Scientific Appraisal of COVID-19 Literature – January 7, 2021 1330

Spectrum Health contact Stefan Jovinge

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Article Title: ***A Neutralizing Monoclonal Antibody for Hospitalized Patients with COVID-19***

Source: *New England Journal of Medicine*

Clinical Field: *Infectious Disease*

Article Type: *Clinical Report*

Study Type: _____

Patient Group: *Inhouse COVID-19 patients*

Intervention: *Ly-CoV555, AB specific to the SPIKE protein of SARS-CoV2*

Reviewer	Stefan Jovinge
Study Design	Minor Concerns
Study Design Concerns	There was a a higher proportion of patients in the control group that had a more extensive mechanical ventilation (≥ 4 L/min). Authors conclude that Spec Ab is not more efficient to get patients to recover when they are given remdesivir as well than placebo. However 2/3 of the study population in each group did not get remdesivir treatment.
Main Results	Primary Outcome (day 5): Pulmonary Ordinal Outcome (1-7); 1. Independently engage in activities with minimal or no symptoms and 7 being death. The OR was calculated Primary efficacy outcome: Time to sustained recovery (discharge with no readmission within 14 days) Primary safety outcome: composite of death, serious adverse events or adverse events (grade 3 or 4) at day 5. No significant difference in Time to sustained recover or Hospital Discharge. No difference in safety or efficacy outcomes either.
Comments	Incl Crit: - Hospitalized - SARS-CoV2 positive Excl Crit: -Symptoms >12 days -Recipient of serum

Article Title: ***Antibody Status and Incidence of SARS-CoV-2 Infection in Health Care***

Source: New England Journal of Medicine

Clinical Field: Infectious Disease

Article Type: Clinical Report

Study Type: Retrospective Study

Patient Group: Healthcare workers

Intervention: Observational study

Reviewer	Stefan Jovinge
Study Design	Minor Concerns
Study Design Concerns	The follow-up was not confirmed to be equal or similar in the studied individuals.
Main Results	90.6% were seronegative at inclusion. 88 seroconverted during the observation period. 68% of the converted healthcare workers reported symptoms. NB. Seropositivity protects against COVID-19 in general but definitively against symptomatic disease
Comments	n=12,541 healthcare workers serum assessed for Spike- and nucleocapsid Abs: day 0 and then Within study study PCR tests were positive at significantly higher proportion of the healthcare workers that were seronegative at inclusion at study start compared to those who were seropositive. Incidence rate (seropositive vs seronegative)) 0.12 (95% 0.03-0.47, p=0.002). No symtomatic infections in seropositive healthcare workers.

Article Title: ***Comparative evaluation of clinical manifestations and risk of death in patients admitted to hospital with COVID-19 and seasonal influenza: cohort study***

Source: BMJ

Clinical Field: Infectious Disease

Article Type: _____

Study Type: _____

Patient Group: Pa

Intervention: _____

Reviewer	Stefan Jovinge
Study Design	Well Designed
Study Design Concerns	The major co-variates of concern age, race (white, black, and other), and sex; history of diseases such as chronic lung disease, cancer, cardiovascular disease, cerebrovascular disease, dementia, diabetes mellitus, hypertension, and peripheral artery disease; history of use of drugs such as statins, angiotensin converting enzyme inhibitors or angiotensin receptor blockers, and non-steroidal antiinflammatory drugs; smoking status (never, former, and current); and estimated glomerular filtration rate and body mass index (underweight <18.50, normal ≥18.50-<25, overweight ≥25-<30, and obese ≥30) were accounted for. Missing values <3% were replaced by mean imputation.
Main Results	COVID-19 vs seasonal influenza (OR, 95% conf interval): - AKI (1.52: 1.37 -1.69) - Renal Replacement Therapy (4.11: 3.13-5.40) - Incident insulin use (1.86: 1.62-2.14) - Severe septic shock (4.04: 3.38-4.83) - Vasopressor use (3.95: 3.46-4.51) - PE (1.50: 1.18-1.90) - DVT (1.50:1.20-1.88) - Stroke (1.62:1.17-2.24) - Myocarditis (7.82:3.53-17.36) - Arrythmias/sudden cardiac death (1.76: 1.40-2.20) - Rhabdomyolysis (1.84:1.54-2.18) - Death (4.97: 4.42-5.58) MV use (4.01:3.53-4.54) - ICU Admission (3.00:2.20-3.80)
Comments	In hospital patients with COVID19 Feb 2020 - June 2020 were compared with seasonal influenza between 2017 and 2019. Outcomes: - Risks of clinical manifestations - healthcare resource use (including use of mechanical ventilation, admission to intensive care, and length of stay) - death Estimated using a doubly robust approach to build propensity scores that were then used along with covariates to adjust the outcome models. COVID has more complications than seasonal flu of which cardiac and kidney are the most striking. Differences in rates of death per 100 patients between COVID-19 and seasonal influenza were most pronounced in people over 75 years of age with chronic kidney disease or dementia and those with black race and obesity, diabetes, or chronic kidney disease. Previous concern of hypertension as risk not confirmed as more prevalent in COVID-19 patients over that of seasonal flu patients.

Article Title: ***Efficacy and Safety of the mRNA-1273 SARS-CoV-2 Vaccine***

Source: New England Journal of Medicine

Clinical Field: Infectious Disease

Article Type: Clinical Study

Study Type: Proper RCT

Patient Group: Healthy people

Intervention: mRNA-1273 SARS-CoV-2 Vaccine

Reviewer	Stefan Jovinge
Study Design	Well Designed
Study Design Concerns	No serious concerns.
Main Results	_____
Comments	Phase 3 trial of MODERNA mRNA vaccine. 99 centers in US. n=30,420 (15,210x2) 96% received both doses. Baseline serologic/mRNA positivity: 2.2%. Serious COVID-19 in 30 cases with one death only in placebo. Efficacy in preventing COVID-19 illness 94.1%, which already was true (ad hoc) 2w after the first dose.

Article Title: ***Safety and Efficacy of the BNT162b2 mRNA COVID-19 Vaccine***

Source: New England Journal of Medicine

Clinical Field: Infectious Disease

Article Type: Clinical Study

Study Type: Proper RCT

Patient Group: Healthy people

Intervention: BNT162b2 mRNA COVID-19 Vaccine Pfizer

Reviewer	Stefan
Study Design	Well Designed
Study Design Concerns	_____
Main Results	Efficacy 2w after second dose 95%.
Comments	Triple blind RCT. n=43,548)21,720 vaccine, 21,728 placebo). Only 50% efficacy dose one until before two doses were given. That is lower than for the MODERNA vaccine (short term before second dose. No difference if both doses are given.

Article Title: ***REGN-COV2, a Neutralizing Antibody Cocktail, in Outpatients with COVID-19***

Source: New England Journal of Medicine

Clinical Field: Infectious Disease

Article Type: Clinical Study

Study Type: Proper RCT

Patient Group: nonhospitalized patients with COVID19

Intervention: Regn-CoV2 Ab at 2.4 g or 8.0g dose

Reviewer	Stefan Jovinge
Study Design	Major Concerns
Study Design Concerns	Only the first 275 patients of an ongoing trial. Despite low numbers reasonable well-balanced study- About half of the patients were Ab titer positive at baseline!
Main Results	Safety endpoint: No significance over placebo of treated. Significant reduction in viral dose if patients were baseline Ab negative. But no difference between the different doses.
Comments	Regeneron Ab efficacious in reducing viral load in pre treatment negative serology. for the highest titers all treated patients treated with the different doses of Ab were more efficiently avoiding titer >10^6/ml. Too many patients in the study so far having positive serology. Unclear number of days with symptoms between groups.

Article Title: ***SARS-CoV-2 Variant - United Kingdom of Great Britain and Northern Ireland***

Source: WHO Report

Clinical Field: Other

Article Type: International Document

Study Type: Other

Patient Group: COVID19

Intervention: Observational

Reviewer	Stefan Jovinge
Study Design	N/A
Study Design Concerns	WHO report.

Main Results	A total of 1108 cases infected with SARS-CoV-2 VUI 202012/01 have been detected in the United Kingdom as of 13 December 2020. The variant was picked up as part of an epidemiological and virological investigation initiated earlier in December 2020 following an unexpected rise in COVID-19 cases in South East England. It was characterized by a more than three-fold increase in the 14-day case notification rate from epidemiological week 41 to week 50 (5 October to 13 December 2020). On average, between 5 - 10% of all SARS-CoV-2 viruses have routinely been sequenced in the United Kingdom and 4% routinely sequenced in South East England since the beginning of the pandemic. From 5 October to 13 December, over 50% of isolates were identified as the variant strain in South East England. Retrospective analysis traced the first identified variant to Kent, South East England, on 20 September 2020, which was followed by a rapid increase of the same variant identified later in November. Most COVID-19 cases from whom this variant has been identified have occurred in people under 60 years of age. A new genetic variant has been discovered. The variant is defined by the presence of a range of 14 mutations resulting in amino acid changes and three deletions. Preliminary reports by the United Kingdom are that this variant is more transmissible than previous circulating viruses, with an estimated increase of between 40% and 70% in transmissibility (adding 0.4 to the basic reproduction number R0, bringing it to a range of 1.5 to 1.7). The herd immunity needed would with the new virus be about 50%.
Comments	The new virus is assumed be taken care of by the new vaccines due to the limited change in the antigen. This remains to be proven. However, the importance to bring down the R0 (the Re) by governmental actions and regulations will most likely be more important. So far there are no reports out there of the severity of the disease vs the more traditional virus.