Long COVID patients:
They are changing how clinicians think

Bishop O.C. Allen III
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Sarath Raju, MD, MPH
April 27, 2021
Association of Nurses in AIDS Care

**Mission:** ANAC fosters the professional development of nurses and others involved in the delivery of health care for persons at risk for, living with, and/or affected by the human immunodeficiency virus (HIV) and its comorbidities. ANAC promotes the health, welfare, and rights of people living with HIV around the world.
COVID-19 Prevention Network (CoVPN)

• CoVPN was formed by the National Institute of Allergy and Infectious Diseases (NIAID)

• Partnership
  • HIV Vaccine Trials Network
  • HIV Prevention Trials Network
  • Infectious Disease Clinical Research Consortium
  • AIDS Clinical Trials Group
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Agenda

• Greetings & Introductions
• Presentation
• Question & Answer
• Closing & Continuing Education (CE) information
Disclosures

The speakers have no relevant conflicts of interest to disclose.
Objectives

• Summarize the post-acute sequelae of SARS-CoV-2 (Long COVID) peer-reviewed and patient-led research

• Examine the nursing perspective in post-acute sequelae of SARS-CoV-2 (Long COVID)

• Describe the lived experience of post-acute sequelae of SARS-CoV-2 (Long COVID)
Presenter Introductions

Bishop O.C. Allen III
Julie Barroso, PhD, RN, ANP, FNAP, FAAN
Sarath Raju, M.D., M.P.H.
Long COVID / Post-Acute COVID-19: A Physician’s Perspective

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Disclosures

• No Relevant Disclosures or Conflicts of Interest
Outline

• Case Presentation
• COVID-19: Where We Are Now
• Overview on Post-Hospital Syndrome
• Post-Acute COVID Syndrome / Long-COVID
• Areas in Need of Research / Models for Care
• Summary
• 49yo w/ PMHx of HIV (VL<20, CD4 600), **Mild Asthma**

• 3/27 – Experiences new shortness of breath / abd pain

• 3/29 – Presented to local ED, COVID19+ via nasal swab; hypoxic with rising oxygen requirement

• 3/30 – Transferred to our ICU given progressive disease
  – Requiring Intubation / Mechanical Ventilation
  – Hospital LOS 22 days
  – Complications: Pulmonary Embolism, Bacterial Pneumonia, and Acute Kidney Injury (Cr 2.0 from 1.0)
Case Presentation

- **Symptoms at Discharge:**
  - Dyspnea, fatigue

- **PACT Physical Therapy PM&R Followup May 2020**
  - Fatigue, Dyspnea and Decreased Physical Function (worse from discharge)

- **PACT Pulmonary Followup Visit June 2020:**
  - Dyspnea
  - Depression
  - Cough
  - Fatigue
  - Complaints of Impaired Memory
COVID-19: Where we are now in the United States

As of April 20, 2021:
• 31,602,676 Cases
• 2,023,259 Hospitalizations
• 561,356 Deaths

https://covid.cdc.gov/covid-data-tracker/#/datatracker-home
### Timeline of Post-Acute COVID-19: AKA Long COVID

**Sub-Acute COVID-19:**
Symptoms present 4-12 weeks beyond acute COVID-19

**Post-COVID-19 Syndrome:**
Symptoms beyond 12 weeks of acute COVID-19 without alternative explanation

<table>
<thead>
<tr>
<th>Acute COVID-19</th>
<th>Post-acute COVID-19</th>
</tr>
</thead>
<tbody>
<tr>
<td>Detection unlikely</td>
<td>PCR positive</td>
</tr>
</tbody>
</table>

- **Fatigue**
- **Decline in quality of life**
- **Muscular weakness**
- **Joint pain**
- **Dyspnea**
- **Cough**
- **Persistent oxygen requirement**
- **Anxiety/depression**
- **Sleep disturbances**
- **PTSD**
- **Cognitive disturbances (brain fog)**
- **Headaches**
- **Palpitations**
- **Chest pain**
- **Thromboembolism**
- **Chronic kidney disease**
- **Hair loss**

Post-Hospital Syndrome in Non-COVID Population

- Acquired, transient period of vulnerability
- Impairments in physical function, cognition and mental health

*1/5 readmitted within 30 days

Krumholtz. NEJM. 2013.
One-Year Outcomes in Survivors of the Acute Respiratory Distress Syndrome

Margaret S. Herridge, M.D., M.P.H., Angela M. Cheung, M.D., Ph.D., Catherine M. Tansey, M.Sc., Andrea Matte-Martyn, B.Sc., Natalia Diaz-Granados, B.Sc., Fatma Al-Saidi, M.D., Andrew B. Cooper, M.D., Cameron B. Guest, M.D., C. David Mazer, M.D., Sangeeta Mehta, M.D., Thomas E. Stewart, M.D., Aiala Barr, Ph.D., Deborah Cook, M.D., and Arthur S. Slutsky, M.D., for the Canadian Critical Care Trials Group.
6MWD improved over 1 year, but still abnormal due to:

- muscle wasting & weakness, foot drop, joint immobility

Table 3. Ability to Exercise and Return to Work and Health-Related Quality of Life among Patients with the Acute Respiratory Distress Syndrome during the First 12 Months after Discharge from the ICU.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>3 Months</th>
<th>6 Months</th>
<th>12 Months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Distance walked in 6 min</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. evaluated</td>
<td>80*</td>
<td>78†</td>
<td>81‡</td>
</tr>
<tr>
<td>Median — m</td>
<td>281</td>
<td>396</td>
<td>422</td>
</tr>
<tr>
<td>Interquartile range — m</td>
<td>55–454</td>
<td>244–500</td>
<td>277–510</td>
</tr>
<tr>
<td>Percentage of predicted value‡</td>
<td>49</td>
<td>64</td>
<td>66</td>
</tr>
<tr>
<td>Returned to work — no./total no. (%)¶</td>
<td>13/83 (16)</td>
<td>26/82 (32)</td>
<td>40/82 (49)</td>
</tr>
<tr>
<td>Returned to original work — no./total no. (%)</td>
<td>10/13 (77)</td>
<td>23/26 (88)</td>
<td>31/40 (78)</td>
</tr>
</tbody>
</table>
COVID-19 Survivorship: Further Complicated by Impaired…..

Cognition

Physical Function

Mental Health
COVID-19 Survivorship: Further Complicated by Impaired.....

- Physical Function
  - Prolonged Mechanical Ventilation
  - Proning
  - Myopathy

- Cognition
  - Prolonged delirium

- Limited essential rehabilitation services

- Visitor restrictions

- Mental Health
  - Media
  - Grief
  - Fear of infecting others

## Post COVID-19 Symptoms Across the Globe

<table>
<thead>
<tr>
<th>COUNTRY</th>
<th>STUDY</th>
<th>NUMBER OF CASES INCLUDED</th>
<th>RESULTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Canada</td>
<td>Wong et al. (2020)</td>
<td>78</td>
<td>• 51% had persistently reduced quality of life and 50% had shortness of breath at 12 weeks after symptom onset</td>
</tr>
<tr>
<td>France</td>
<td>Carvalho-Schneider et al. (2020)</td>
<td>130</td>
<td>• 40% reported persistent fatigue and 30% breathlessness at 60 days after symptom onset</td>
</tr>
<tr>
<td>Italy</td>
<td>Carfi, Bernabei &amp; Landi (2020)</td>
<td>143</td>
<td>• 87% had symptoms, 55% had three or more symptoms at 60 days after discharge</td>
</tr>
<tr>
<td>United Kingdom</td>
<td>Cruz et al. (2020)</td>
<td>119</td>
<td>• 68% reported persistent fatigue, 57% sleep disturbance and 32% breathlessness at 60 days after discharge</td>
</tr>
<tr>
<td></td>
<td>Arnold et al. (2020)</td>
<td>110</td>
<td>• 74% had persistent symptoms, typically breathlessness and fatigue and 10% had persistent anomalies on chest X-ray or respiratory function testing at 12 weeks after discharge</td>
</tr>
<tr>
<td>USA</td>
<td>Donnelly et al. (2020)</td>
<td>2,179</td>
<td>• 19.9% were readmitted, 9.1% died and 27% were readmitted or died within 60 days after discharge</td>
</tr>
<tr>
<td>China</td>
<td>Huang et al. (2021)</td>
<td>1,733</td>
<td>• 76% reported persistent symptoms, and 50% had residual anomalies on chest imaging 6 months after discharge</td>
</tr>
</tbody>
</table>

Persistent Symptoms Seen Across the Globe among both hospitalized and non-hospitalized patients
- N=767; N=66 (9%) ICU
  - Median 105d (IQR 84-127) post-Sx onset

- 51% ≥1 symptom (fatigue, dyspnea)

- Pulmonary: Dyspnea: N=228 (31%) (N=52 (7%) > mild)
  PFTs: 19% w/ DLCO <80%

- Mental Health: 31% PTSD; 11% anxiety; 5% depression

- Physical Function: 16% no longer independent

- Fatigue: N=334 (44%) (145 (19%) ≥ moderate)

- <10% with palpitations, GI symptoms, HA, cough, loss of taste/smell
N=1733 – 6 month f/u

- 1265 (76%) ≥1 symptom
  - most common fatigue/muscle weakness (N=1038 (63%))

- Pulmonary: Dyspnea - mMRC ≥1 (26%)
  PFTs - DLCO < 80% (56% in ICU population)

- Mental Health: Anxiety/depression - 23% (Measured via EQ5D)

- Physical function: Impaired 6MWT 23%

Greater proportion in the post-ICU group w/ dyspnea, decreased mobility, anxiety/depression
• Approximately 3 months after acute illness:
  – >50% with at least mild cognitive impairment
  • Almost all domains impaired
  • Impairments in BOTH ICU & non-ICU survivors
    – Impairments greater in ICU vs non-ICU survivors

  – Substantial mental health impairments

<table>
<thead>
<tr>
<th>Domain</th>
<th>Instrument</th>
<th>ICU (N=33)</th>
<th>Non-ICU (N=16)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Mean (SD)</td>
<td>N (%) above threshold</td>
</tr>
<tr>
<td>Anxiety</td>
<td>GAD-7</td>
<td>5.2 (4.3)</td>
<td>4 (12%)</td>
</tr>
<tr>
<td>Depression</td>
<td>PHQ-9</td>
<td>6.4 (4.6)</td>
<td>6 (18%)</td>
</tr>
<tr>
<td>PTSD</td>
<td>IES-6</td>
<td>1.3 (1.5)</td>
<td>9 (27%)</td>
</tr>
</tbody>
</table>

*English-speaking only
Cardiac Disease Post-COVID: Varying Reports of Post-COVID Cardiac Inflammation

Concern for Cardiac Inflammation (Myocarditis) Post – COVID-19:

Puntman (JAMA Card 7/20): 60/100 (60%) with ongoing cardiac inflammation seen via MRI
• Numbers much higher than seen in other practices

Rajpal (JAMA Card 9/20): Myocarditis in young athletes recovering – M 4 / 26 (15%)

Starekova (JAMA Card 1/2021): Found lower prevalence of myocarditis in athletes recovering = N 2/145 (1.4%)
Characterising long-term covid-19: a rapid living systematic review

- "Living" Systematic Review: January 1 2020 – September 28 2020 →
  - Inclusion criteria: > 21d after symptom onset or post-hospital discharge

- 28 studies, 9442 people, 13 countries
  - Limited by variable symptom reporting and definition of "long-COVID"

- Most frequently reported symptoms:
  - Increased dependency in ADLs (48%)
  - Breathlessness – 13 studies (46%)
  - Smell/taste disturbance – 12 studies (43%)
  - Fatigue – 11 studies (39%)
  - Also reported: psychological symptoms anxiety > depression > PTSD symptoms

*Robust research needed to describe Post-COVID Syndrome*
Unknowns: Areas in Need of Investigation

1. Risk Factors/ True Etiology of post-COVID-19 Syndrome

2. Interventions for post-COVID-19 Syndrome

3. True Prevalence of post-COVID-19 Syndrome

4. Natural History of post-COVID-19 Syndrome

5. The Impact of post-COVID-19 Syndrome in Low-Income / Disadvantaged Communities
Multidisciplinary Care Will Be Key


- **Pulmonary/cardiovascular**: Symptom assessment through virtual/in-person follow-up at 4–6 weeks and at 12 weeks post-discharge.
- **Dyspnea/persistent oxygen requirement**: Consider 6MWT, PFT, chest X-ray, PE work up, echocardiogram and HRCT of the chest as indicated.
- **Hematology**: Consider extended thromboprophylaxis for high-risk survivors based on shared decision-making.
- **Neuropsychiatry**: Screening for anxiety, depression, PTSD, sleep disturbances and cognitive impairment.
- **Renal**: Early follow-up with nephrologists after discharge for patients with COVID-19 and AKI.
- **Primary care**: Consideration of early rehabilitation, Patient education, Consider enrollment in clinical research studies, Active engagement with patient advocacy groups.

COVID-19 clinic
Multidisciplinary Post-COVID Clinics: Johns Hopkins PACT Clinic

- **Conception:** March 2020
  - First patient: April 7, 2020

- **Multi-Disciplinary Clinic**
  - Pulmonary and Critical Care Medicine
  - Physical Medicine and Rehabilitation

- **Weekly multi-D meetings**
JH PACT –
Need for Standardized Assessments Post-COVID

<table>
<thead>
<tr>
<th>Domain</th>
<th>Instrument</th>
</tr>
</thead>
<tbody>
<tr>
<td>Health-related Quality of Life</td>
<td>EQ5D</td>
</tr>
<tr>
<td></td>
<td>PROMIS Global 10</td>
</tr>
<tr>
<td>Mental Health</td>
<td></td>
</tr>
<tr>
<td>Depression</td>
<td>PHQ9</td>
</tr>
<tr>
<td>Anxiety</td>
<td>GAD7</td>
</tr>
<tr>
<td>PTSD</td>
<td>IES-6</td>
</tr>
<tr>
<td>Cognition</td>
<td>Telephone cognitive battery</td>
</tr>
<tr>
<td></td>
<td>MoCA-Blind</td>
</tr>
<tr>
<td>Pain</td>
<td>EQ5D pain question</td>
</tr>
<tr>
<td>Physical Function</td>
<td>AM-PAC Surgical Short Form</td>
</tr>
<tr>
<td>Respiratory Symptoms</td>
<td>BCSS, mMRC</td>
</tr>
<tr>
<td>Employment</td>
<td>Qualitative</td>
</tr>
<tr>
<td>Readmissions</td>
<td>Qualitative</td>
</tr>
</tbody>
</table>

Johns Hopkins Post-Acute COVID-19 Team (JH PACT): Care Will Be a Group Effort

- **PCCM**
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- **Otolaryngology**
  - Simon Best, MD

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- **Otolaryngology**
  - Simon Best, MD

- **Hepatology**
  - Tinsay Woreta, MD
Summary

• COVID-19 Survivors may face health issues beyond their acute illness
• More work is needed to understand the prevalence and cause of Long COVID/ Post-Acute COVID-19
• Survivors are at risk for pulmonary, neurologic, and mental health consequences
• Investment in multi-disciplinary care/resources is required to help COVID-19 survivors
• Research into effective treatments is required
Long COVID: Crowd-Sourced Studies and Patient Perspectives

Julie Barroso, PhD, RN, ANP, FNAP, FAAN
Sadie Sommer, MPH, Research Assistant
Patient-driven definition:

A collection of symptoms that develop during or following a confirmed or suspected case of COVID-19 infection, and which continue for more than 28 days.
Long COVID has a strong claim to be the first illness created through patients finding one another on Twitter and other social media.
Timeline to recognition

- Shared experiences on social media
- First-person newspaper accounts
- Patient-founded support groups on Facebook and social media
- Medical journals published provider accounts
- Used to validate symptoms to providers
Publication timeline

► May 2020: an all-patient team published first survey of prolonged symptoms
► Followed by more patient-lead initiatives
► Most recent included >3,400 respondents
► Director of NIH called them “citizen scientists”
Many studies include people who have not had a positive diagnostic test for COVID-19

- Lack of testing services/supplies
- False negative tests
- Did not seek testing
  - Stigma, income, caretaker status, self-isolating
- Tested too early or late to indicate positive infection
If we don’t truly know the number, we don’t know how to provide support and care, nor do we know the true effect of the pandemic.

- Acknowledge the limitations
- Similar data regardless of positive diagnostic test with exception of taste and/or smell
- Johns Hopkin’s study w/ 25,000 recruitment goal will include symptomatic people without positive test

[Johns Hopkins COVID Long Study](https://covid-long.com) Participation includes a one-time, 10-15 minute survey.
Crowd-sourced Long COVID studies

- Body Politic COVID-19 support group survey
- Symptoms for more than 2 weeks
- Patient-centric, participatory research methods
- Respondents (n=640) to survey April-May 2020
- Survey questions and symptoms were aggregated and curated by patients
- Analyzed by patients with appropriate expertise
Top 10 symptoms

- mild shortness of breath
- mild tightness of chest
- moderate fatigue
- mild fatigue
- chills or sweats
- mild body aches
- dry cough
- elevated temperature (98.8-100 F)
- mild headache
- brain fog/concentration challenges
Respondents reported:

- Volatile recovery
- Relapse lasting 6 weeks or more
- Major decline in physical activity for most
- Returning symptoms for many who did re-engage in physical activity
Study highlighted the critical need for early and accurate testing

47% of respondents were denied testing or not tested

- Positive respondents reported loss of smell and taste more often
- Stigma and a lack of understanding by healthcare professionals compromised access to healthcare and quality of support
Other crowd-sourced Long COVID studies

- 1567 respondents
- Many from Facebook groups, Survivor Corps
- Reported similar findings, 98 symptoms
- Painful symptoms reported by 26% or respondents
Expanded Body Politic Survey

- Illness lasting over 28 days
- Onset prior to June 2020
- Distributed online
- Objective: to characterize 1) symptom profile and time course  
  2) impact on daily life, work and return to baseline health
- 3,762 respondents from 57 countries
- Respondents reported 205 symptoms in 10 organ systems, with 66  
symptoms traced over 7 months.
Most people suffering from Long COVID had more than one symptom, often had multiple symptoms, and **no body system was spared**.

These symptoms led to **profound functional limitations** with people being unable to return to work full-time or at all.

The **most common** symptoms were consistent across studies.
Most common symptoms:

- Fatigue
- Muscle and body aches
- Cognitive dysfunction
- Shortness of breath
- Headaches and dizziness
- Cough
- Loss of taste or smell
It is urgent that we start to answer some of the many questions surrounding Long COVID.

► We have consistent research on the symptoms that are suffered by Long COVID patients

► Next step should be to determine which symptoms cluster together – my proposed work

The occurrence of symptom clusters appears to worsen patient outcomes.
Identifying and examining clusters may allow us to identify risk for a higher symptom burden.

- Understanding a “driving” symptom that triggers other symptoms is needed
- Identifying the mechanisms that underlie symptom clusters
  - co-occurrence and severity
- One-time survey (n=500)
- Administer to participants recruited from online support groups
- Examine symptom clusters’ impact on functioning via interview (n=100 of the original 500)
Our long-term goal is to further our scientific knowledge about the symptoms of Long COVID in order to develop interventions to ameliorate their impact.

- **Aim #1**: examine the symptom clusters found in sample

- **Aim #2**: build on the results of the cluster analysis to determine the impact of clusters on functional activities through in-depth interviews with randomly selected participants from each cluster.

Nursing care:
► For all patients with COVID; there are no specific nursing interventions for those with Long COVID
► Unusual symptoms:
  _ GI disorders – N/V, diarrhea
  _ Loss of smell, taste
  _ CVA, blood clots
  _ COVID toes – purple toes
  _ Children have different symptoms
► Not everyone will need to be hospitalized
► Rapid deterioration days 8-10
Monitoring and diagnostics:

- Chest xray/CT scan
- CBC w diff, metabolic profile (hepatic, renal function)
- Inflammatory markers (d-dimer, lactate, ferritin, C reactive protein)
- ECG
- Scoring tools help us determine level of care
Nursing assessment:

- Comorbidities
- Vital signs
- Pulse oximetry
- Lung sounds
- Mental status
- Capillary refill
- Urinary output
Nursing interventions:

► Goals of care – assessed on admission, reevaluated
► Prognosis
► Improving or declining
► What are the patient’s wishes?
  - Advanced directives
  - Discussion with family or healthcare representative
Delirium prevention and treatment – assess each shift; cognitive activities; sleep/wake cycle; hearing aids/eyeglasses; mobility; hydration; pain management

Early progressive mobility – helps with delirium and deconditioning

Oxygenation – close monitoring for deterioration; prone positioning - proning ventilated patients improves outcomes; for non-ventilated patients, improves secretion clearance, recruits posterior lung regions, improves ventilation/perfusion matching

Nutrition – early initiation of parenteral feeding (small bore feeding tube in the small intestine)
 ► Social isolation – increases risk of delirium; video conferencing, engaging the individual – be reassuring, smile behind the mask

 ► IV pumps outside of the room – decreases the exposure of the nurse inside the room; saves PPE; can respond more quickly to patient needs

 ► Standards of care – you have to decide what can be changed...bed changes and baths every 24 hours?
References


Reflections on experiencing post-acute sequelae of SARS-CoV-2 (Long COVID)

Bishop O.C. Allen III
Q & A Discussion

Additional questions?
Email Kara: kara@anacnet.org
Continuing Nursing Education

After the webinar an email will be sent to you with a link to the slides and evaluation form. To be awarded contact hours for this webinar, complete the evaluation at that link or it can be found at

https://www.classmarker.com/online-test/start/?quiz=tm9605393aa7c260

You will be asked to create a login. This is a temporary account that will allow you to return to the evaluation if you do not finish it. This is not the same login as your ANAC account.

Additional Questions?
Email Kara at kara@anacnet.org

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