

Scientific Appraisal of COVID-19 Literature – January 21, 2021 1315

Spectrum Health contact Stefan Jovinge

Document reviewed: 1/21/2021

Article Title: *Drug treatments for covid-19: living systematic review and network meta-analysis*

<https://www.bmj.com/content/370/bmj.m2980>

Source: BMJ

Clinical Field: Infectious Disease

Article Type: Clinical Report

Study Type: Other

Patient Group: COVID19 patients

Intervention: Multiple Interventional Trials meta-analysis

Reviewer	Stefan Jovinge
Study Design	Minor Concerns
Study Design Concerns	It is a meta-analysis for multiple treatments and thus for some treatments few studies are included.
Main Results	Of all treatments analyzed (azithromycin, colchicine, corticosteroids, favipiravir, hydroxychloroquine, hydroxychloroquine+azithromycin, IFN β , IFN γ , IFN κ +trefoil factor2, lopinavir+ritonavir, Nitazoxanide, rHG-CSF, Remdesivir, Tocilizumab, Umifenovir) against all outcomes (mortality, mechanical ventilation, adverse events, admission to hospital, viral clearance at 7 days, hospital stay duration, ICU LoS, Duration of Mechanical ventilation, Time to symptom relief, time to viral clearance, ventilator free days) the only effect that at least was moderately certain of a benefit was corticosteroids towards; mortality, mechanical ventilation, ventilator free days. No harm was detected.
Comments	In practical terms only corticosteroids effect towards mortality, mechanical ventilation, ventilator free days seem to be of benefit

Article Title: *Comparison of Saliva and Nasopharyngeal Swab Nucleic Acid Amplification Testing for Detection of SARS-CoV-2 A Systematic Review and Meta-analysis*

<https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2775397>

Source: JAMA Internal Medicine

Clinical Field: Other

Article Type: Clinical Report

Study Type: Retrospective Study

Patient Group: Patients sampled for PCR diagnostics

Intervention: Comparison NPH swab vs saliva

Reviewer	Stefan Jovinge
Study Design	Minor Concerns
Study Design Concerns	Not all included used the same technique for the diagnostics.
Main Results	<p>Pooled saliva sensitivity of 83.2% (95% CrI, 77.4%-91.4%) and a pooled saliva specificity of 99.2% (95% CrI, 98.2%-99.8%)</p> <p>Nasopharyngeal swab performed similarly with a pooled sensitivity of 84.8% (95% CrI, 76.8%-92.4%) and a pooled specificity of 98.9% (95% CrI, 97.4%-99.8%).</p> <p>In a comparison between the sampling types the the sensitivity didn't differ but there was a slight difference of specificity, favoring NPH.</p>
Comments	Saliva a reasonable good sampling fluid compared to NPH swab.

Article Title: *Multisystem Inflammatory Syndrome in U.S. Children and Adolescents*

<https://www.nejm.org/doi/full/10.1056/NEJMoa2021680>

Source: New England Journal of Medicine

Clinical Field: Critical Care

Article Type: Clinical Report

Study Type: Retrospective Study

Patient Group: Pats with Multi-inflammatory syndrome due to COVID < age 21

Intervention: Observational

Reviewer	Stefan Jovinge	Vinu Perinjilil
Study Design	Major Concerns	N/A
Study Design Concerns	Observational read out without any comparison towards non-multi inflammatory syndrome patients	<ul style="list-style-type: none"> - Case series data without a comparison group, does not attempt to infer risk factors or incidence of MIS-C (multi system inflammatory syndrome in children) - Pathogenesis of MIS-C not detailed
Main Results	<p>MI the hardest hit state. The peak of incidence about 5 weeks after testpositivity peak.</p> <p>Most prominent (freq) components of involvement: cardiac, GI, blood. But 71% had ≥ 4 organ systems involvement, 70% survival rate, 80% ICU need</p>	<p>This published case series characterizes 186 pediatric cases from March 2020 to May 2020 of MIS-C at participating health centers part of the "overcoming COVID-19 study"</p> <ul style="list-style-type: none"> - MIS-C is a consequence of immune mediated injury by COVID-19 based on lab markers of inflammation, timing of onset, and similarities to adults. - 70% of patients with MIS-C were RT-PCR positive for COVID-19, antibody testing or both and 30% had an epidemiological link to a COVID-19 individual. Most without underlying health issues (70%) - Median interval based on available data from symptoms of covid-19 to onset of MIS-C was 25 days. - Involved at least 4 organ systems in a majority of patients, mainly GI (92%) and the cardiovascular system (80%), hematologic (76%) and respiratory (74%) - 80% of patients required hospitalization - Out of deceased patients, half (2 out of 4) had underlying conditions -40% had fever for 4 or more days and 4 or 5

		Kawasaki like features. 1 in 12 have coronary artery aneurysms
Comments	Multi-inflammatory syndrome comes with multiorgan (≥ 4) impact and the need of ICU (80%) and good survival 70%. Survival is improving.	<ul style="list-style-type: none"> - Manifestation of MIS-C has a strong temporal link with COVID-19 through confirmation of nucleic acid or antibody testing in a majority of patients. Most patients infected 1-2 weeks prior to onset of MIS-C - Kawasaki like features were evident in patients however 60% of patients met incomplete criteria for this disease - Cardiac sequelae involvement should support providers considering Kawasaki guidelines for frequent echocardiograph imaging at 1-2 weeks and 4-6 weeks after treatment - There is a role for antiviral agents and immunomodulatory agents, depending on if immune dysregulation is evident or if organ damage is mediated by ongoing viral replication. This study does not evaluate effectiveness of these therapies but treatment methods should be guided by the method of organ damage

Article Title: *Efficacy of Tocilizumab in Patients Hospitalized with Covid-19*

<https://www.nejm.org/doi/full/10.1056/NEJMoa2028836>

Source: New England Journal of Medicine

Clinical Field: Infectious Disease

Article Type: _____

Study Type: Proper RCT

Patient Group: _____

Intervention: _____

Reviewer	Stefan Jovinge
Study Design	Minor Concerns
Study Design Concerns	Negative trial with no power calculation provided. n=161 tocilizumab and n= 81 placebo
Main Results	Prim end-point (intubation or death) negative as all secondary end-point.
Comments	No support for Tocilizumab as a general treatment which is also the current guidelines: no Tocilizumab outside a clinical study.

Article Title: *Vitamin D status and outcomes for hospitalised older patients with COVID-19*

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7456620/>

Source: Postgrad Med J

Clinical Field: Infectious Disease

Article Type: Clinical Study

Study Type: Retrospective Study

Patient Group: Patients with COVID19 inhouse >64 years

Intervention: None, prospective cohort w/o intervention

Reviewer	Stefan Jovinge
Study Design	Major Concerns
Study Design Concerns	Only n=105 and no power calculation
Main Results	Among patients with vitamin D deficiency, there was higher peak D-dimer level (1914.00 µgFEU/L vs 1268.00 µgFEU/L) (p=0.034) and higher incidence of NIV support and high dependency unit admission (30.77% vs 9.68%) (p=0.042). No increased mortality was observed between groups.
Comments	There is no support to supplement Vit D to COVID 19 patients. If a patient is vitD deficient, as for any other deficiency it might be helpful to supplement. However an interventional RCT of vit D supplementation is needed to recommend vit supplementation for older COVID19 patients.

Article Title: *Post-exertion oxygen saturation as a prognostic factor for adverse outcome in patients attending the emergency department with suspected COVID-19: A substudy of the PRIEST observational cohort study*

<https://emj.bmj.com/content/38/2/88>

Source: Emergency Medicine Journal

Clinical Field: Internal Medicine

Article Type: Clinical Report

Study Type: Other

Patient Group: Patients with COVID19 at ER

Intervention: None

Reviewer	Stefan Jovinge
Study Design	Major Concerns
Study Design Concerns	Not actively intervention of measuring post-exertion saturation. Thus, only selecting patients on which this was available and therefore a risk for selection bias. 54 patients were excluded because their data was "unfeasible" - unclear what that meant.
Main Results	Post-exertion saturation showed have a predictability of organ support or death at day 30 by AUC in ROC of 0,589 (95% CI 0,465 - 0.713). Also in a multivariable analysis postexertion sat didn't survive as an independent predictor, when baseline clinical assessment was built into the model
Comments	Thus, in conclusion saturation being an important measure to assess e.g the need for immediate oxygen therapy; post-exertion sat doesn't add anything beyond clinical judgement.