TGIF to all

Today I selected 5 articles for your reading enjoyment. The first is a pre-publication article where investigators sequenced the genomes of 5,085 SARS-CoV-2 strains causing two COVID-19 disease waves in metropolitan Houston, Texas. This is the first analysis of the molecular architecture of SARS-CoV-2 in two infection waves in a major metropolitan region. The next 2 articles look at different approaches to predict severity of SARS-CoV-2. The last 2 articles are from the CDC. The first article documents the changing age distribution of people infected with SARS-CoV-2 and the last article looks at influence of SARS-CoV-2 on rates of influenza looking at both the Northern and Southern hemispheres.

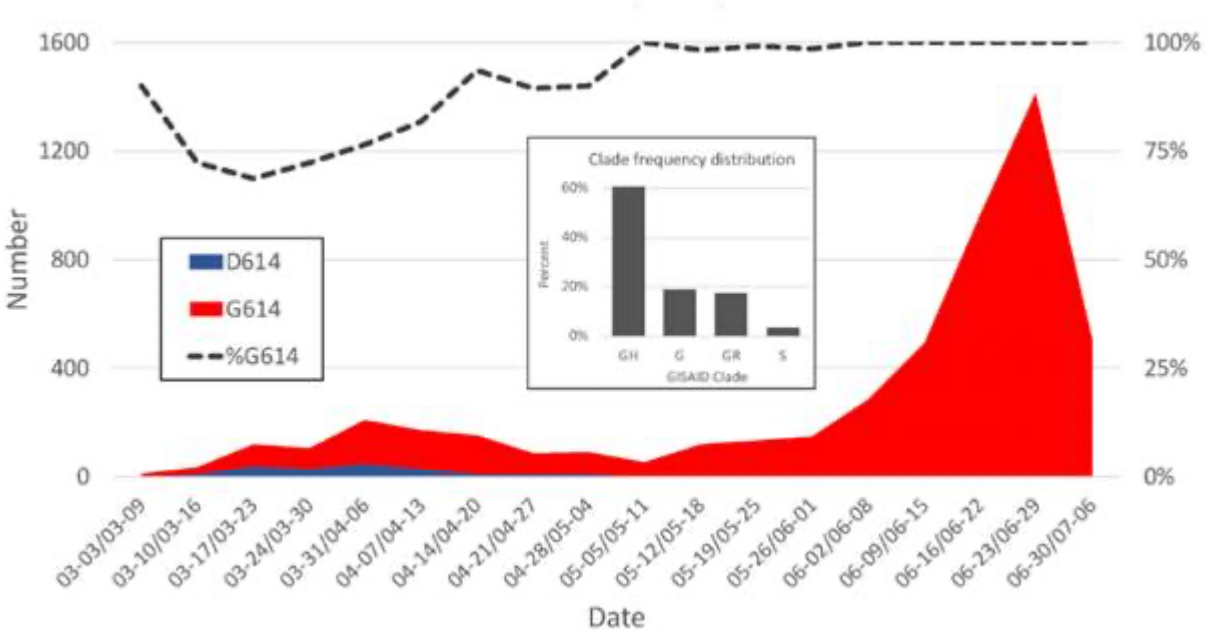
Have a wonderful weekend

Ed

Molecular Architecture of Early Dissemination and Massive Second Wave of the SARS-CoV-2 Virus in a Major Metropolitan Area

medRvix published online September 23, 2020 article provided by Cesar Arias

The researchers sequenced the genomes of 5,085 SARS-CoV-2 strains causing two COVID-19 disease waves in metropolitan Houston, Texas, with seven million residents. The genomes were from viruses recovered in the earliest recognized phase of the pandemic in Houston, and an ongoing significant second wave of infections. The virus was originally introduced into Houston from several sources independently. Virtually all strains in the second wave have a Gly614 amino acid replacement in the spike protein, a polymorphism that has been linked to increased transmission and infectivity. Patients infected with the Gly614 variant strains had significantly higher virus loads in the nasopharynx. They found no evidence between virus genotypes and altered virulence. They exploited the genomic data to generate defined single amino acid replacements in the receptor binding domain of spike protein that, importantly, produced decreased recognition by the neutralizing monoclonal antibody CR30022.



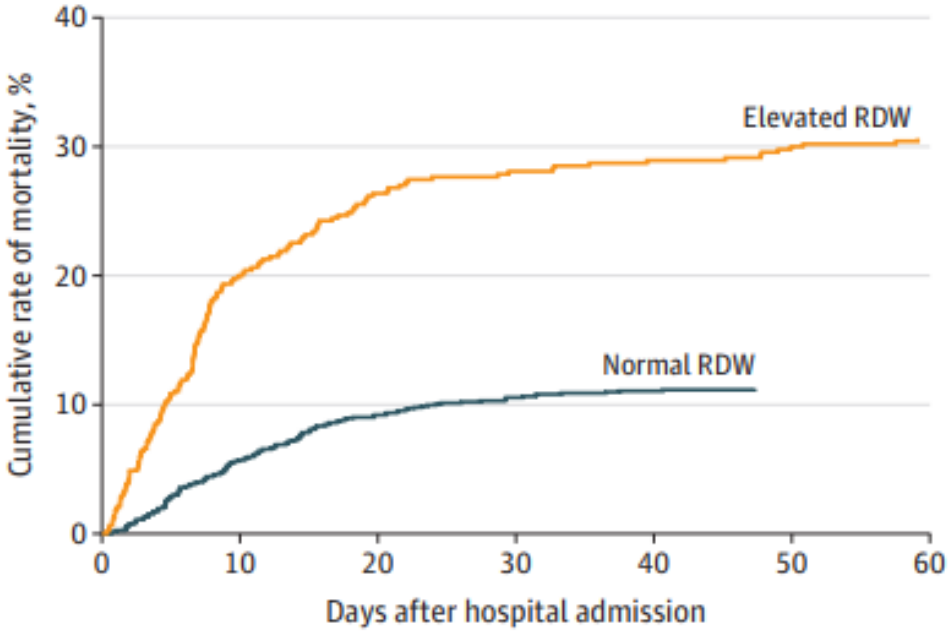
Comment: To my knowledge this is the first analysis of the molecular architecture of SARS-CoV-2 in two infection waves in a major metropolitan region. The findings will hopefully help us to understand the origin, composition, and possible trajectory of future waves, and the potential effect of the host immune response and effectiveness of antivirals on SARS- CoV-2. The Daily Briefing reviewed an article from Cell in July that highlighted the shift to G614 and did demonstrate higher viral loads but as this report shows no evidence of increased virulence. The genomics and 3-D images are excellent. This publication has not gone through peer review yet.

Association of Red Blood Cell Distribution Width with Mortality Risk in Hospitalized Adults With SARS-CoV-2 Infection

JAMA Netw Open published online September 23, 2020

The study tracked RDW for 1,641 adults admitted to one of four Boston-area hospitals from March 4 to April 28. Patients with high RDW at the time of hospital admission (RDW > 14.5%), or whose RDW increased during their hospital stay, had a higher mortality rate than patients with normal RDW. Patients who had RDW values above the normal range on hospital admission had a 2.7-times higher risk of dying, with a mortality rate of 31%, compared with 11% in patients who had normal RDW values. The association of RDW and increased mortality risk was observed across all age-groups and independent of demographic factors and comorbidities.

Although the mechanism behind COVID-19–elevated RDW is unclear, the authors suggest that it may reflect a clinical state in which RBC production and turnover have slowed in the setting of increased production and turnover of leukocytes or platelets such as would occur in inflammation.



No. at risk						
Normal RDW	1173	1106	1065	1049	1043	1041
Elevated RDW	468	374	344	336	332	328

Comment: While the study shows value for RDW as a diagnostic indicator for higher risk of complications, conclusions are limited by the small number of younger adults included in the study, its restriction to hospitalized patients, and the failure to capture socioeconomic data. More research is needed to better determine if RDW may be helpful for patient risk stratification.

The BAS²IC Score: A Useful Tool to Identify Patients at High Risk of Early Progression to Severe COVID-19

OFID published online September 23, 2020

The investigators used data collected from a prospective non-interventional cohort study, which included adult patients with confirmed COVID-19 hospitalized in March 2020 in Strasbourg University and Mulhouse hospitals in France. Severe disease was defined as admission to the intensive care unit (ICU) or death within 7 days after admission. Overweight and obesity were defined according to the WHO as a body mass index (BMI) of ≥25 kg/m² and ≥30 kg/m^2, respectively. Dyspnea was defined as a score >0 according to the modified Medical Research Council breathlessness scale. We chose an early time-point at day 7 as majority of ICU transfers or deaths occurred within the first week of hospitalization. They performed a Bayesian logistic regression to identify risk factors for severe COVID-19. All demographic, clinical and biological variables with a Pr(diff>0) <0.025 or a Pr(diff>0) >0.975 in the univariate analysis, or of clinical relevance, were included in the multivariate model. Variables collected were: age, sex, BMI, comorbidities (hypertension, diabetes, chronic lung disease, immunosuppression, chronic kidney disease, chronic heart failure, chronic hepatic failure, cancer, hematological malignancy, active smoking), pregnancy, symptoms at admission (fever, dyspnea, headache, chills, cough, fatigue, myalgia, chest pain, diarrhea, abdominal pain, confusion, anosmia or ageusia, oxygen level at admission), biological markers (C-reactive protein, neutrophil count, lymphocyte count, aspartate aminotransferase, alanine aminotransferase, hemoglobin level, platelet count, serum creatinine, serum sodium, lactate), radiological findings (chest computed tomography (CT) described as typical, bilateral involvement, ground-glass opacities, micronodules), treatments in the previous month (non-steroidal anti-inflammatory drugs, angiotensin-converting enzyme inhibitors, angiotensin-2 receptor antagonists, insulin, corticosteroids, hydroxychloroquine), antibiotic in the seven days prior to admission (beta lactam, macrolide).

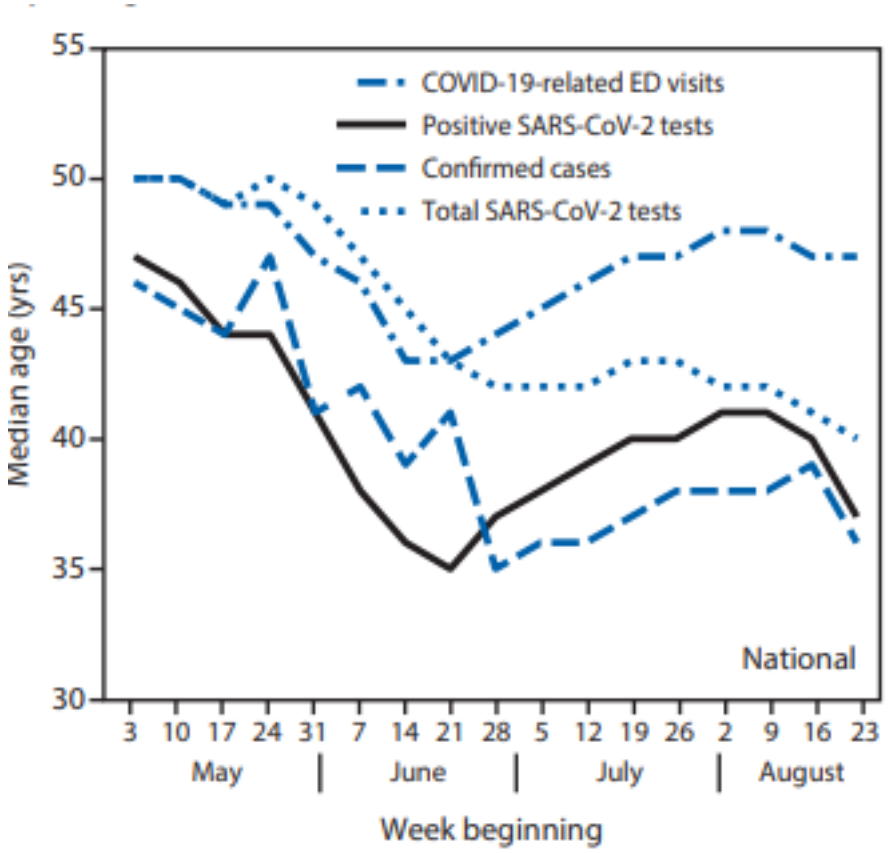
The factors associated with severe disease identified by multivariate analysis were: advanced age (β coefficient = 0.4), male sex (β coefficient = 0.735), overweight (BMI ≥ 25 and < 30 kg/m²: β coefficient = 0.490 ; BMI ≥ 30 kg/m²: β coefficient = 0.776), dyspnea (β coefficient = 0.913), inflammatory parameters at admission (C-reactive protein level ≥ 100 and < 200 mg/L (β coefficient = 0.489), C-reactive protein level ≥ 200 mg/L (β coefficient = 1.397), neutrophil count ≥ 8000 per µL (β coefficient = 0.747) and lymphocyte count < 1000 per µL (β coefficient = 0.364)) [3]. To build the score, these coefficients have been multiplied by 4 and rounded to the nearest half-integer. The score was evaluated (positive predictive value [PPV], negative predictive value [NPV], sensitivity, specificity) on the derivation cohort and clinically relevant cut offs (NPV >85% and PPV >60%) were determined.

Patients with a score ≤6 points could be considered at a low risk of developing severe disease, with an NPV of 87%; hence, this score may help to decide which patients can be discharged. On the contrary, those with score >14 were requiring rapid implementation of appropriate measures, such as hospitalization and consideration of specific therapeutics (e.g. dexamethasone, remdesivir)

a. BAS²IC score calculation	
Variables	Points assigned
BMI ≥ 25 kg/m^2 and < 30 kg/m^2	2
BMI ≥ 30 kg/m^2	3
Age > 65 years	1.5
Sex, male	3
Shortness of breath (dyspnea) at admission	3.5
Inflammatory parameters at admission	
Neutrophil count ≥ 8000 per µL	3
Lymphocyte count < 1000 per µL	1.5
CRP ≥ 100 mg/L and < 200 mg/L	2
CRP ≥ 200 mg/L	5.5
b. Interpretation of the score and suggested management	
≤6 points: low risk	Outpatient management may be possible.[a]
>6 and ≤14 points: intermediate risk	Consider hospitalization.[a] Outpatient management may be possible with close monitoring.
>14 points: high risk	Hospitalization required. Consider specific therapies (e.g. dexamethasone, remdesivir).

Comment: This score could be easily implemented in routine clinical practice to help clinicians classify patients at low risk and those at high risk, who should be closely monitored and thus, might benefit quickly from appropriate therapy. The score includes overweight parameter and certain inflammatory parameters, two important risk factors that have not been taken into account in previously published scores. [reviewed the last few months in the Daily Briefing] The use of inflammatory parameters is of particular relevance in terms of the results of dexamethasone administration for COVID-19 treatment. It may also serve as a predictor for use of antivirals and plasma. Some risk factors, such as high levels of D-dimer and IL-6, which have been associated with a poor outcome, were not considered when developing this score. D-dimer is readily available, but most sites do not do routine IL-6 levels. This simple score may be useful for triage of patients with SARS-CoV-2 infection in terms of admission or early treatment before progression.

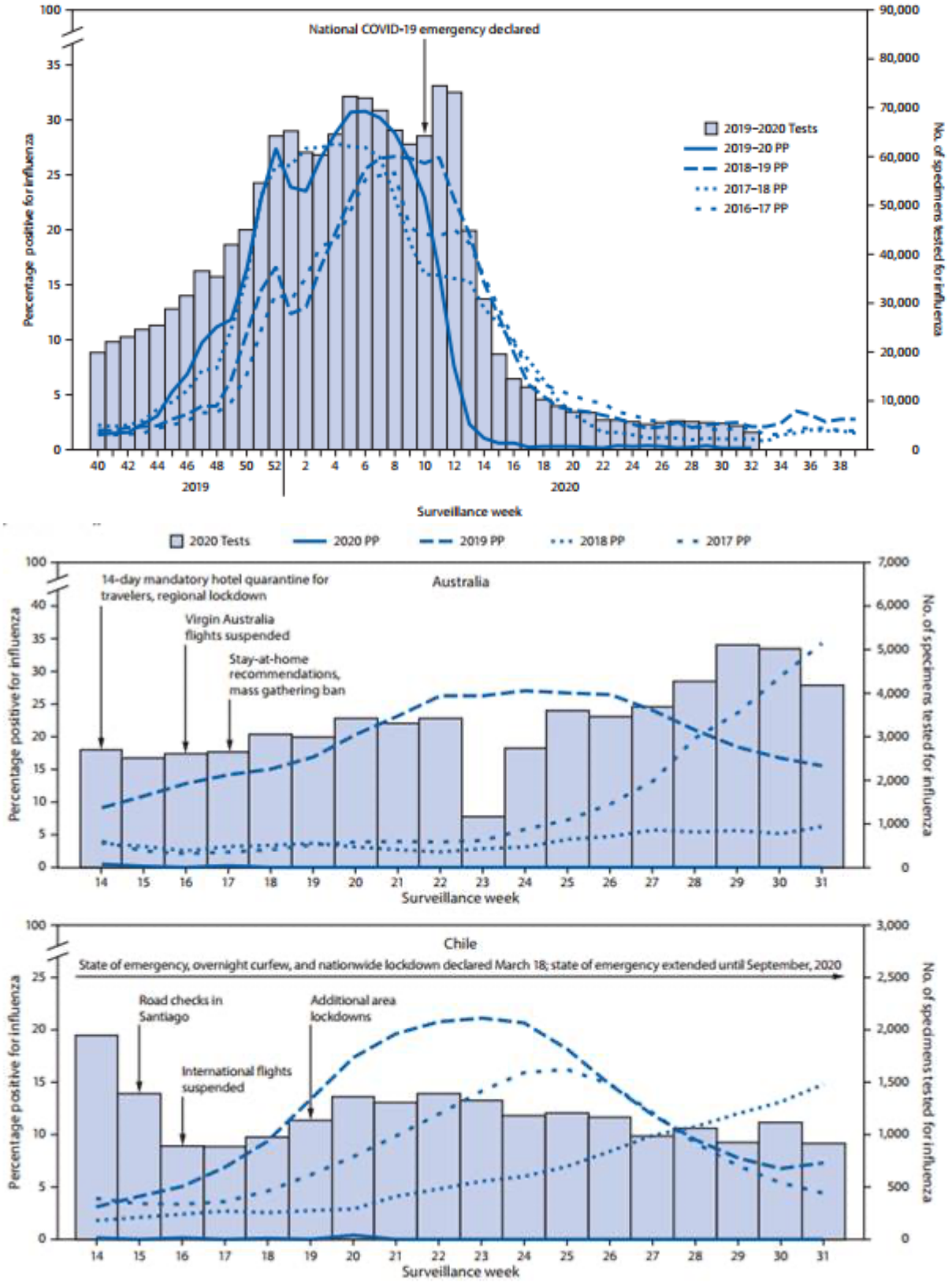
Changing Age Distribution of the COVID-19 Pandemic — United States, May–August 2020
MMWR published online September 23, 2020
That shift in the age of who is getting infected was highlighted today by the CDC in its latest Morbidity and Mortality Weekly Report. An analysis of age trends by the CDC COVID-19 Response Team found that, from June to August, COVID-19 incidence was highest among people aged 20 to 29, a trend seen in all regions of the country. Nationwide, the median age of COVID-19 cases declined from 46 years in May to 37 years in July and 38 years in August. Across the southern United States in June 2020, increases in percentage of positive SARS-CoV-2 test results among adults aged 20–39 years preceded increases among those aged ≥60 years by 4–15 days.



Comment: This report also provides evidence that younger adults can contribute to community transmission of COVID-19 to older adults. Strict adherence to community mitigation strategies and personal preventive behaviors by younger adults is needed to help reduce infection and subsequent transmission to persons at higher risk for severe illness. This includes restricting in-person gatherings and events, recommending mask use and social distancing in settings where persons socialize, implementing safe practices at on-site eating and drinking venues. We see this playing out across college campuses where infections have increased as student come back to campus. Several studies reviewed in the Daily Briefing the last few weeks have demonstrated the increased risk associated with indoor dining and bars.

Decreased Influenza Activity During the COVID-19 Pandemic — United States, Australia, Chile, and South Africa, 2020
MMWR 2020; 69:1305-1309
In the United States, influenza virus circulation declined sharply within 2 weeks of the COVID-19 emergency declaration and widespread implementation of community mitigation measures, including school closures, social distancing, and mask wearing, although the exact timing varied by location. The decline in influenza virus circulation observed in the United States also occurred in other Northern Hemisphere countries and the tropics, and the Southern Hemisphere temperate climates have had virtually no influenza circulation. (see graphs below)

FIGURE 1. Number of respiratory specimens tested and percentage testing positive for influenza, by year — United States, 2016–17 through 2019–20 seasons



Comment: Like SARS-CoV-2, influenza viruses are spread primarily by droplet transmission; the lower transmissibility of seasonal influenza virus (R0 = 1.28) compared with that of SARS-CoV-2 (R0 = 2–3.5) likely contributed to a more substantial interruption in influenza transmission. These findings suggest that certain community mitigation measures might be useful adjuncts to influenza vaccination during influenza seasons, particularly for populations at highest risk for developing severe disease or complications. It is difficult to separate the effect that individual community mitigation measures might have had on influenza transmission this season. There is evidence to support the use of masks by infected persons to reduce transmission of viral respiratory illnesses to others and growing evidence to support their use in the health care setting, in households, and in the community to protect the healthy wearer from acquiring infection. Data from the current pandemic may help answer critical questions about the effect of community mitigation measures on transmission of influenza or other respiratory diseases. Other factors, such as the sharp reductions in global travel or increased vaccine use, might have played a role in decreasing influenza spread; however, these were not assessed. Another important factor may be the concept of viral interference which might help explain the lack of influenza during a pandemic caused by another respiratory virus that might outcompete influenza in the respiratory tract. We saw this in 2009-2010 during the H1N1 pandemic.