



CLINICAL EXPERTISE
NURSING PRACTICE
SYSTEMS INNOVATION

NACNS

National Association of Clinical Nurse Specialists

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Medications for Covid (Nov 2021 edition)

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HENRY FORD
ALLEGIANCE HEALTH

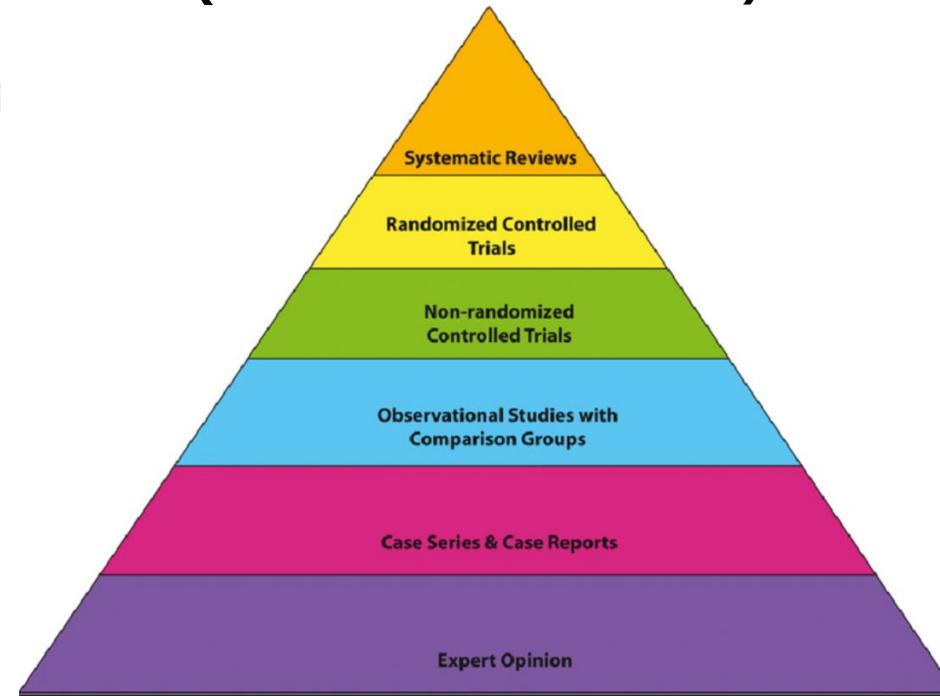
Goals and Objectives

- Discuss difficulties surrounding literature evaluation and Covid
- Discuss medications used in Covid



Covid literature

- Over 185,000 articles published (as of Nov 2021)
 - Various quality of research and reporting
 - REMAP CAP
 - RECOVERY Collaborative
 - NIH treatment guidelines
- = 357 pages



Example

- Intravenous high-dose vitamin C for the treatment of severe Covid-10: study protocol for a multicentre randomized controlled trial (BMJ June 25, 2020)
- Trials Test Mushrooms and Herbs as Anti-covid-19 agents (JAMA Nov 3, 2021)



REMAP CAP

- REMAP = randomized embedded multifactorial adaptive platform
- Ongoing, international, multicenter, open-label trial
- Combines adaptive platform with point of care
- Multifactorial statistical model allows comparison of multiple interventions across multiple subgroups
- Over time allows for preferential assignment to interventions showing promise at interim analysis



BMJ and WHO recommendations

Population

This recommendation applies only to people with these characteristics:



Disease severity



Non-severe	Severe	Critical
Absence of signs of severe or critical disease	Oxygen saturation <90% on room air Signs of pneumonia Signs of severe respiratory distress ⁱ	Requires life sustaining treatment Acute respiratory distress syndrome Sepsis Septic shock

Interventions

Casirivimab and imdevimab
Neutralising monoclonal antibodies


Recommendation in favour (conditional)
For those with highest risk of hospitalisation ⁱ


Recommendation in favour (conditional)
For those with seronegative status ⁱ
Assessed by accurate and rapid testing

IL-6 receptor blockers
Interleukin-6 receptor blockers


Recommendation in favour (strong)



Steroids

- Choice of steroids
- Mechanism decrease pulmonary inflammation

Steroid	Approximate equivalent dose (mg)	Anti-inflammatory potency	Mineralocorticoid Potency
Dexamethasone	0.75	25	0
Methylprednisolone	4	5	0
Hydrocortisone	20	1	1
Prednisone	5	4	0.8



Steroids in Covid Hydrocortisone

- REMAP CAP domain
- Fixed 7 day course vs shock dependent dose vs none
- 7 day = 50-100 mg every 6 hours
- Shock dependent = 50 mg every 6 hours while in shock
- Domain closed early due to dexamethasone data release
- Outcome = organ support free days within 21 days
- 93% (7 day) compare 80% (shock) compared to none

Steroid Dexamethasone

- 7 randomized trials = reduced short term mortality
- Recovery trial = 6 mg/day x 10 days
- 6 other trials = 12 mg/day
- COVID STEROID 2 trial
 - Compared 6 mg to 12 mg dose
 - No statistical difference

Steroid Methylprednisolone

- 6 mg dexamethasone = 32 mg methylprednisolone
- Multiple studies showing efficacy of methylprednisolone
- Comparison study showed equal efficacy
- Drug shortages
- Familiarity

Steroid outpatients

- Not currently recommended
 - Prednisone
 - Methylprednisolone (oral)
 - Budesonide (inhaled)



Monoclonal Anti-bodies (Regen Cov)

- Non-hospitalized patients with mild to moderate disease
- Hospitalized = insufficient evidence effect on outcome
- HFHS = casirivimab 600 mg + imdevimab 600 mg (Regen Cov)
- Within 10 days of symptom onset



IL-6 inhibitors (tocilizumab)

- Mechanism
 - IL-6 proinflammatory cytokine
 - Elevated levels associated with increased incidence of ARDS
- Study summaries
 - REMAP CAP and RECOVERY showed mortality benefit in severely ill patients with rapid deterioration, increased O₂ requirements, and significant inflammatory response
 - 29% of patient received second dose
 - Doses administered within 24 hours of requiring mechanical ventilation



IL-6 inhibitors (tocilizumab)

- Dose = 8 mg/kg rounded to nearest vial size
- Avoid use
 - Immunosuppressed
 - ALT > 5 times upper limit of normal
 - Signs and symptoms of infection
 - ANC < 500
 - Platelet < 50



Jak inhibitor (baricitinib)

- Immunomodulators
- Janus Kinase inhibitors
 - Prevent phosphorylation of key proteins
 - Decrease cellular response to inflammatory cytokines (e.g. IL-6)
- Baricitinib or tofacitinib
- Do not use if signs/symptoms infection
- Oral only



Jak inhibitor (baricitinib)

- Study summaries
 - Most effective mild moderate with elevated inflammatory markers
 - Insufficient evidence with invasive mechanical ventilation
 - Used on combination with corticosteroids
 - Increased risk of infection, reactivation of HSV, myelosuppression, elevated LFT, GI perforation



Remdesivir

- Antiviral = prevents viral replication
- Effective in patients with mild moderate disease
- Use in combination with steroids
- No difference outcome mechanical ventilation
- Contraindicated elevated LFT (> 10 times normal) or renal failure with CrCl < 30 ml/min



Ivermectin

- Mechanism
- Suppression of viral transmission by inhibiting transport proteins
- May have anti-inflammatory properties
- Doses
 - In vitro data indicates doses required may be 100-fold greater than currently approved doses
 - Neurotoxicity, tetatogenic



Ivermectin

- Study summaries
 - Studied previous dengue, Zika, HIV, and yellow fever = no clinical benefit
 - Multiple small studies
 - Combination with other agents
 - NIH = insufficient evidence
 - Warning against using ivermectin intended for animals



Vitamin C (ascorbic acid)

- Ascorbic acid
- Mechanism
 - Antioxidant
 - Cofactor for production of catecholamines, vasopressin, and cortisol
 - Inhibition of proinflammatory cytokine production (IL-6)

Vitamin C (ascorbic acid)

- Dose
 - 1000 mg up to 24 grams
 - 1 vial Vitamin C = 500 mg
- Study summaries
 - High dose may improve oxygenation
 - No difference in mortality, mechanical ventilation, or SOFA scores
 - NIH treatment guidelines= insufficient evidence

Antibiotics and antifungal

- Potential secondary infection
- New lobar infiltrate, leukocytosis, elevated lactate, microbiologic data, shock
- Reassess daily and discontinue when no longer indicated (7-10 days unless other indications)



Anticoagulation

- COVID associated with coagulation abnormalities
 - Full dose versus prophylaxis
 - Full dose if other indication for anticoagulation (e.g. PE)
- Prophylaxis enoxaparin 1 mg/kg/day versus 40 mg/day
 - No difference efficacy (all cause mortality and VTE)
 - Slightly increased bleeding and thrombocytopenia in high dose group

Heparin dosing with Covid

- MUE heparin dosing patients with COVID
 - Higher degree of variability
 - Higher number of dose adjustments
 - Longer time requirement to get therapeutic





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