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Where Rheumatology Meets

COVID-19 Outcomes in Patients Living with Rheumatic Diseases

Kristin M. D'Silva, April Jorge, Na Lu, Yuqing Zhang, Zachary S. Wallace, Hyon K. Choi

Division of Rheumatology, Allergy, and Immunology

Clinical Epidemiology Program, Mongan Institute

Department of Medicine

Massachusetts General Hospital

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COI DISCLOSURE INFORMATION

Kristin M. D'Silva

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I have no financial relationships to disclose.

The COVID-19 Pandemic: October 2020

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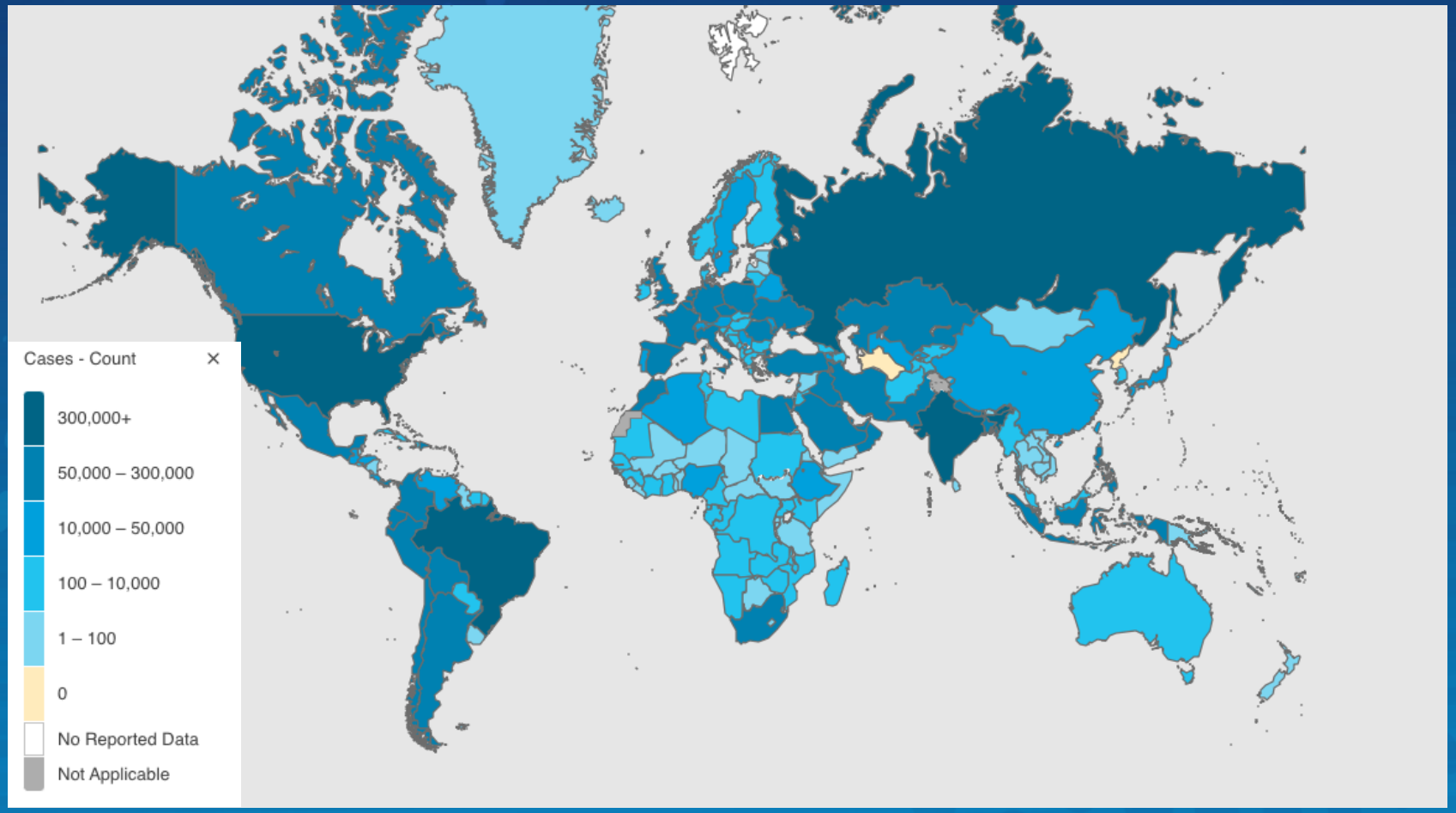

Worldwide:
>36 million cases
>1 million deaths

Covid19.who.int

The COVID-19 Pandemic

Impact on Patients with Rheumatic Disease

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- Continued concerns regarding potentially increased risk of poor COVID-19 outcomes due to
  - Underlying immunosuppression
  - Chronic inflammatory state
  - Comorbidities
  - Racial, ethnic, and socioeconomic disparities

COVID-19 Outcomes in Patients with Rheumatic Diseases

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- Early center-specific studies from Wuhan, China, and Boston, MA
  - Up to 3-fold higher odds of mechanical ventilation in patients with rheumatic disease vs. comparators
- Global Rheumatology Alliance
  - No higher odds of hospitalization in patients on conventional, biologic, or targeted synthetic DMARDs
  - Two-fold higher odds of hospitalization in patients on prednisone-equivalent doses ≥ 10 mg daily

Ye et al., Ann Rheum Dis 2020
D'Silva & Serling-Boyd et al., Ann Rheum Dis 2020
Gianfrancesco et al., Ann Rheum Dis 2020

Objective

- To determine COVID-19 outcomes in patients living with systemic autoimmune rheumatic diseases (SARDs) versus the general population
- At two timepoints:
  - 4 months
  - 6 months

Ye et al., Ann Rheum Dis 2020
D'Silva & Serling-Boyd et al., Ann Rheum Dis 2020
Gianfrancesco et al., Ann Rheum Dis 2020

Methods: Data Source

- **TriNetX**: Multicenter research network with real-time electronic health record data across 35 healthcare organizations in the US
- Includes
  - Greater than 52 million patients
  - Academic and community practices
  - Demographics, diagnoses, procedures, medications, laboratory values, vital status
- Previously used to study COVID-19 outcomes in malignancy, liver disease, and inflammatory bowel disease

www.trinetx.com
Alkhouli et al. Mayo Clinic Proceedings 2020
Annie et al. Am J Cardiol 2020
London et al. JCO Clinical Cancer Informatics 2020
Singh, et al. Gastroenterology 2020

Methods: Study Cohort

- COVID-19 infection: ICD-10 codes or positive COVID-19 PCR testing (January 20, 2020, to June 1, 2020)
- SARDs: ≥ 2 ICD-10 codes, >2 months apart, but within 2 years

Inflammatory arthritis	• Rheumatoid arthritis • Psoriatic arthritis • Ankylosing spondylitis
Connective tissue diseases	• Systemic lupus erythematosus • Sjögren's syndrome • Systemic sclerosis • Idiopathic inflammatory myopathy • Mixed or undifferentiated connective tissue diseases
Systemic vasculitis	• ANCA-associated vasculitis • Polyarteritis nodosa • Giant cell arteritis • Takayasu arteritis • Behçet's disease

Bernatsky et al., J Rheumatol 2011

Methods: Analysis

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- Real-time online platform for up-to-date analyses
- 1:1 matching of patients with SARDs to comparators using exposure score based on age, sex, and race/ethnicity
- Baseline characteristics assessed in 1 year prior to COVID-19 infection
- Outcomes assessed up to 3 months after COVID-19 infection
  - Hospitalization, intensive care unit (ICU) admission, mechanical ventilation, acute kidney injury (AKI), death
- Calculated risk ratio (RR) and 95% CI for each outcome

Greenland S. Wiley StatsRef 2015.

Baseline Characteristics

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	COVID-19 with SARD (n=716)	COVID-19 without SARD (n=716)
Age, years, mean (SD)	57 ± 16	57 ± 16
Female, n (%)	569 (79%)	569 (79%)
Race/ethnicity, n (%)		
White	388 (54%)	388 (54%)
Black/African American	241 (34%)	241 (34%)
Asian	13 (2%)	13 (2%)
Hispanic/Latinx	47 (7%)	47 (7%)
Body mass index, kg/m^2, mean (SD)	31 ± 8	32 ± 9
Creatinine, mg/dL, mean (SD)	1.2 ± 1.4	1.0 ± 0.8
Hypertension, n (%)	349 (49%)	228 (32%)
Diabetes mellitus, n (%)	173 (24%)	120 (17%)
Chronic kidney disease, n (%)	136 (19%)	47 (7%)
Asthma, n (%)	129 (18%)	67 (9%)
Chronic obstructive pulmonary disease, n (%)	25 (3%)	13 (2%)

Baseline Characteristics of Rheumatic Diseases: Diagnoses

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	Rheumatic disease (n, %) (n=716)
Rheumatoid arthritis	325 (45%)
Systemic lupus erythematosus	128 (18%)
Sjögren's syndrome	71 (10%)
Systemic sclerosis	25 (3%)
Idiopathic inflammatory myositis	20 (3%)
Mixed or undifferentiated connective tissue disease	34 (5%)
Systemic vasculitis	61 (9%)
Psoriatic arthritis	44 (6%)
Ankylosing spondylitis	22 (3%)

Baseline Characteristics of Rheumatic Diseases: Medications

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	Rheumatic disease medication (n, %) (n=716)
Prednisone	289 (40%)
Hydroxychloroquine	140 (20%)
Methotrexate	98 (14%)
TNF Inhibitors	84 (12%)
Rituximab	28 (4%)
Abatacept	12 (2%)
Tofacitinib	11 (2%)
Tocilizumab	10 (1%)

TNF, tumor necrosis factor

COVID-19 Outcomes

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COVID-19 Outcome	Risk in People with SARD, n (%) (n=716)	Risk in People without SARD, n (%) (n=716)	Risk Ratio (95% CI)
Hospitalization	175 (24%)	142 (20%)	**1.23 (1.01, 1.50)**
Intensive care unit admission	49 (7%)	28 (4%)	**1.75 (1.11, 2.75)**
Mechanical ventilation	39 (5%)	22 (3%)	**1.77 (1.06, 2.96)**
Acute kidney injury	42 (6%)	23 (3%)	**1.83 (1.11, 3.00)**
Death	36 (5%)	31 (4%)	1.16 (0.73, 1.86)

Six Months into the Pandemic

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- Extended study period until August 15, 2020
- Assessed 30-day outcomes
  - Added new outcomes: renal replacement therapy, venous thromboembolism (VTE), ischemic stroke
- Primary model: Exposure score including age, sex, race/ethnicity

Six Months into the Pandemic

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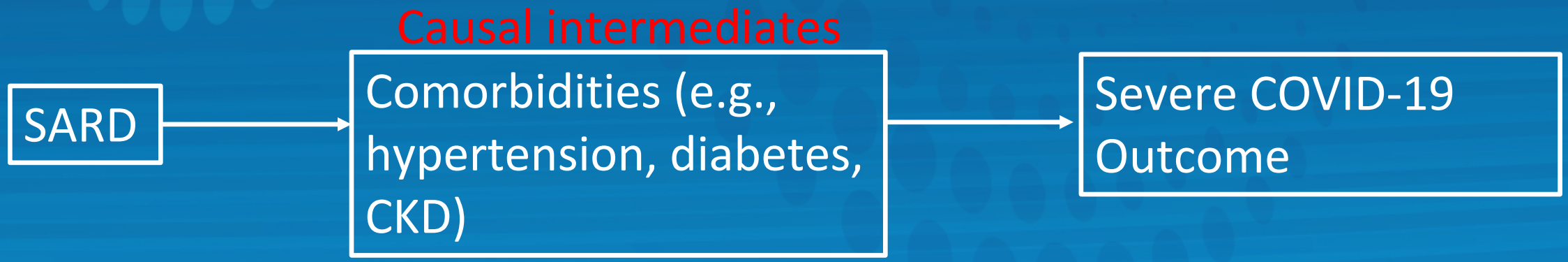
- Extended model: primary model (age/sex/race/ethnicity) +
  - Comorbidities (hypertension, ischemic heart disease, chronic kidney disease, diabetes, asthma, COPD)
  - Health care utilization (prior hospitalization within 1 year)
- Chosen as extended model given that comorbidities are likely causal intermediates rather than confounders



Baseline Characteristics

	COVID-19 with SARD (n=2,379)	COVID-19 without SARD (n=2,379)
Age, years, mean (SD)	58 ± 16	57 ± 16
Female, n (%)	1,873 (79)	1,873 (79)
Race/ethnicity, n (%)		
White	1,295 (54)	1,295 (54)
Black/African American	649 (27)	649 (27)
Hispanic/Latinx	312 (13)	312 (13)
Body mass index, kg/m^2, mean (SD)	30.7 ± 8.2	30.6 ± 7.8
Creatinine, mg/dL, mean (SD)	1.1 ± 1.3	1.1 ± 1.2
Hypertension, n (%)	1,206 (51)	758 (32)
Diabetes mellitus, n (%)	599 (25)	384 (16)
Asthma, n (%)	372 (16)	200 (8)
Chronic obstructive pulmonary disease, n (%)	87 (4)	34 (1)
Chronic kidney disease, n (%)	376 (16)	183 (8)
Ischemic heart disease, n (%)	360 (15)	165 (7)
Prior hospitalizations, n (%)	360 (15)	187 (8)

COVID-19 Outcomes, Matched on Age, Sex, Race/ethnicity

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30-Day Outcomes	Risk in People with SARD, n (%) (n=2,379)	Risk in People without SARD, n (%) (n=2,379)	Risk Ratio (95% CI)
Hospitalization	620 (26)	546 (23)	**1.14 (1.03, 1.26)**
Intensive care unit admission	142 (6)	108 (5)	**1.32 (1.03, 1.68)**
Mechanical ventilation	78 (3)	74 (3)	1.05 (0.77, 1.44)
Acute kidney injury	157 (7)	87 (4)	**1.81 (1.40, 2.33)**
Renal replacement therapy	38 (2)	21 (1)	**1.81 (1.07, 3.07)**
Venous thromboembolism	85 (4)	49 (2)	**1.74 (1.23, 2.45)**
Ischemic stroke	42 (2)	28 (1)	1.50 (0.93, 2.41)
Death	94 (4)	87 (4)	1.08 (0.81, 1.44)

COVID-19 Outcomes, Matched on Age, Sex, Race/ethnicity, Comorbidities, Health Care Utilization

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30-Day Outcomes	Risk in People with SARD, n(%) (n=2,374)	Risk in People without SARD, n(%) (n=2,374)	Risk Ratio (95% CI)
Hospitalization	616 (26)	579 (24)	1.06 (0.96, 1.17)
Intensive care unit admission	141 (6)	134 (6)	1.05 (0.84, 1.32)
Mechanical ventilation	77 (3)	85 (4)	0.91 (0.67, 1.23)
Acute kidney injury	154 (6)	116 (5)	**1.33 (1.05, 1.68)**
Renal replacement therapy	38 (2)	41 (2)	0.93 (0.60, 1.44)
Venous thromboembolism	85 (4)	53 (2)	**1.60 (1.14, 2.25)**
Ischemic stroke	42 (2)	39 (2)	1.08 (0.70, 1.66)
Death	93 (4)	79 (3)	1.18 (0.88, 1.58)

Conclusions

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- After extending the study period to 6 months,
  - Persistently higher risk of hospitalization, ICU admission, acute kidney injury, and renal replacement therapy in patients with SARDs vs. comparators
    - Risks attenuated after adjusting for comorbidities (likely causal intermediates)
  - Persistently higher risk of VTE (RR 1.60)
  - No higher risk of mechanical ventilation (unlike at 4 months)

Strengths and Limitations

- Strengths
  - Generalizability: Large multi-center national cohort
  - Real-time data allowing timely analyses
- Limitations:
  - Residual confounding, inaccuracies in ICD-10 coding, incomplete capture of outcomes
  - Potential collider bias (study population selection conditioned on COVID-19 diagnosis → bias towards null)

Choi et al., Nat Rev Rheumatol 2014

Overall Conclusions

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- Improvement in mechanical ventilation risk over time
- Patients with rheumatic disease appear to be at higher risk of some severe COVID-19 outcomes, likely mediated by comorbidities
  - Rheumatic disease may contribute to risk of VTE even beyond the mediating effects of comorbidities
  - Patients with rheumatic disease should be monitored closely for VTE during COVID-19 infection

Kim et al., Arthritis Care Res 2013

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Contact information:

kmdsilva@partners.org

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Division of Rheumatology, Allergy & Immunology
Massachusetts General Hospital

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American College of Rheumatology
2200 Lake Boulevard NE
Atlanta, GA 30319
Phone: 404-633-3777, ext. 815