



# COVID-19: Implications for Pharmacists - Round 3

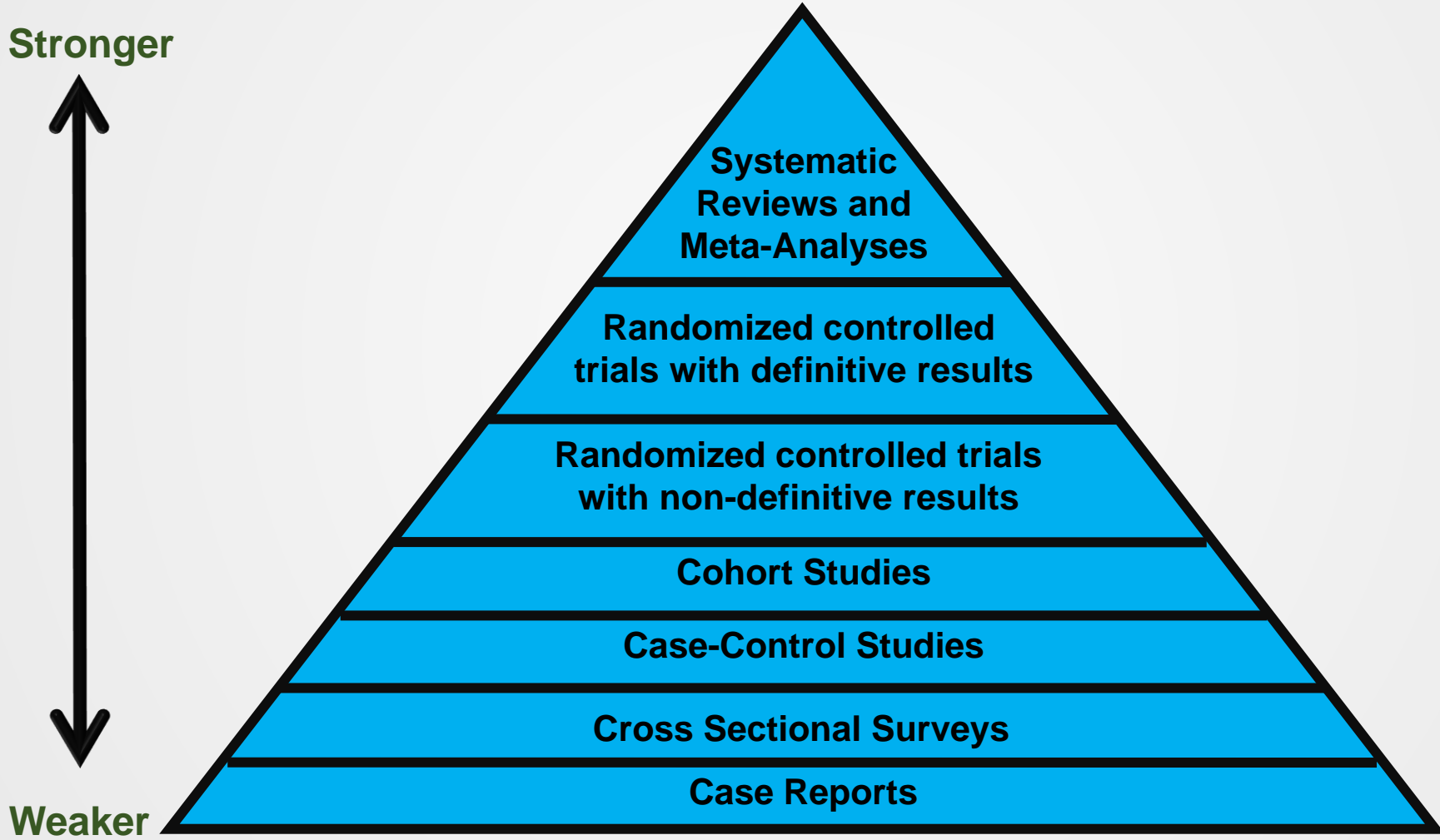
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# Objectives

1. Summarize the NIH/HHS recommendations regarding treatment of COVID-19
2. Describe the data regarding supplement use for treatment or prevention of COVID-19
3. Review the available tests to detect for presence of or immunity from COVID-19
4. State the potential role of pharmacists in testing for COVID-19

# Hierarchy of Evidence



# The Current Norm...

- ▶ Rapid release of information
- ▶ Hypotheses and loose associations turn into potential treatments
- ▶ Pre-publication before completion of peer review
- ▶ Recommendations from non-healthcare professionals



The NEW ENGLAND  
JOURNAL of MEDICINE

## Use of Commercial Disinfectants to Treat Novel Coronavirus (Covid-19) through Oral Administration or Subdermal Injection

Amanda Kerri, M.D., Andre Young, M.D., Trapper John, M.D., Meredith Gray, M.D., Douglas E. Powers, M.D.

Article

### BACKGROUND

On March 23<sup>rd</sup>, 2020, President Donald J. Trump, during his daily briefings on the response to Covid-19, suggested the use of disinfectants to treat patients infected with the novel coronavirus Covid-19. We conducted a study on the efficacy of using commercial disinfectants through oral administration or subdermal injection.

### METHOD

We read the labels on the bottles we found in the janitors closet.

### CONCLUSION

This will kill you. Don't do it.

# Coronavirus Disease 2019 (COVID-19) Treatment Guidelines

VIEW GUIDELINES

Available at <https://covid19treatmentguidelines.nih.gov>

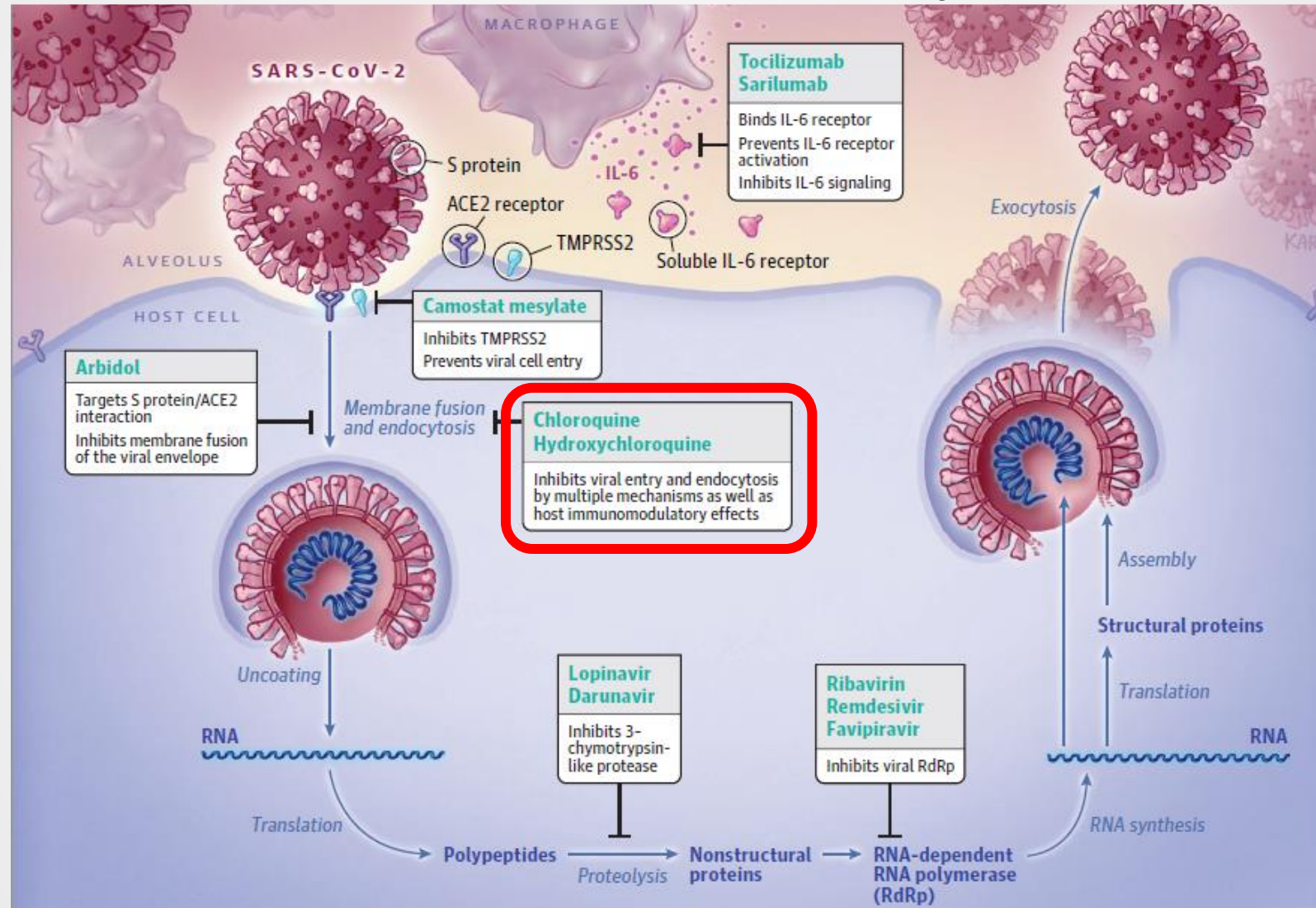
Developed by panel representing:

- ▶ American College of Chest Physicians
- ▶ American College of Emergency Physicians
- ▶ American Thoracic Society
- ▶ Biomedical Advanced Research and Development Authority
- ▶ Centers for Disease Control and Prevention
- ▶ Department of Defense
- ▶ Department of Veterans Affairs
- ▶ Food and Drug Administration
- ▶ Infectious Diseases Society of America
- ▶ National Institutes of Health
- ▶ Pediatric Infectious Diseases Society
- ▶ Society of Critical Care Medicine
- ▶ Society of Infectious Diseases Pharmacists

# Coronavirus Disease 2019 (COVID-19) Treatment Guidelines

- ▶ The COVID-19 Treatment Guidelines Panel does not recommend the use of any agents for **pre-exposure prophylaxis** against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) (A III)
- ▶ The Panel does not recommend the use of any agents for **post-exposure prophylaxis** against SARS-CoV-2 infection (A III)
- ▶ At present, no drug has been proven to be safe and effective for treating COVID-19. There are insufficient data to recommend either for or against the use of any antiviral or immunomodulatory therapy in patients with COVID-19 who have mild, moderate, severe, or critical illness (A III)

# Purported Pharmacotherapy for COVID-19



# Hydroxychloroquine (HCQ) in COVID-19

- ▶ Retrospective analysis; 368 hospitalized US Veterans
  - Death: 27.8% with HCQ; 22.1% with HCQ/AZ; 11.4%, neither
  - Ventilation: 13.3% with HCQ; 6.9% with HCQ/AZ; 14.1%, neither
- ▶ Open-label, randomized controlled trial; 150 patients from China
  - 28-day negative seroconversion:
    - 85.4% with HCQ vs 81.3% without (P=0.34)
  - Symptoms resolved quicker with HCQ



# HCQ with Azithromycin

## Drug-Drug Interactions (1)

Drugs:

AZITHROMYCIN –  
HYDROXYCHLOROQUINE SULFATE

Severity:



Documentation:

Good

Summary:

Concurrent use of HYDROXYCHLOROQUINE and QT PROLONGING AGENTS may result in increased risk of QT-interval prolongation.

Coadministration is not recommended (Prod Info PLAQUENIL® oral tablets, 2017) as life-threatening additive effects on the QT interval, including torsades de pointes, may occur

- ▶ University of Liverpool COVID-19 drug-interactions (<http://www.covid19-druginteractions.org/>)

# Drug Interactions on QTc in Exploratory COVID-19 Treatment

## Recommendations to minimize arrhythmia risk:

1. ECG/QT interval monitoring
  - Withhold medications if baseline QT  $\geq$ 500 msec, or known congenital long QT
  - Stop medications if QT becomes  $\geq$ 500 msec
2. Correct electrolyte abnormalities
  - Hypokalemia to  $>$ 4 mEq/L
  - Hypomagnesemia to  $>$ 2 mg/dL
3. Avoid other QTc prolonging medications whenever feasible

# Chloroquine (CQ)

- ▶ Double-blind trial in hospitalized with severe COVID-19 randomized to
  - High-dose CQ: 600 mg twice daily x 10 days
  - Low-dose CQ: 450 mg twice daily day 1 then once daily x 4 days
  
- ▶ Results:
  - Death at day 13: 39.0%, high-dose vs 15.0%, low-dose
  - QTc prolongation: 18.9%, high-dose vs. 11.1%, low-dose



## FDA Drug Safety Communication

FDA cautions against use of hydroxychloroquine or chloroquine for COVID-19 outside of the hospital setting or a clinical trial due to risk of heart rhythm problems

*Close supervision is strongly recommended*

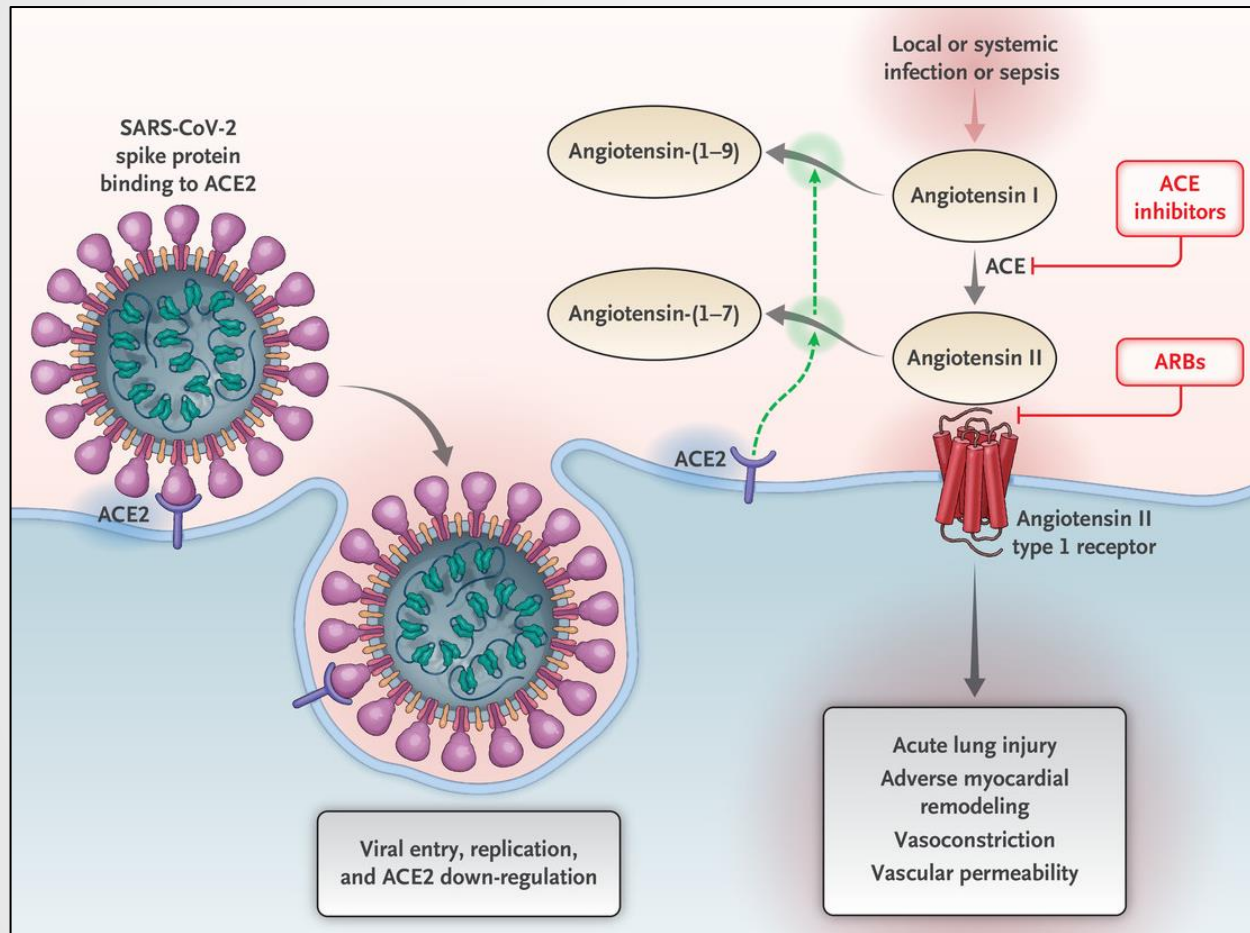
**Safety Announcement [04-24-2020]**

# Coronavirus Disease 2019 (COVID-19) Treatment Guidelines

- ▶ Persons with COVID-19 who are prescribed an **ACEi or ARB** for cardiovascular disease (or other indications) should continue these medications

(A III)

# SARS-CoV-2 and the RAAS are Related



- ▶ ACEi or ARB therapy can upregulate ACE2 expression in animal models
- ▶ ACEi or ARB therapy might increase SARS-CoV-2 attachment and COVID-19
- ▶ Observational data suggest COVID-19 patients with CVD/risk factors have worse outcomes

# ACEi/ARB use in COVID-19 from China

- ▶ Retrospective case series; 1178 hospitalized patients
  - 32.9% ACEi/ARB users had severe disease, 30.7% in non-users (P=.65)
  - 27.3% non-survivors used ACEi/ARB vs 33.0% in survivors (P=.34)
- ▶ Retrospective study; 1128 hospitalized patients with hypertension
  - ACEi/ARB users (n=188) compared to non-users (n=940)
    - Mortality rate lower in the ACEi/ARB group (3.7% vs. 9.8%; P = 0.01)
      - Adjusted for variables HR, 0.37 (95% CI, 0.15-0.89; p=0.03)
      - Compared to other antihypertensives HR, 0.30 (95% CI, 0.12-0.70; p=0.01)

# Coronavirus Disease 2019 (COVID-19) Treatment Guidelines

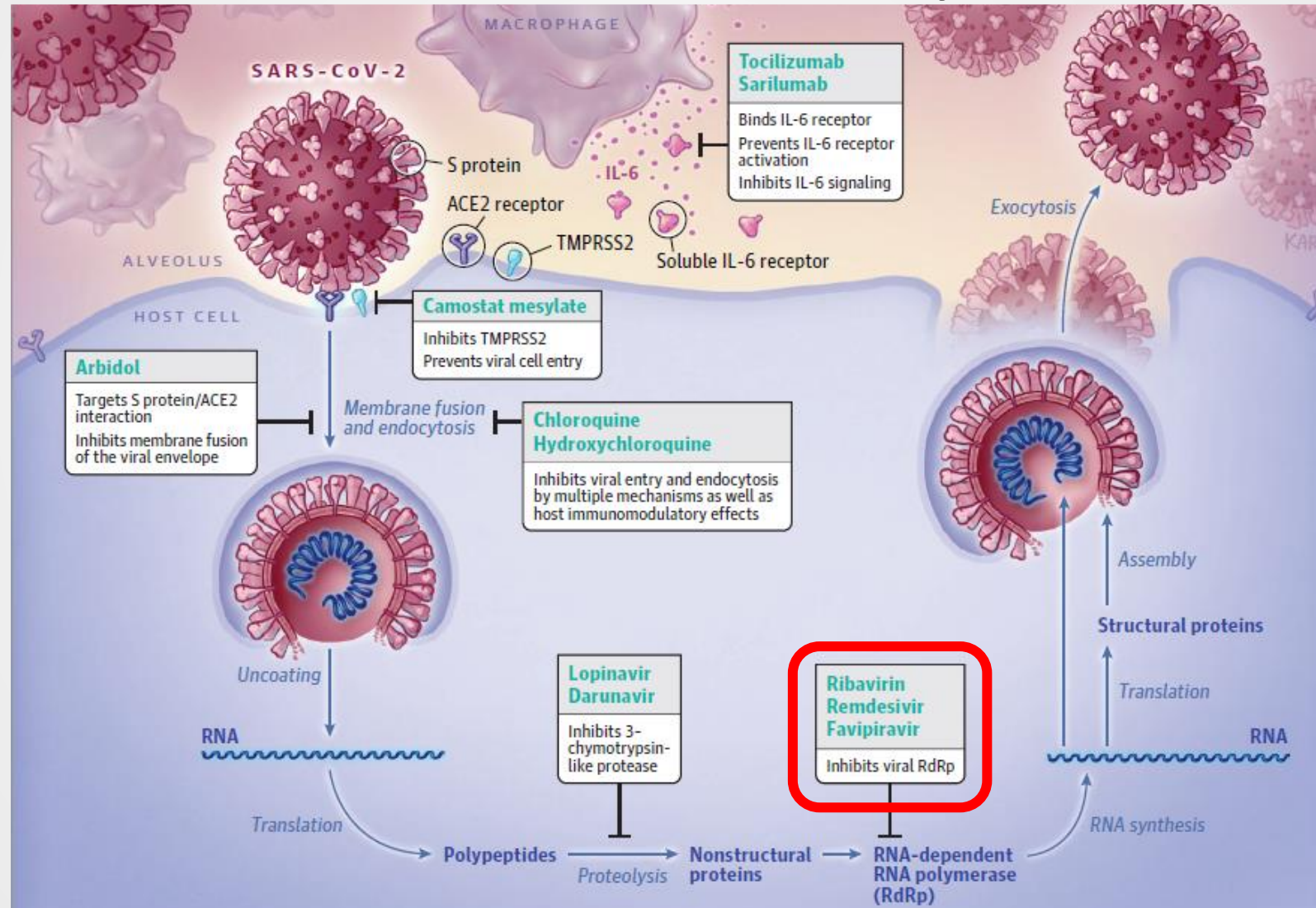
- ▶ Persons with COVID-19 who are prescribed **statin** therapy for the treatment or prevention of cardiovascular disease should continue these medications (A III)



# Coronavirus Disease 2019 (COVID-19) Treatment Guidelines

- ▶ **Oral corticosteroid therapy** used prior to COVID-19 diagnosis for another underlying condition (e.g., primary or secondary adrenal insufficiency, rheumatological diseases) should not be discontinued (A III)
- ▶ **Inhaled corticosteroids** used daily for patients with asthma and chronic obstructive pulmonary disease for control of airway inflammation should not be discontinued in patients with COVID-19 (A III)
- ▶ Persons with COVID-19 who are taking **NSAIDs** for a co-morbid condition should continue therapy as previously directed by their physician (A III)
- ▶ The Panel recommends that there be no difference in the use of **antipyretic strategies** (e.g., with acetaminophen or NSAIDs) between patients with or without COVID-19 (A III)

# Purported Pharmacotherapy for COVID-19



Sanders JM, et al. JAMA. doi:10.1001/jama.2020.6019 Published online April 13, 2020.

# Emerging Treatments: Possibly Effective

## ▶ Remdesivir

- 61 hospitalized patients requiring oxygen support
- Compassionate use provided for 10 days
  - 36 of 53 (68%) had clinical improvement in oxygen support
  - 25 of 53 (47%) were discharged
  - 7 of 53 (13%) died
  - No placebo group

## ▶ Convalescent Plasma

- Case series of five critically ill patients with COVID-19 and ARDS
- Treatment provided between days 10 and 22
- All five patients clinically improved
  - 3 were discharged
  - 2 in stable condition 37 days post treatment

# Want Ongoing COVID Updates?



- ▶ Ongoing ECHO sessions held virtually Mon/Wed/Fri 7:00 - 8:00 AM MST
  - Featured topic by local experts,
  - CO epidemiology updates
  - Medication updates
- ▶ Sign up:
  - <https://projectcore.echocolorado.org/Series/Registration/258>



# Supplements: Should we recommend them?

# Vitamin C: Does it help?

- ▶ Observational data suggests high-dose Vitamin C may benefit patients with sepsis and ARDS
- ▶ Upregulates protein channels regulating alveolar clearance
- ▶ RCT in China evaluating IV Vitamin C in patients with SARS CoV-2: 12g every 12 hours for 7 days
  - Primary outcome measure: # of ventilator free days
  - Expected completion date: September 2020

# Vitamin C: Does it help?

## BOTTOM LINE:

- There is only observational data with high-dose IV vitamin C in ARDS
- No evidence to support oral vitamin C can prevent or treat COVID-19

# What about Vitamin D?

- Metanalysis of 25 trials of patients with acute respiratory tract infections
  - NOT COVID-19 patients
  - Daily or weekly dosing of vitamin D decreased the risk of respiratory track infection
    - Most benefit seen in patients that had significant vitamin D deficiencies
  - The pandemic started during the winter when vitamin D levels are low



# Surely, elderberry can help, can't it?

- ▶ One relatively small (n=312) study claimed elderberry extract decreased the incidence and duration of cold symptoms
- ▶ Another small study (n=60) claimed elderberry syrup, started within 48 hours of flu symptoms, decreased symptoms four days earlier than those patient who received placebo
  
- ▶ **BOTTOM LINE:**
  - NO evidence that elderberry can prevent or treat COVID-19

# Emerging Treatments: Hope and Hype

- ▶ Bacille Calmette-Guérin (BCG) vaccine:
  - Ongoing trials
  - Unpublished study shows COVID-19 mortality lower among BCG-using countries
- ▶ Zinc lozenges
  - May shorten duration of the common cold.
  - Speculation that hydroxychloroquine helps the zinc enter SARS-CoV-2 infected cells and might then exert antiviral effects

# And more hype.....

## Missouri Sues Televangelist Jim Bakker For Selling Fake Coronavirus Cure

March 11, 2020 · 4:35 PM ET

Silver Solution "has been proven by the government that it has the ability to kill every pathogen it has ever been tested on, including SARS and HIV," Sellman continued. Four 4-ounce bottles could be yours, a message on the screen said, for just \$80.



Date: April 27, 2020

RE: Unapproved and Misbranded Products Related to Coronavirus Disease 2019 (COVID-19)

This is to advise you that the United States Food and Drug Administration (FDA) and the Federal Trade Commission (FTC) reviewed your website at the Internet address <https://hopewelloils.com> on April 13, 2020 and April 16, 2020, respectively. The FDA has observed that your website offers essential oils and herbal products in the United States and that these products are intended to mitigate, prevent, treat, or cure COVID-19 in people. Based on our review



**WARNING LETTER**

Date: April 27, 2020

RE: Unapproved and Misbranded Product Related to Coronavirus Disease 2019 (COVID-19)

This is to advise you that the United States Food and Drug Administration (FDA) and the Federal Trade Commission (FTC) reviewed your website at the Internet address <https://defendpatch.com> on April 16, 2020 and April 23, 2020, respectively. The FDA has observed that your website offers the "Defend™ Patch," a transdermal patch containing a "composition of botanical oils," for sale in the United States and that this product is intended to mitigate, prevent, treat, diagnose, or cure COVID-19<sup>[1]</sup> in people. Based on our review





# Testing

# Emergency Use Authorization (EUA)

- ▶ Allows unapproved products or unapproved uses of an approved product
- ▶ Public health emergency
- ▶ No adequate, approved or available alternatives
- ▶ Includes labs, PPE, ventilators






# Testing: What we know

- ▶ Pharmacists may administer CLIA-waived tests, provided they have a CLIA waiver
- ▶ All current CLIA-waived tests (as of 4/29/20 at noon) are for detecting the presence of virus
  - AKA, “molecular” or “PCR”
  - Variable approaches
    - Collection only (in partnership with a lab)
    - Collection and testing
    - Home testing
  - CLIA waiver only needed if the pharmacy runs the test

# Testing: What we know

- ▶ Antibody testing
  - AKA, serology tests
- ▶ There are no CLIA-waived tests for antibodies
  - Questionable sensitivity and specificity
  - Important from a public health perspective to detect viral prevalence in a community
  - Does NOT indicate an individual is immune

# CLIA-waived tests

Company	Test Name	Collection method	Timing of results	Product image
Abbott Diagnostics	ID Now COVID-19	Nasal, nasopharyngeal, or throat	5-13 mins	
Mesa Biotech Inc	Accula SARS-CoV-2 Test	Nasal or throat	30 mins	
Cepheid	Xpert Xpress SARS-CoV-2 Test	Nasal, mid-turbinate, nasopharyngeal	45 mins	



# Other considerations

## ► DORA/Governor's Communication (4/28/20)

- Make sure to include appropriate patient identifiers on all specimens
- State contacts:
  - Ben Henderson, Director of Operations ([Benjamin.s.henderson@state.co.us](mailto:Benjamin.s.henderson@state.co.us))
  - Alicia Cronquist, Chief of the Public Health Informatics, Reporting, and Refugee Branch ([alicia.cronquist@state.co.us](mailto:alicia.cronquist@state.co.us))

## ► Reimbursement



# Resources

## ▶ HHS Pharmacist Guidance

- <https://www.hhs.gov/sites/default/files/authorizing-licensed-pharmacists-to-order-and-administer-covid-19-tests.pdf>

## ▶ COVID-19 Tests

- <https://www.360dx.com/coronavirus-test-tracker-launched-covid-19-tests>

## ▶ Antibody Tests

- <https://www.centerforhealthsecurity.org/resources/COVID-19/serology/Serology-based-tests-for-COVID-19.html#sec2>

## ▶ FDA

- <https://www.fda.gov/medical-devices/emergency-situations-medical-devices/emergency-use-authorizations#ivdnote1>

# Continuing Education

## How to claim credit (pharmacists & pharmacy technicians)

1. Navigate to [UCDenver.edu/pharmacy/continuingeducation](https://UCDenver.edu/pharmacy/continuingeducation)
2. Select **Online CE**
3. Select Today's Webinar

Questions: [sop.continuingeducation@cuanschutz.edu](mailto:sop.continuingeducation@cuanschutz.edu)

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