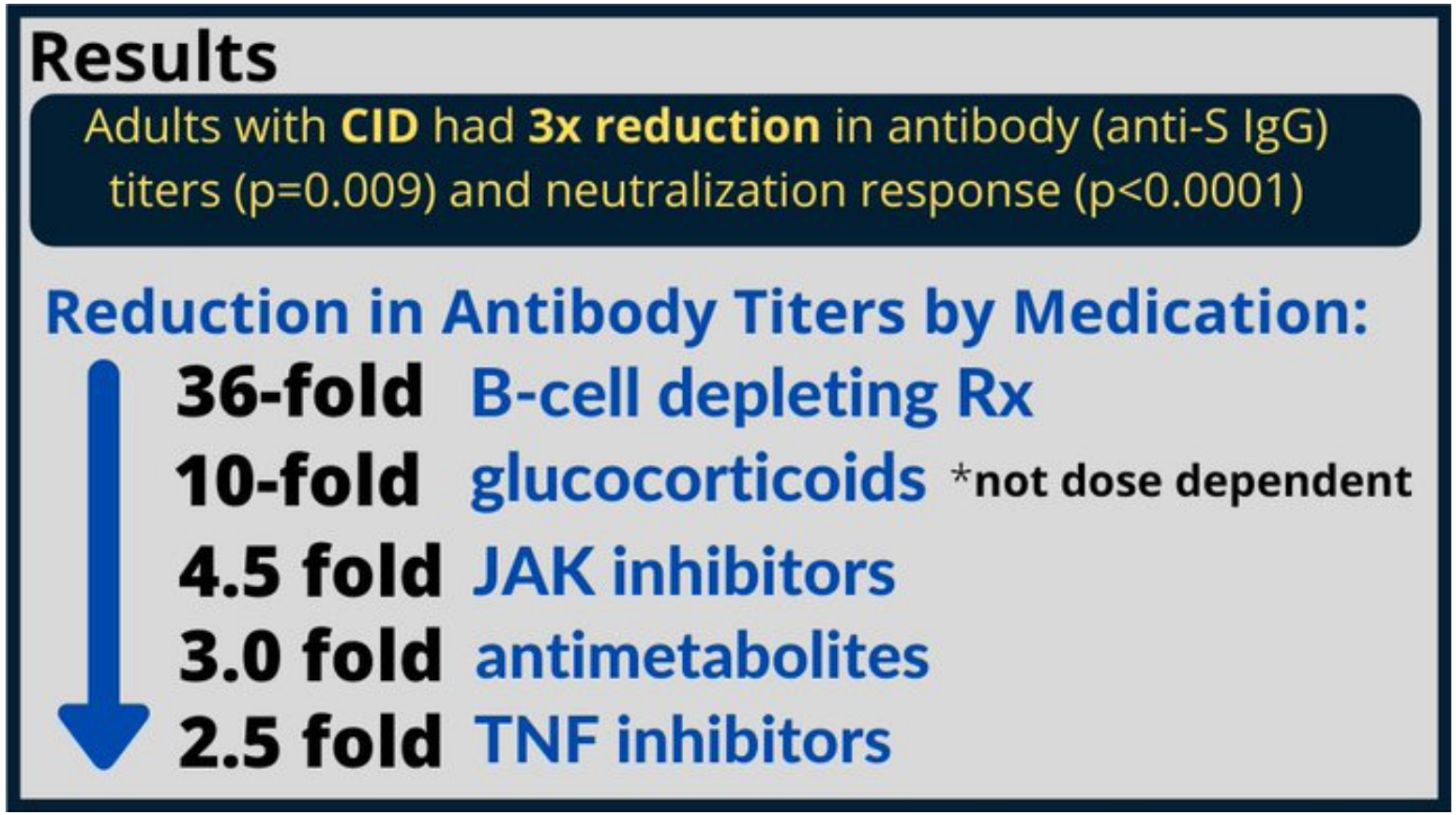
Geisen UM, et al. Immunogenicity and safety of anti-SARS-CoV-2 mRNA vaccines in patients with chronic inflammatory conditions and immunosuppressive therapy in a monocentric cohort. Ann Rheum Dis. 2021.

Vaccine Response in Patients with Immune-Mediated Disease

- COVaRiPAD Study
- 133 adults with chronic inflammatory diseases (CIDs) and 53 immunocompetent controls
- Average age 45 years, 74% female, 88% white
- The most common diagnoses included:
  - Inflammatory bowel disease (Crohn's disease and ulcerative colitis): 30%
  - Rheumatoid arthritis: 27%
  - Spondyloarthritis (such as axial spondyloarthritis and psoriatic arthritis): 15%
  - Lupus: 11%
  - Multiple sclerosis: 7%
- The most common immunosuppressive medications were anti-TNF biologics (29%) and methotrexate (22%)

https://www.medrxiv.org/content/10.1101/2021.04.05.21254656v1

Vaccine Response in Patients with Immune-Mediated Disease



- Positive antibodies:
  - 98% in controls
  - 92% in CID participants off prednisone
  - 65% in CID participants on prednisone

https://twitter.com/alhkim
https://www.medrxiv.org/content/10.1101/2021.04.05.21254656v1.full

Vaccine Response Summary

- Solid organ transplant – 38-59% develop antibodies
- Hematologic malignancy – 52-54% develop antibodies
- Solid tumor – 95% develop antibodies
- Immune-mediated disease – Most develop antibodies but 3-fold reduction in titers
  - Rituximab (36-fold reduction) and steroids (10-fold reduction)

Do COVID-19 Vaccines Provide Strong Protection in Patients with Sarcoidosis?

- Most patients with immune-mediated diseases mount only a moderately decreased antibody response to the COVID-19 vaccine compared to healthy controls
- Even if the COVID-19 vaccine is some degree less effective for those on immunosuppressive medications, it can still provide lifesaving protection and prevent illness
- **Unclear how reduced levels of antibodies exactly translate to protection against COVID-19**
  - Does not mean the vaccine is not providing protection
  - More time and research needed to understand how antibody levels, as well as other parts of the immune system, correlate with infection and severity of disease
  - Duration of protection remains unknown

https://creakyjoints.org/living-with-arthritis/coronavirus/covid-19-vaccines/immunosuppressant-medication-response-to-covid-19-vaccine-study/

Should You Get An Antibody Test Right Now?

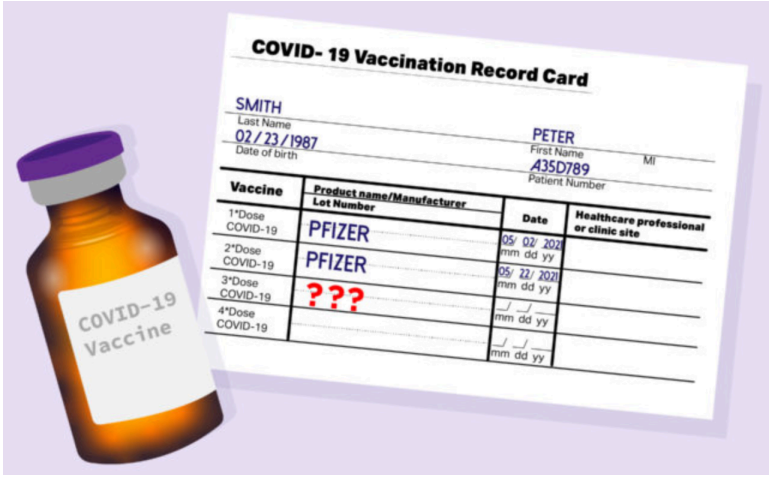
- Currently, there are **no good data to correlate protection with antibody test results**
- The CDC specifically advises that people should not use the antibody tests to check the efficacy of the vaccine
- Most of the advertised tests expressly disclaim the ability to determine a level of immunity
- Vaccines induce antibodies to specific viral proteins
  - Many of the antibody tests will be negative in persons without history of previous natural infection if the test used does not detect antibodies induced by the vaccine

PROBABLY NOT

https://www.medrxiv.org/content/10.1101/2021.04.02.21254493v1
https://www.cdc.gov/coronavirus/2019-ncov/lab/resources/antibody-tests-guidelines.html

What Should You Do?

- Understand that if you were vaccinated while receiving certain treatments such as glucocorticoids or rituximab, you likely have less protection
- However, you probably have some protection!
- Anticipate validated tests with meaningful cutoffs to be developed to help us assess immunity
- Wait for booster shots
  - May incorporate variants
  - Will augment the initial vaccine response



https://creakyjoints.org/living-with-arthritis/coronavirus/covid-19-vaccines/covid-19-vaccine-boosters-immunocompromised-patients/

Altering Medications Around the Vaccine

Medication	Timing Considerations for Immunomodulatory Therapy and Vaccination*	Level of Task Force Consensus
Hydroxychloroquine; IVIG; glucocorticoids, prednisone-equivalent dose <20mg/day	No modifications to either immunomodulatory therapy or vaccination timing	Strong-Moderate
Sulfasalazine; Leflunomide; Mycophenolate; Azathioprine; Cyclophosphamide (oral); TNFi; IL-6R; IL-1; IL-17; IL-12/23; IL-23; Belimumab; oral calcineurin inhibitors; Glucocorticoids, prednisone-equivalent dose ≥ 20mg/day**	No modifications to either immunomodulatory therapy or vaccination timing	Moderate
Methotrexate	Hold MTX 1 week after each vaccine dose, for those with well-controlled disease; no modifications to vaccination timing	Moderate
JAKi	Hold JAKi for 1 week after each vaccine dose; no modification to vaccination timing	Moderate
Abatacept SQ	Hold SQ abatacept both one week prior to and one week after the first COVID-19 vaccine dose (only); no interruption around the second vaccine dose	Moderate
Abatacept IV	Time vaccine administration so that the first vaccination will occur four weeks after abatacept infusion (i.e., the entire dosing interval), and postpone the subsequent abatacept infusion by one week (i.e., a 5-week gap in total); no medication adjustment for the second vaccine dose	Moderate
Cyclophosphamide IV	Time CYC administration so that it will occur approximately 1 week after each vaccine dose, when feasible	Moderate
Rituximab	Assuming that patient's COVID-19 risk is low or is able to be mitigated by preventive health measures (e.g., self-isolation), schedule vaccination so that the vaccine series is initiated approximately 4 weeks prior to next scheduled rituximab cycle; after vaccination, delay RTX 2-4 weeks after 2nd vaccine dose, if disease activity allows	Moderate

- Hold methotrexate for 1 week after each vaccine dose
- No need to modify TNF inhibitor use

https://www.rheumatology.org/Portals/0/Files/COVID-19-Vaccine-Clinical-Guidance-Rheumatic-Diseases-Summary.pdf

Should You Get a Third Shot?

Here's Why This Doc Got a Third Vaccine Dose

— A transplant surgeon, a heart recipient himself, saw robust antibody response after third dose

by Kristina Fiore, Director of Enterprise & Investigative Reporting, MedPage Today May 20, 2021

NOT YET

- NIH phase 1/2 clinical trial underway
- Fully vaccinated adults who will receive booster doses of various COVID-19 vaccines to determine safety and efficacy

https://www.medpagetoday.com/special-reports/exclusives/92698?vpass=1

CDC Recommendations for Immunocompromised People

Antibody testing is not recommended to assess for immunity to SARS-CoV-2 following COVID-19 vaccination. At this time, revaccination is not recommended after people who received COVID-19 vaccines during chemotherapy or treatment with other immunosuppressive drugs regain immune competence. Recommendations on re-vaccination or additional doses of COVID-19 vaccines may be updated when additional information is available.

People should be counseled about the unknown vaccine safety profile and effectiveness in immunocompromised populations, the potential for reduced immune responses, and the need to continue to follow current guidance to protect themselves against COVID-19.

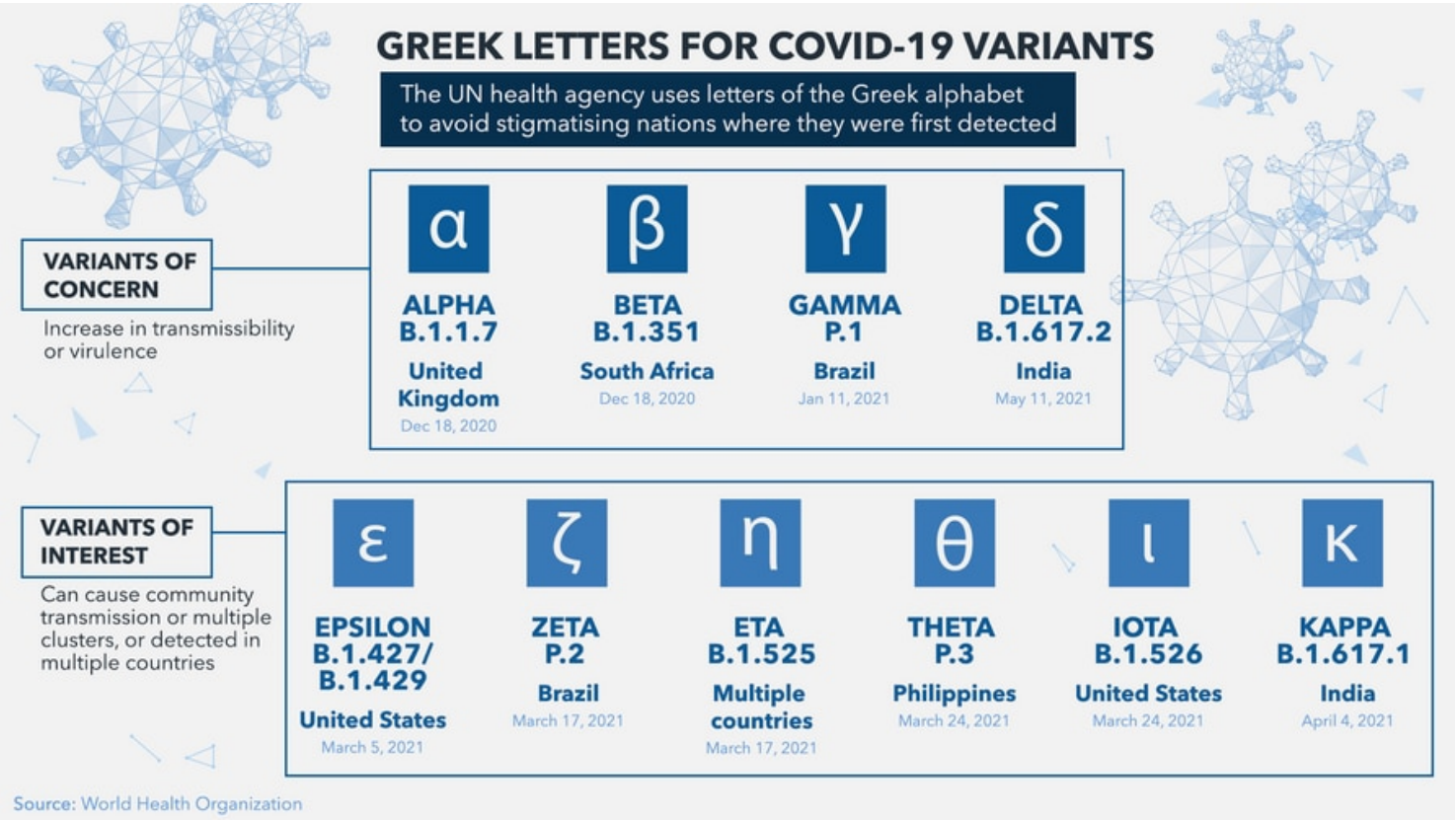
https://www.cdc.gov/vaccines/covid-19/clinical-considerations/covid-19-vaccines-us.html#underlying-conditions

Current Recommendations for Sarcoidosis Patients

- Get vaccinated!
- If you are vaccinated, you almost certainly have some protection
- Likely need to continue precautions such as masking and distancing
- Work with your treating physician to minimize steroids and potentially use alternatives to rituximab
  - Keeping disease under control is equally important
- Keep up to date on potential booster shots in the future
  - Particularly if you received the vaccination after rituximab or on glucocorticoids

https://creakyjoints.org/living-with-arthritis/coronavirus/covid-19-vaccines/covid-19-vaccine-boosters-immunocompromised-patients/

SARS-CoV-2 Variants



- Recent UK study shows:
  - Pfizer vaccine 88% effective against symptomatic disease from the Delta variant
  - AstraZeneca 60% effective
- No data on Delta variant in patients with sarcoidosis

https://www.voanews.com/covid-19-pandemic/infection-numbers-continue-decline-covid-19-response-team-warns-about-variants
https://www.gov.uk/government/news/vaccines-highly-effective-against-b-1-617-2-variant-after-2-doses

Key Takeaways

- Are COVID-19 vaccines safe for sarcoidosis patients? YES
- Do COVID-19 vaccines protect sarcoidosis patients? YES
- Does your underlying treatment for sarcoidosis affect your response to the vaccine? YES
- Should you check your anti-spike antibody level? PROBABLY NOT
- Should you seek out a third vaccination shot now? NO

FOUNDATION FOR
SARCOIDOSIS RESEARCH

Thank you!