CDC/IDSA COVID-19 Clinician Call

March 27, 2021

Welcome & Introduction

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Vice President, Clinical Affairs & Guidelines
IDSA

- 60th in a series of weekly calls, initiated by CDC as a forum for information sharing among frontline clinicians caring for patients with COVID-19
- The views and opinions expressed here are those of the presenters and do not necessarily reflect the official policy or position of the CDC or IDSA. Involvement of CDC and IDSA should not be viewed as endorsement of any entity or individual involved.
- This webinar is being recorded and can be found online at www.idsociety.org/cliniciancalls.

COVID-19 Outcomes in Immunosuppressed Individuals with Autoimmune Disease; Variants Q&A

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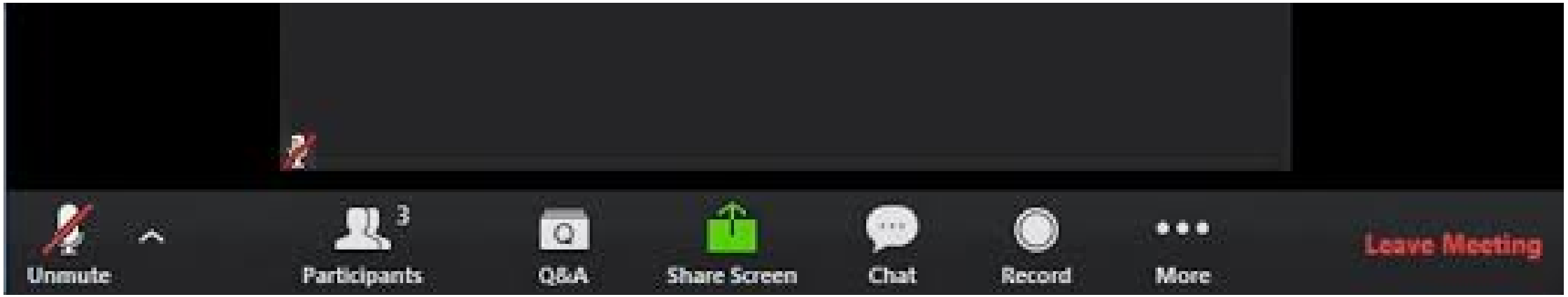
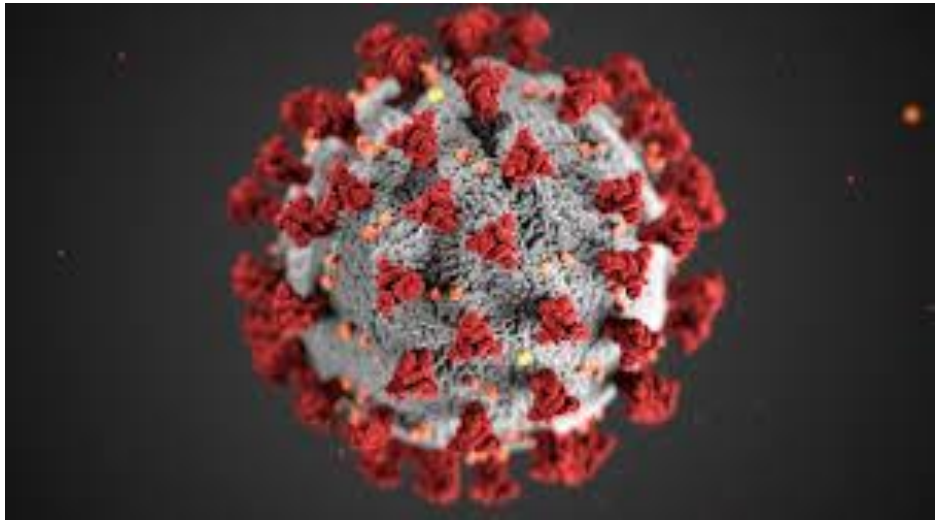
Question?
Use the “Q&A” Button

Comment?
Use the “Chat” Button





MANAGING IMMUNOMODULATING THERAPIES AND IMMUNOCOMPROMISED PATIENTS DURING THE COVID-19 PANDEMIC

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DISCLOSURES

- **Research program support:**
  - NIH/NIAMS
  - Agency for Healthcare Research and Quality
  - Centers for Disease Control and Prevention

- **Research-related Consulting or Grants:**
  - Astra Zeneca, Gilead, BMS, Eli Lilly, Pfizer, Aurinia

OBJECTIVES

Review epidemiological evidence addressing 3 questions:

1. Are people receiving immunosuppressive drugs more susceptible to initial infection with SARS-CoV-2?
2. What are the outcomes of COVID-19 in immunosuppressed individuals?
3. Are COVID-19 outcomes more severe with specific immunosuppressive drugs?

OUR RHEUMATOLOGY PERSPECTIVE

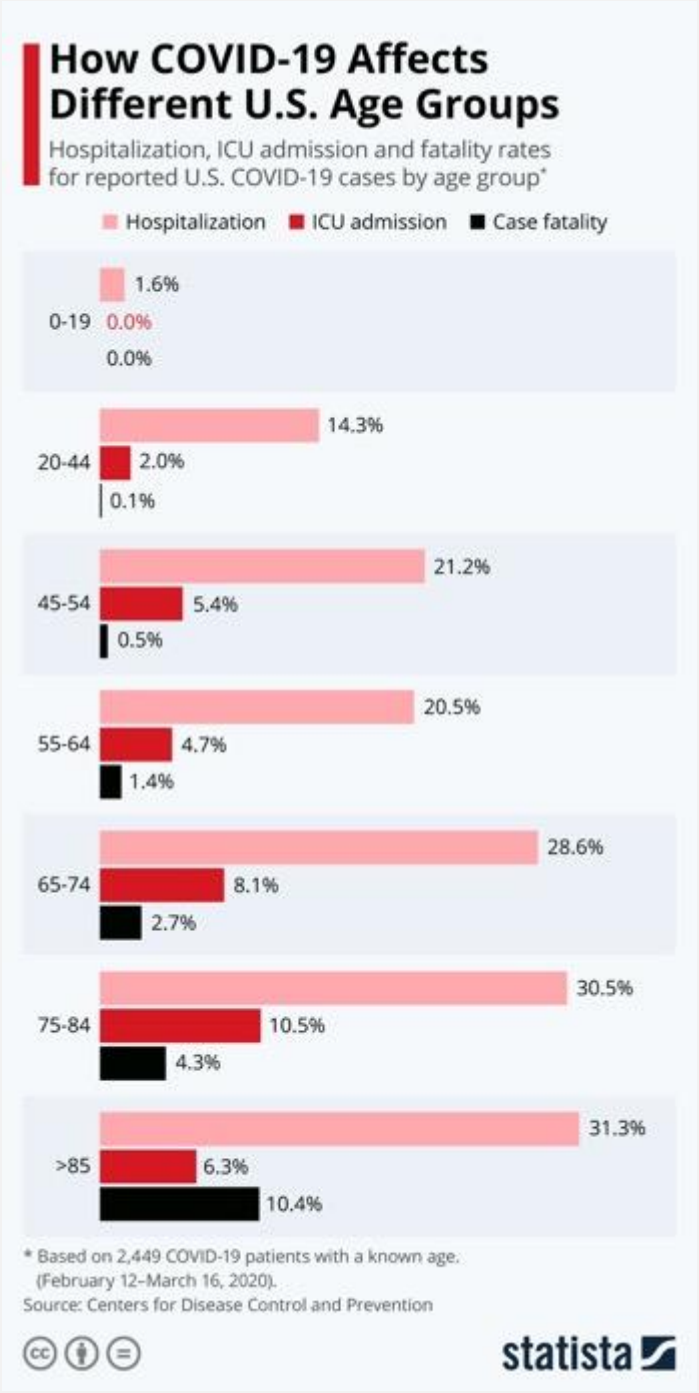
- Aberrant immune responses can lead to organ damage in COVID-19, just as they do in autoimmune diseases
- Production of autoantibodies in COVID-19
- Many drugs commonly used to treat autoimmune disease have been tested in COVID-19 (HCQ, anti-IL-1, anti-IL-6, JAK inhibitors, steroids)

Lessons from the Targeted Immunomodulation Era of Rheumatology
Peripheral blood cytokine levels are imperfect biomarkers of immunopathology
Few biomarkers exist to identify most aberrant immune responses; applications of multi-omics data to patient care has largely been elusive
Enormous immunological heterogeneity between individuals
Many autoimmune diseases require "multi-target" therapy

WHAT ARE THE RISK FACTORS FOR POOR OUTCOMES?

Comorbidities associated with severe illness and mortality

- Cardiovascular disease
- Diabetes mellitus
- Hypertension
- Chronic lung disease
- Cancer
- Chronic kidney disease
- Obesity
- *Immunocompromising conditions?*



ARE PEOPLE RECEIVING IMMUNOSUPPRESSIVE DRUGS SIGNIFICANTLY MORE SUSCEPTIBLE TO INITIAL INFECTION WITH SARS-COV-2?

LOW PREVALENCE OF INFECTION AMONG IMMUNOSUPPRESSED PATIENTS

- Survey of 995 rheumatology patients in Lombardy between February and April
  - 98% response
- The incidence of confirmed COVID-19 similar to the general population (0.62% vs 0.66%; p=0.92)
- No severe complications or deaths

Favalli et al. *Arthritis & Rheum*, June 2020

POPULATION-BASED STUDY IN HONG KONG

- 1067 cases of COVID-19 diagnosed in Hong Kong which has a population of 7.5 million
  - Only 5 patients with rheumatic disease developed COVID-19
- The incidence of COVID-19 was 1.26 cases per 100,000 patients with rheumatologic diseases, compared to 1.42 per 100,000 in the general population

Fhkam et al. *Seminars in Arthritis and Rheum*, July 24, 2020.

IMMUNOSUPPRESSIVE DRUGS NOT ASSOCIATED WITH HIGHER COVID-19 INCIDENCE IN IBD

- National VA data between Jan and April 2020
- 37, 821 Veterans with inflammatory bowel disease:
  - 36 cases of COVID-19
  - No increase among TNFi users or thiopurine users

Khan et al. *Gastroenterology*, May 29, 2020.

SUMMARY OF CURRENT RESEARCH

- In almost all studies, incidence of COVID-19 in immunosuppressed individuals with autoimmune disease similar to the general population
- *Caveat*: People who are immunosuppressed may be more likely to follow COVID-19 precautions

- High attack rates in vulnerable populations (*prison inmates, homeless individuals, nursing home residents*) illustrate that initial infection is most strongly associated with high-risk exposures

	N tested	+SARS-COV-2 N (%)
Diamond Princess Cruise Ship	3,711	**712 (19.2)**
Charles de Gaulle aircraft carrier crew	1,760	**1,046 (59.4)**
Boston homeless shelter occupants	408	**147 (36.0)**
Los Angeles homeless shelter occupants	178	**43 (24.2)**
NYU OB patients	214	**33 (15.4)**
King County, Washington nursing home residents	76	**48 (63.2)**

https://www.scripps.edu/science-and-medicine/translational-institute/about/news/sarc-cov-2-infection/index.html

PEOPLE WITH AUTOIMMUNE DISEASES DO NOT APPEAR TO HAVE HIGHER RATES OF INITIAL INFECTION WITH SARS-COV-2 COMPARED TO THE GENERAL POPULATION

ACR Guidance:
Patients should be counseled on general preventive measures, e.g., distancing and masks

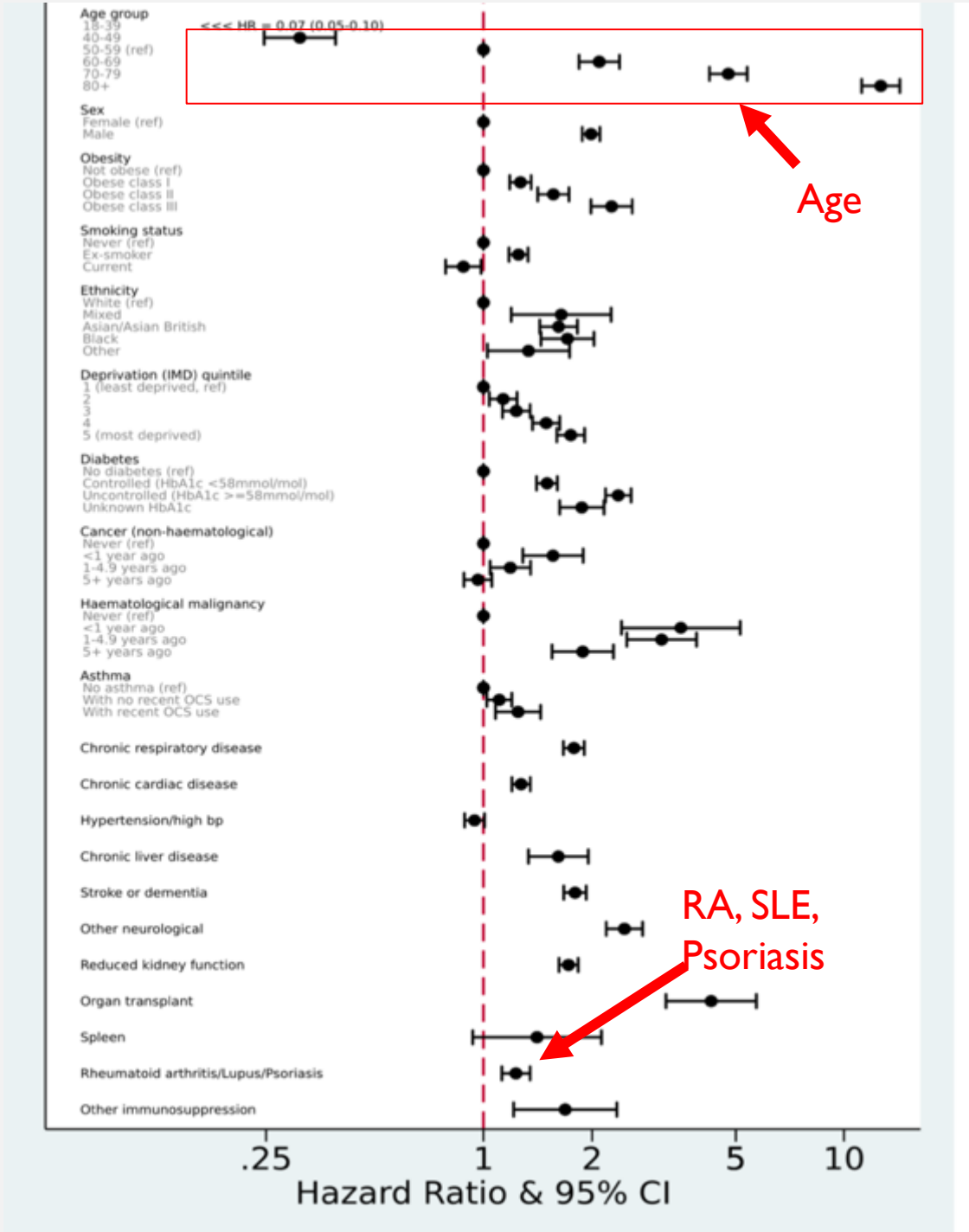
https://www.rheumatology.org/Portals/0/Files/ACR-COVID-19-Clinical-Guidance-Summary-Patients-with-Rheumatic-Diseases.pdf

WHAT ARE THE OUTCOMES OF COVID-19 IN IMMUNOSUPPRESSED INDIVIDUALS?

DO RHEUMATIC DISEASE PATIENTS HAVE HIGHER MORTALITY FROM COVID-19?

- **Study Design**: Observational cohort from UK electronic health record data on 17 million individuals
- **Outcome**: Hospital deaths
- **Findings**:
  - Confirmed many risk factors like age, obesity, comorbidities
  - Highlighted risk of poverty/social determinants
  - 885,000 with "RA/SLE/Psoriasis" had slightly higher risk (HR1.23, 1.12-1.35)

Williamson, et al. *Nature* (2020).



NYC AND BOSTON STUDIES

- **NYC study (Haberman, *N Engl J Med*. 2020 Jul 2;383(1):85-88)**
  - 86 COVID-19 positive patients with autoimmune disease
    - Incidence of hospitalization (16%) was consistent with that of the corresponding general population (26%); only one patient died
- **Multi-site study (D'Silva, *Arthritis Rheum* 2020 Dec 10)** 2,379 autoimmune disease patients with COVID-19 and 142,750 matched controls
  - Slightly higher risks of hospitalization (RR 1.14, 95% CI 1.03-1.26) and ICU admission (RR 1.32, 95% CI 1.03-1.68), but not death in cases and controls
  - After matching for comorbidities, risks attenuated, except for venous thromboembolism

SWEDISH NATIONAL REGISTERS

Table 3 Absolute and relative risks for COVID-19-related events and other outcomes in Swedish residents with rheumatoid arthritis (RA), and other inflammatory joint diseases (IJDs, defined as ankylosing spondylitis, psoriatic arthritis, other spondyloarthropathies and juvenile idiopathic arthritis) compared with matched general population comparator subjects 1 March through September 2020

Condition	Outcome	N events (risk, %) in the IJD cohort	N events (risk, %) in the general population	Crude excess risk per 100 patients*	HR model 1†	HR model 2‡
All						
	Hospitalisation, all causes	8971 (8.1%)	24 273 (5.0%)	3.1	1.65 (1.61 to 1.69)	1.18 (1.15 to 1.21)
	Hospitalisation, COVID-19	581 (0.5%)	1443 (0.3%)	0.2	1.77 (1.61 to 1.95)	1.32 (1.19 to 1.46)
	Admission to ICU, COVID-19	45 (0.04%)	162 (0.03%)	0.01	1.22 (0.88 to 1.70)	1.17 (0.82 to 1.66)
	Death, all causes	1310 (1.2%)	3036 (0.6%)	0.6	1.90 (1.78 to 2.02)	1.13 (1.05 to 1.21)
	Death, COVID-19	161 (0.10%)	338 (0.07%)	0.03	2.09 (1.73 to 2.52)	1.18 (0.97 to 1.44)

Bower H, et al. Ann Rheum Dis. doi:10.1136/ annrheumdis-2021-219845

THE RISK OF SEVERE OUTCOMES IN PATIENTS WITH RHEUMATIC DISEASES IS CLOSELY TIED TO AGE AND COMORBIDITIES, LIKE THE GENERAL POPULATION

ACR and EULAR Guidance: Immunosuppressive medications should be continued in non-infected individuals to reduce the risk of disease flare

ACR COVID Guidance: https://www.rheumatology.org/Portals/0/Files/ACR-COVID-19-Clinical-Guidance-Summary-Patients-with-Rheumatic-Diseases.pdf
EULAR COVID Guidance: https://ard.bmj.com/content/79/7/851

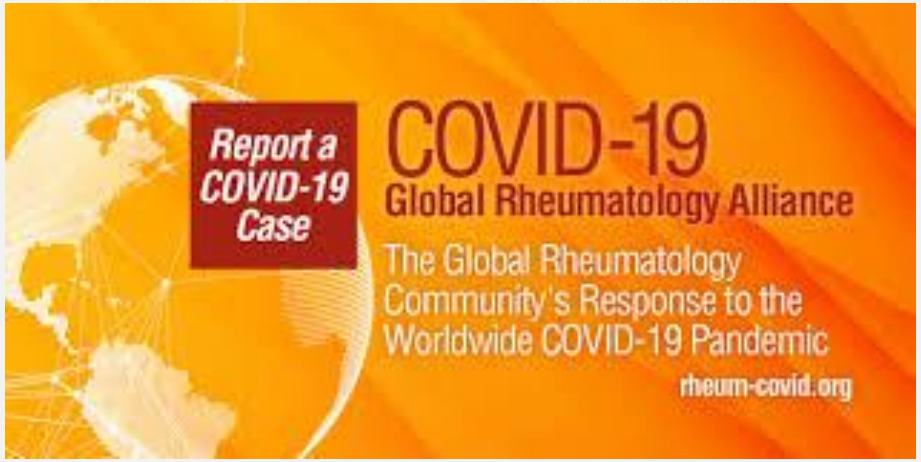
ARE COVID-19 OUTCOMES MORE SEVERE WITH SPECIFIC IMMUNOSUPPRESSIVE DRUGS?

- The Nebraska Rheumatology Society
- The Australian Rheumatology Association (ARA)
- International League of Associations for Rheumatology (ILAR)
- British Society of Rheumatology

COVID-19 COLLABORATION
288 ORGANIZATIONS
>300 INVESTIGATORS
WORLDWIDE

ENGAGED PATIENT ADVISORY BOARD

- Turkish Society for Rheumatology
- Netherlands Component to European Network for Children with Arthritis and Auto-inflammatory diseases (KAISZ)
- Arthritis Consumer Experts
- Childhood Arthritis and Rheumatology Research Alliance (CARRA)
- National Organization of Rheumatology Managers (NORM)
- French Society of Rheumatology (SFR)
- New Zealand Rheumatology Association (NZRA)
- CreakyJoints & The Global Healthy Living Foundation (GHLF)
- South African Rheumatism & Arthritis Association (SARAA)
- Mexican College of Rheumatology
- Lupus Research Alliance
- Irish Society of Rheumatology (ISR)
- Autoinflammatory Alliance

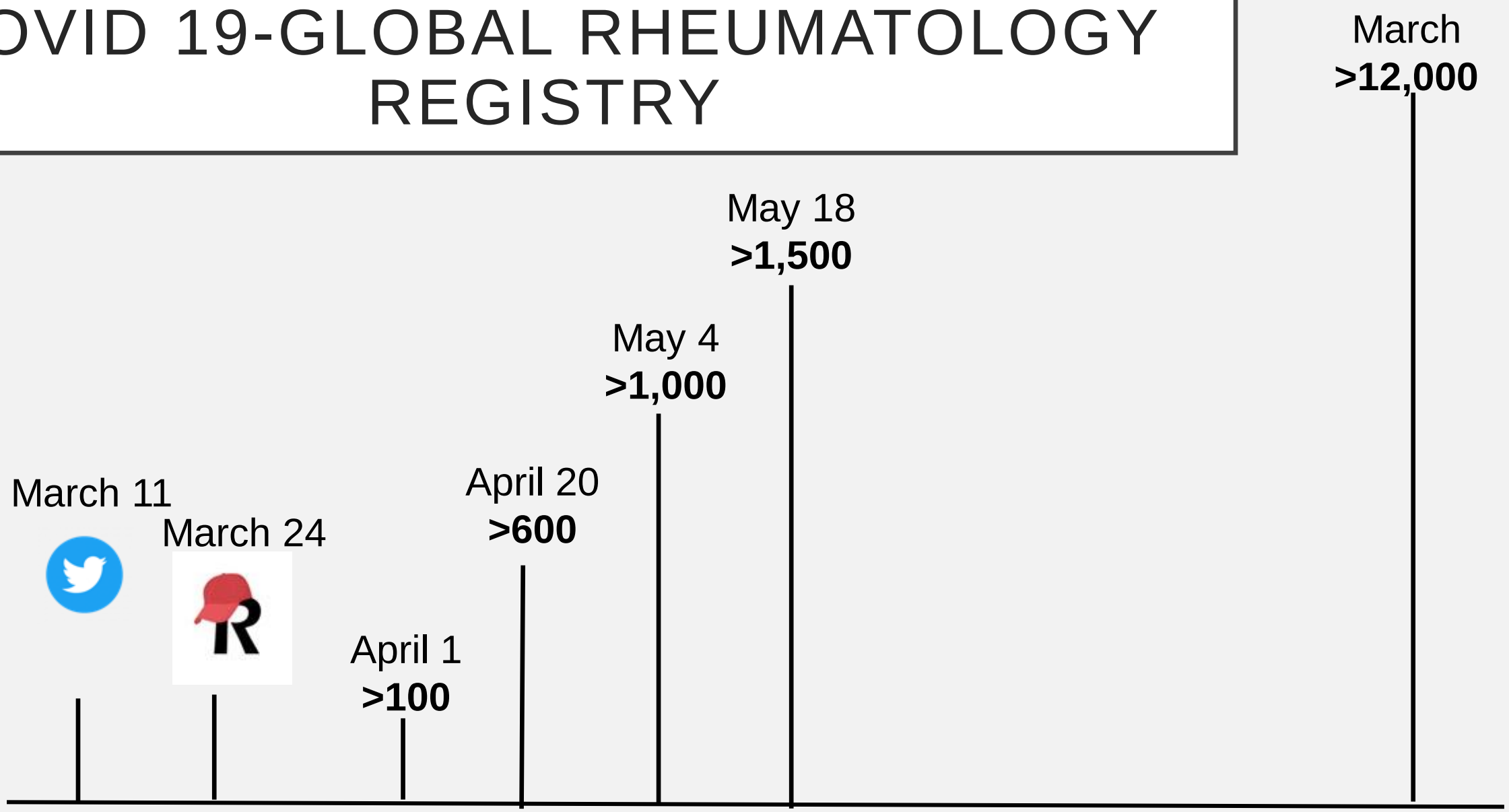


WHAT ARE WE TRYING TO ACCOMPLISH?

Two main questions:

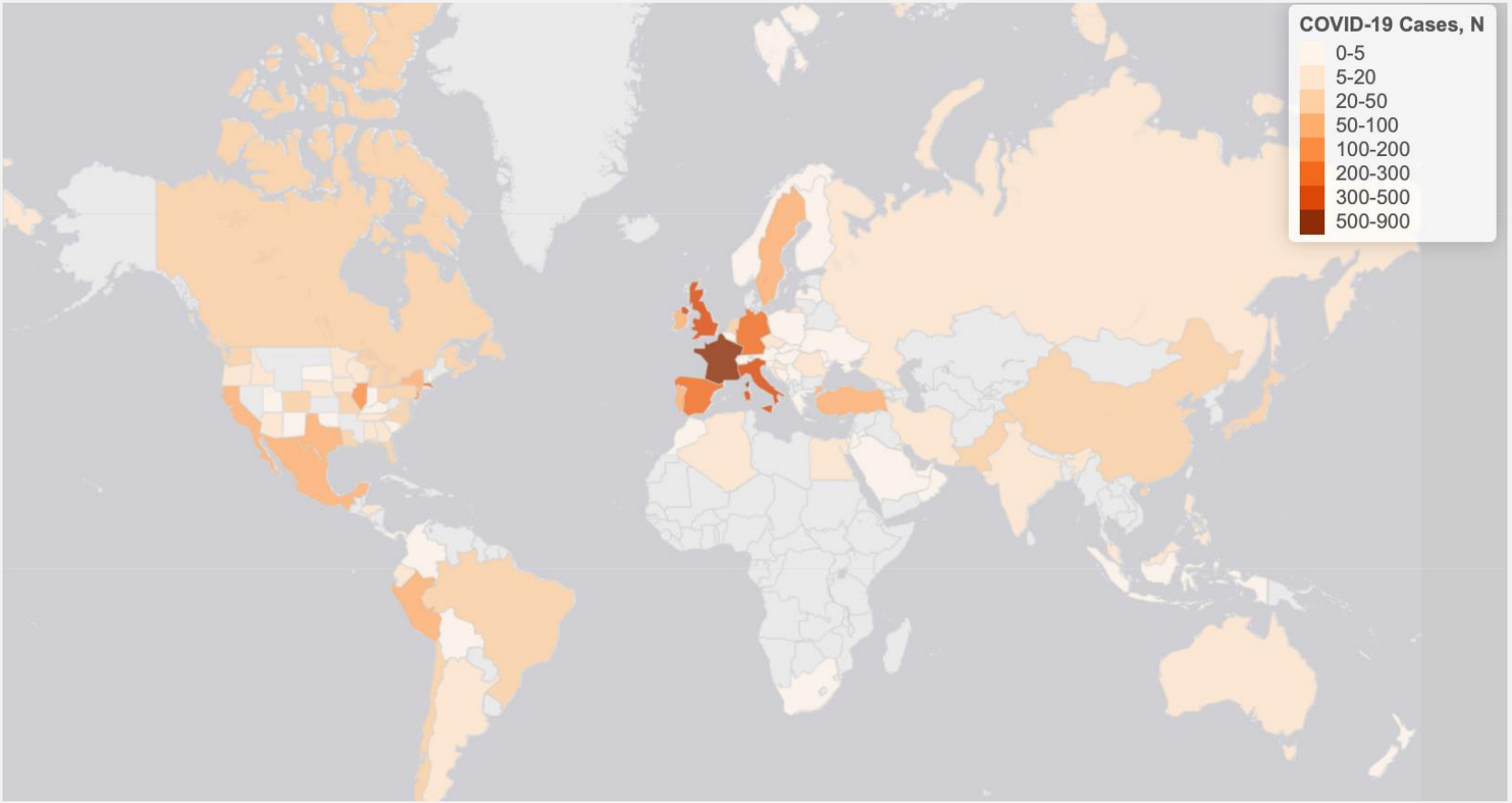
- What are the outcomes of patients with rheumatic disease with COVID19?
- Can we make any inferences about immunomodulating drugs?

COVID 19-GLOBAL RHEUMATOLOGY REGISTRY



PHYSICIAN REGISTRY, INITIAL RESEARCH QUESTION:
WHAT ARE RISK FACTORS FOR HOSPITALIZATION?

Rheum COVID-19 cases submitted between March 24-April 20, 2020



rheum-covid.org/map

Map as of Aug 1, 2020

RESULTS: CHARACTERISTICS OF 600 PATIENTS

- Patients have inflammatory rheumatic disease
- Which cases are entered?
  - Sick enough to receive COVID-19 diagnosis/testing
  - Only some practices have systems for capturing all COVID-19 cases

Characteristic	**N (%)**
Female	423 (71)
Age, Median (IQR)	56 (45 - 67)
Common rheumatic diagnoses:	
RA	230 (38)
SLE	85 (14)
SpA - PsA	74 (12)
SpA – AS or other	48 (8)
Vasculitis	44 (7)
Common comorbidities	
HTN	199 (33)
Lung Disease	127 (21)
Diabetes	69 (12)
CVD	63 (11)
CKD/ESRD	40 (7)
Smoking	
Ever	129 (22)
Never	389 (65)
Unknown	82 (14)
Medications	
No DMARD	97 (16)
csDMARD only, including anti-malarial	272 (45)
csDMARD only, excluding anti-malarial	122 (20)
Anti-malarial, with or without other DMARD	130 (22)
Anti-malarial only	52 (9)
b/tsDMARD only	107 (18)
csDMARD + b/tsDMARD combination	124 (21)
NSAIDs	111 (21)
Prednisone-Equivalent Glucocorticoids (N=592)	
None	403 (68)
1-9 mg/day	125 (21)
more than 10 mg/day	64 (11)
Hospitalized	**277 (46)**
Deceased	**55 (9)**

Gianfrancesco et al. *Ann Rheum Dis*. 2020 Jul;79(7):859-866.

RESULTS: HOSPITALIZATION STATUS

- Risk factors for hospitalization
  - Older age & comorbidities
  - Prednisone ≥10 mg/day
    - *Steroid effect remained after adjusting for disease activity*
- Fewer hospitalizations among those on b/ts DMARD only

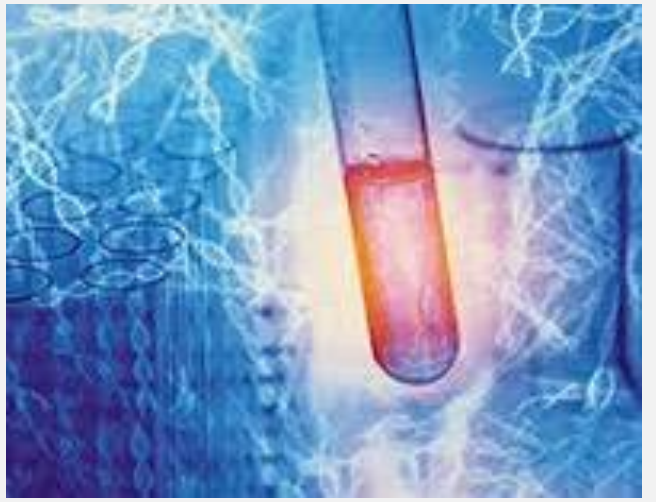
Characteristic	OR (95% CI)	*P*-value
Female	0.83 (0.54,1.28)	0.39
Age, Median (IQR)	**2.56 (1.62, 4.04)**	**<0.01**
Common rheumatic diagnoses:		
RA	*Ref*	--
SLE	1.80 (0.99, 3.29)	0.06
SpA -PsA	0.94 (0.48, 1.83)	0.85
SpA – AS or other	1.11 (0.50, 2.42)	0.80
Vasculitis	1.56 (0.66, 3.68)	0.31
Other	0.94 (0.55, 1.62)	0.82
Common comorbidities		
HTN or CVD	**1.86 (1.23, 2.81)**	**<0.01**
Lung Disease	**2.48 (1.55, 3.98)**	**<0.01**
Diabetes	**2.61 (1.39, 4.88)**	**<0.01**
CKD/ESRD	**3.02 (1.21, 7.54)**	**0.02**
Medications		
No DMARD	*Ref*	--
csDMARD only	1.23 (0.70, 2.16)	0.48
b/tsDMARD only	**0.46 (0.22, 0.93)**	**0.03**
csDMARD + b/tsDMARD	0.74 (0.37, 1.46)	0.38
Prednisone-Equivalent		
None	*Ref*	--
1-9 mg/day	1.03 (0.64, 1.66)	0.91
≥10 mg/day	**2.05 (1.06, 3.96)**	**0.03**
NSAIDs	0.64 (0.39, 1.06)	0.08

*Models adjusting for smoking and disease activity yielded similar results

Gianfrancesco et al. *Ann Rheum Dis*. 2020 Jul;79(7):859-866.

RESULTS: MORE ON HCQ AND BIOLOGIC DMARDS

- TNFi users have fewer hospitalizations in adjusted models (**OR 0.40**, 95% CI 0.19, 0.81)
- No significant association between antimalarials and hospitalization in adjusted models (**OR 0.94**, 95% CI 0.57, 1.57)



Gianfrancesco et al. *Ann Rheum Dis*. 2020 Jul;79(7):859-866.

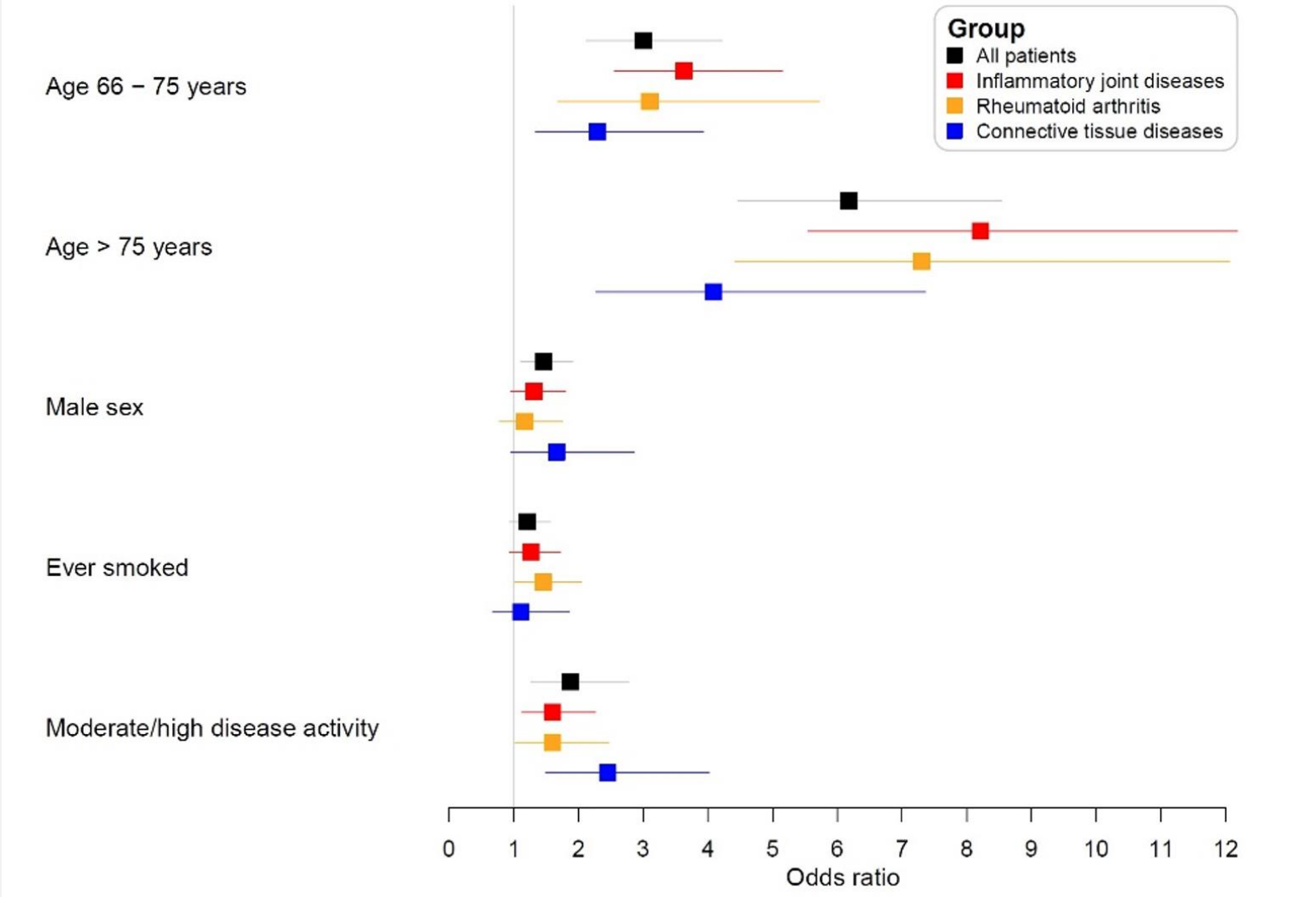
RISK OF MORTALITY AMONG 3729 INDIVIDUALS WITH RHEUMATIC DISEASES (*ANN RHEUM DIS. 2021 JAN 27*)

Epidemiology

EPIDEMIOLOGICAL SCIENCE

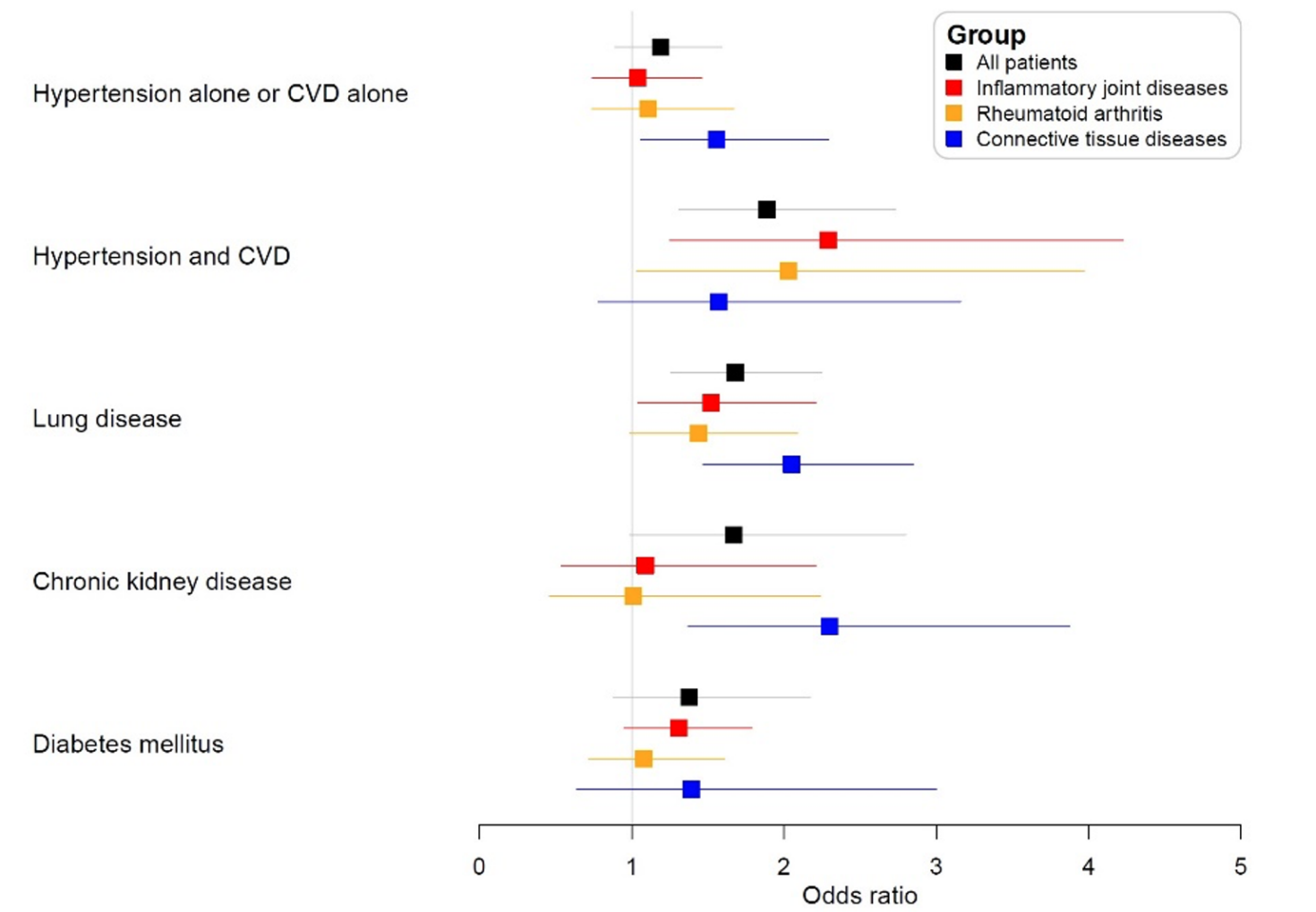
Factors associated with COVID-19-related death in people with rheumatic diseases: results from the COVID-19 Global Rheumatology Alliance physician-reported registry

Anja Strangfeld ,[1] Martin Schäfer,[1] Milena A Gianfrancesco,[2] Saskia Lawson-Tovey,[3,4] Jean W Liew,[5] Lotta Ljung ,[6,7] Elsa F Mateus,[8,9] Christophe Richez ,[10] Maria J Santos ,[11,12] Gabriela Schmajuk,[2] Carlo A Scirè ,[13] Emily Sirotich,[14,15] Jeffrey A Sparks,[16] Paul Sufka,[17] Thierry Thomas,[18,19,20] Laura Trupin,[2] Zachary S Wallace,[21] Sarah Al-Adely,[4,22] Javier Bachiller-Corral ,[23,24] Suleman Bhana,[25] Patrice Cacoub,[26,27,28] Loreto Carmona ,[29] Ruth Costello ,[22] Wendy Costello,[30] Laure Gossec ,[31,32] Rebecca Grainger,[33] Eric Hachulla ,[34] Rebecca Hasseli ,[35] Jonathan S Hausmann ,[36,37] Kimme L Hyrich ,[4,22] Zara Izadi,[2] Lindsay Jacobsohn,[2] Patricia Katz,[2] Lianne Kearsley-Fleet ,[22] Philip C Robinson ,[38,39] Jinoos Yazdany,[2] Pedro M Machado ,[40,41,42] COVID-19 Global Rheumatology Alliance



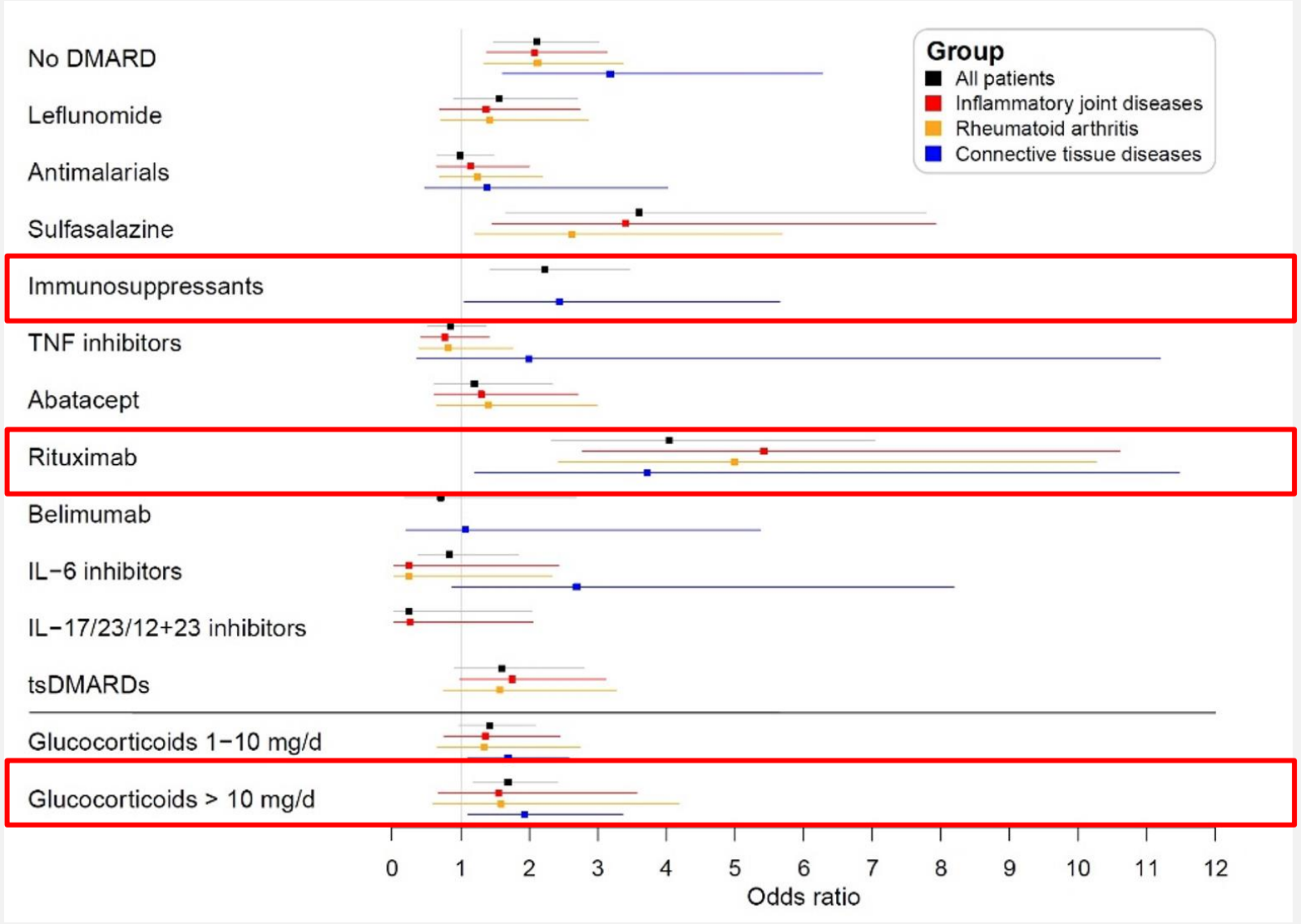
*Models also adjusted for other comorbidities, smoking, additional diseases, and several other classes of DMARDs and biologics and disease activity yielded similar results

COMORBIDITIES INCREASE RISK OF MORTALITY AMONG RHEUMATIC DISEASE PATIENTS



Strangfeld A, et al. *Ann Rheum Dis*. 2021 Jan 27.

HIGHER RISK OF MORTALITY WITH SSZ, RITUXIMAB, IMMUNOSUPPRESSANTS, STEROIDS



Strangfeld A, et al. *Ann Rheum Dis*. 2021 Jan 27.

RHEUMATOID ARTHRITIS PATIENTS IN GRA **N=1,673 BIOLOGIC USERS**

Odds of increase in ordinal severity scale among individuals with RA.

	Abatacept		**Rituximab**		IL-6 inhibitors		**JAKi**		TNFi
	OR (95% CI)	p-value	**OR (95% CI)**	**p-value**	OR (95% CI)	p-value	**OR (95% CI)**	**p-value**	Ref
Multivariable adjusted (primary analysis)	1.24 (0.78, 2.19)	0.36	**3.60 (3.40, 3.80)**	**<0.01**	0.83 (0.50, 1.37)	0.46	**1.59 (1.11, 2.28)**	**0.01**	Ref
Excluding patients with ILD or cancer*	1.24 (0.78, 1.96)	0.36	**4.15 (2.95, 5.84)**	**<0.01**	0.66 (0.40, 1.07)	0.09	**1.76 (1.25, 2.47)**	**<0.01**	Ref
Restricted to US and additionally adjusted for race**	1.00 (0.48, 2.12)	0.99	**3.82 (2.72, 5.37)**	**<0.01**	0.66 (0.40, 1.07)	0.09	**1.67 (1.19, 2.35)**	**<0.01**	Ref
Propensity score matched***	1.72 (0.99, 2.98)	0.05	**3.36 (2.11, 5.34)**	**<0.01**	0.68 (0.35, 1.32)	0.25	**1.56 (1.01, 2.42)**	**0.047**	Ref

**Unpublished*

DATA FROM SWEDISH NATIONAL REGISTERS

- Higher COVID-19 related mortality for those on rituximab and JAKi

Table 4 Occurrence and relative risks of COVID-19-related events and other outcomes in individuals with chronic inflammatory joint diseases (rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis, other spondyloarthropathies and juvenile idiopathic arthritis), 1 March through September 2020, according to DMARD treatment status 1 March

Outcome	Cohort	N events	Crude risk (%)	HR (95% CI)*
Death due to COVID-19	csDMARD	52	0.2	1 (ref)
	TNFi	7	0.0	1.03 (0.40 to 2.61)
	Abatacept	1	0.1	–
	Tocilizumab	2	0.2	–
	Rituximab	9	0.4	3.20 (1.19 to 8.57)
	JAKi	5	0.3	10.03 (2.35 to 42.76)
	All b/tsDMARDs	24	0.1	1.26 (0.60 to 2.64)

Bower H, et al. *Ann Rheum Dis*. doi:10.1136/ annrheumdis-2021-219845

DATA FROM POOLED IBD AND RHEUMATOLOGY REGISTRIES

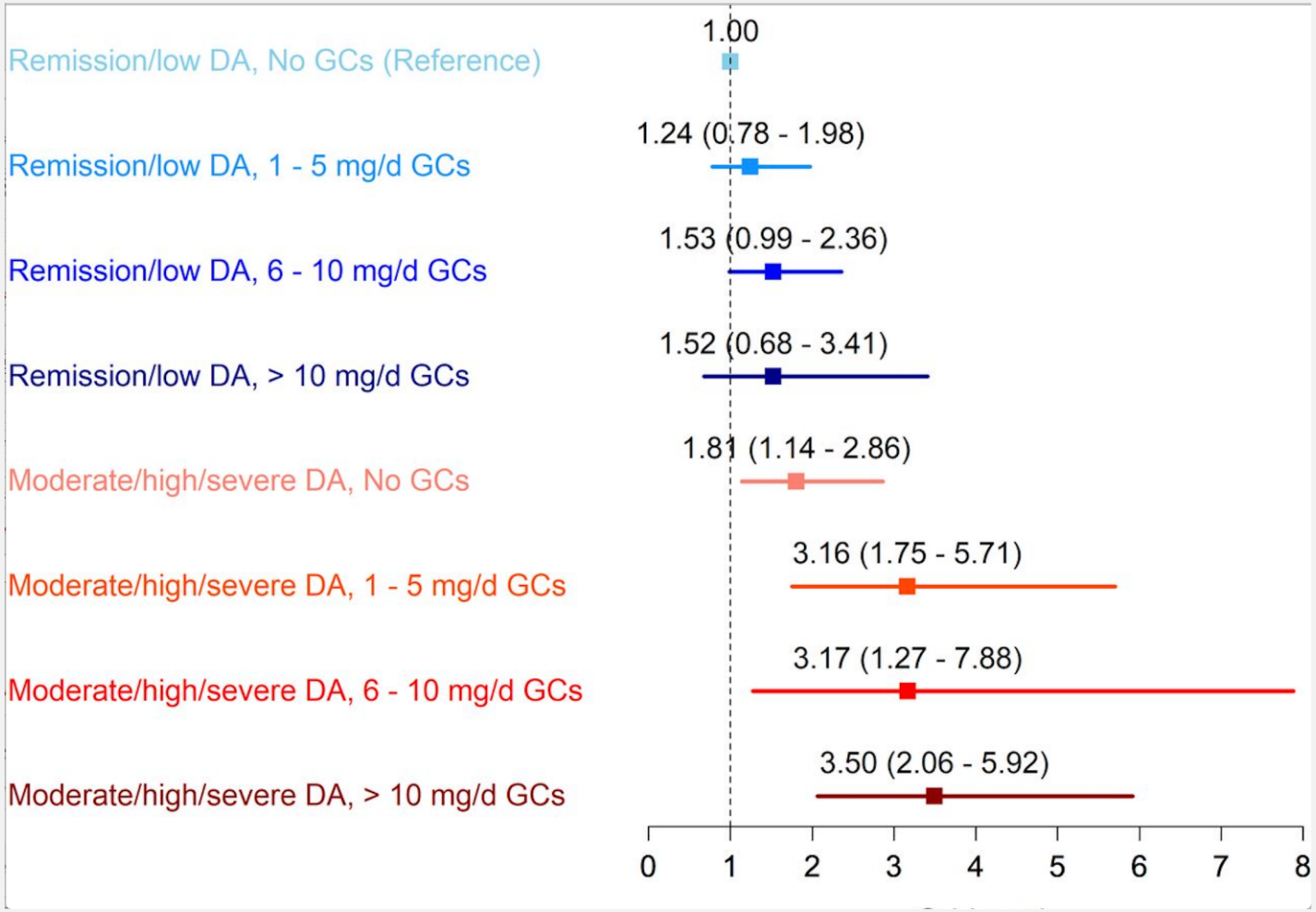
- **2208 cases, ~ half from each registry**
- Analyses controlled for age, sex, smoking status, diagnosis, disease activity, and number of comorbidities.

Figure 1: Pooled adjusted odds ratios using data from GRA and SECURE-IBD registries (N=2,208)

We are in the process of pooling data from the GRA, SECURE-IBD and Psoriasis registries

**Unpublished*

INTERACTION BETWEEN STEROIDS AND DISEASE ACTIVITY



Schäfer M, et al. *Ann Rheum Dis*. 2021 Mar 1:annrheumdis-2021-220134.

CONCLUSIONS

- COVID-19 outcomes for people taking immunosuppression for autoimmune diseases driven by older age and comorbidities
- Consistent signal of worse outcomes with moderate or high doses of steroids
- Worse outcomes with **rituximab, JAKi** and several immunosuppressants (**CYC, MMF, AZA, TAC**)
  - These patients should be prioritized for monoclonal antibody therapy as outpatients

ACKNOWLEDGEMENTS

- Global Rheumatology Community
- American College of Rheumatology (ACR)
- European League Against Rheumatism (EULAR)

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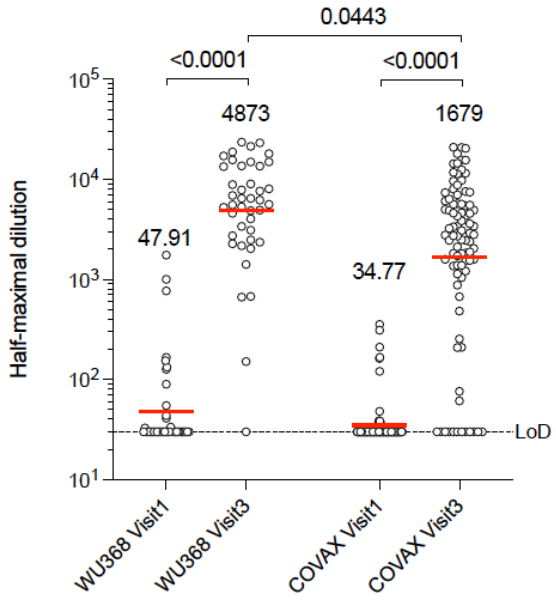
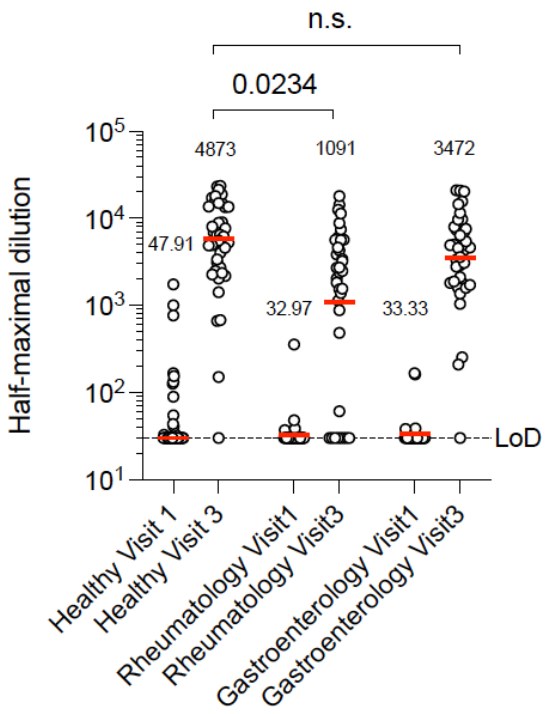
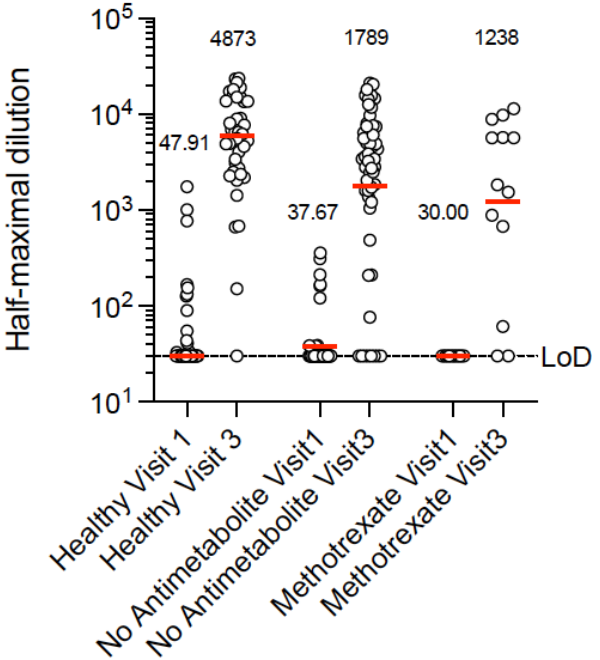
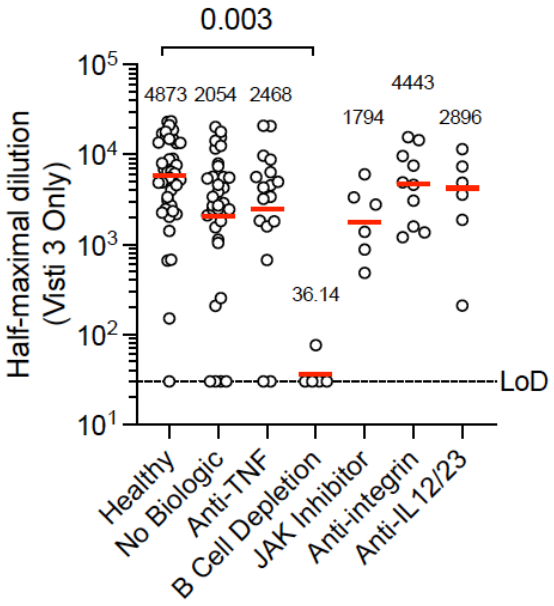
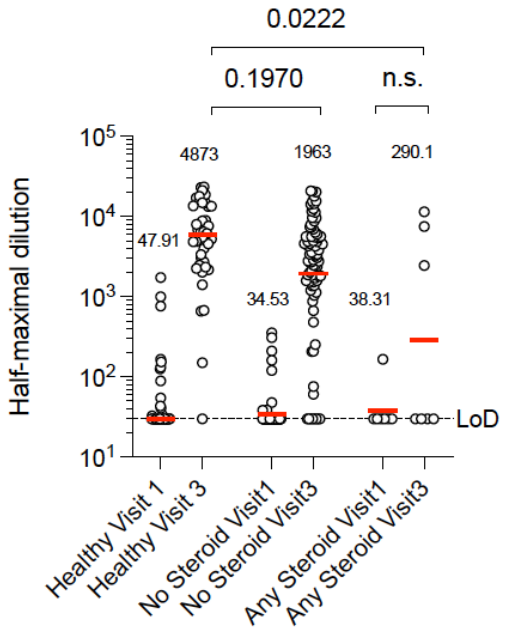
Anti-IgG spike protein
N=37 controls
N=90 autoimmune disease patients

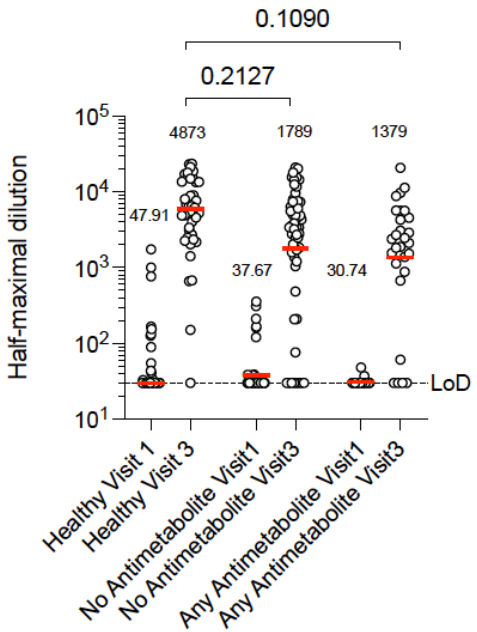








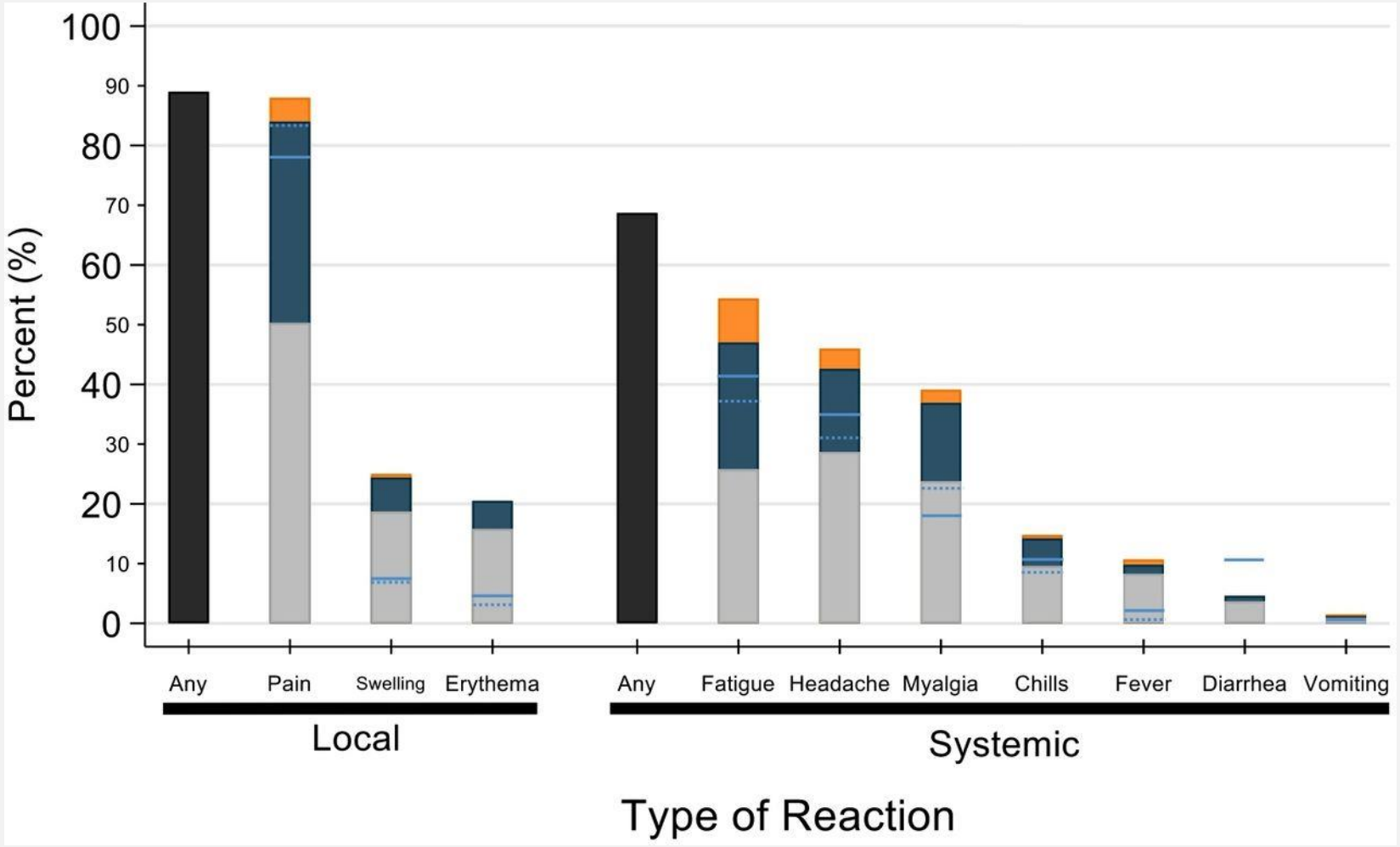




Courtesy of Dr. Alfred Kim at Washington U

Local site and systemic adverse reactions in patients with rheumatic and musculoskeletal diseases within the first week following the first dose of the SARS-CoV-2 vaccination.

The most common diagnoses were inflammatory arthritis (38%), SLE (28%) and overlap CTD (19%).



Caoilfhionn M Connolly et al. Ann Rheum Dis
doi:10.1136/annrheumdis-2021-220231

ARD

CLINICAL SCIENCE

Immunogenicity and safety of anti-SARS-CoV-2 mRNA vaccines in patients with chronic inflammatory conditions and immunosuppressive therapy in a monocentric cohort

Ulf M Geisen,[1] Dennis K Berner,[1] Florian Tran,[2,3] Melike Sümbül,[4] Lena Vullriede,[1] Maria Ciripoi,[1] Hayley M Reid,[1] Annika Schaffarzyk,[5] Ann C Longardt,[6] Jeanette Franzenburg,[7,8] Paula Hoff,[9] Jan H Schirmer,[1] Rainald Zeuner,[1] Anette Friedrichs,[2] Andrea Steinbach,[1] Christine Knies,[10] Robert DH Markewitz ,[11] Peter J Morrison,[4] Sascha Gerdes,[4] Stefan Schreiber,[7,12] Bimba F Hoyer [1]

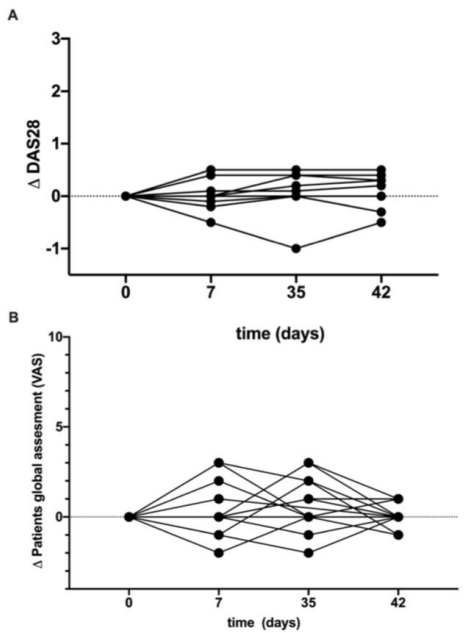


Figure 2 Disease activity does not increase over time after SARS-CoV-2 vaccination. (A) Delta DAS28 for patients with inflammatory arthritis during the 42-day study period. (B) Delta patients global assessment in patients with CID from baseline to day 42. Disease activity was assessed before the first and the second immunisation and 7 days after each vaccination. Each symbol represents one patient. CID, chronic inflammatory disease; DAS28, disease activity score 28.

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

NSAIDs, non-steroidal anti-inflammatory drugs.

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COVID-19 Vaccine Clinical Guidance Summary for Patients with Rheumatic and Musculoskeletal Diseases

Developed by the ACR COVID-19 Vaccine Clinical Guidance Task Force

This draft summary was approved by the ACR Board of Directors on February 8, 2021, and updated on March 4, 2021.

Table 3: Guidance Related to the Use and Timing of Vaccination and Immunomodulatory Therapies in Relation to COVID-19 Vaccination Administration in RMD Patients*

Medication	Timing Considerations for Immunomodulatory Therapy and Vaccination*	Level of Task Force Consensus
Hydroxychloroquine; apremilast; 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

RMD = rheumatic and musculoskeletal disease; IVIG = intravenous immunoglobulin; TNFi = tumor necrosis factor inhibitor; IL = interleukin; JAKi = janus kinase inhibitor; CYC = cyclophosphamide; RTX = rituximab; IV = intravenous; SQ = subcutaneous

**guidance to 'hold' a therapy was made based on the assumption that the patient had well-enough controlled disease to allow for a temporary interruption; if not, decision-making should be determined on a case-by-case basis, considering the circumstances involved*

Q&A and Discussion

SARS-CoV-2 Variants Q&A

Judith A. Aberg, MD, FIDSA, FACP
Dean of System Operations for Clinical Sciences
Dr. George Baehr Professor of Medicine
Icahn School of Medicine at Mount Sinai
Chief, Division of Infectious Diseases
Mount Sinai Health System

Gregory Armstrong, MD, FIDSA
Director, Advanced Molecular Detection Program
Centers for Disease Control and Prevention

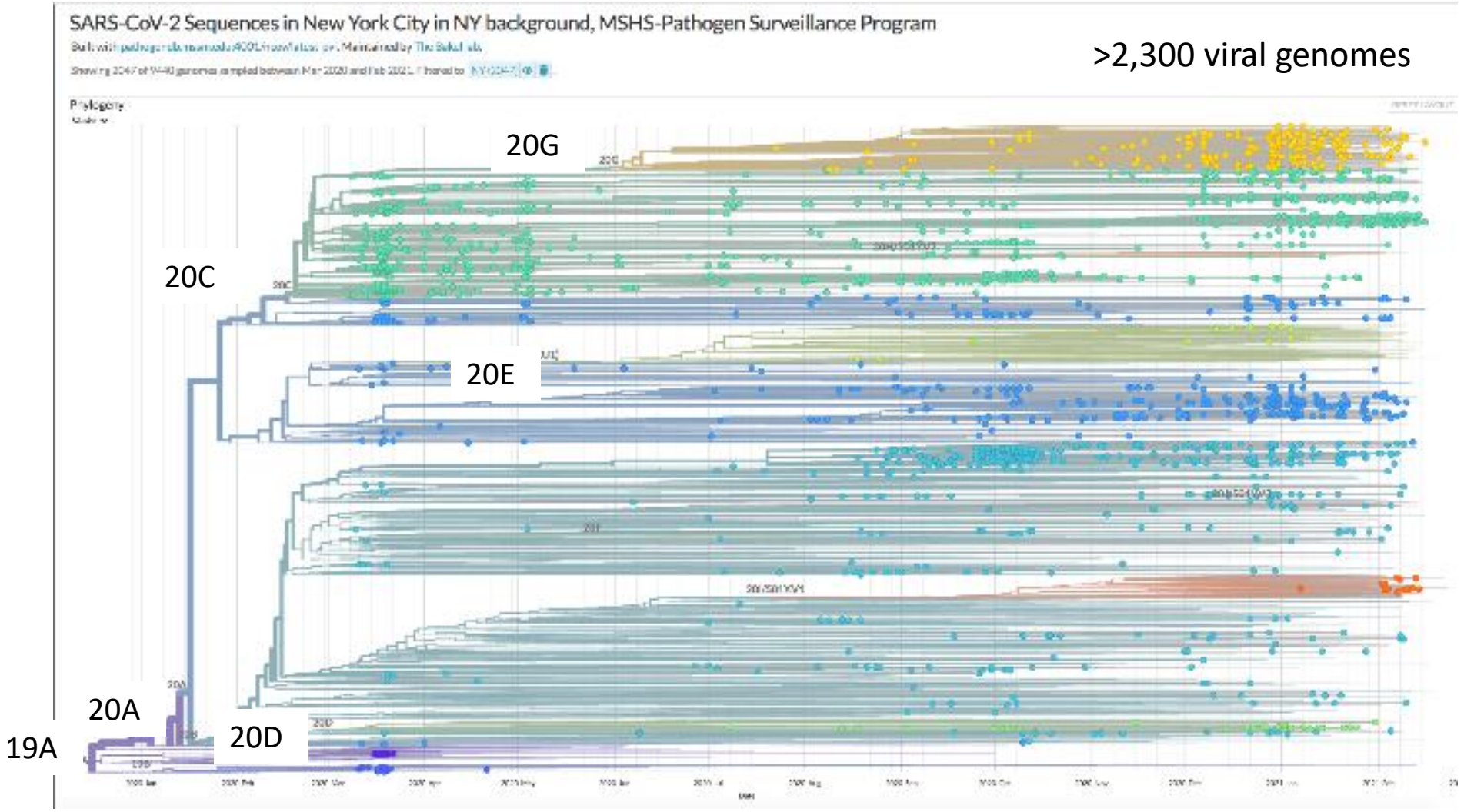
Disclosures

- **Judith A. Aberg, MD, FIDSA, FACP** was on scientific advisory boards for Merck (>1 year ago) and Gilead (>2 years ago).
- **Gregory Armstrong, MD, FIDSA –** nothing to disclose

SARS-CoV-2 Variants

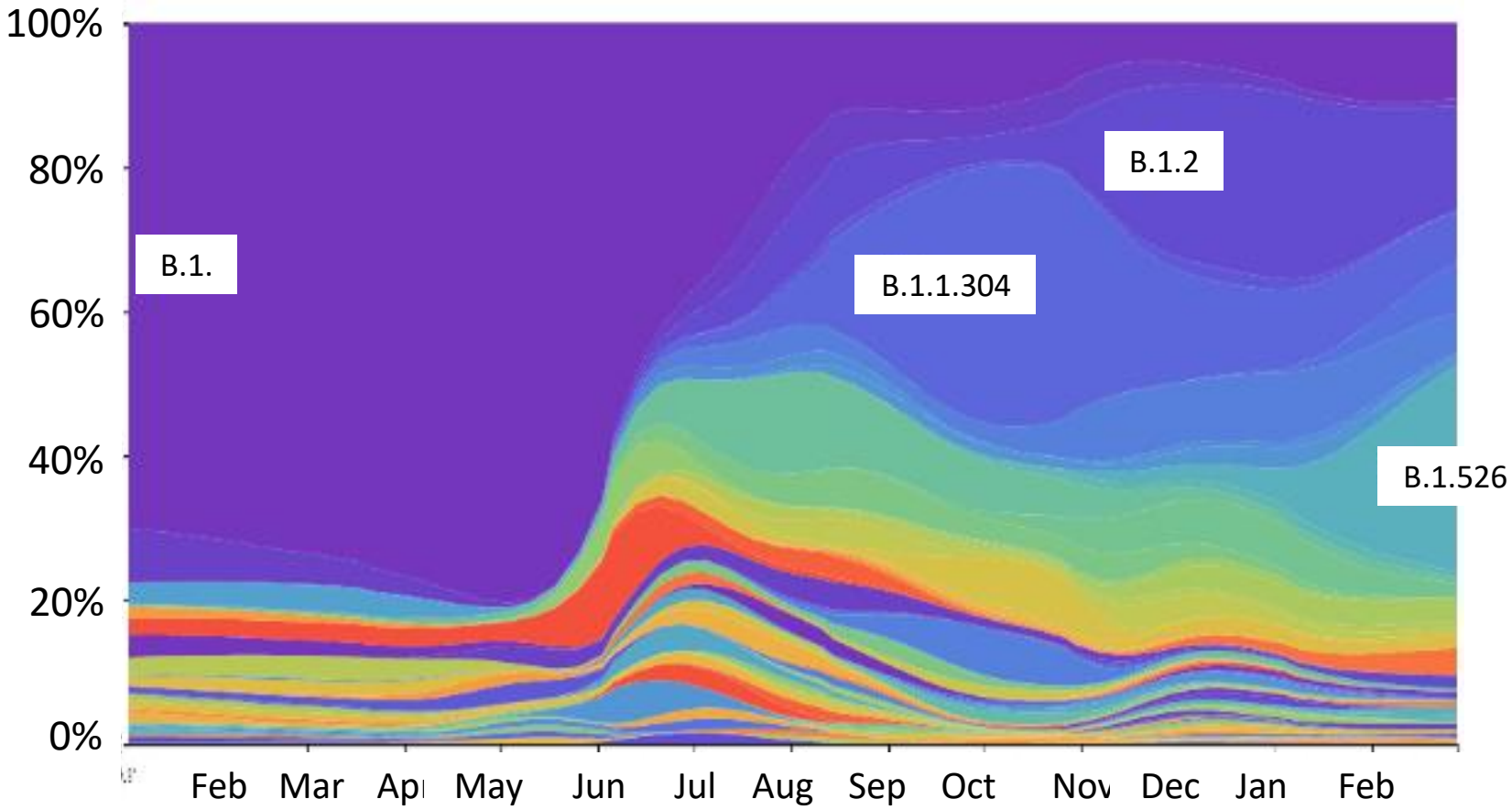
Variant Lineage with Spike Protein Substitution	Key Mutation(s)
B.1.1.7 (UK Origin)	N501Y
B.1.351 (South Africa Origin)	K417N, E484K, N501Y
P.1 (Japan/Brazil Origin)	K417T, E484K, N501Y
B.1.427/B.1.429 (California Origin)	L452R
B.1.526 (New York Origin)	E484K (not all isolates of the lineage)

SARS-CoV-2 isolates from MSHS patients represent the global viral diversity



Mount Sinai Pathogen

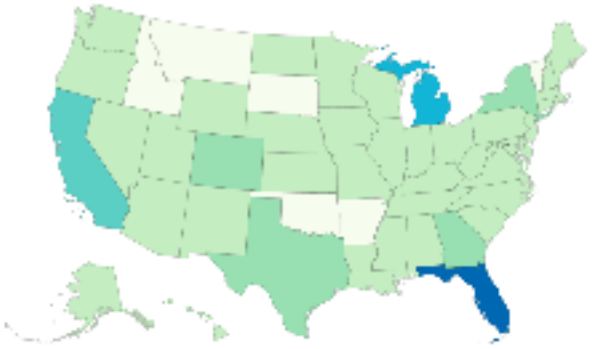
The genetic makeup of SARS-CoV-2 in NYC has changed over time



Mount Sinai Pathogen

Variants of Concern Cases in the US and in the Mount Sinai Health Care System

B.1.1.7



P.1

B.1.351

CDC, Feb 28

MSSM Surveillance

Week ending on:	2-Jan	9-Jan	16-Jan	23-Jan	30-Jan	6-Feb	13-Feb	20-Feb	27-Feb
B.1.1.7 (UK)	0.00%	0.76%	0.00%	0.00%	0.00%	5.43%	11.94%	14.29%	14.29%
P.1 (Brazil)	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%
B.1.351 (S. Africa)	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%
B.1.526 (NYC)	1.40%	1.53%	6.41%	8.43%	10.87%	26.09%	38.81%	46.94%	23.81%

Mount Sinai Pathogen

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ID Division
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Wanni Mendez
Ben Mulder
Kayla Rousso
Miti Saksena
Ashley Salimbangon
Komal Srivastava
Levy Sominsky
Amber Shin
Mahmoud Awawda
Rachel Chernet
Lilly Eaker
Emily Ferreri
Daniel Floda
+ many volunteers

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Shirish Huprikar
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Employee Health
Ismail Nabeel

Medina Lab (PUC)
Leo Almonacid et al.

Perez Lab (UGA)
Lucia Ortiz

Robin Chemers Neustein Postdoctoral Fellowship

Marion Alban MSCIC Scholars Award

Institutional and philanthropic funding

Links from Today's call

- **Slide 13 -** https://www.scripps.edu/science-and-medicine/translational-institute/about/news/sarc-cov-2-infection/index.html
- **Slide 14** -https://www.rheumatology.org/Portals/0/Files/ACR-COVID-19-Clinical-Guidance-Summary-Patients-with-Rheumatic-Diseases.pdf
- **Slide 19 -ACR** COVID Guidance: https://www.rheumatology.org/Portals/0/Files/ACR-COVID-19-Clinical-Guidance-Summary-Patients-with-Rheumatic-Diseases.pdf
- **Slide 19 - EULAR** COVID Guidance: https://ard.bmj.com/content/79/7/851

Additional Resources: SARS-CoV-2 Variant Surveillance

CDC updates about emerging variants and ongoing strain surveillance
https://www.cdc.gov/coronavirus/2019-ncov/more/science-and-research/scientific-brief-emerging-variants.html

Variants of Interest, Concern: CDC updates on U.S. variant tracking and classification:
https://www.cdc.gov/coronavirus/2019-ncov/cases-updates/variant-surveillance/variant-info.html

Variant Proportions in the U.S.: CDC genomic surveillance dashboard providing an overview of SARS-CoV-2 variant circulation in the U.S.
https://www.cdc.gov/coronavirus/2019-ncov/cases-updates/variant-proportions.html

CDC updated webpages to provided information regarding variants of concern by State.
https://www.cdc.gov/coronavirus/2019-ncov/cases-updates/variant-proportions.html

Additional Resources: SARS-CoV-2 Variants & Treatment

HHS will stop the distribution of bamlanivimab alone starting March 24, 2021.
https://www.phe.gov/emergency/events/COVID19/investigation-MCM/Bamlanivimab/Pages/default.aspx

The Fact Sheets for the bamlanivimab, bamlanivimab and etesevimab, and REGEN-COV EUAs were modified to include the following statement and updated virology information regarding variants and the particular mAb(s):

> Circulating SARS-CoV-2 viral variants may be associated with resistance to monoclonal antibodies. Health care providers should review the Antiviral Resistance information in Section 15 of this Fact Sheet for details regarding specific variants and resistance, and refer to the CDC website (https://www.cdc.gov/coronavirus/2019-ncov/cases-updates/variant-proportions.html) as well as information from state and local health authorities regarding reports of viral variants of importance in their region to guide treatment decisions.
>
> Updated Fact Sheets available at: https://www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/emergency-use-authorization#coviddrugs

Additional Resources: COVID-19 Vaccine Efficacy

Lack of efficacy of Oxford/AZ vaccine in S. Africa was in the NEJM this week.
https://www.nejm.org/doi/full/10.1056/NEJMoa2102214

Preliminary evidence that B.1.1.7 may be more severe. https://www.nature.com/articles/s41586-021-03426-1

Evaluating COVID-19 booster and new vaccine variants- Pfizer/BioNTech's third-dose study to understand the effect of a booster on immunity against COVID-19 caused by circulating and potential newly emerging SARS-CoV-2 variants

https://www.pfizer.com/news/press-release/press-release-detail/pfizer-and-biontech-initiate-study-part-broad-development

Current trials to create variant-specific vaccine candidates (i.e., Moderna's variant-specific vaccine candidate mRNA-1273.351

https://investors.modernatx.com/news-releases/news-release-details/moderna-announces-it-has-shipped-variant-specific-vaccine

SPECIAL NOTICE - UPCOMING WEBINAR

ASCO/IDSA Global COVID webinar - Vaccinations

Tuesday, March 30th - 8 a.m. ET/ 5 a.m. PT

Hosted by the American Society of Clinical Oncology and the Infectious Diseases Society of America

Join ASCO and IDSA for an important COVID-19 vaccines webinar at 8 a.m. EST on March 30th.
Following a short presentation on currently available vaccines, a panel of invitees from the Infectious Diseases Society of America (IDSA), a nurse, a medical oncologist, a hematologist, and a patient advocate will discuss and answer questions for the remaining hour. Shaheenah S. Dawood, MBBCh, MPH, FACP, FRCP a Consultant Medical Oncologist at Mediclinic Middle East in Dubai, UAE will moderate.

This webinar is not part of the CDC/IDSA COVID-19 Clinician Call series and requires separate registration.

To Register: https://asco1.zoom.us/webinar/register/WN_B5a0zz4JR1yqdb4zseu6jA

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IDSA Infectious Diseases Society of America

COVID-19 Real-Time Learning Network

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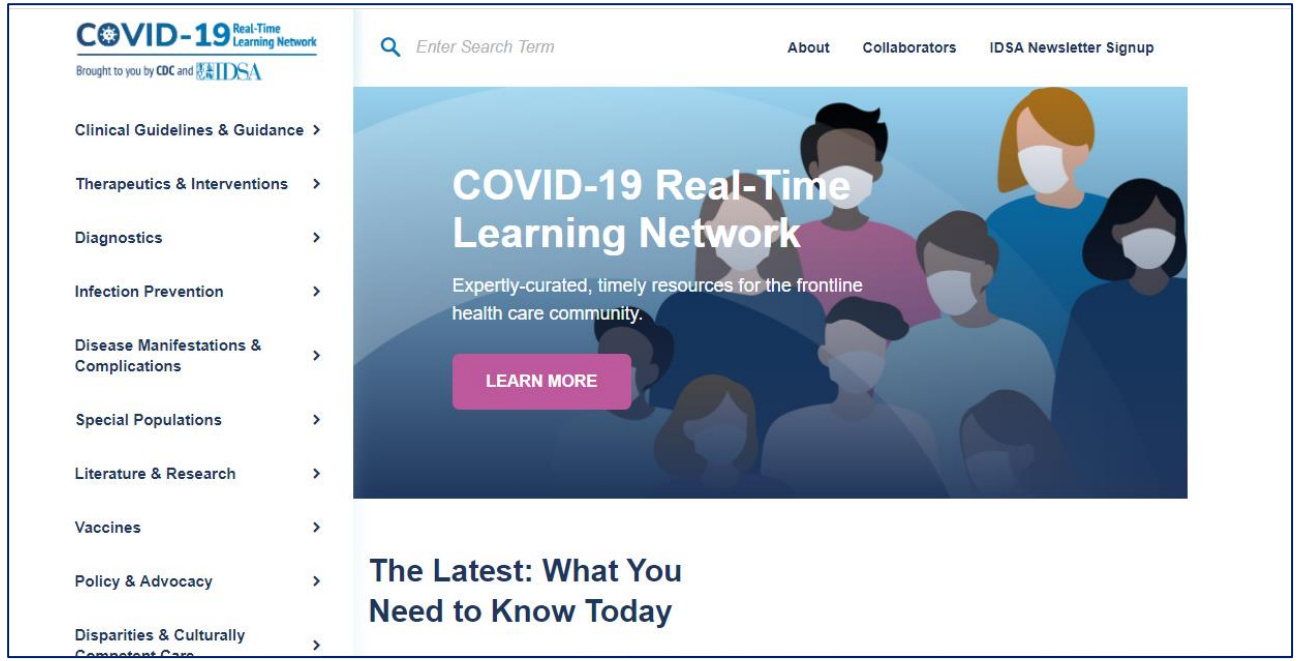

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CDC-IDSA Partnership: Clinical Management Call Support

FOR WHOM?

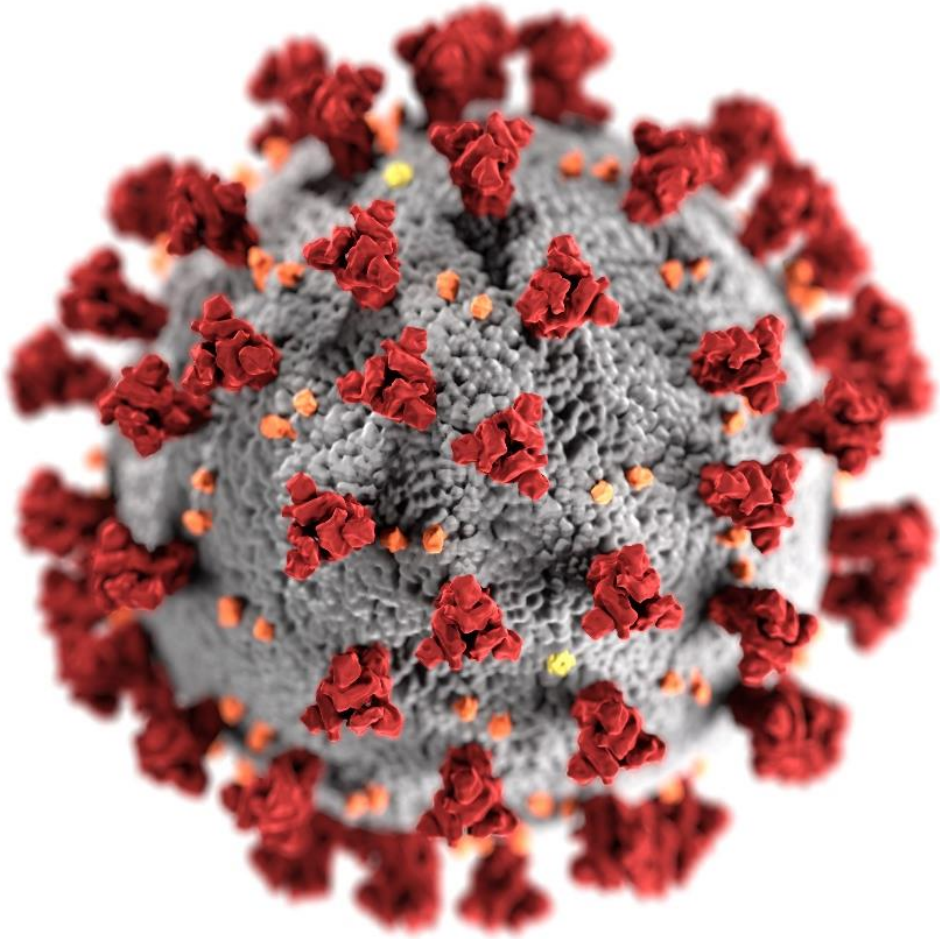
- Clinicians who have questions about the clinical management of COVID-19

WHAT?

- Calls from clinicians will be triaged by CDC to a group of IDSA volunteer clinicians for peer-to-peer support

HOW?

- Clinicians may call the main CDC information line at 800-CDC-INFO (800-232-4636)
- To submit your question in writing, go to www.cdc.gov/cdc-info and click on Contact Form



IDSA
Infectious Diseases Society of America

cdc.gov/coronavirus

Continue the conversation on Twitter

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#RealTimeCOVID19

We want to hear from you! Please complete the post-call survey.

No Call Next Week

Next Call: **Saturday, April 10th**

A recording of this call will be posted at **www.idsociety.org/cliniciancalls**

-- library of all past calls now available --

Contact Us:

Dana Wollins (dwollins@idsociety.org)
Deirdre Lewis (dlewis@idsociety.org)