Learning Objectives

• Discuss the proposed roles and mechanisms of action for vitamin use in illness
• Describe the evidence for use of vitamins in the treatment of conditions similar to COVID-19
• Describe potential renin-angiotensin system (RAS) disruptions secondary to COVID-19 infection
• Summarize the literature on the benefits and risks of RAS inhibitors, mainly ACE inhibitors and ARBs, for prevention and treatment of COVID-19 infection
Audience Participation

Control Panel

COVID-19 Resources

Speakers

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Critical Care Clinical Specialist III – Medical ICU
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Disclosures

In this session:

• Alexander H. Flannery reports grant funding from KidneyCure/American Society of Nephrology and La Jolla Pharmaceutical Company to study renin-angiotensin system in critical illness.

• All other planners, presenters, reviewers, and ASHP staff report no financial relationships relevant to this activity.

Webcast Recording

This webcast is being recorded.

To access go to: covid19.sccm.org/webcast or https://www.ashp.org/COVID-19
The Society of Critical Care Medicine (SCCM) and the American Society of Health-System Pharmacists (ASHP) partnered to produce this webinar on COVID-19.

Vitamin Treatment in COVID-19

Michael Sirimaturos, Pharm.D., BCNSP, BCCCP, FCCM
Critical Care Clinical Specialist III – Medical ICU
Houston Methodist Hospital, Houston, TX, USA

COVID-19 Resources
Learning Objectives

• Discuss the proposed roles and mechanisms of action for vitamin use in illness

• Describe the evidence for use of vitamins in the treatment of conditions similar to COVID-19

Vitamin Use in COVID-19

• Why vitamin use during COVID-19?
  • Role in essential cellular processes
  • Search for therapies to reduce inflammation, morbidity, mortality
  • Use in other critical care related illnesses
    • Acute Respiratory Distress Syndrome (ARDS)
    • Acute Lung Injury (ALI)
    • Sepsis

• Immunonutrition – modulation of the immune system with dietary nutrients
  • Clinical trials
    • Heterogeneous
    • Include multiple agents (i.e. vitamins, minerals, fatty acids, etc.)
    • Difficult to pinpoint a beneficial agent, if any

doi: 10.3390/nu12092550
Vitamin A

COVID-19 Resources

• Fat-soluble vitamin; also known as carotenoids (i.e. beta-carotene) or retinoids (i.e. retinoic acid)
  • Carotenoids are provitamins converted to retinoids in the body
    • Commonly found in fruits and vegetables
  • Retinoids regulate gene transcription, vision, epithelial membrane, and bone metabolism
    • Commonly found in animal sources (i.e. meat, fish, eggs)
• Reference daily intake (RDI) = 900 mcg (retinol activity equivalents – RAE)
• Vitamin A deficiency dosing
  • 30,000 mcg RAE (100,000 IU) IM x 3 days, then
  • 15,000 mcg RAE (50,000 IU) IM x 14 days, then
  • 3,000-6,000 mcg RAE (10,000-20,000 IU) PO daily x 2 months
Vitamin A

- Proposed benefits
  - Lung – studied in COPD, asthma, ARDS
  - Controls expression of surfactant proteins
  - Reverses airway hyper-responsiveness; down-regulates oxidative stress
  - Potential antimicrobial qualities attributed to immune modulating factors
  - Influences production of IL1-β and IL-1 receptor antagonist by alveolar macrophages and subsequent pulmonary infiltration of neutrophils
  - Immunoregulatory processes
  - Promote proliferation of T-lymphocytes (increase in IL-2) and differentiation into regulatory T cells
    - Used as an adjunct to vaccines (i.e. influenza, measles) → increase effect of antibody response

Vitamin A in COVID-19

- Sept 2020 (n=10)
  - Vitamin A as primary therapy (n=1)
  - No completed RCTs
  - Combination therapy

<table>
<thead>
<tr>
<th>Name</th>
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<th>Dose</th>
<th>Primary Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>NCT04323228</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Saudi Arabia</td>
<td>40</td>
<td>Vitamin A 1500 mcg (with other vitamins and minerals)</td>
<td>Inflammatory markers (CRP, IL-6, ferritin, TNF-α) &amp; change in NRS-2002 score @ 3 mo.</td>
</tr>
</tbody>
</table>

Vitamin B

COVID-19 Resources

Vitamin B
• Water-soluble vitamins

<table>
<thead>
<tr>
<th>Vitamin</th>
<th>Chemical Name</th>
<th>Role</th>
<th>Reference Daily Intake</th>
</tr>
</thead>
<tbody>
<tr>
<td>B1</td>
<td>Thiamine</td>
<td>Dextrose and amino acid catabolism</td>
<td>1.2 mg</td>
</tr>
<tr>
<td>B2</td>
<td>Riboflavin</td>
<td>Flavoprotein enzyme reactions</td>
<td>1.3 mg</td>
</tr>
<tr>
<td>B3</td>
<td>Niacin</td>
<td>Various metabolic processes</td>
<td>16 mg</td>
</tr>
<tr>
<td>B5</td>
<td>Pantothenic acid</td>
<td>Precursor of coenzyme A</td>
<td>5 mg</td>
</tr>
<tr>
<td>B6</td>
<td>Pyridoxine</td>
<td>Various metabolic processes</td>
<td>1.7 mg</td>
</tr>
<tr>
<td>B7</td>
<td>Biotin</td>
<td>Gluconeogenesis and fatty acid synthesis</td>
<td>30 mcg</td>
</tr>
<tr>
<td>B9</td>
<td>Folate</td>
<td>DNA synthesis and repair</td>
<td>400 mcg</td>
</tr>
<tr>
<td>B12</td>
<td>Cyanocobalamin</td>
<td>DNA, fatty acid, &amp; amino acid metabolism</td>
<td>2.4 mcg</td>
</tr>
</tbody>
</table>

doi: 10.3390/nu12092550
https://www.fda.gov/media/99069/download
Vitamin B
• Proposed benefits
  • Theoretical benefits in sepsis (Vitamin B1)
    • Hydrocortisone, ascorbic acid, thiamine (“HAT therapy”)
    • Glucose metabolism - Cofactor for pyruvate dehydrogenase; converts pyruvate to acetyl-CoA (Krebs cycle)
      • Low thiamine levels lead to impaired aerobic respiration → increased lactic acidosis
    • Important in antioxidant pathway via generation of NADPH and glutathione cycling and cellular anabolism
  • Reduction of viral titers in MERS-CoV (Vitamin B2)
  • Possible binding affinity to SARS-CoV-2 protease (Vitamins B3, B9, B12)

Vitamin B in COVID-19
• Sept 2020 (n=6)
  • Vitamin B as primary therapy (n=3)
  • No completed RCTs
  • Primarily combination therapy

<table>
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<tr>
<th>Name</th>
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<th>Location</th>
<th>Size</th>
<th>Dose</th>
<th>Primary Outcomes</th>
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</thead>
<tbody>
<tr>
<td>NCT04407390</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Denmark</td>
<td>N=100</td>
<td>Nicotinamide 1 g daily x 14 days</td>
<td>Need for O₂</td>
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<tr>
<td>NCT04354428</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>USA</td>
<td>N=630</td>
<td>Folate 800 mcg x 1, then 400 mcg x 4 days</td>
<td>Lower respiratory tract infections</td>
</tr>
<tr>
<td>NCT04507867</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Mexico</td>
<td>N=240</td>
<td>Folate 5 mg BID</td>
<td>57 primary endpoints listed</td>
</tr>
</tbody>
</table>
Vitamin C

COVID-19 Resources

- Water-soluble vitamin; also known as ascorbic acid
- Role
  - Antioxidant; support host defenses against infection and oxidative stress
  - Infections may decrease Vitamin C concentrations
  - Selective interest recently for repurposing Vitamin C
    - Common cold
    - ARDS
    - Sepsis/septic shock
    - COVID-19
- Reference Daily Intake = 90 mg
- Scurvy dosing
  - up to 1,000 mg PO daily in divided doses x 2-4 weeks
  - 200 mg IV daily x 1-2 weeks

https://www.fda.gov/media/99069/download
Vitamin C

- Proposed benefits
  - Reduction of reactive oxygen species (ROS)
  - Inhibition of nitric oxide expression \(\rightarrow\) decrease in vasodilation
  - Decreased endothelial and microvascular dysfunction
  - Bacteriostatic effects
  - Biosynthesis of norepinephrine

COVID-19 Resources

Could Vitamin C Be the Cure for Deadly Infections?
A new protocol that includes this common nutrient could save millions of lives—and has already sparked a major debate among doctors.
Vitamin C

- Vitamin C in sepsis
  - Marik et al. 2017
  - Treatment vs. standard of care (pre-treatment cohort)
    - High dose IV Vitamin C 1.5 g q 6 hrs (6 g/day) x 4 days
    - Hydrocortisone 50 mg q 6 hrs (200 mg/day) x 7 days
    - Thiamine 200 mg BID (400 mg/day) x 4 days
  - Primary outcome: Hospital mortality – 8.5% vs. 40.4%; p < 0.001
  - Impact: yet to be seen
  - Controversy
    - Beneficence? Mega dosage strategy (Vitamin C 6 g/day)
    - Generalizability? Single center, non-randomized, retrospective before-after study
    - Reproducibility? High rate of mortality at baseline
    - Too simple? Too good to be true?

Vitamin C

- Vitamin C in sepsis
  - Nov 2017 (n=11)
**Vitamin C**

- Vitamin C in sepsis
  - Sept 2020 (n=40)

---

**Vitamin C**

- Vitamin C in infections
  - Common cold
    - Cochrane Systematic Review (Hemila 2013)
      - 29 trials; 11,306 participants; Decreased duration of symptoms
    - Meta-Analysis (Hindawi 2018)
      - 9 trials; Decreased symptom duration only with regular supplementation
  - Sepsis/septic shock
    - Marik, et al., CITRIS-ALI, VITAMINS, ORANGES, HYVCTSSS

<table>
<thead>
<tr>
<th>Mortality</th>
<th>Marik et al.</th>
<th>CITRIS-ALI</th>
<th>VITAMINS</th>
<th>ORANGES</th>
<th>HYVCTSSS</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(+)¹</td>
<td>(+)¹</td>
<td>(-)²</td>
<td>(-)²</td>
<td>(-)²</td>
</tr>
<tr>
<td>Vasopressor</td>
<td>(-)²</td>
<td>N/A</td>
<td>(+)¹</td>
<td>(+)¹</td>
<td>(+)²</td>
</tr>
<tr>
<td>duration</td>
<td>(-)¹</td>
<td>(-)¹</td>
<td>(+)¹</td>
<td>(+)¹</td>
<td>(+)²</td>
</tr>
<tr>
<td>SOFA score</td>
<td>(-)¹</td>
<td>(-)¹</td>
<td>(+)¹</td>
<td>(+)¹</td>
<td>(+)²</td>
</tr>
</tbody>
</table>

¹ = Primary endpoint; ² = Secondary endpoint; (+) = in favor of vitamin C; (-) = not in favor of vitamin C
Vitamin C

• Vitamin C in COVID-19
  • Sept 2020 (n=39)
  • No completed RCTs
  • Majority combination therapy


<table>
<thead>
<tr>
<th>Name</th>
<th>Blind</th>
<th>Placebo</th>
<th>RCT</th>
<th>Location</th>
<th>Dose</th>
<th>Primary Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>NCT04357782 (AVoCaDO)</td>
<td>N</td>
<td>N</td>
<td>N</td>
<td>USA</td>
<td>50 mg IV q 6h x 4d</td>
<td>Incidence of adverse events</td>
</tr>
<tr>
<td>NCT04342728 (COVIDAtoZ)</td>
<td>N</td>
<td>N</td>
<td>Y</td>
<td>USA</td>
<td>8 g/d divided +/- zinc</td>
<td>Time to 50% symptom reduction</td>
</tr>
<tr>
<td>NCT04395768</td>
<td>N</td>
<td>N</td>
<td>Y</td>
<td>Australia</td>
<td>50 mg/kg IV q 6h x 1d, 100 mg/kg IV q 6h x 7d</td>
<td>Death @ 15d &amp; 45d</td>
</tr>
<tr>
<td>NCT04363216</td>
<td>N</td>
<td>N</td>
<td>Y</td>
<td>USA</td>
<td>0.3 g/kg IV x 1, 0.6 g/kg x 1, 0.9 g/kg x 4d</td>
<td>Clinical improvement @ 3d</td>
</tr>
<tr>
<td>NCT03680274 (LOVIT)</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Canada</td>
<td>50 mg/kg IV q 6h x 4d</td>
<td>Death &amp; organ dysfunction in septic or COVID-19 @ 28d</td>
</tr>
<tr>
<td>NCT04401150 (LOVIT-COVID)</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Canada</td>
<td>50 mg/kg IV q 6h x 4d</td>
<td>Death &amp; organ dysfunction @ 28d</td>
</tr>
<tr>
<td>NCT04344184 (EVICT-CORONA-ALI)</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>USA</td>
<td>100 mg/kg IV q 8h x 3d</td>
<td>Vent free days @ 28d</td>
</tr>
</tbody>
</table>

70 kg
28 g/d
63 g/d

COVID-19 Resources
Vitamin C

• Takeaways
  • Increasing number of studies with high dose Vitamin C will add to safety data (or lack thereof)
    • Calcium oxalate (kidney stones)
      • Thiamine = protective effect
    • Severe hypernatremia – Vitamin C formulations contain sodium
      • 1.5 g q 6 hrs = ~7,000 mg Na
      • 50 mg/kg q 6 hrs = ~16,000 mg Na
    • “Hyperglycemia” or masked hypoglycemia
      • Interference with oxidative-reduction reaction-based tests (i.e. glucometers)
  • However, “limited major safety issues” + lack of sufficient efficacy data = caution in use
  • Unapproved IV products removed from the market = nationwide shortage

Vitamin D

COVID-19 Resources
**Vitamin D**

- Fat-soluble vitamin; also known as ergocalciferol (D2), cholecalciferol (D3), calcifediol, and calcitriol
  - Dietary sources: oily fish (D3), egg yolks (D3), plants (D2)
  - De novo synthesis in the skin (D3) with ultraviolet B light
- Primary function: mineral homeostasis (Ca, Mg, Phosphate)
- Deficiency affects up to 1 billion people worldwide, especially dark skinned, elderly, and those distant from the equator
  - Drug-drug interactions
    - Antiepileptic agents: phenobarbital, carbamazepine, phenytoin, primidone
    - Corticosteroids: dexamethasone
    - Antiretrovirals: efavirenz
- Reference daily intake = 20 mcg (800 IU)
- Vitamin D deficiency dosing
  - 1250 mcg (50,000 IU) PO weekly x 6 weeks OR
  - 25-50 mcg (1,000-2,000) IU PO daily

**Proposed benefits**

- Antimicrobial effects
  - Augments natural protective barriers – preserves tight, gap, and adheren junctions between epithelial cells; suppress CD26/DDP4 (adhesion molecules) – pathway for host cell access in COVID-19
  - Enhances innate cellular immunity – promotes release of defensins & cathelicidins within the cell
    - Cathelicidins have direct antimicrobial effects against enveloped (i.e. coronavirus) & non-enveloped viruses
- Boosts adaptive immunity
- Inflammatory mediation (ALI, ARDS)
  - Stimulates Th2 cells and regulatory T cells; attenuates Th1 cells – decrease in proinflammatory cytokines (TNF-α, INF-γ)
  - Respiratory epithelium converts vitamin D to active form
    - Modulates expression of angiotensin converting enzyme I (ACE1) and ACE2 in the Renin-angiotensin system (RAS) → decrease in alveolar permeability → decreased pulmonary edema, hypoxemia, and pulmonary hypertension
    - Calcitriol upregulates pulmonary ACE2 and downregulates renin and angiotensin II → decreasing progression of infection-induced ARDS
Vitamin D

**Vitamin D in Respiratory Tract Infections**
- Martineau AR; BMJ 2017
  - Systematic review & meta-analysis
  - 25 RCT, double blind, placebo controlled trials
  - n= 10,933
  - Vitamin D supplementation for prevention of acute respiratory tract infections (RTI)
  - Primary endpoint: reduction in RTI; OR 0.88; p=0.003
    - Moderate heterogeneity (I² = 53.3%)
  - Subgroup analyses
    - Baseline vitamin D levels < 25 vs. > 25 nmol/L
      - OR 0.58; p=0.002 vs. OR 0.89; p=0.15
    - Daily or weekly dosing vs. bolus (30,000+ IU)
      - OR 0.81; p<0.001 vs. OR 0.97; p=0.67

**Vitamin D in Critical Illness**
- VITdAL-ICU study; JAMA 2017
  - Effect of High-Dose Vitamin D₃ on Hospital Length of Stay in Critically Ill Patients with Vitamin D Deficiency
  - RCT, double blind, placebo controlled, single center, Austrian, phase 2 study
  - n = 475 with Vitamin D level < 20 ng/mL; Vitamin D 540,000 IU x 1, then 90,000 IU/month x 5 months vs. placebo
  - Primary endpoint: Hospital LOS; 20.1 vs. 19.3 days; p=0.98
  - Subgroup analysis
    - Hospital mortality in severe vitamin D deficiency vs. placebo
      - 28.6% vs. 46.1%; HR 0.51; p=0.009
    - 6-month mortality in severe vitamin D deficiency vs. placebo
      - 34.7% vs. 50.0%; HR 0.60; p=0.12
Vitamin D

- Vitamin D in Critical Illness
  - VIOLET study; *NEJM* 2019
    - Early High-Dose Vitamin D for Critically Ill, Vitamin D-Deficient Patients
    - The National Heart, Lung, and Blood Institute PETAL Clinical Trials Network study
    - RCT, double blind, placebo controlled, phase 3 study
    - n = 1,078 with Vitamin D level < 20 ng/mL; Vitamin D 540,000 IU x 1 or placebo
    - Primary endpoint: 90 day all-cause mortality; 23.5% vs. 20.6%; CI -2.1 to 7.9; p=0.26
  - Subgroup analysis
    - Mortality higher in the Vit D group: sepsis, pneumonia, infection, and pre-randomized ARDS

- Vitamin D in COVID-19
  - Sept 2020 (n=45)
  - No completed RCTs
  - Majority combination therapy

Vitamin D doi: 10.1056/NEJMoa1911124

Vitamin D in Critical Illness

Early High-Dose Vitamin D for Critically Ill, Vitamin D-Deficient Patients

The National Heart, Lung, and Blood Institute PETAL Clinical Trials Network study

RCT, double blind, placebo controlled, phase 3 study

n = 1,078 with Vitamin D level < 20 ng/mL; Vitamin D 540,000 IU x 1 or placebo

Primary endpoint: 90 day all-cause mortality; 23.5% vs. 20.6%; CI -2.1 to 7.9; p=0.26

Subgroup analysis

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Vitamin D in COVID-19

Sept 2020 (n=45)

No completed RCTs

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Vitamin D in COVID-19

Sept 2020 (n=45)

No completed RCTs

Majority combination therapy

Vitamin D doi: 10.1056/NEJMoa1911124
Vitamin E

COVID-19 Resources

- Fat-soluble vitamin; also known as tocopherols (α-tocopherol) and tocotrienols
  - Dietary sources: nuts, legumes, avocados, sunflower seeds
- Primary functions:
  - Lipid component of cell membranes
  - Antioxidant → neutralizes free radicals and reactive oxygen species
  - Enhance immune response
- Reference daily intake = 15 mg
- Vitamin E deficiency dosing: 40-50 mg (60-75 IU) PO daily
Vitamin E

• Proposed benefits
  • Enhanced immune response
    • Decrease production of nitrogen oxide → prostaglandin E2 down regulation and inhibits cyclooxygenase-2 (COX-2)
    • Initiation of T-lymphocyte signaling
    • Modulation of Th1/Th2 balance (cellular/humoral immune response)
    • Inhibition of protein kinase C (PKC) → affecting the proliferation of monocytes, macrophages, neutrophils, and smooth muscle cells
    • Reduce superoxide free radical production

Vitamin E in COVID-19
• Sept 2020 (n=9)
  • Vitamin E as primary therapy (n=1)
• No completed RCTs
• Combination therapy

### Vitamin E in COVID-19 Trials

<table>
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<tr>
<th>Name</th>
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<td>Saudi Arabia</td>
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<td>Vitamin E 90 mg (with other vitamins and minerals)</td>
<td>Inflammatory markers (CRP, IL-6, ferritin, TNF-α) &amp; change in NRS-2002 score @ 3 mo.</td>
</tr>
</tbody>
</table>

Vitamin Guidance in COVID-19

**COVID-19 Resources**

- American Society of Parenteral and Enteral Nutrition (ASPEN)
  - Published May 27, 2020; Robert Martindale, Beth Taylor, Stephen McClave
  - "No recommendation is made other than that supported by the societal guidelines"
  - "Caution must be exercised before wide acceptance of unsubstantiated or unstudied recommendations are made in patients with COVID-19 infections"

- The European Society for Clinical Nutrition and Metabolism (ESPEN)
  - Published: June 1, 2020
  - "Subjects with malnutrition should ensure sufficient supplementation with vitamins and minerals"
  - "There is no established evidence that routine, empirical use of supraphysiologic or supratherapeutic amount of micronutrients may prevent or improve clinical outcomes of COVID-19...we suggest that provision of daily allowances for vitamins and trace elements be ensured to malnourished patients"
Vitamin Guidance in COVID-19

- National Institutes of Health (NIH)
  - Updated: July 17, 2020
  - Vitamin C
    - Non-critically ill - Insufficient data to recommend for or against use
      - No compelling reason to use – less oxidative stress or severe inflammation
    - Critically ill – Insufficient data to recommend for or against use
      - No completed RCTs
  - Vitamin D
    - Insufficient data to recommend for or against use

Takeaways

- No COVID-19 RCTs are available to indicate treatment dose of vitamin therapy cause benefit/harm
  - Most RCT results most likely will not have definitive answers
    - Underpowered
    - Multiple confounding therapies
- Non-COVID-19 clinical trials for treatment dose vitamin therapy demonstrate mixed results
  - Majority non-inferiority
  - Few superiority
  - Few inferiority/harm
- No current national clinical guidelines/guidance recommend use of treatment dose vitamin therapy
  - Caution for supratherapeutic treatment dosing unless in a clinical trial
  - Supplemental therapy may benefit malnourished patients or those with vitamin deficiency
    - Unlikely to cause harm if used at the Reference Daily Intake (RDI)

doi: 10.1016/j.clinu.2020.03.022
Vitamin Treatment in COVID-19

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COVID-19 Resources

RAS Inhibition in COVID-19

Alexander H. Flannery, Pharm.D., FCCM, BCCCP, BCPS
Assistant Professor
University of Kentucky College of Pharmacy

COVID-19 Resources
Objectives

- Following the presentation, the attendee will be able to:
  - Describe potential renin-angiotensin system (RAS) disruptions secondary to COVID-19 infection
  - Summarize the literature on the benefits and risks of RAS inhibitors, mainly ACE inhibitors and ARBs, for prevention and treatment of COVID-19 infection
COVID-19 and RAS

SARS-CoV-2 receptor-binding domain affinity for ACE2

ACE Inhibitors & ARBs

- ACE Inhibitors
  - Block ACE, not ACE2
- ARBs
  - Block ATR1
“The HFSA, ACC, and AHA recommend continuation of RAAS antagonists for those patients who are currently prescribed such agents for indications for which these agents are known to be beneficial, such as heart failure, hypertension, or ischemic heart disease. In the event patients with cardiovascular disease are diagnosed with COVID-19, individualized treatment decisions should be made according to each patient’s hemodynamic status and clinical presentation. Therefore, be advised not to add or remove any RAAS-related treatments, beyond actions based on standard clinical practice.”
Should non-COVID-19 patients stop taking ACEI/ARB?

Living Systematic Review

- Limited to observational data, primarily of symptomatic patients
- 3 studies with over 8,000 patients driving recommendation
- “Moderate-certainty evidence” no association between RAS inhibition and positive test
Should non-COVID-19 patients stop taking ACEI/ARB?

Most likely not.

For patients testing positive for COVID-19, should we stop ACEI/ARB?
BRACE CORONA

Multicenter trial (Brazil) from 29 centers
Patients hospitalized with COVID-19
n = 659

Temporarily stopping ACEI/ARB for 30 days vs.
continuing therapy

Key exclusion: > 3 antihypertensive drugs,
sacubitril/valsartan, or hemodynamically unstable

Primary outcome: days alive and out of hospital

Results: 21.9 (stopped) vs. 22.9 (continued) days
Difference: -1.1 days (95% CI -2.33 to 0.17)

Mortality similar: 2.7% (stopped) vs. 2.8% (continued)
For patients testing positive for COVID-19, should we stop ACEI/ARB?

No (level I evidence)
Future Work

20+ active clinical trials
Questions?
Thank you for attending!

• The recording will be available soon, to access go to: covid19.sccm.org/webcast or https://www.ashp.org/COVID-19

• The Society of Critical Care Medicine and the American Society of Health-System Pharmacists would like to thank you for attending today.