

# COVID CLINICAL UPDATE ROUNDS

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OCT 8, 2020

# COVID UPDATE ROUNDS

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- Recurring
- Interactive
  - Slido/**#MedicalStaffCOVID**
- Choose your own adventure (send us requests for topics)
  - [medstaffengagement@viha.ca](mailto:medstaffengagement@viha.ca), omar.ahmad@viha.ca
- Knowing local response is paramount

# PREVIOUSLY ON RECURRING ROUNDS

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- Cases remain low on the Island
  - 0 hospitalized, 0 in ICU, 11 active cases
- Canadian ICU Mortality:
  - ICU 26%
  - Ventilated 31%
  - Vancouver 15 (20)%
  - RJH 20%

# PREVIOUSLY ON RECURRING ROUNDS

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- Critical care management:
  - Look at the work of breathing and physiology
  - HFNC --> NIV → IMV
  - Standard fare ARDS mgt
    - Low TV, conservative/judicious fluids
    - Consider proning, higher PEEP trials in severe ARDS
    - Look at the driving pressure and maintain less than 15
      - $DP = P_{lat} - PEEP$
    - L vs H phenotypes?

# PREVIOUSLY ON RECURRING ROUNDS

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- Critical care management:
  - Look at the work of breathing and physiology
  - HFNC → NIV → IMV → ECLS

# PREVIOUSLY ON RECURRING ROUNDS

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- Critical care management:
  - Standard fare ARDS mgt
    - Low TV, conservative/judicious fluids
    - Consider proning, higher PEEP trials in severe ARDS
    - Look at the driving pressure and maintain less than 15
      - $DP = P_{lat} - PEEP$
    - L vs H phenotypes?
      - Measure the lung compliance

# PREVIOUSLY ON RECURRING ROUNDS

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- Critical Care Management:
  - Adam Thomas has seen a lot of COVID
  - Beware the PTX
  - Bronchs and Trach appear safe

# OBJECTIVES, OCT 8TH

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- Be aware of cohort protocols
- Be updated on epidemiology
- Review recent BC CDC Code blue 'draft' protocol
- Be aware of mask policy for patients and visitors
- Be aware of COVID research occurring at Island Health
- Review VTEp and VTE therapy
- Be updated on recent critical care literature



# TODAY'S SPEAKERS AND SUPPORT STAFF

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- Dr. Omar Ahmad
- Dr. Gordon Wood
- Dr. Shavaun MacDonald
- Dr. Adam Thomas
- Dr. Daniel Ovakim
- Matt Erickson
- Lisa Young
- Victoria Schmid
- Tara Holmes
- Kyja Levitt

# DISCLOSURES/CONFLICTS OF INTEREST

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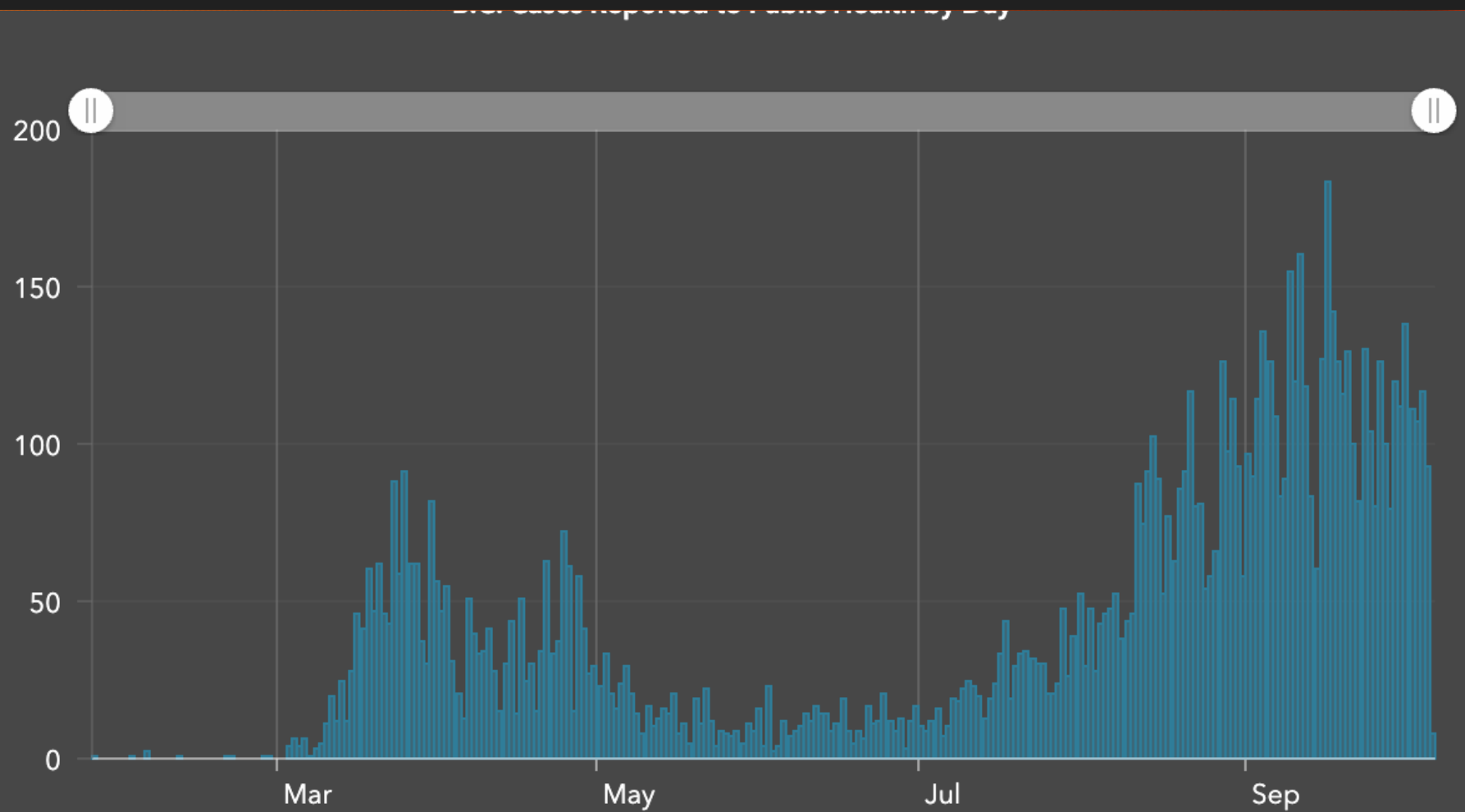
- None

# COVID 19 UPDATE

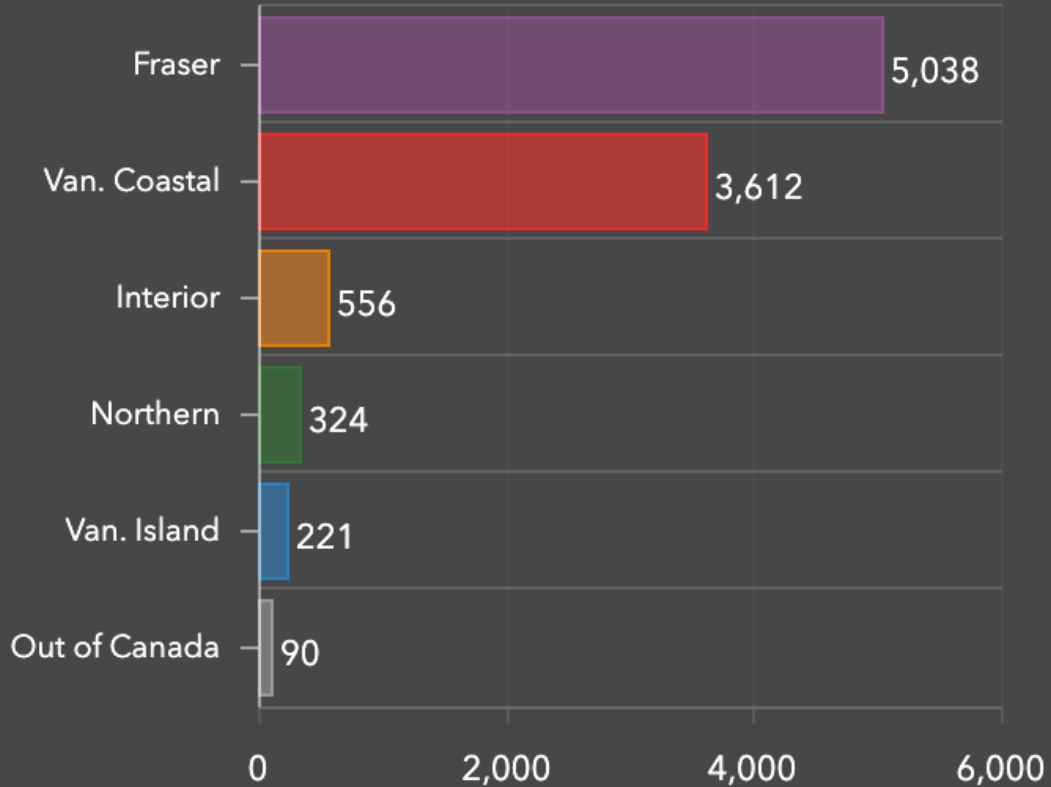
OCT. 7, 2020

# EPIDEMIOLOGY

# COVID CASES BC



### Total Cases Reported by Health Authority



Total Cases  
**9,841**

Laboratory Diagnosed

**9,665**

Epi-Linked

**176**

Currently Hospitalized



**71**

Total to Date: 809

Currently Admitted to ICU



**16**

Confirmed Deaths



**244**

Recovered



**8,184**

Last Update

**10/6/2020, 4:30 PM**



New Cases



Active Cases



Total Cases  
 **221**

Laboratory Diagnosed  
**217**

Epi-Linked  
**4**

Currently Hospitalized



Total to Date: 25

Currently Admitted to ICU



Confirmed Deaths



Recovered

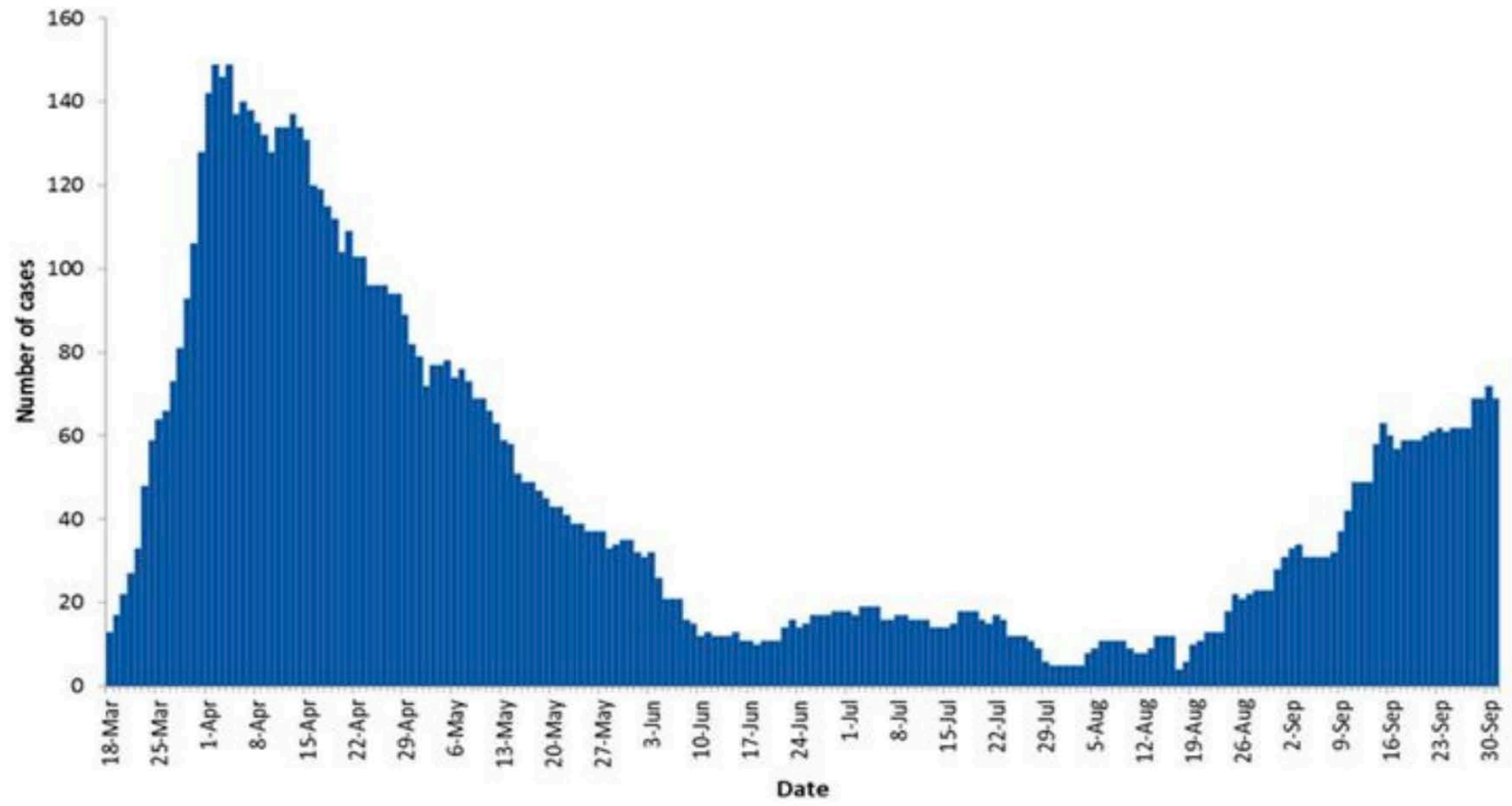


Last Update  
**10/6/2020, 4:30 PM**



# Number of COVID-19 Cases in Hospital by Day, BC, March 18 - October 1, 2020

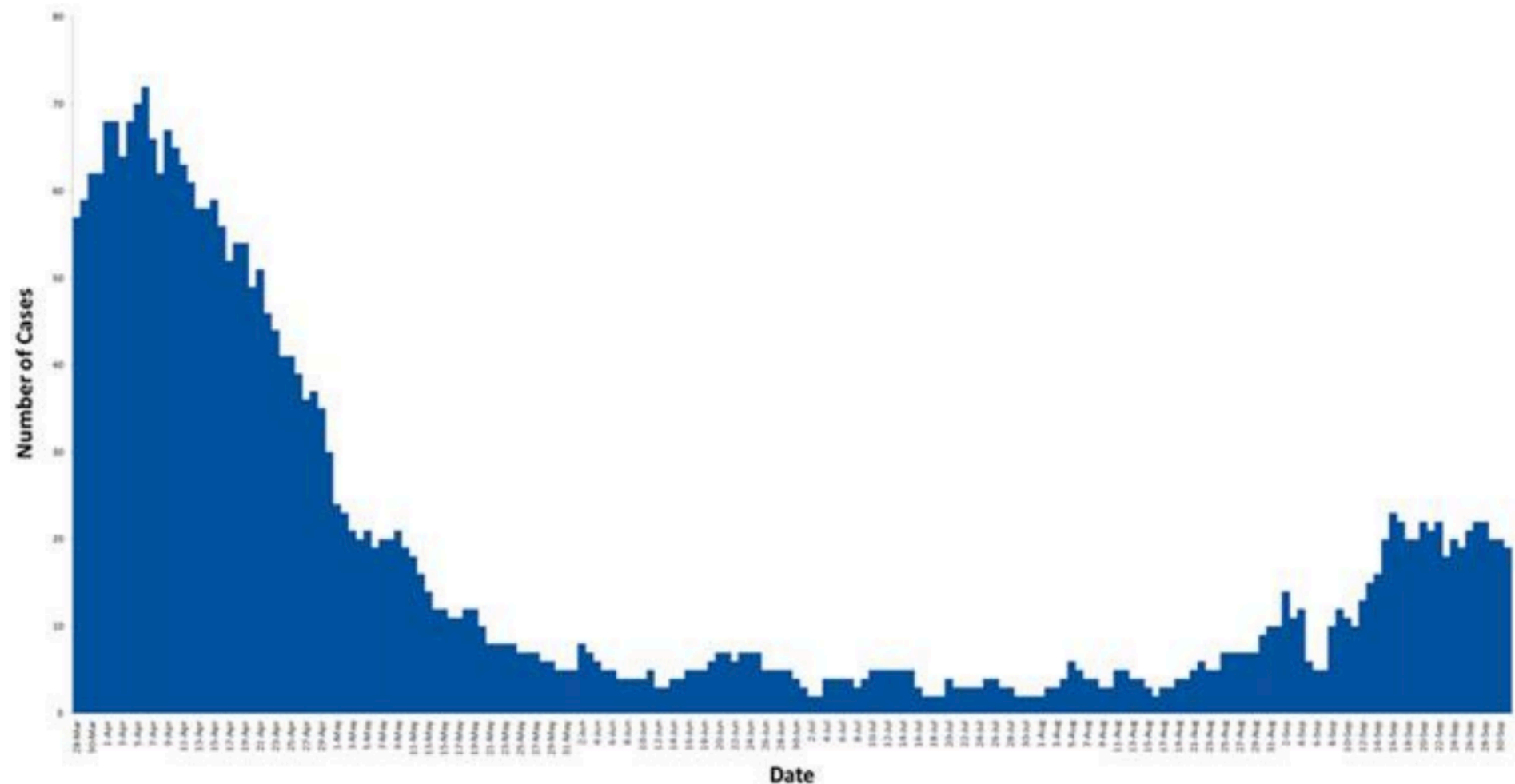
The number of cases currently in hospital is lower than in April.



Data available starting March 18. For dates with no data available (April 12; Sundays from May 10 onwards; and Saturdays from June 7 onwards).

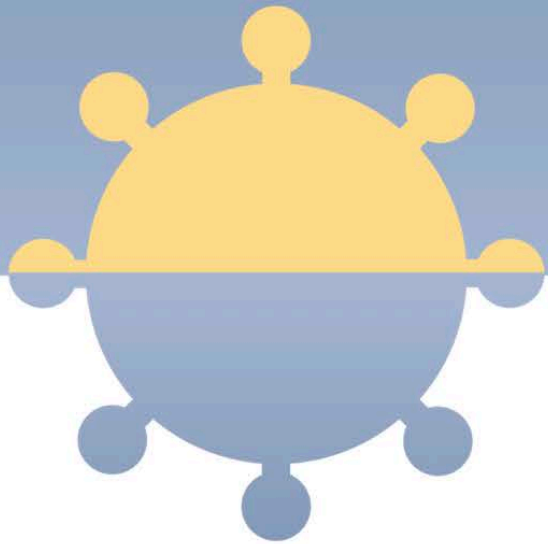
# Total COVID-19 Cases in Critical Care by Day, BC, March 25 – October 1, 2020

The number of cases currently in critical care is lower than in April.



Data source: PHSA October 1, 2020.  
Note: critical care data may change over time due to small adjustments and improvements in data quality.

# CODE BLUE RESPONSE



# Coronavirus COVID-19

BC Centre for Disease Control | BC Ministry of Health



Infection Prevention and Control (IPC) Protocol During Code Blue for Adult Patients at **Unknown** for COVID-19 in a Time of Low Community Covid-19 Prevalence

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In patients with circulatory arrest, *early* bystander CPR improves survival and neurological outcomes. The likelihood of a patient having COVID-19 outside of designated COVID-19 units in acute care is low. Patients are risk-assessed on admission to health authority facilities for the possibility of COVID-19.

Time-motion studies by Alberta Health Services<sup>2</sup> suggest that it takes at least 3 minutes to don airborne PPE. Delay in commencing or stopping CPR may decrease the survival rate by at least 2%<sup>3</sup>. It is therefore advised to minimize any delay or interruptions to CPR.

## A. Location/Environment

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- Patients may experience a Code Blue/medical emergency in any part of the hospital. This includes the emergency department (ED), intensive care unit (ICU), ward, operating room, outpatient areas or common areas.
- Minimizing the amount of people present during a Code Blue enhances the safety and effectiveness of the care provided and limits the health care workers (HCWs) potential exposure to pathogens.
- As with any Code Blue, the environment should be optimized to provide adequate access to the patient and enhance safety. This may include moving the patient to a designated resuscitation area.
- When transporting patients during a cardiac arrest (e.g. from ambulance to resuscitation area) ensure CPR and assisted ventilations through a bag valve mask (BVM) and high efficiency hydrophobic filter, supraglottic airway or secured airway continues uninterrupted by HCWs wearing airborne and contact PPE (N95 respirator, gown, gloves and eye protection).
- CPR should not be interrupted to transport the patient.

## B. Patient COVID-19 Risk Assessment

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- All patients entering a hospital should be screened with an appropriate risk assessment tool, such as the PCRA tool, including all outpatient areas. Those screened as at risk (red) should be immediately isolated and referred for evaluation for COVID-19.
- All patients risk screen status should be displayed clearly on their chart and communicated with their treating team.
- All patients should be regularly re-evaluated on their COVID-19 risk status and the chart updated and transferred to an appropriate area if suspected or confirmed.
- The patient's COVID-19 risk screen status should be known at the point of commencing basic life support (BLS). However it is not always known, this should not delay the commencement of chest compressions.

## C. Patient Assessment – Determining if a Code Blue Should be Activated

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- Each facility should have a process for identifying the code status or advanced care directive of admitted patients. If there is uncertainty of the code status, a code blue should be activated inline with the patient assessment.
- Follow local guidelines, policies and training when activating a Code Blue.
- The HCW assessing the patient should wear standard PPE for the patient as outlined by local guidelines.



## D. Initiating CPR

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- Prior to commencing chest compressions a covering (surgical mask, cloth or oxygen mask) should be placed over the patients nose and mouth to minimize the risk of exposure to droplets.
- For patients who are **not suspected or not known to be COVID-19 positive**, CPR should be commenced as per local CPR guidelines.
- When responding to a Code Blue:
  - a. The first person on scene should commence chest compressions (after calling for assistance) wearing their current level of PPE (i.e. the first responder **should not** change/don PPE prior to commencing CPR).
  - b. If there is uncertainty about the patients COVID-19 status the first person on scene should continue chest compressions until assistance arrives before donning additional PPE.

## PATIENT RISK CATEGORY TABLE:

<i>Does the patient have a risk factor for COVID-19 exposure?</i>	<i>Does the patient have new onset COVID-19 like symptoms that cannot be explained otherwise?</i>	<i>COVID-19 test result (if applicable)</i>	<b>Risk Category</b>
NO	NO	NOT REQUIRED	GREEN
NO	YES	NEGATIVE	GREEN
YES	NO	NEGATIVE	GREEN
YES	YES	NEGATIVE	GREEN
YES	UNKNOWN	NEGATIVE	GREEN
UNKNOWN	UNKNOWN	PENDING/NOT DONE	YELLOW
YES	UNKNOWN	PENDING/NOT DONE	RED
NO	UNKNOWN	PENDING/NOT DONE	RED
YES	YES*	PENDING/NOT DONE	RED
NO	YES	PENDING/NOT DONE	RED
YES	YES	PENDING/NOT DONE	RED
-	-	<b>POSITIVE</b>	RED

## E. Airway Management During a Code Blue

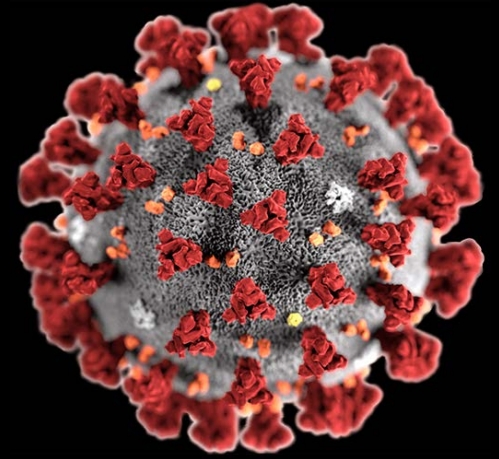
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- If intubation is required for:
  - Patients with low risk of COVID-19 (GREEN) the treating team should don droplet precaution PPE (surgical mask, eye protection, gown and gloves) prior to the procedure
  - Patients with unknown risk of COVID-19 (YELLOW) the treating team should don airborne and contact PPE (N95 respirator, gown, gloves and eye protection) prior to the procedure.
- If assisted ventilation via a BVM is required prior to intubation for:
  - Patients with low risk of COVID-19 (GREEN) the treating team should don droplet precaution PPE (surgical mask, eye protection, gown and gloves) prior to commencing breaths.
  - Patients with unknown risk of COVID-19 (YELLOW) the treating team should don airborne PPE (N95 respirator, gown, gloves and eye protection) prior to commencing breaths.

# Critical Care Rounds

## COVID-19: An Update

### Therapeutics & Clinical Trials



October 8, 2020



## **Conflict of Interests**

- No relevant conflicts of interest

### **Outline**

1. Review the current recommendations for Antimicrobial and Immunomodulatory Therapy for COVID-19
2. (Re)Introduce the Clinical Trials and research occurring at Island Health for inpatients with COVID-19 (next session)
  - CATCO
  - CONCOR
  - ATTACC

# 1. COVID Therapeutics



Rita Panahi

@RitaPanahi

Professor of epidemiology at Yale School of Public Health Dr Harvey Risch said we'd slash COVID-19 death rate dramatically if we prescribed hydroxychloroquine & zinc to high risk patients early in the infection.

Interview on NOW @SkyNewsAust



The key to defeating COVID-19 already exists. Contrary to what you hear, there is clear evidence of the efficacy of hydroxychloroquine.

newsweek.com

5:15 PM · Sep 5, 2020

2.5K ⚡ See the latest COVID-19 information on Twitter



Rep Andy Biggs

@RepAndyBiggsAZ

Arizona should embrace President Trump's plan to give Americans the right to try hydroxychloroquine.



6:55 PM · Sep 5, 2020



AssocAmerPhys&Surg

@AAPSONline

Canadian doctor: Smear against Hydroxychloroquine drug in stopping COVID 'needs to stop' | News | LifeSite



DR. KULVINDER KAUR GILL

Canadian doctor: Smear against Hydroxychloroquine drug in stopping ... Ontario-based doctor Kulvinder Gill said bans on the drug have caused an 'unprecedented violation of the doctor-patient relationship.'

lifesitenews.com

7:54 PM · Sep 5, 2020

470 ⚡ See the latest COVID-19 information on Twitter

# WUWT Watts Up With That?

The world's most viewed site on global warming and climate change

Daily Coronavirus Graph Page Home About Climate FAIL Files Climategate Reference Pages

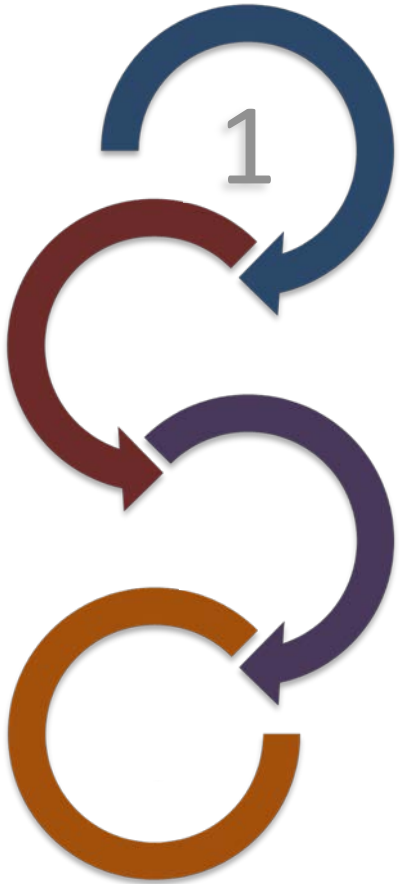
## Hydroxychloroquine in COVID-19 Treatment, Actual Usage in the USA

Leo Goldstein / 2 weeks ago August 24, 2020

Preprint. August 23, 2020.

Key Words: hydroxychloroquine, COVID-19, SARS-CoV-2, Wuhan





## **Therapeutic Recommendations**

- Antiviral therapy
- Antibacterial therapy
- Immunomodulatory therapy
- Other therapies

**Antimicrobial and Immunomodulatory Therapy in Adult Patients with COVID-19**

last updated August 24th, 2020

Recommendations in this document apply to patients > 18 years of age. For details including special populations, refer to the complete summary document.	There is limited clinical evidence to guide antiviral therapy for patients with COVID-19.			
Specialist consultation (e.g., Critical Care, Infectious Disease, Hematology, or Rheumatology) is recommended if any investigational treatment is offered to a patient with COVID-19 outside of approved clinical trials. Informed consent should be obtained from the patient or the substitute decision maker.				
SEVERITY OF ILLNESS	ANTIVIRAL THERAPY Unless otherwise specified, recommendations include antivirals alone or in combination	ANTIBACTERIAL THERAPY	IMMUNOMODULATORY THERAPY	OTHER THERAPEUTICS
<b>Critically Ill COVID-19 Patients</b> <i>Hospitalized, ICU-based</i> Patients requiring mechanical ventilatory and/or vasopressor/inotropic support	<p><b>Chloroquine</b> or <b>Hydroxychloroquine</b> is <b>not</b> recommended for the treatment of COVID-19</p> <p><b>Lopinavir/ritonavir</b> is <b>not</b> recommended outside of approved clinical trials</p> <p><b>Remdesivir*</b> has received conditional approval by Health Canada for the treatment of COVID-19. Remdesivir shortened time to clinical recovery but failed to show any survival benefit in the ACTT-1 trial. In British Columbia availability of remdesivir remains limited to clinical trials at this time.</p> <p><b>Ribavirin/Interferon</b> is <b>not</b> recommended outside of approved clinical trials</p>	<p><b>Ceftriaxone 1-2 g IV q24h x 5 days</b> is recommended if there is concern for bacterial co-infection (alternative for severe beta-lactam allergy: moxifloxacin 400 mg IV q24h x 5 days)</p> <p><b>Azithromycin 500 mg IV q24h x 3 days</b> is recommended if atypical bacterial infection is suspected (not required if on moxifloxacin)</p> <p>De-escalate on the basis of microbiology results and clinical judgment</p>	<p><b>Dexamethasone 6 mg IV/PO q24h for up to 10 days is strongly recommended</b> (RECOVERY trial), unless higher doses are indicated**. If Dexamethasone is not available, methylprednisolone 30 mg IV q24h is the preferred alternative.</p> <p><b>Tocilizumab</b> or <b>sarilumab</b> is <b>not</b> recommended outside of approved clinical trials; where clinical trials are not available, expert consultation is recommended (Infectious Diseases, Hematology, Rheumatology)</p>	<p><b>Enoxaparin 30 mg SC q12h</b> is suggested for VTE prophylaxis</p> <p><b>ACE inhibitors</b> and <b>ARBs</b> should not be discontinued solely on the basis of COVID-19</p> <p><b>NSAIDs</b> should not be discontinued solely on the basis of COVID-19</p>
<b>Severely Ill COVID-19 Patients</b> <i>Hospitalized, ward-based, long-term care</i> Patients requiring supplemental oxygen therapy	<p><b>Chloroquine</b> or <b>Hydroxychloroquine</b> is <b>not</b> recommended for the treatment of COVID-19</p> <p><b>Lopinavir/ritonavir</b> is <b>not</b> recommended outside of approved clinical trials</p> <p><b>Remdesivir*</b> has received conditional approval by Health Canada for the treatment of COVID-19. Remdesivir shortened time to clinical recovery but failed to show any survival benefit in the ACTT-1 trial. In British Columbia availability of remdesivir remains limited to clinical trials at this time.</p> <p><b>Ribavirin/Interferon</b> is <b>not</b> recommended outside of approved clinical trials</p>	<p>Antibacterial therapy is <b>not</b> routinely recommended outside of approved clinical trials unless other indications justify its use (e.g., suspected bacterial co-infection in COVID-19 positive patients)</p>	<p><b>Dexamethasone 6 mg IV/PO q24h for up to 10 days is recommended</b> (RECOVERY trial), unless higher doses are indicated**. If Dexamethasone is not available, methylprednisolone 30 mg IV q24h or prednisone 40 mg PO q24h are the preferred alternatives. If dexamethasone supplies are limited, they should be reserved for critically ill patients.</p> <p><b>Tocilizumab</b> or <b>sarilumab</b> is <b>not</b> recommended outside of approved clinical trials</p>	<p><b>Enoxaparin 30 mg SC q12h</b> should be considered for VTE prophylaxis in severely ill hospitalized patients</p> <p><b>ACE inhibitors</b> and <b>ARBs</b> should not be discontinued solely on the basis of COVID-19</p> <p><b>NSAIDs</b> should not be discontinued solely on the basis of COVID-19</p>
<b>Mildly Ill COVID-19 Patients</b> <i>Ambulatory, outpatient, long-term care</i> Patients who do not require supplemental oxygen, intravenous fluids, or other physiological support	<p><b>Chloroquine</b> or <b>Hydroxychloroquine</b> is <b>not</b> recommended for the treatment of COVID-19</p> <p><b>Lopinavir/ritonavir</b> is <b>not</b> recommended outside of approved clinical trials</p> <p><b>Remdesivir*</b> is <b>not</b> recommended outside of approved clinical trials</p> <p><b>Ribavirin/Interferon</b> is <b>not</b> recommended outside of approved clinical trials</p>	<p>Antibacterial therapy is <b>not</b> routinely recommended outside of approved clinical trials unless other indications justify its use (e.g., suspected bacterial co-infection in COVID-19 positive patients)</p>	<p><b>Corticosteroids</b> are <b>not</b> recommended outside of approved clinical trials unless otherwise indicated**</p> <p><b>Tocilizumab</b> or <b>sarilumab</b> is <b>not</b> recommended outside of approved clinical trials</p>	<p><b>ACE inhibitors</b> and <b>ARBs</b> should not be discontinued solely on the basis of COVID-19</p> <p><b>NSAIDs</b> should not be discontinued solely on the basis of COVID-19</p>
<b>Prophylaxis</b> Patients with known COVID-19 exposure	<b>Chloroquine</b> or <b>hydroxychloroquine</b> is <b>not</b> recommended for prophylaxis in patients with known COVID-19 exposure			

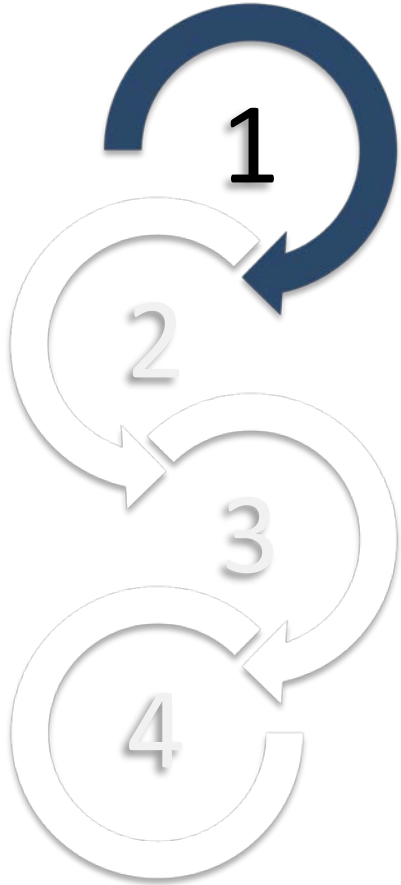
\* Currently unavailable in Canada

\*\* e.g., asthma exacerbation, refractory septic shock, history of chronic steroid use, obstetric use for fetal lung maturation

This document is dynamic and addresses key therapeutic areas of concern for clinicians. The complete and most up-to-date version of the guidelines is available at <http://www.bccdc.ca/health-professionals/clinical-resources/covid-19-care/clinical-care/treatments>

## Antiviral Therapy

- Chloroquine and Hydroxychloroquine
- Lopinovir/Ritonovir (Kaletra®)
- Ribavirin/Interferon
- Remdesivir



### ANTIVIRAL THERAPY

Unless otherwise specified, recommendations include antivirals alone or in combination

**Chloroquine** or **Hydroxychloroquine** is **not** recommended for the treatment of COVID-19

**Lopinavir/ritonavir** is **not** recommended outside of approved clinical trials

**Remdesivir\*** has received conditional approval by Health Canada for the treatment of COVID-19. Remdesivir shortened time to clinical recovery but failed to show any survival benefit in the ACTT-1 trial. In British Columbia availability of remdesivir remains limited to clinical trials at this time.

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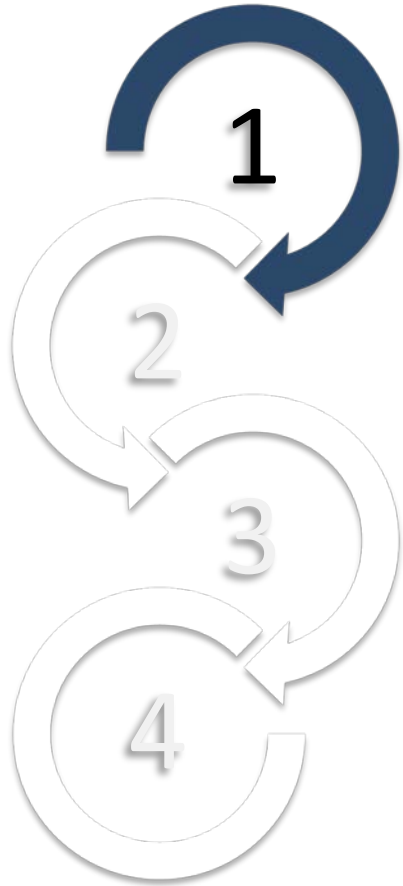
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**Remdesivir\*** is **not** recommended outside of approved clinical trials

**Ribavirin/Interferon** is **not** recommended outside of approved clinical trials

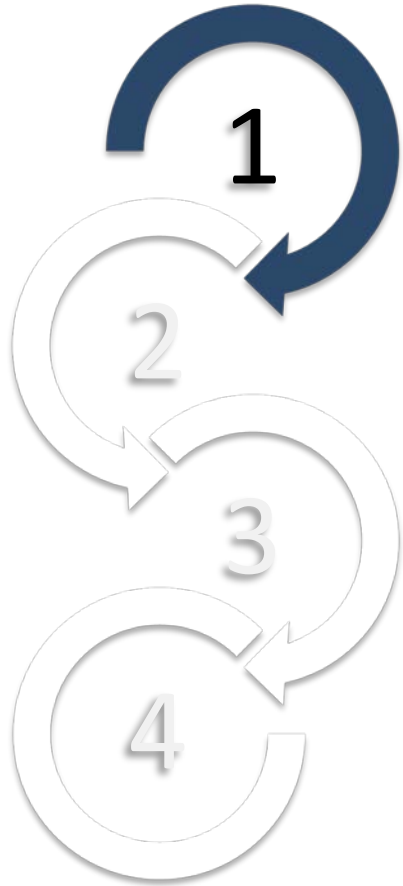


## Antiviral Therapy

### Chloroquine and Hydroxychloroquine

- Antimalarial agent
- Primarily used in rheumatologic disease
- NOT recommended
  - Treatment of all forms of disease
  - Prophylaxis after known COVID-19 exposure

<b>Critically Ill COVID-19 Patients</b> <i>Hospitalized, ICU-based</i>	<b>Chloroquine</b> or <b>Hydroxychloroquine</b> is <b>not</b> recommended for the treatment of COVID-19
<b>Severely Ill COVID-19 Patients</b> <i>Hospitalized, ward-based, long-term care</i>	<b>Chloroquine</b> or <b>Hydroxychloroquine</b> is <b>not</b> recommended for the treatment of COVID-19
<b>Mildly Ill COVID-19 Patients</b> <i>Ambulatory, outpatient, long-term care</i>	<b>Chloroquine</b> or <b>Hydroxychloroquine</b> is <b>not</b> recommended for the treatment of COVID-19



## Antiviral Therapy

### Chloroquine and Hydroxychloroquine

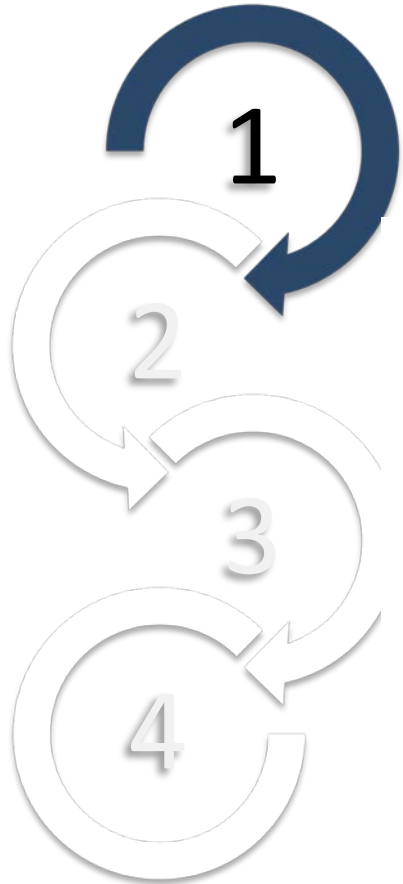
**Conclusion:** Despite its small sample size, our survey shows that hydroxychloroquine treatment is significantly associated with viral load reduction/disappearance in COVID-19 patients and its effect is reinforced by azithromycin.

Hydroxychloroquine and azithromycin as a treatment of COVID-19: results of an open-label non-randomized clinical trial <sup>☆</sup>

Philippe Gautret<sup>a,b,\$</sup>, Jean-Louis Lagier<sup>a,c,\$</sup>, Philippe Parola<sup>a,b</sup>, Van Thuan Hoang<sup>a,b,d</sup>, Line Meddeb<sup>a</sup>, Morgane Halime<sup>a</sup>, Barbara Doudier<sup>a</sup>, Johan Courjon<sup>e,f,g</sup>, Valérie Giordano<sup>a</sup>, Vera Esteves Vieira<sup>a</sup>, Hervé Tissot Dupont<sup>a,c</sup>, Stéphane Honoré<sup>ij</sup>, Philippe Colson<sup>a</sup>, Eric Chabrière<sup>a,c</sup>, Bernard La Scola<sup>a,c</sup>, Jean-Marc Rolain<sup>a,c</sup>, Philippe Brouqui<sup>a,c</sup>, Didier Raoult<sup>a,c,\*</sup>

International Journal of Antimicrobial Agents 56 (2020) 105949

**EXPRESSION OF CONCERN**



## Antiviral Therapy

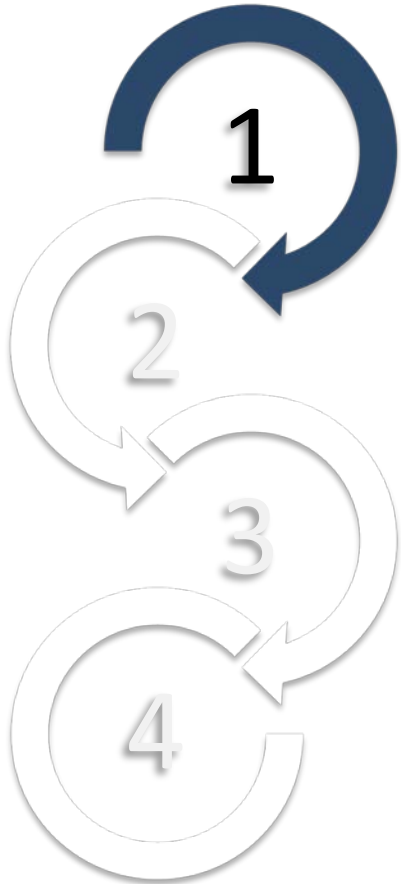
### Chloroquine and Hydroxychloroquine

#### CONCLUSIONS

In this observational study involving patients with Covid-19 who had been admitted to the hospital, hydroxychloroquine administration was not associated with either a greatly lowered or an increased risk of the composite end point of intubation or death. Randomized, controlled trials of hydroxychloroquine in patients with Covid-19 are needed. (Funded by the National Institutes of Health.)

Joshua Geleris, M.D., Yifei Sun, Ph.D., Jonathan Platt, Ph.D., Jason Zucker, M.D., Matthew Baldwin, M.D., George Hripcsak, M.D., Angelena Labella, M.D., Daniel Manson, M.D., Christine Kubin, Pharm.D., R. Graham Barr, M.D., Dr.P.H., Magdalena E. Sobieszczyk, M.D., M.P.H., and Neil W. Schluger, M.D.

May 7, 2020  
Observational  
1446 Patients



## Antiviral Therapy

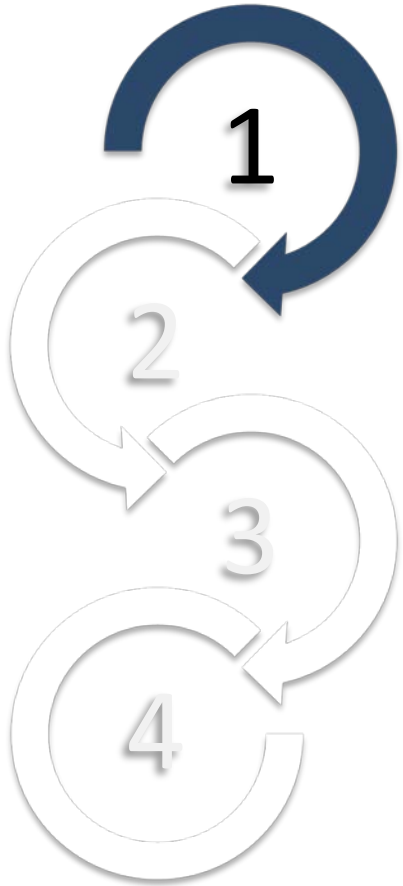
### Chloroquine and Hydroxychloroquine

**CONCLUSIONS AND RELEVANCE** Among patients hospitalized in metropolitan New York with COVID-19, treatment with hydroxychloroquine, azithromycin, or both, compared with neither treatment, was not significantly associated with differences in in-hospital mortality. However, the interpretation of these findings may be limited by the observational design.

Association of Treatment With Hydroxychloroquine or Azithromycin With In-Hospital Mortality in Patients With COVID-19 in New York State

Eli S. Rosenberg, PhD; Elizabeth M. Dufort, MD; Tomoko Udo, PhD; Larissa A. Wilberschied, MS; Jessica Kumar, DO; James Tesoriero, PhD; Patti Weinberg, PA; James Kirkwood, MPH; Alison Muse, MPH; Jack DeHovitz, MD; Debra S. Blog, MD; Brad Hutton, MPH; David R. Holtgrave, PhD; Howard A. Zucker, MD

May 11, 2020  
Observational  
1428 Patients



## Antiviral Therapy

### Chloroquine and Hydroxychloroquine

#### CONCLUSIONS

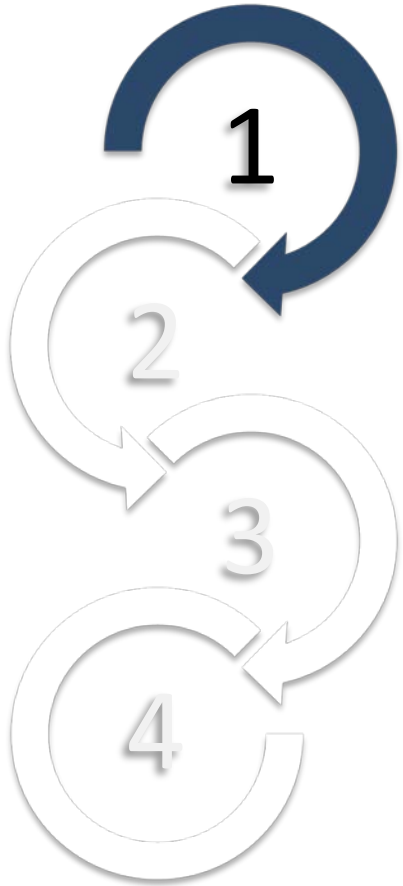
Among patients hospitalized with mild-to-moderate Covid-19, the use of hydroxychloroquine, alone or with azithromycin, did not improve clinical status at 15 days as compared with standard care. (Funded by the Coalition Covid-19 Brazil and EMS Pharma; ClinicalTrials.gov number, NCT04322123.)

#### Azithromycin in Mild-to-Moderate Covid-19

A.B. Cavalcanti, F.G. Zampieri, R.G. Rosa, L.C.P. Azevedo, V.C. Veiga, A. Avezum, L.P. Damiani, A. Marcadenti, L. Kawano-Dourado, T. Lisboa, D.L.M. Junqueira, P.G.M. de Barros e Silva, L. Tramujas, E.O. Abreu-Silva, L.N. Laranjeira, A.T. Soares, L.S. Echenique, A.J. Pereira, F.G.R. Freitas, O.C.E. Gebara, V.C.S. Dantas, R.H.M. Furtado, E.P. Milan, N.A. Golin, F.F. Cardoso, I.S. Maia, C.R. Hoffmann Filho, A.P.M. Kormann, R.B. Amazonas, M.F. Bocchi de Oliveira, A. Serpa-Neto, M. Falavigna, R.D. Lopes, F.R. Machado, and O. Berwanger, for the Coalition Covid-19 Brazil I Investigators\*

July 23, 2020  
Randomized  
Open label  
Max 4L O<sub>2</sub>





## Antiviral Therapy

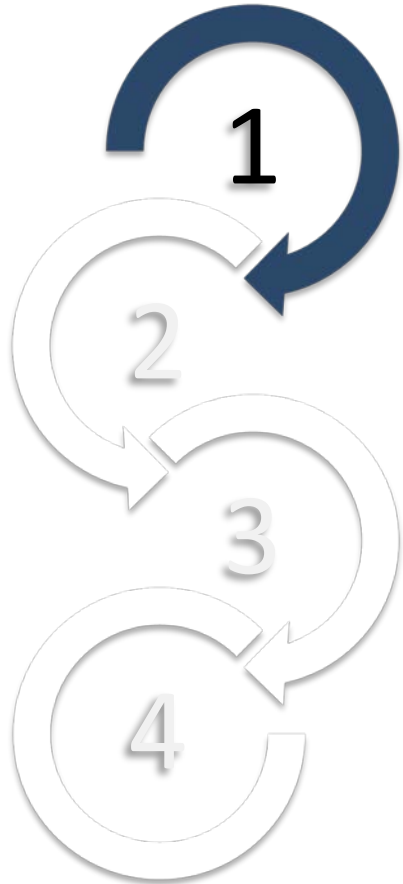
### Chloroquine and Hydroxychloroquine

**CONCLUSIONS AND RELEVANCE** In this cohort study, patients who received hydroxychloroquine for the treatment of pneumonia associated with COVID-19 were at high risk of QTc prolongation, and concurrent treatment with azithromycin was associated with greater changes in QTc. Clinicians should carefully weigh risks and benefits if considering hydroxychloroquine and azithromycin, with close monitoring of QTc and concomitant medication usage.

for Coronavirus Disease 2019 (COVID-19)

Nicholas J. Mercuro, PharmD, BCIDP; Christina F. Yen, MD; David J. Shim, MD, PhD; Timothy R. Maher, MD; Christopher M. McCoy, PharmD, BCPS(AQ-ID), BCIDP; Peter J. Zimetbaum, MD; Howard S. Gold, MD

May 1, 2020  
Observational  
Boston



## Antiviral Therapy

### Lopinavir/Ritonavir

- Antiretroviral combination used in HIV
- Previously shown to have *in vitro* activity against SARS-CoV (2003)

#### Critically Ill COVID-19 Patients

Hospitalized, ICU-based  
Patients requiring mechanical ventilation

**Lopinavir/ritonavir** is **not** recommended outside of approved clinical trials

#### Severely Ill COVID-19 Patients

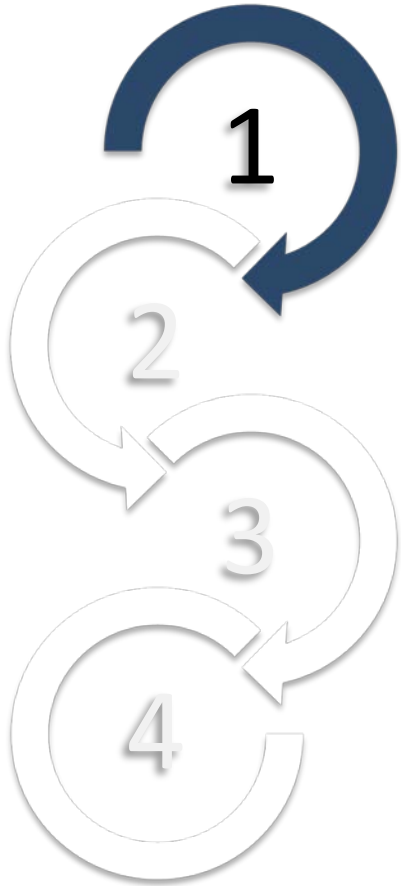
Hospitalized, ward-based, long-term care  
Patients requiring supplemental oxygen therapy

**Lopinavir/ritonavir** is **not** recommended outside of approved clinical trials

#### Mildly Ill COVID-19 Patients

Ambulatory, outpatient, long-term care  
Patients who do not require oxygen

**Lopinavir/ritonavir** is **not** recommended outside of approved clinical trials



## Antiviral Therapy

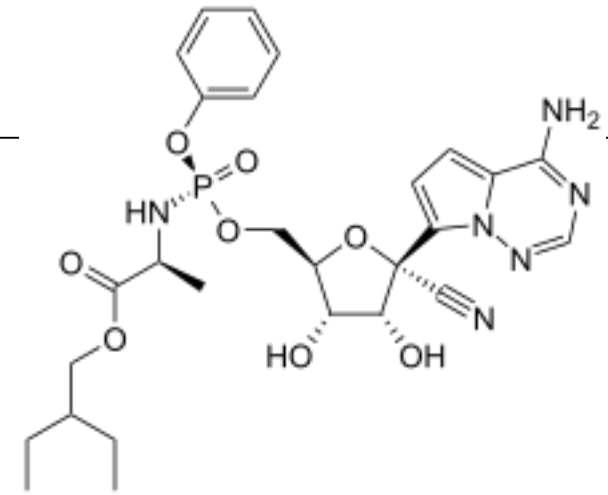
### Lopinavir/Ritonavir

#### CONCLUSIONS

In hospitalized adult patients with severe Covid-19, **no benefit was observed with lopinavir-ritonavir treatment beyond standard care.** Future trials in patients with severe illness may help to confirm or exclude the possibility of a treatment benefit. (Funded by Major Projects of National Science and Technology on New Drug Creation and Development and others; Chinese Clinical Trial Register number, ChiCTR2000029308.)

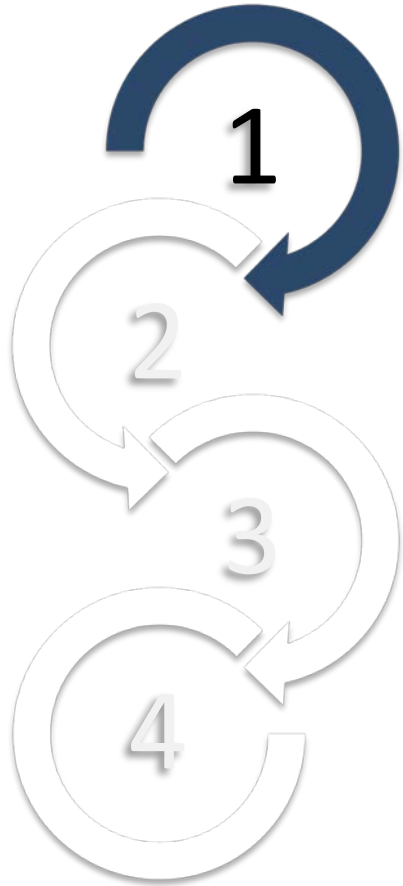
B. Cao, Y. Wang, D. Wen, W. Liu, Jingli Wang, G. Fan, L. Ruan, B. Song, Y. Cai, M. Wei, X. Li, J. Xia, N. Chen, J. Xiang, T. Yu, T. Bai, X. Xie, L. Zhang, C. Li, Y. Yuan, H. Chen, Huadong Li, H. Huang, S. Tu, F. Gong, Y. Liu, Y. Wei, C. Dong, F. Zhou, X. Gu, J. Xu, Z. Liu, Y. Zhang, Hui Li, L. Shang, K. Wang, K. Li, X. Zhou, X. Dong, Z. Qu, S. Lu, X. Hu, S. Ruan, S. Luo, J. Wu, L. Peng, F. Cheng, L. Pan, J. Zou, C. Jia, Juan Wang, X. Liu, S. Wang, X. Wu, Q. Ge, J. He, H. Zhan, F. Qiu, L. Guo, C. Huang, T. Jaki, F.G. Hayden, P.W. Horby, D. Zhang, and C. Wang

March 18, 2020  
Randomized  
China

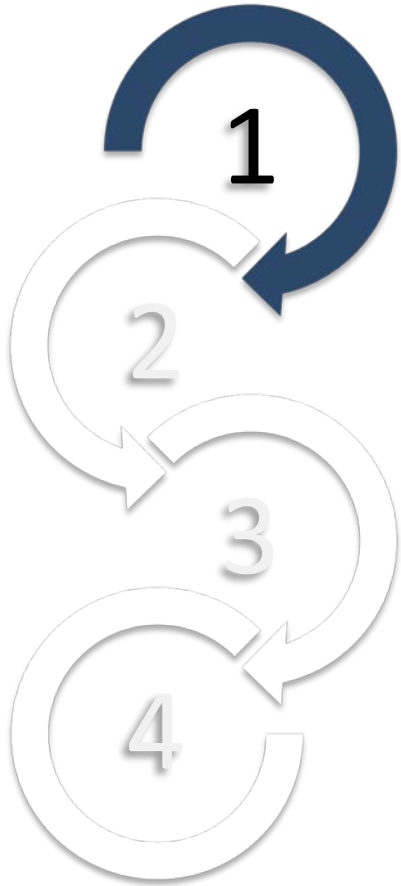


## Antiviral Therapy

### Remdesivir (AKA Tamiflu 2020)



**Remdesivir\*** has received conditional approval by Health Canada for the treatment of COVID-19. Remdesivir shortened time to clinical recovery but failed to show any survival benefit in the ACTT-1 trial. In British Columbia availability of remdesivir remains limited to clinical trials at this time.



## Antiviral Therapy

### Remdesivir (AKA Tamiflu 2020)

#### CONCLUSIONS

Remdesivir was superior to placebo in shortening the time to recovery in adults hospitalized with Covid-19 and evidence of lower respiratory tract infection. (Funded by the National Institute of Allergy and Infectious Diseases and others; ACCT-1 ClinicalTrials.gov number, NCT04280705.)

J.H. Beigel, K.M. Tomashek, L.E. Dodd, A.K. Mehta, B.S. Zingman, A.C. Kalil, E. Hohmann, H.Y. Chu, A. Luetkemeyer, S. Kline, D. Lopez de Castilla, R.W. Finberg, K. Dierberg, V. Tapson, L. Hsieh, T.F. Patterson, R. Paredes, D.A. Sweeney, W.R. Short, G. Touloumi, D.C. Lye, N. Ohmagari, M. Oh, G.M. Ruiz-Palacios, T. Benfield, G. Fätkenheuer, M.G. Kortepeter, R.L. Atmar, C.B. Creech, J. Lundgren, A.G. Babiker, S. Pett, J.D. Neaton, T.H. Burgess, T. Bonnett, M. Green, M. Makowski, A. Osinusi, S. Nayak, and H.C. Lane, for the ACTT-1 Study Group Members\*

May 22, 2020  
ACTT-1 study  
DBRCT  
NIAID-sponsored

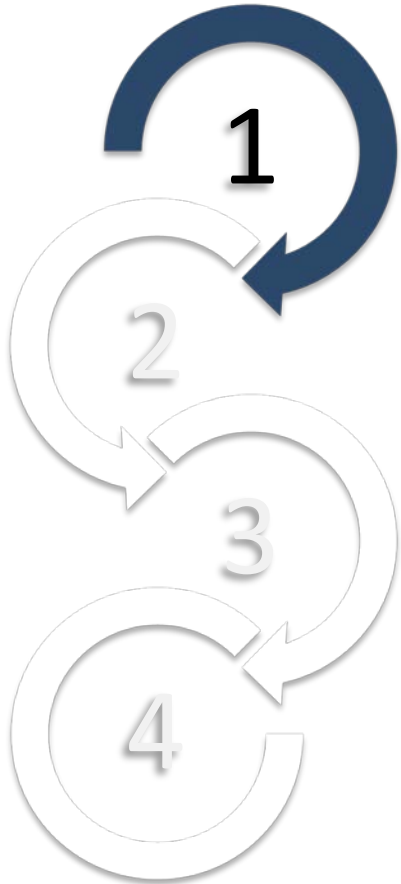
## Remdesivir for the Treatment of Covid-19 — Preliminary Report

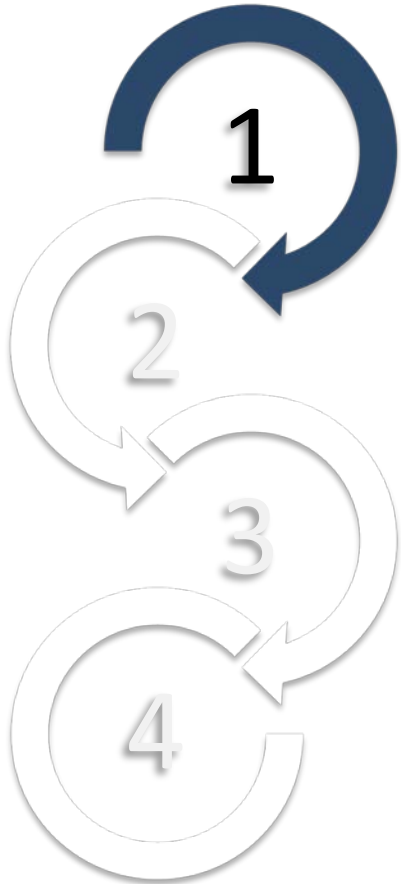
J.H. Beigel, K.M. Tomashek, L.E. Dodd, A.K. Mehta, B.S. Zingman, A.C. Kalil, E. Hohmann, H.Y. Chu, A. Luetkemeyer, S. Kline, D. Lopez de Castilla, R.W. Finberg, K. Dierberg, V. Tapson, L. Hsieh, T.F. Patterson, R. Paredes, D.A. Sweeney, W.R. Short, G. Touloumi, D.C. Lye, N. Ohmagari, M. Oh, G.M. Ruiz-Palacios, T. Benfield, G. Fätkenheuer, M.G. Kortepeter, R.L. Atmar, C.B. Creech, J. Lundgren, A.G. Babiker, S. Pett, J.D. Neaton, T.H. Burgess, T. Bonnett, M. Green, M. Makowski, A. Osinusi, S. Nayak, and H.C. Lane, for the ACTT-1 Study Group Members\*

## Antiviral Therapy

### Remdesivir (NIAID Study)

- Randomized, double-blinded, placebo-controlled
- Multiple centres/countries
- COVID-19 positive requiring oxygen (NP to ECMO)
- Primary outcome = recovery (discharge)
- Median time to recovery shorter (11 vs. 15d)
- More benefit in those not yet critically ill





## Antiviral Therapy

### Remdesivir (Goldman et al.,)

#### CONCLUSIONS

In patients with severe Covid-19 not requiring mechanical ventilation, our trial did not show a significant difference between a 5-day course and a 10-day course of remdesivir. With no placebo control, however, the magnitude of benefit cannot be determined. (Funded by Gilead Sciences; GS-US-540-5773 ClinicalTrials.gov number, NCT04292899.)

Jason D. Goldman, M.D., M.P.H., David C.B. Lye, M.B., B.S., David S. Hui, M.D.,  
Kristen M. Marks, M.D., Raffaele Bruno, M.D., Rocio Montejano, M.D.,  
Christoph D. Spinner, M.D., Massimo Galli, M.D., Mi-Young Ahn, M.D.,  
Ronald G. Nahass, M.D., Yao-Shen Chen, M.D., Devi SenGupta, M.D.,  
Robert H. Hyland, D.Phil., Anu O. Osinusi, M.D., Huyen Cao, M.D.,  
Christiana Blair, M.S., Xuelian Wei, Ph.D., Anuj Gaggar, M.D., Ph.D.,  
Diana M. Brainard, M.D., William J. Towner, M.D., Jose Muñoz, M.D.,  
Kathleen M. Mullane, D.O., Pharm.D., Francisco M. Marty, M.D.,  
Karen T. Tashima, M.D., George Diaz, M.D., and Aruna Subramanian, M.D.,  
for the GS-US-540-5773 Investigators\*

May 27, 2020  
Open-label  
No placebo  
Gilead-sponsored

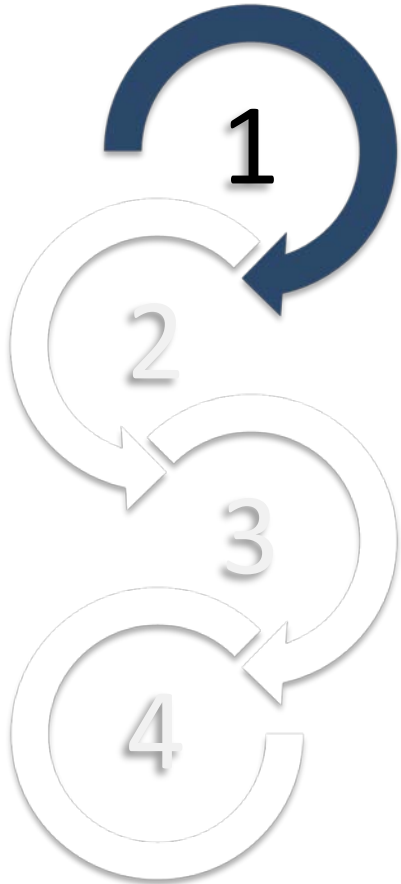
## Remdesivir for 5 or 10 Days in Patients with Severe Covid-19

Jason D. Goldman, M.D., M.P.H., David C.B. Lye, M.B., B.S., David S. Hui, M.D., Kristen M. Marks, M.D., Raffaele Bruno, M.D., Rocio Montejano, M.D., Christoph D. Spinner, M.D., Massimo Galli, M.D., Mi-Young Ahn, M.D., Ronald G. Nahass, M.D., Yao-Shen Chen, M.D., Devi SenGupta, M.D., Robert H. Hyland, D.Phil., Anu O. Osinusi, M.D., Huyen Cao, M.D., Christiana Blair, M.S., Xuelian Wei, Ph.D., Anuj Gaggar, M.D., Ph.D., Diana M. Brainard, M.D., William J. Towner, M.D., Jose Muñoz, M.D., Kathleen M. Mullane, D.O., Pharm.D., Francisco M. Marty, M.D., Karen T. Tashima, M.D., George Diaz, M.D., and Aruna Subramanian, M.D., for the GS-US-540-5773 Investigators\*

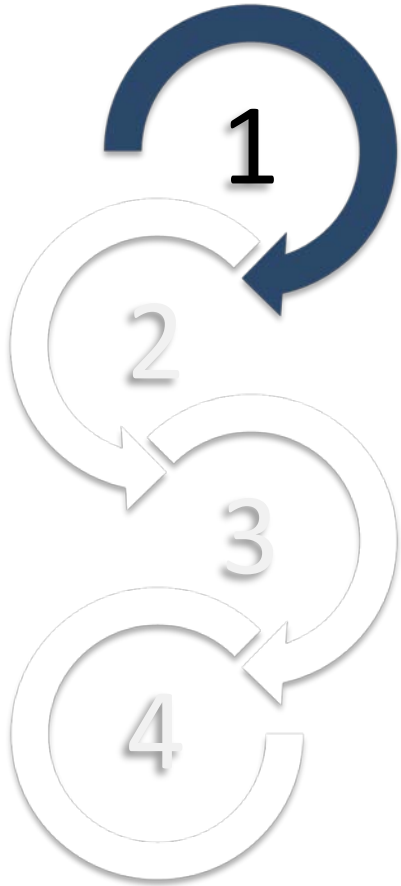
## Antiviral Therapy

### Remdesivir (Goldman et al.,)

- Randomized, open label study
- Severely ill patients (MV, ECMO) excluded
- No difference in 5 vs. 10d course (may guide future clinical treatment course)
- Mortality lower in 5 vs. 10d course (NSS)  
Patients allocated to 10d were sicker at baseline







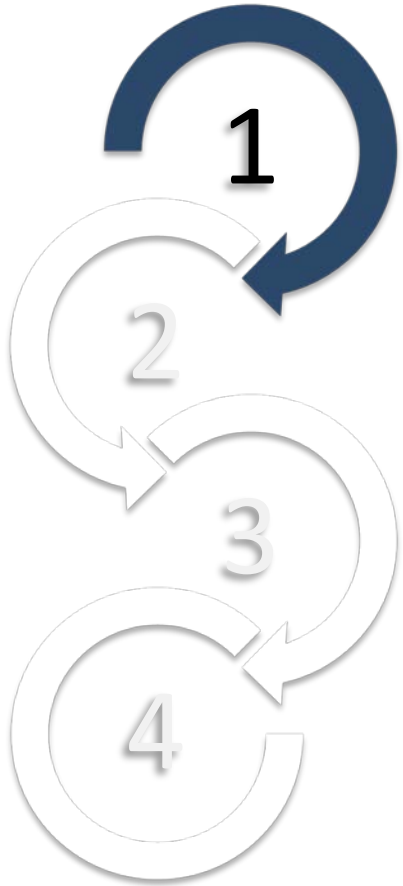
## Antiviral Therapy

### Remdesivir (Spinner et al.,)

**CONCLUSIONS AND RELEVANCE** Among patients with moderate COVID-19, those randomized to a 10-day course of remdesivir did not have a statistically significant difference in clinical status compared with standard care at 11 days after initiation of treatment. **Patients randomized to a 5-day course of remdesivir had a statistically significant difference in clinical status compared with standard care, but the difference was of uncertain clinical importance.**

Louis Yi Ann Chai, MD; Meta Roestenberg, MD; Owen Tak Yin Tsang, MD; Enos Bernasconi, MD; Paul Le Turnier, MD; Shan-Chwen Chang, MD; Devi SenGupta, MD; Robert H. Hyland, DPhil; Anu O. Osinusi, MD; Huyen Cao, MD; Christiana Blair, MS; Hongyuan Wang, PhD; Anuj Gaggar, MD, PhD; Diana M. Brainard, MD; Mark J. McPhail, MD; Sanjay Bhagani, MD; Mi Young Ahn, MD; Arun J. Sanyal, MD; Gregory Huhn, MD; Francisco M. Marty, MD; for the GS-US-540-5774 Investigators

August 21, 2020  
Open-label  
No placebo  
Gilead-sponsored



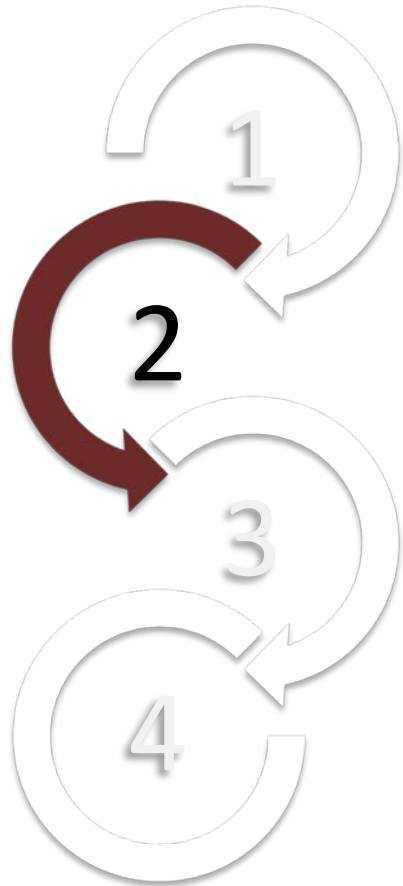
## Antiviral Therapy

### Remdesivir: Issues

- Allocation (only 78 vials in BC)
- Which patients benefit?
  - Unknown who will do better (or worse)
- Cost: \$3000/5 day course (vs. fewer days in hospital)
- Reserve for Clinical Trials (CATCO) only (next week)
- Which hospitals get it?
- Transfers/patient demands etc...

## Antibacterial therapy

- Empiric antibiotics depending on disease severity



### Critically Ill COVID-19 Patients

*Hospitalized, ICU-based*  
Patients requiring mechanical ventilation

**Ceftriaxone 1-2 g IV q24h x 5 days** is recommended if there is concern for bacterial co-infection (alternative moxifloxacin 400 mg IV q24h x 5 days)

**Azithromycin 500 mg IV q24h x 3 days** is recommended if atypical bacterial infection is suspected

### Severely Ill COVID-19 Patients

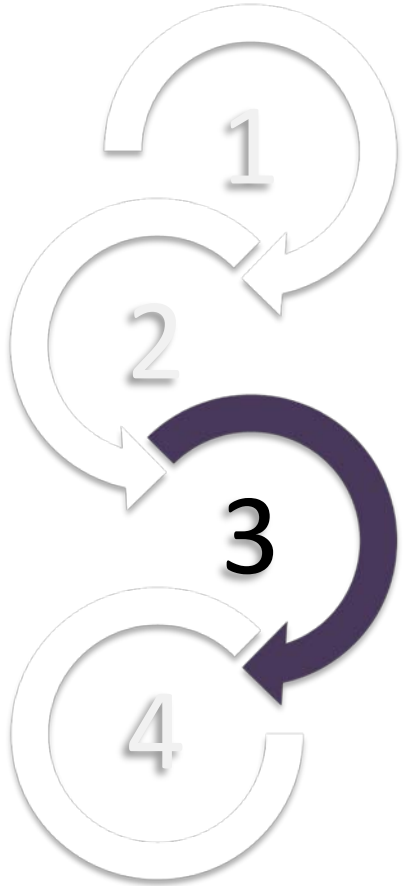
*Hospitalized, ward-based, long-term care*  
Patients requiring supplemental oxygen therapy

Antibacterial therapy is **not** routinely recommended outside of approved clinical trials unless other indications justify its use

### Mildly Ill COVID-19 Patients

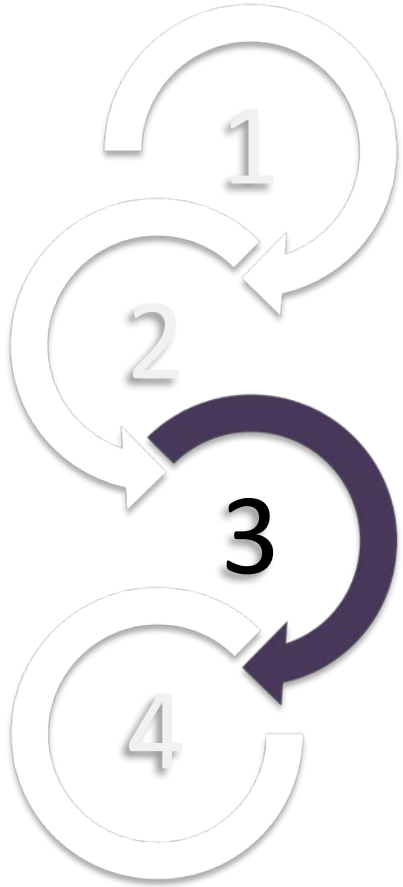
*Ambulatory, outpatient, long-term care*  
Patients who do not require oxygen

Antibacterial therapy is **not** routinely recommended outside of approved clinical trials unless other indications justify its use



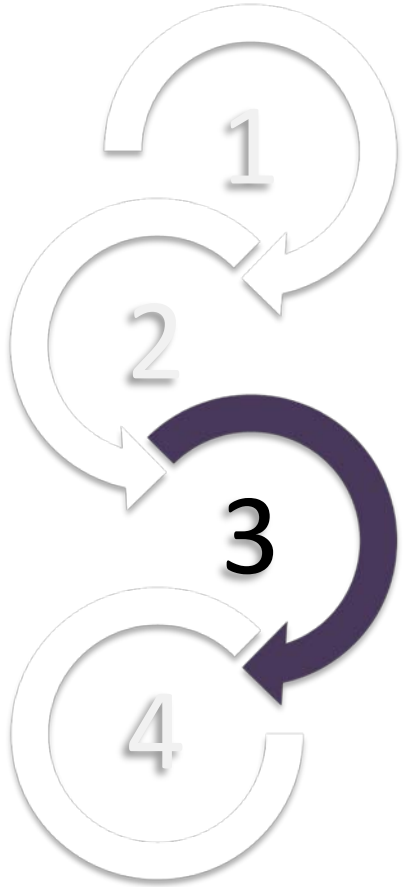
## Immunomodulatory therapy

- Corticosteroids
  - Dexamethasone
  - Hydrocortisone
- Biologic agents
  - Tocilizumab
  - Sarilumab



### The saga of steroids in the ICU

- Decades of research in using steroids:
  - Pneumonia
  - Septic shock
  - ARDS
- Inconclusive data due to study limitations
- Recent data suggest benefit in septic shock (APROCCHSS and ADRENAL)
- DEXA-ARDS (2019): Improved mortality in patients with moderate to severe ARDS

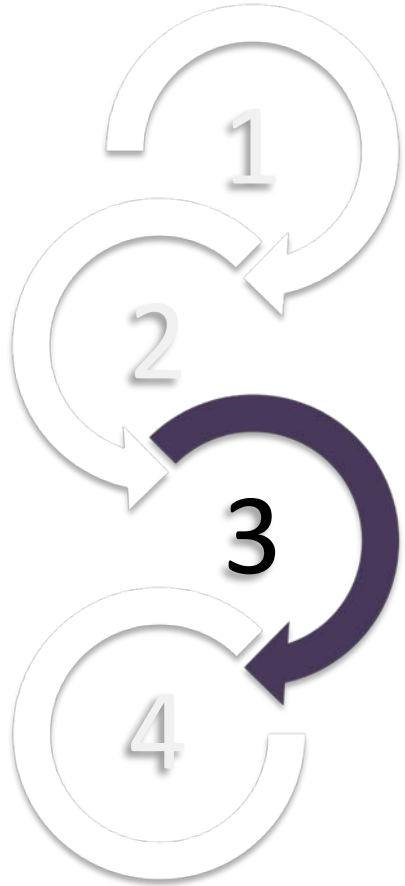


### **The saga of steroids in the ICU**

- Previous studies of other viral pneumonias (SARS/MERS) suggested poor viral clearance
- Associated with increased mortality in influenza related pneumonia

## **Steroids and COVID-19**

Mixed guidance  
regarding steroids



**January 2020**

**March 2020**

[Home](#) / [News](#) / [Low-cost dexamethasone reduces death by up to one third in hospitalised patients with severe respiratory complications of COVID-19](#)

# Low-cost dexamethasone reduces death by up to one third in hospitalised patients with severe respiratory complications of COVID-19

16 June 2020

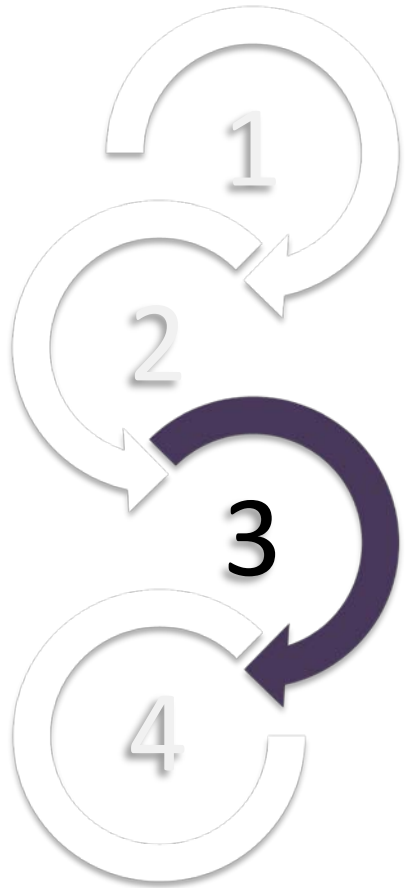
Statement from the Chief Investigators of the Randomised Evaluation of COVid-19 thERapY (RECOVERY) Trial on dexamethasone, 16 June 2020



**June 2020**



## **Steroids and COVID-19**

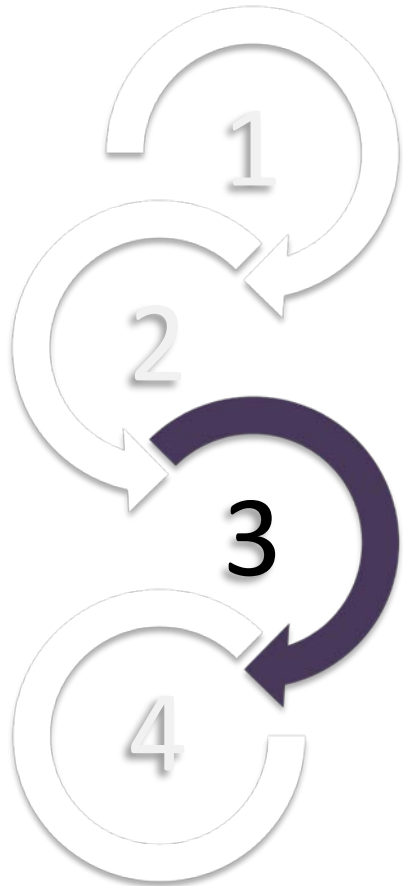


June 16, 2020  
RECOVERY trial  
press release  
Change of clinical  
practice

**June 2020**

**September 2020**

## Corticosteroids for COVID-19



**Critically Ill COVID-19 Patients**  
*Hospitalized, ICU-based*  
Patients requiring mechanical ventilation

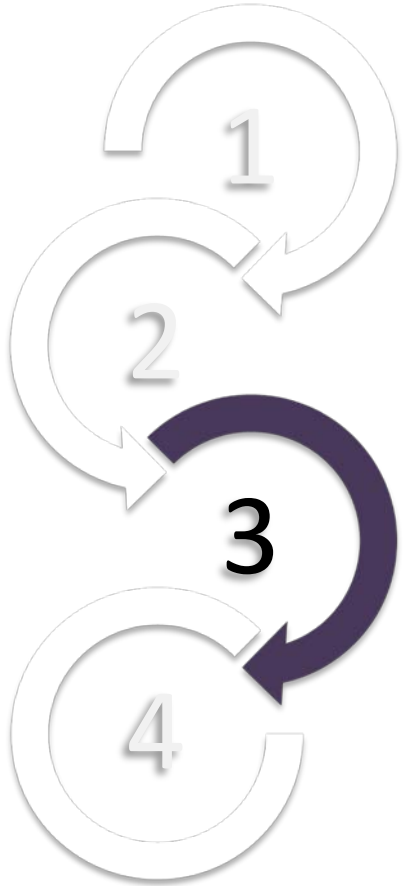
**Dexamethasone 6 mg IV/PO q24h for up to 10 days is strongly recommended** (RECOVERY trial), unless higher doses are indicated\*\*. If Dexamethasone is not available, methylprednisolone 30 mg IV q24h is the preferred alternative.

**Severely Ill COVID-19 Patients**  
*Hospitalized, ward-based, long-term care*  
Patients requiring supplemental oxygen therapy

**Dexamethasone 6 mg IV/PO q24h for up to 10 days is recommended** (RECOVERY trial), unless higher doses are indicated\*\*. If Dexamethasone is not available, methylprednisolone 30 mg IV q24h or prednisone 40 mg PO q24h are the preferred alternatives. If dexamethasone supplies are limited, they should be reserved for critically ill patients.

**Mildly Ill COVID-19 Patients**  
*Ambulatory, outpatient, long-term care*  
Patients who do not require oxygen

**Corticosteroids are not recommended** outside of approved clinical trials unless otherwise indicated\*\*



## Corticosteroids for COVID-19

### Dexamethasone: RECOVERY

ORIGINAL ARTICLE

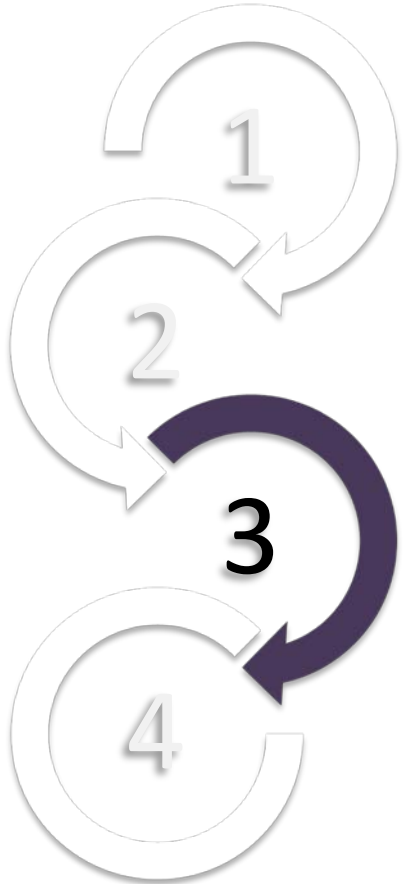
## Dexamethasone in Hospitalized Patients with Covid-19 — Preliminary Report

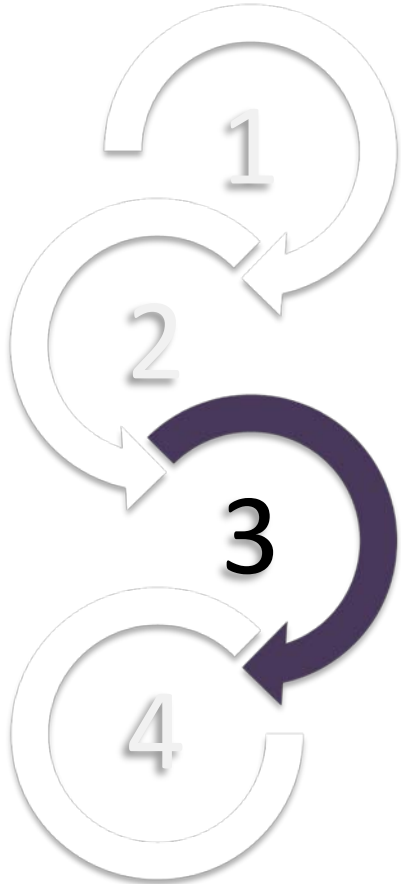
The RECOVERY Collaborative Group\*

## Corticosteroids for COVID-19

### Dexamethasone: RECOVERY

- Largest trial to date to show improved survival for *any* intervention in COVID-19
- High quality study and considered indisputable
- All other steroid trials were subsequently halted
- Mortality results:
  - Mechanical ventilation: 29.3% vs. 41.4%
  - Oxygen alone: 23.3 vs. 26.2%
  - No oxygen: 17.8% vs. 14% (NS)





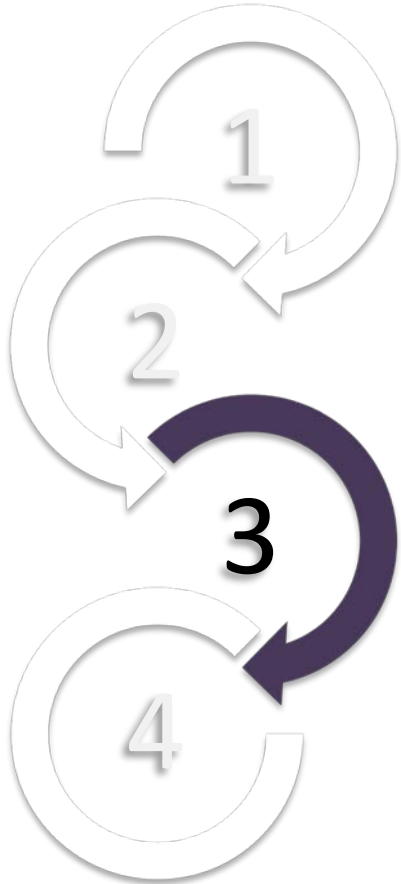
## Corticosteroids for COVID-19

### Dexamethasone: CoDEX (Brazil)

JAMA | **Original Investigation** | **CARING FOR THE CRITICALLY ILL PATIENT**

#### Effect of Dexamethasone on Days Alive and Ventilator-Free in Patients With Moderate or Severe Acute Respiratory Distress Syndrome and COVID-19 The CoDEX Randomized Clinical Trial

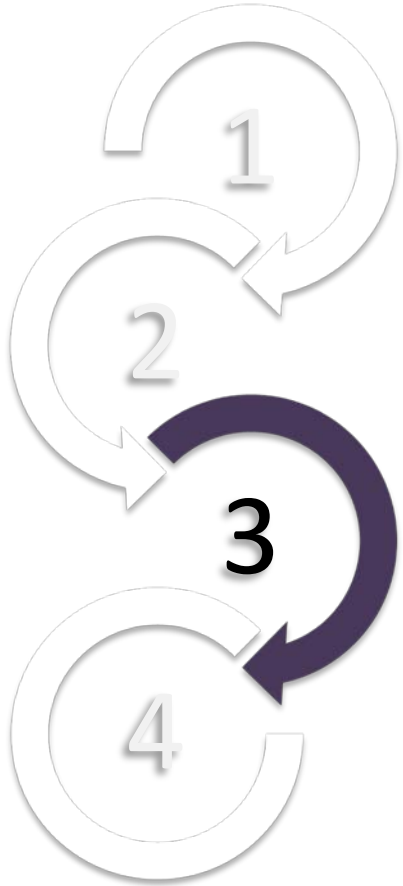
Bruno M. Tomazini, MD; Israel S. Maia, MD, MSc; Alexandre B. Cavalcanti, MD, PhD; Otavio Berwanger, MD, PhD; Regis G. Rosa, MD, PhD; Viviane C. Veiga, MD, PhD; Alvaro Avezum, MD, PhD; Renato D. Lopes, MD, PhD; Flavia R. Bueno, MSc; Maria Vitoria A. O. Silva; Franca P. Baldassare; Eduardo L. V. Costa, MD, PhD; Ricardo A. B. Moura, MD; Michele O. Honorato, MD; Andre N. Costa, MD, PhD; Lucas P. Damiani, MSc; Thiago Lisboa, MD, PhD; Letícia Kawano-Dourado, MD, PhD; Fernando G. Zampieri, MD, PhD; Guilherme B. Olivato, MD; Cassia Righy, MD, PhD; Cristina P. Amendola, MD; Roberta M. L. Roepke, MD; Daniela H. M. Freitas, MD; Daniel N. Forte, MD, PhD; Flávio G. R. Freitas, MD, PhD; Caio C. F. Fernandes, MD; Livia M. G. Melro, MD; Gedealvares F. S. Junior, MD; Douglas Costa Morais; Stevin Zung, MD, PhD; Flávia R. Machado, MD, PhD; Luciano C. P. Azevedo, MD, PhD; for the COALITION COVID-19 Brazil III Investigators



## Corticosteroids for COVID-19

### Dexamethasone: CoDEX (Brazil)

- High dose Dexamethasone
  - 20 mg x 5d; 10 mg x 5 days
- No mortality difference
- Ventilator free days
  - 6.6d dexamethasone vs. 4.0d standard care



## Corticosteroids for COVID-19

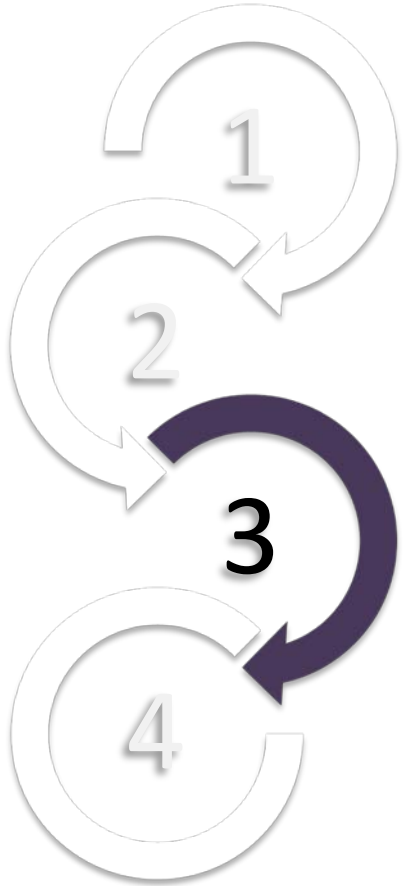
### Hydrocortisone: REMAP-CAP

JAMA | **Original Investigation** | **CARING FOR THE CRITICALLY ILL PATIENT**

**Effect of Hydrocortisone on Mortality and Organ Support in Patients With Severe COVID-19**

**The REMAP-CAP COVID-19 Corticosteroid Domain Randomized Clinical Trial**

The Writing Committee for the REMAP-CAP Investigators

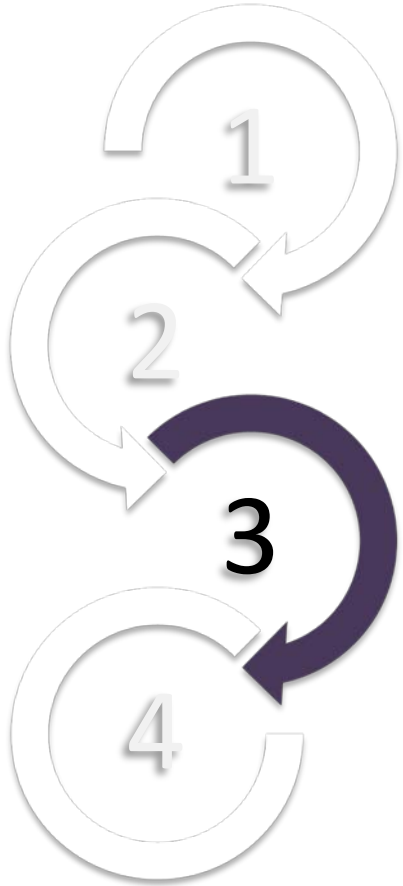


## Corticosteroids for COVID-19

### Hydrocortisone: REMAP-CAP

- Fixed dose (50 mg or 100 mg IV q6h) vs. shock-dependent (50 mg IV q6h) with shock vs. none
- Primary outcome: organ support-free days
- Results
  - 93% vs. 80% probability of superiority with regards to improvement in primary outcome

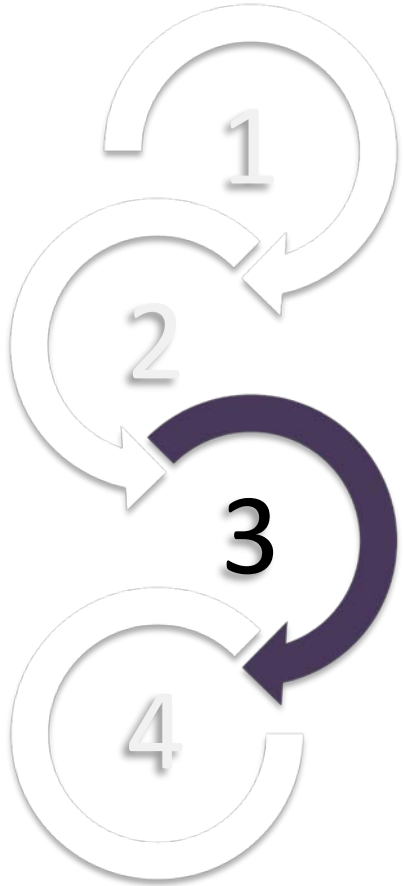




## **Corticosteroids for COVID-19**

### **Summary**

- Solid evidence for both dexamethasone and hydrocortisone for COVID-19 patients requiring oxygen
- CTC Recommendations will be updated to include hydrocortisone



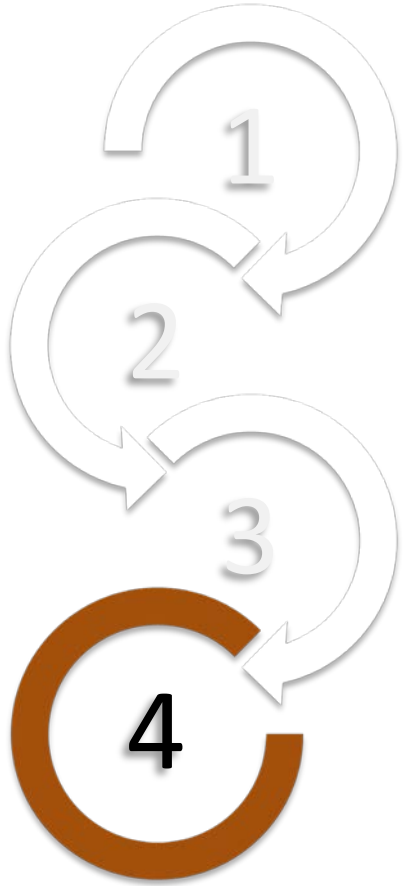
### Biologics/IL-6 inhibitors

- “Indicated” in cases of COVID-related Cytokine Storm
- Controversial
- Currently NOT recommended outside of clinical trials
- If being considered, expert consultation recommended

#### Critically Ill COVID-19 Patients

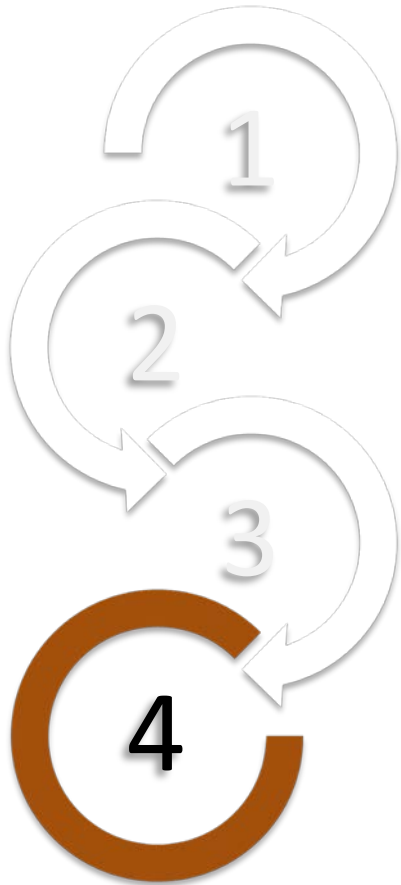
Hospitalized, ICU-based  
Patients requiring mechanical ventilation

**Tocilizumab** or **sarilumab** is **not** recommended outside of approved clinical trials; where clinical trials are not available, expert consultation is recommended (Infectious Diseases, Hematology, Rheumatology)



## Other therapies

- DVT Prophylaxis
- NSAIDS
- ACE-I/ARBs



## Other therapies

### DVT Prophylaxis

- Controversial
- Living SBAR document available on Island Health intranet

**Critically Ill COVID-19 Patients**  
*Hospitalized, ICU-based*  
Patients requiring mechanical ventilation

**Enoxaparin 30 mg SC q12h is suggested** for VTE prophylaxis

**Severely Ill COVID-19 Patients**  
*Hospitalized, ward-based, long-term care*  
Patients requiring supplemental oxygen therapy

**Enoxaparin 30 mg SC q12h is suggested** for VTE prophylaxis

#### PREPARED BY:

**Anna Maruyama, PharmD (ICU)**

**Jolanta Piszczek, PharmD (AMS)**

**Celia Culley, PharmD (CCU/ CVU)**

**Dr. Shavaun MacDonald, MD FRCPC (Emerg/ICU)**

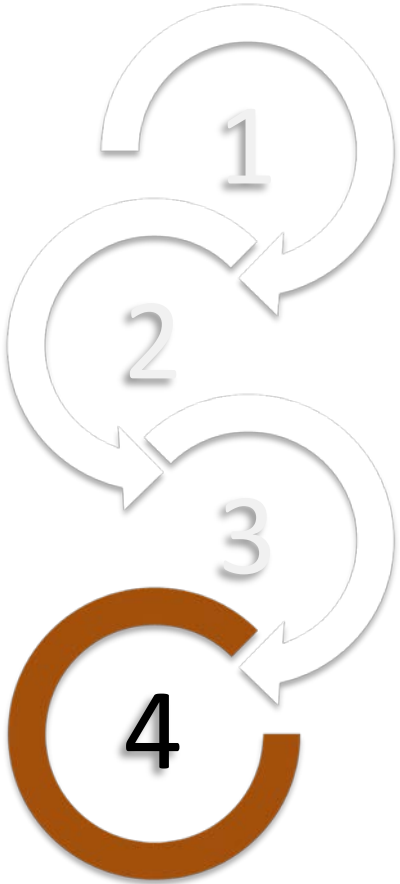
**Erica Otto, PharmD (ICU)**



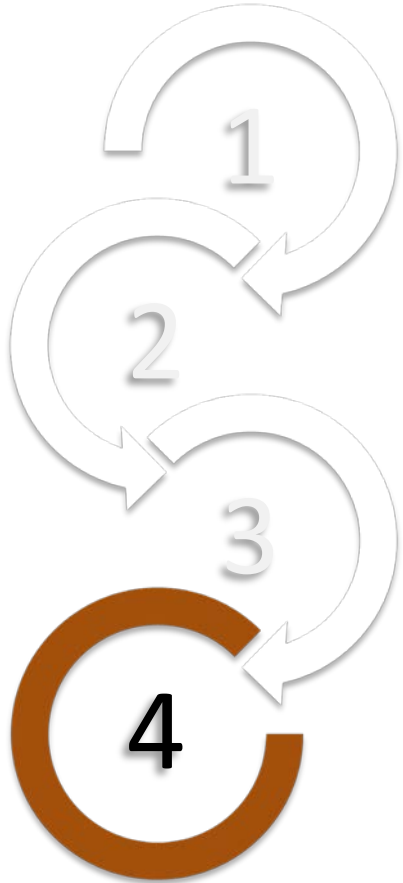
## Other therapies

### DVT Prophylaxis

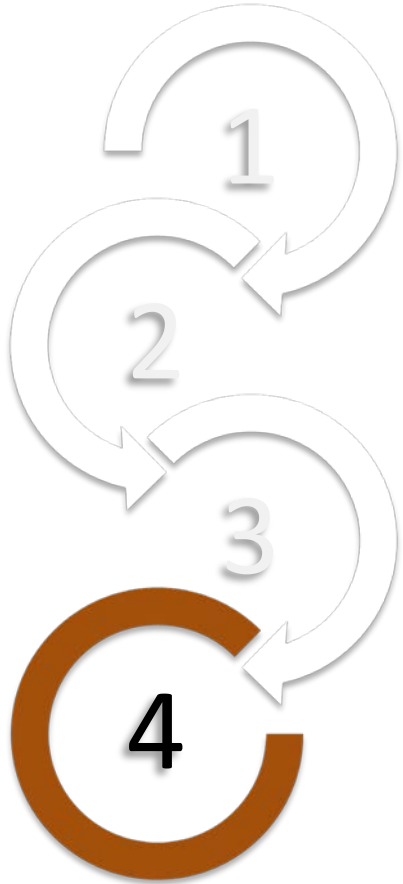
- Severe COVID-19 infection is likely a hypercoagulable state
- Increased risk of DVT/PE
- Studies of alternate DVT prophylaxis dosing or empiric therapeutic anticoagulation are in progress.



## Other therapies



	Dose based on estimated glomerular filtration rate (eGFR)		
Weight (kg)	eGFR greater than or equal to 30mL/min	eGFR 20 to 29mL/min	eGFR less than 20mL/min
40-100	Enoxaparin 30mg SUBCUT q12h	Enoxaparin 40 mg SUBCUT q24h	Heparin 5000 units SUBCUT q8h  OR Consider clinical pharmacy consult for consideration of non- formulary Tinzaparin
Greater than 100	Enoxaparin 40mg SUBCUT q12h	Enoxaparin 60 mg SUBCUT q24h	Heparin 7500 units SUBCUT q8h  OR Consider clinical pharmacy consult for consideration of non- formulary Tinzaparin



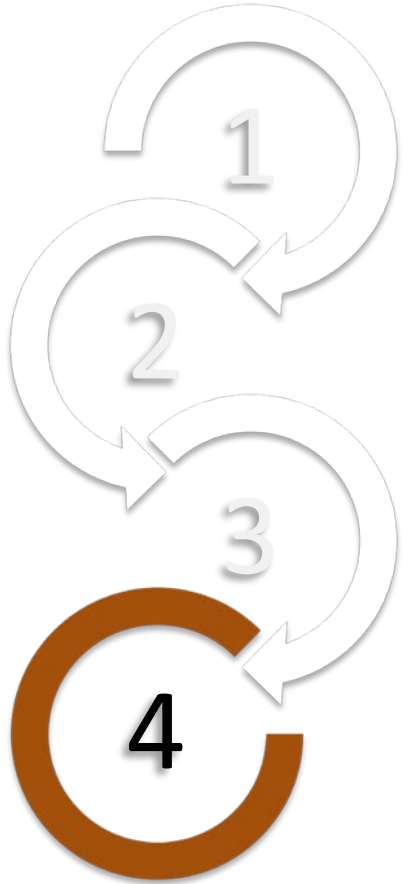
## Other therapies

### NSAIDS and ACE-I/ARB

**ACE inhibitors** and **ARBs** should not be discontinued solely on the basis of COVID-19

**NSAIDs** should not be discontinued solely on the basis of COVID-19

# COVID-19 Therapeutics



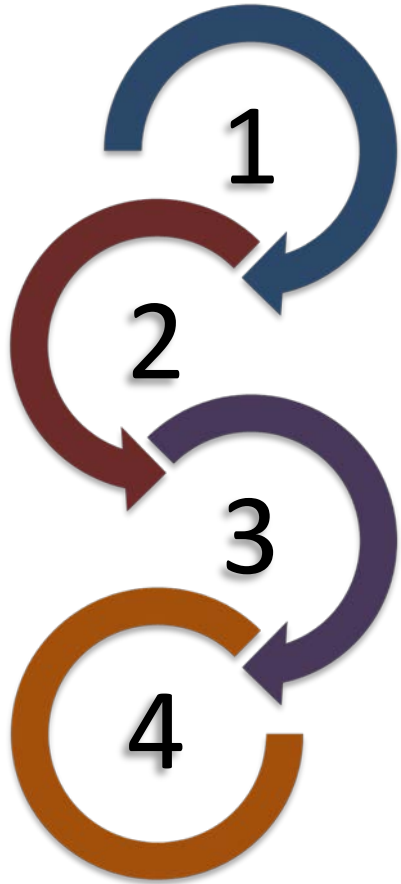
## Other therapies

### Other other therapies

- Colchicine
- Zinc
- Vitamin D
- Oleander
- Bleach
- Unicorn tears







## Therapeutic Recommendations

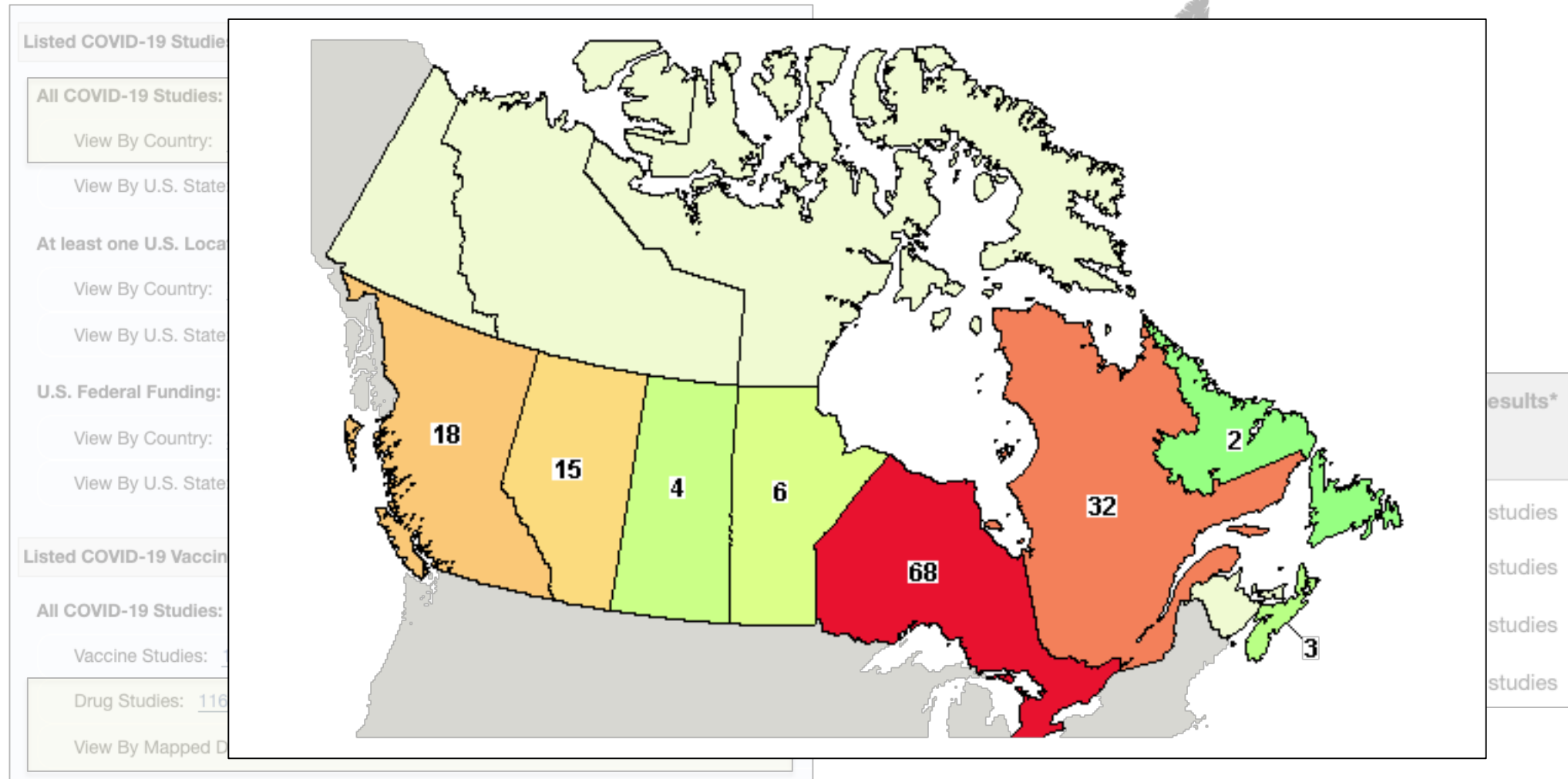
- Antiviral therapy
- Antibacterial therapy
- Immunomodulatory therapy
- Other therapies



Questions:  
[dovakim@gmail.com](mailto:dovakim@gmail.com)

# COVID-19: Clinical Trials at VIHA

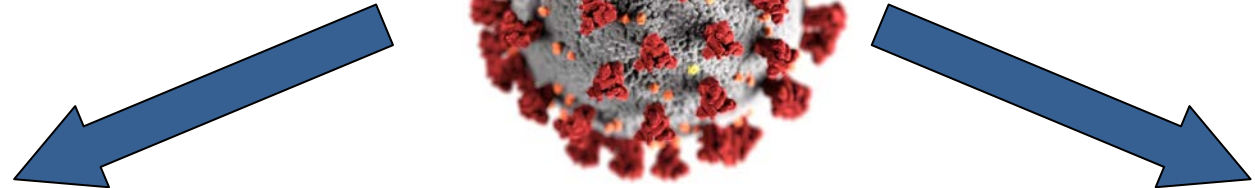
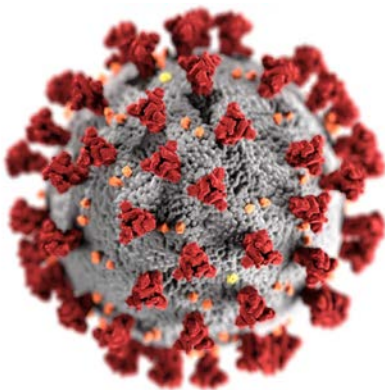
## Clinical Trials



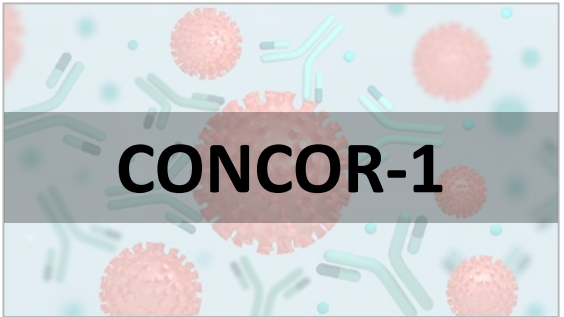


# COVID-19: Clinical Trials at VIHA

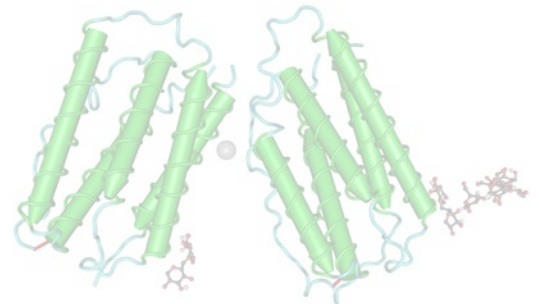
## Clinical Trials



**CATCO**



**CONCOR-1**



**ATTACC**

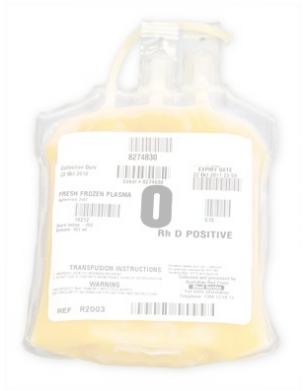
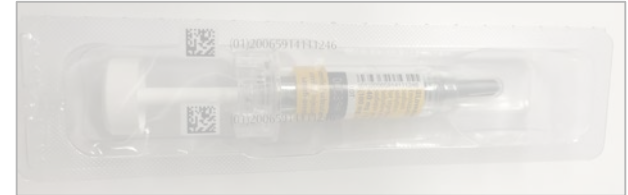
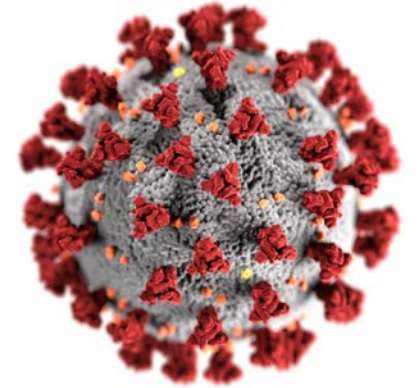


Photo credit: Dr. Anna Maruyama

## **Commonalities**



- Confirmed SARS-CoV-2 via PCR
- Randomized, open-label studies
- Hospitalized
- Co-enrollment permitted (with other ICU trials too)
- Optimized supportive care
  - Supplementary oxygen
  - Dexamethasone 6 mg IV daily (for patients on O<sub>2</sub>)
  - Routine ward vs. ICU care (ARDS management)

## COVID-19: Clinical Trials at VIHA

### CATCO

### Canadian Treatments for CCOVID-19

- Run in conjunction with the global WHO SOLIDARITY trial
- Adaptive, open-label, controlled trial
- Hospitalized patients with COVID-19
- Randomized to one of the following groups:
  1. Remdesivir 200 mg IV Day 1, 100 mg IV daily x 9 days
  2. Interferon-beta-1a 44 mcg SC on days 1, 3, 6
  3. Optimized supportive care only



## **CATCO: Rationale**

### **Remdesivir**

- Broad-spectrum nucleotide prodrug that inhibits RNA-dependent RNA polymerase
- Thought to slow down viral replication

## **CATCO**

### **Inclusion criteria**

- Adults  $\geq$  18 years of age
- Laboratory confirmed SARS-CoV-2 infection
- Hospitalized

### **Exclusion criteria**

- Will be transferred to non study site
- Moribund state

## **CATCO: Outcomes**

### **Primary**

- All cause mortality

### **Exploratory**

- Viral clearance

### **Secondary**

- Clinical severity
  - Ordinal scales: Time to improvement
  - Oxygenation: Oxygen free days, new oxygen use
  - Mechanical ventilation: Ventilator free days, new MW
- Duration of hospitalization
- Safety



## CATCO: Outcomes

### Primary

- All cause mortality

### Secondary

- Clinical severity
  - Ordinal scale
  - Oxygenation
  - oxygen use
  - Mechanical ventilation
  - days, new
- Duration of
- Safety

Patient State	Descriptor	Score
<i>Uninfected</i>	Uninfected; no viral RNA detected	0
<i>Ambulatory</i>	Asymptomatic; viral RNA detected	1
	Symptomatic; Independent	2
	Symptomatic; Assistance needed	3
<i>Hospitalized: Mild disease</i>	Hospitalized; no oxygen therapy	4
	Hospitalized; oxygen by mask or nasal prongs	5
	Hospitalized; Oxygen by NIV or High flow	6
	Intubation & Mechanical ventilation, $pO_2/FIO_2 \geq 150$ or $SpO_2/FIO_2 \geq 200$	7
	Mechanical ventilation $pO_2/FIO_2 < 150$ ( $SpO_2/FIO_2 < 200$ ) or vasopressors	8
<i>Hospitalized: Severe disease</i>	Mechanical ventilation $pO_2/FIO_2 < 150$ and vasopressors, dialysis, or ECMO	9
	Dead	10

Ordinal Scale for evaluating clinical status

## *COVID-19: Clinical Trials at VIHA*

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### **CATCO**

#### **Status**

- Ready to enroll
- Remdesivir on site (2 patients)
- Interferon not ready

## **ATTACC**

### **Anthrombotic Therapy To Ameliorate Complications of COVID-19**

- Prospective, open-label, randomized, adaptive clinical trial
- Establish whether therapeutic anticoagulation improves outcomes in patient with COVID-19

## **ATTACC: Rationale**

### **COVID & Hypercoaguability**

- COVID-19 is associated with a hypercoagulable state
- Many patients experience significant cardiac and pulmonary thrombotic complications
- Heparin induces a conformational change in the SARS-CoV-2 receptor spike protein limiting invasion
- Heparin has anti-inflammatory effects
- D-dimer levels could potentially be used to risk stratify patients

## **ATTACC**

### **Inclusion criteria**

- Adults  $\geq$  18 years of age
- Laboratory confirmed SARS-CoV-2 requiring hospital admission
- Anticipated to be in hospital  $\geq$  72h
- Enrolled  $<$  72h of hospital admission

## **ATTACC**

### **Exclusion criteria**

- Invasive mechanical ventilation
- Active bleeding
- Risk factors for bleeding
- Thrombocytopenia/DIC
- Hg < 80
- DAPT
- Independent indication for therapeutic anticoagulation
- Pregnancy

#### **Risk factors for bleeding**

- intracranial surgery or stroke within 3 months
- history of intracerebral AVM
- cerebral aneurysm or mass lesions of CNS
- intracranial malignancy
- history of intracranial bleeding
- history of bleeding diatheses
- GIB within previous 3 months
- thrombolysis within the previous 7 days
- presence of an epidural or spinal catheter
- recent major surgery <14 days
- uncontrolled hypertension
- physician-perceived contraindications

## **ATTACC: Study Protocol**

### **Intervention**

- Therapeutic-dose parenteral anticoagulation
  - Up until 14 days, or recovery (discharge or liberation from oxygen)
- Preference is for LMWH
  - Enoxaparin is the preferred LMWH (viral inhibitory properties)
- IV UFH can be used if LMWH contraindicated
- Control group to receive standard prophylactic dosing based on institutional practices

## **ATTACC: Outcomes**

### **Primary**

- Outcome at 30 days
  - No IMV
  - IMV
  - Death

### **Secondary**

- Safety of therapeutic anticoagulation
  - Laboratory confirmed HIT
  - Major bleeding
- Efficacy of therapeutic anticoagulation
  - Mortality/Intubation/ICU-free days
  - NIV or HFNC
  - Symptomatic VTE at 30 and 90 days
  - MI at 30 and 90 days



## *COVID-19: Clinical Trials at VIHA*

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### **ATTACC**

#### **Status**

- Ready to go
- Eligible patients from ward, HAU, ICU

## **CONCOR-1**

### **CONvalescent plasma for COVID-19 Respiratory Illness**

- Randomized, open label trial using plasma from patients known to have recovered from COVID-19
- To establish whether COVID-19 Convalescent Plasma (CCP) can reduce poor outcomes from COVID-19

## **CONCOR-1: Rationale**

### **Immunologic response to COVID-19**

- Recovered patients have been shown to have high levels of neutralizing antibodies (compared to those that died)
- Insufficient viral clearance may lead to a hyperimmune response to virus (“cytokine storm”)
- Antibody response may determine outcome
- Passive immunization may facilitate viral neutralization and prevent a disproportional immune response

## **CONCOR-1**

### **Inclusion criteria**

- Adults  $\geq$  16 years of age
- Laboratory confirmed SARS-CoV-2 requiring hospital admission
- *Receiving supplemental oxygen*
- 500 mL of ABO compatible Convalescent Plasma is available

## **CONCOR-1**

### **Exclusion criteria**

- Onset of symptoms >12 days prior
- Intubated or to be intubated imminently
- Contraindication to plasma

## **CONCOR-1: Study Protocol**

### **Intervention**

- 2:1 randomization (CCP:standard care)
- Stratified by centre and age
- COVID-19 Convalescent plasma (CCP)
  - One unit of 500 mL (single donor) or
  - Two units of 250 mL each (from one or two donors)
- Control patients to receive standard of care

## **CONCOR-1: Outcomes**

### **Primary**

- Intubation or death at Day 30

### **Secondary**

- Intubation before Day 30
- Time to intubation
- Death at Day 30
- Length of ICU/hospital stay
- Need for ECMO
- Need for RRT
- Myocarditis
- Serious adverse events (SAE)

## **CONCOR-1**

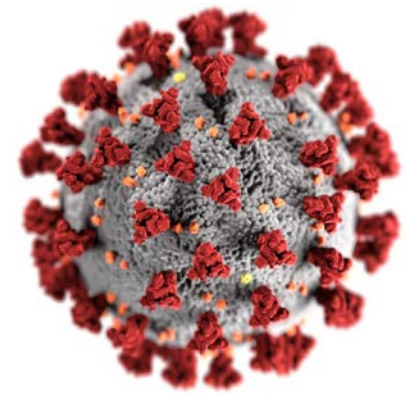
### **Status**

- Ready to go, CCP on site
- Eligible patients from ward, HAU, ICU





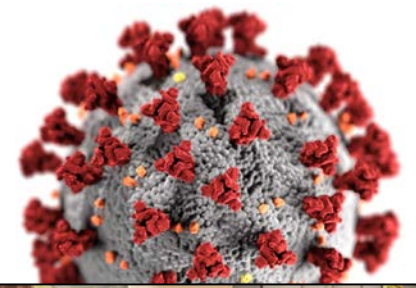
# COVID-19: Clinical Trials at VIHA



## Summary

Study	Population (SARS-CoV-2 PCR positive)	Intervention	Comparator	Outcome	Status
<b>CATCO</b>	Hospitalized	Remdesivir or Interferon	Optimized supportive care	All cause mortality Clinical severity	Remdesivir on site Ready to enroll
<b>ATTACC</b>	Hospitalized <i>Not intubated</i>	Therapeutic anticoagulation		Outcome at 30d (IMV/death)	Ready to enroll
<b>CONCOR-1</b>	Hospitalized <i>Receiving oxygen</i>	Convalescent Plasma		CCP on site Ready to enroll	

## COVID-19: Clinical Trials at VIHA



### Who to contact?

#### Research Team

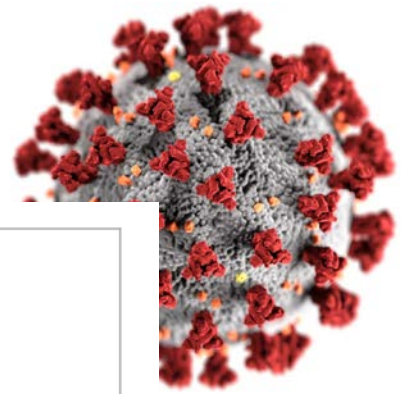
- Fiona Auld
- Deb Parfett
- Gayle Carney

#### Investigators

- Daniel Ovakim
- Gordon (🇺🇸) Wood
- Eric Partlow
- Matt Moher
- David Forrest (NRGH)



# COVID-19: Clinical Trials at VIHA



## Clinical Order Set

Demographics

### COVID-19 Treatment Adult Suspected or Confirmed (Module)

Page 1 of 4

**Key:** Req – Requisition   MAR – Medication Administration Record   K – Kardex   Dis – Discontinued

**Instructions for completing this order set:**

- Indicates a pre-selected order. To delete a pre-selected order, draw a line through it
- Must tick the box for order to be implemented. Orders not checked will not be implemented
- Fill in blank spaces as needed/appropriate
- Indicates an item for consideration by Provider; is NOT an order

Key

Phase

It (Module)

### COVID-19 Treatment Adult (Module)

778 (\*NRGH and Victoria sites only)

250-213-7778

## *COVID-19: Clinical Trials at VIHA*

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