William J. Bommer, MD, FACP, FACC

Chairman, Right Care Initiative Capital Region University of Best Practices; Executive Committee, American College of Cardiology, California Chapter; Professor, Division of Cardiovascular Medicine, University of California, Davis

Dr. Bommer’s service to the American College of Cardiology includes his current role on the California Executive Committee; as well as former roles as President, Vice-President, Governor, and Member of the Board of Governors. As an accomplished UC Davis Clinical Professor of Medicine, he directs UC Davis Cardiology’s Noninvasive Services; directs the Cardiology Fellowship Training Program and sees patients in the CCU. As the longest-tenured UCD Training Director, he has trained over 200 practicing cardiologists. Dr. Bommer has been the Principal Investigator or Co-Investigator of multiple NIH, NHLBI, and international research trials. He is a member of 50 international, national, state, and university education commissions and committees. Dr. Bommer founded and is a Board Member of numerous hardware and software startup companies and is an inventor or co-inventor of patents for xerography, color-flow ultrasound imaging, and contrast echocardiography. His public service includes consulting with the State of California and directs multiple programs including CA Pilot PCI (offsite) Program, CA Elective PCI (offsite) Program, and CA Cardiac Surgery and Intervention Outcomes Program. He has authored over 250 scientific publications, received over 100 Honors and Awards, presented over 1000 papers at International, National, and Statewide meetings, and coauthored California Legislation including SB 357 and SB 906. A Physics and Chemistry graduate of Cornell University, he received his medical degree from the State University of New York. He is an Honorary Lifetime Member of the British Cardiovascular Society and an accomplished marathon runner.
COVID-19: THE MOST LETHAL PANDEMIC IN 102 YEARS
RIGHT CARE INITIATIVE
MAY 11, 2020

WILLIAM BOMMER, MD FACC
UNIVERSITY OF CALIFORNIA, DAVIS
Structural and genetic organization of SARS CoV2

SARS CoV-2 fully assembled

- Spike Glycoprotein
- Ribonucleoprotein
- Envelope
- Membrane protein

SARS CoV-2 gene structure

5'UTR  pp1ab  pp1a  S  3a  E  M  7a  8b  N  3'UTR

16 untranslated regions
4 translated regions: S, E, M, N
156 mutations are known

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WHAT ARE SOME OF THE THINGS PEOPLE LIVING WITH CHRONIC CONDITIONS CAN DO TO PROTECT THEMSELVES AGAINST THIS VIRUS?

SARS-CoV
SARS from 2002-2003

&

SARS-CoV-2
COVID-19

The spike protein of SARS-CoV-2 is primed by TMPRSS2

Activation

Attachment

Angiotensin converting enzyme (ACE2)

SARS-CoV-2 uses the ACE2 receptor for host cell entry

HOST CELL

IHOST CELL WALL

Attachment protein “spike”

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Environmental Protection

SARS-CoV-1/2 environmental sensitivity

- Enveloped virus (with a plasma membrane), disrupted by surfactants/detergents, 60-80% alcohol, bleach.

- Sensitive to UV
  - 2–3x more sensitive than influenza virus to UV (Pubmed [17880524, 16254359]).
  - Estimated 10-fold survival decrease after 2–3h direct sunlight

- Sensitive to temperature
  - 10-fold survival decrease with 5°C temperature increase (Pubmed [22312351])
  - Killed by 30min 75°C heat (Pubmed [14631830])
WHAT TO DO AND BE AWARE OF IF A HIGH-RISK INDIVIDUAL CONTRACTS THE VIRUS

Contact your Healthcare Provider

FEVER: Contact your Healthcare Provider

- Headache 14%
- Nasal congestion 5%
- Sore throat 14%
- Dry cough 68%
- Productive cough 33%
- Dyspnea 19%
- Nausea/emesis 5%
- Diarrhea 4-14%
- Myalgias 15%
Progression to late disease varies by age

**B cells**
- Robust secretion of high-avidity antibodies

**CD8+ CD28+ T cells**
- Diverse repertoire
- Robust response to antigens

**CD4+ T cells**
- Diverse repertoire
- Robust response to antigens

**Salutary environment**

**Strength of immune response**

**Aging**

**B cells**
- Reduced antibody avidity and/or number of responding cells

**CD8+ T cells**
- Expansion of CD8+ CD28- cells
- Skewed repertoire

**CD4+ T cells**
- Increase differentiation into Th17 cells

**Inflammatory environment**

To respiratory viruses, such as flu and SARS.

[https://doi.org/10.1098/rspe.2020.0435](https://doi.org/10.1098/rspe.2020.0435)
WHAT MAKES AN INDIVIDUAL HIGH-RISK FOR CORONAVIRUS COMPLICATIONS?

WHY ARE PEOPLE WITH CERTAIN CHRONIC CONDITIONS MORE SEVERELY AFFECTED THAN OTHERS?

Underlying conditions among adults hospitalized with COVID-19


Source: MMWR. 2020 Apr 8:69(early release):1-7

<table>
<thead>
<tr>
<th>Demographics and clinical characteristics</th>
<th>Total (n=191)</th>
<th>Non-survivor (n=54)</th>
<th>Survivor (n=137)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>56.0 (46.0-67.0)</td>
<td>69.0 (63.0-76.0)</td>
<td>52.0 (45.0-58.0)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Sex</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>Female</td>
<td>72 (38%)</td>
<td>16 (30%)</td>
<td>56 (41%)</td>
<td>--</td>
</tr>
<tr>
<td>Male</td>
<td>119 (62%)</td>
<td>38 (70%)</td>
<td>81 (59%)</td>
<td>--</td>
</tr>
<tr>
<td>Exposure history</td>
<td>73 (38%)</td>
<td>14 (26%)</td>
<td>59 (43%)</td>
<td>0.028</td>
</tr>
<tr>
<td>Current smoking</td>
<td>41 (53%)</td>
<td>4 (9%)</td>
<td>57 (44%)</td>
<td>0.21</td>
</tr>
<tr>
<td>Comorbidty</td>
<td>91 (48%)</td>
<td>36 (67%)</td>
<td>55 (40%)</td>
<td>0.0010</td>
</tr>
<tr>
<td>Hypertension</td>
<td>58 (30%)</td>
<td>26 (48%)</td>
<td>32 (23%)</td>
<td>0.0008</td>
</tr>
<tr>
<td>Diabetes</td>
<td>36 (19%)</td>
<td>17 (31%)</td>
<td>19 (14%)</td>
<td>0.0051</td>
</tr>
<tr>
<td>Coronary heart disease</td>
<td>15 (8%)</td>
<td>13 (24%)</td>
<td>2 (1%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Chronic obstructive lung disease</td>
<td>6 (3%)</td>
<td>4 (7%)</td>
<td>2 (1%)</td>
<td>0.047</td>
</tr>
<tr>
<td>Carcinoma</td>
<td>2 (1%)</td>
<td>0</td>
<td>2 (1%)</td>
<td>0.37</td>
</tr>
<tr>
<td>Chronic kidney disease</td>
<td>2 (1%)</td>
<td>2 (4%)</td>
<td>0</td>
<td>0.024</td>
</tr>
<tr>
<td>Other</td>
<td>22 (77%)</td>
<td>11 (29%)</td>
<td>11 (8%)</td>
<td>0.016</td>
</tr>
</tbody>
</table>
WHAT MAKES AN INDIVIDUAL HIGH-RISK FOR CORONAVIRUS COMPLICATIONS?

- Hypertension is associated with a higher risk of severe COVID-19 disease and greater mortality rates.
- Until further studies reveal the impact of pre-existing or de novo RAS blockade on COVID-19 disease progression or severity, there is no justification to omit RAS blockers in COVID-19 patients.

Recent retrospective data may be consistent with this hypothesis. In this study, the use of ARBs in hypertensive patients with COVID-19 was associated with lower risk of adverse outcomes (OR of severe disease=0.343). Another study in their retrospective
Figure 1: Etiology of troponin elevation in patients with SARS-COV-2 infection and its prognostic implication

AMI: Acute myocardial infarction, PE: pulmonary embolism, AHF: acute heart failure, MI: myocardial infarction, ICU: intensive care unit
Acute Coronary Syndrome in the COVID-19 Pandemic Era: how to triage and when to resort to invasive strategies

Take Home Points:

- Timely primary percutaneous coronary intervention (PCI) remains the mainstay treatment for ST-elevation myocardial infarction (STEMI).

- In case of patient- or system-related delays in mechanical reperfusion in the contemporary COVID-19 era, fibrinolytic therapy within door-to-balloon of 30 minutes may be an alternative treatment for STEMI in the absence of contraindications.

- An invasive strategy is highly recommended for patients with non-ST-elevation acute coronary syndrome (NTE-ACS) who are at high risk.

- In the COVID-19 era, and especially when the local community outbreak is increasing and the healthcare system is overwhelmed, moderate- and low-risk patients with NSTE-ACS can be treated with an ischemia-guided approach.
Figure 3. Invasive Therapies for ACS Patients in the COVID-19 Era.

Emergent invasive angiography for reperfusion / revascularization*

Critically-ill ACS
- Cardiogenic shock
- Hemodynamically unstable
- Refractory heart failure
- Mechanical complications^
- Malignant ventricular arrhythmias
- Out-of-hospital cardiac arrest

ACS Presentation in the COVID-19 Era

STEMI
- Low-risk or known COVID-19 (-)
- Large area of myocardial injury on EKG
- High-risk features (e.g., on cardiac imaging evidence of large myocardium in jeopardy, severe & new LV dysfunction)

- Primary PCI*
- Fibrinolytic Therapy**

NSTE-ACS
- Confirmed COVID-19 (+)
- Highly suspicious for COVID-19
- Unsafe healthcare setting to healthcare workers and/or patients****

- Low- to Moderate-Risk Patients^^
- Ischemia Guided Strategy***
- High-Risk Patients^^

- Refractory ischemic symptoms or dynamic ECG changes despite IOMT
- GRACE score > 140
- High-risk features (e.g., on cardiac imaging evidence of large myocardium in jeopardy, severe & new LV dysfunction)

- Invasive Strategy*
Putative mechanisms of cardiac injury in COVID-19 patients

- 2019-nCoV infection
  - ACE2-mediated direct damage
    - Increased affinity to ACE2
    - Reduced ACE2 expression
    - Dysregulated RAS
  - Hypoxia-induced myocardial injury
    - Oxidative stress
    - Intracellular acidosis
    - Mitochondrial damage
  - Cardiac microvascular damage
    - Perfusion defect
    - Vessel hyperpermeability
    - Angiospasm
  - Systemic inflammatory response syndrome
    - Cytokine storm
    - Dysregulated immunocyte
    - Uncontrolled inflammation

Acute cardiac injury

- High IL1-beta, IL-6, IFN gamma
- IL1-inhibitors
- IL6-inhibitors
- JAK-inhibitors
WHAT MAKES AN INDIVIDUAL HIGH-RISK FOR CORONAVIRUS COMPLICATIONS?

- A significant proportion of patients with COVID-19 have evidence of myocardial injury, which portends a higher risk of ICU admission and death.

- Elevated troponin levels are frequently seen in patients with COVID-19 disease; and are associated with increased severity of disease and risk of death.

- In the absence of a specific etiology, elevated levels of troponins are likely due to myocardial injury from inflammation or a direct effect of SARS-CoV-2 infection.

- All patients with COVID-19, where clinically indicated, should be commenced on statins and antiplatelet therapy, if not already on them. Currently, there is no evidence to stop cardioprotective therapy, assuming no contra-indications.

- Cardiovascular healthcare professionals are at risk of contracting COVID-19, and best practices should be implemented to reduce the risk of patient-provider and provider-provider exposure.
WHAT MAKES AN INDIVIDUAL HIGH-RISK FOR CORONAVIRUS COMPLICATIONS?

- Vascular events appear to be a common complication of COVID-19 infection.
- The increased burden of vascular comorbidities among people with severe infection is only a partial explanation or such increased risk of events.
- Broad elevations of chemokines and cytokines occur in SARS-CoV2 infection, similar to cytokine release syndrome (CRS) seen in cancer patients on immune-modulating therapy.

Yet, some overlap with troponin elevation has been seen.

- COVID-19 is associated with a high inflammatory burden that may cause arrhythmias due to increased metabolic demand, hypoxia and/or sympathetic stimulation in patients with and without pre-existing cardiovascular disease.
- New-onset ventricular arrhythmias combined with elevated troponin-T levels in the setting of COVID-19 should raise suspicion of myocarditis.
- Antiviral therapy for COVID-19 may lead to electrical disturbances (most often QTc prolongation) and increased arrhythmic risk.
WHAT ARE SOME OF THE TREATMENT OPTIONS FOR PEOPLE LIVING WITH CHRONIC CONDITIONS?

SARS-CoV-1/2 life cycle

1. Spike protein (S) binds to ACE2.
2. The transmembrane protease TMPRSS or endosomal cathepsin L cleaves S to activate membrane fusion.
3. Cellular ribosomes translate a nonstructural polyprotein from the positive-strand RNA.
4. Embedded viral proteases process the polyprotein to create the replicase.
5. The replicase produces full-length copies of both strands and subgenomic mRNAs.
6. Ribosomes translate the subgenomic mRNAs to produce structural proteins.
7. Structural proteins package the positive-strand RNA and bud off into exocytic vehicles.

doi.org/10.1038/nrmicro2090

Treatment Protocols
Reopening Strategy: • the ability to monitor and protect communities through testing, tracking positive cases, properly isolate and support individuals who are positive and/or exposed to COVID-19.
• the ability to prevent infection in high-risk groups, including older residents, the homeless and those with underlying health conditions.
• the ability for hospitals and health care systems to handle a potential surge in cases through adequate staffing, hospital beds and supplies including ventilators, masks and other personal protective equipment.
• the ability to develop therapeutics to meet the demand.
• the ability for businesses, schools and child care facilities to support physical distancing guidelines as well as provide supplies and equipment to workforces and customers to keep them safe from illness.
• developing guidelines to determine when to reinstitute certain measures, such as Safer at Home guidelines, if necessary, based on relevant data.

Governor Gavin Newsom
Testing Window and Workflow – PHASE IV PLAN (April 2020)

Secondary 6800 for increased throughput and back-up

Random Access Testing (no batched testing):
90 tests/hour for IgM and IgG Serology

Complete Clinical Molecular and Serology Solutions → 2 people per shift

TODAY

1,180 tests/day

1,034 tests/day

720 tests/day
QUESTIONS AND ANSWERS BACKUP SLIDES
TELEHEALTH POST-COVID 19

Adult and Pediatric Telehealth Services

We’re proud to connect physicians and their patients with specialists at UC Davis Health

Adult Specialties

- Cardiology*
- Dermatology* (Store and Forward)
- Emergency Medicine
- Endocrinology*
- Genomic Medicine*
- Hepatology* (Hepatitis)
- Infectious Disease*
- Nephrology*
- Neurology*
- Neuromuscular Disease Medicine
- Neurosurgery*
- Nutrition*
- Ophthalmology* (Store and Forward)
- Orthopaedics
- Otolaryngology
- Perinatology*
- Plastic and Reconstructive Surgery
- Psychiatry*
- Psychology
- (Mental Health and Behavior)
- Pulmonary and Critical Care*
- Rheumatology*
- Thoracic Surgery
- Trauma
- Urology
- Vascular Surgery

Pediatric Specialties

- Allergy and Immunology
- Behavior and Development*
- Cardiology
- Critical Care
- Dermatology* (Store and Forward)
- Emergency Medicine*
- Endocrinology*
- Gastroenterology
- Genomic Medicine*
- Hematology/Oncology
- Infectious Disease
- Nephrology
- Neonatology*
- Neurology*
- Neuromuscular Disease Medicine
- Otolaryngology
- (Cleft and Craniofacial)
- Pediatric Hospital Medicine
- Psychiatry*
- Psychology*
- (Mental Health and Behavior)
- Psychology*
- (Mental Health and Evaluations)
- Pulmonary
- Urology

Collectively, more than 150 articles, abstracts, book chapters and reports have been submitted by faculty exploring various aspects of telemedicine and telehealth services since 1997. We frequently receive requests from other UC Davis departments and outside organizations to collaborate on telehealth research and publications.


