Surviving COVID-19: Long-Term Cognitive and Mental Health Effects on Patients and Their Caregivers

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IADRC Outreach and Recruitment Core Leader, IUSM
Conflicts of Interest

• No conflicts of interest

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Overview

• Background and Epidemiology of COVID-19
• Neurologic symptoms of COVID-19
• Post-intensive care syndrome (PICS)
• Post-intensive care syndrome family (PICS-F)
Biology of COVID-19

• Belongs to a family of viruses, known as coronaviruses
• Corona = crown, coronet (spikes)
• Same family as the SARS virus
• Not living and must “hijack” living cells to reproduce
• Mainly spread through aerosol transmission
Biology of COVID-19

- Gray = envelope containing genetic material
- Orange = “identifying” proteins on the surface of the cell (M = membrane)
- Yellow = proteins for replication, assembly, and release (E = envelope)
- Red = proteins for viral entry (S = spike)
## Epidemiology of COVID-19

### Statewide Demographics for Deaths*

<table>
<thead>
<tr>
<th>Age</th>
<th>% of Deaths</th>
<th>% of Indiana population</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-19</td>
<td>0.1%</td>
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</tr>
<tr>
<td>20-29</td>
<td>0.2%</td>
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<tr>
<td>30-39</td>
<td>0.7%</td>
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<tr>
<td>40-49</td>
<td>1.9%</td>
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<tr>
<td>50-59</td>
<td>5.3%</td>
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<tr>
<td>60-69</td>
<td>16.5%</td>
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<tr>
<td>70-79</td>
<td>24.2%</td>
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<tr>
<td>80+</td>
<td>51%</td>
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<tr>
<td>Unknown</td>
<td>0%</td>
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</tbody>
</table>

*Note: The demographic data is as of the latest update and may not represent the current situation.

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**Race**

<table>
<thead>
<tr>
<th>Race</th>
<th>% of Deaths</th>
<th>% of Indiana population</th>
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</thead>
<tbody>
<tr>
<td>White</td>
<td>64.8%</td>
<td>85.1%</td>
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<tr>
<td>Black or African American</td>
<td>15.4%</td>
<td>9.8%</td>
</tr>
<tr>
<td>Other Race</td>
<td>12.3%</td>
<td>2.6%</td>
</tr>
<tr>
<td>Asian</td>
<td>0.4%</td>
<td>2.5%</td>
</tr>
<tr>
<td>Unknown</td>
<td>7.1%</td>
<td>0%</td>
</tr>
</tbody>
</table>
Symptoms of COVID-19

- Fever or chills
- Cough
- Shortness of breath or difficulty breathing
- Fatigue
- Muscle or body aches
- Headache
- New loss of taste or smell
- Sore throat
- Congestion or runny nose
- Nausea or vomiting
- Diarrhea
Neurologic Symptoms of COVID-19

- Encephalopathies
  - Meningoencephalitis
  - Neuromuscular disorders
  - Psychiatric disorders
  - Neurodegenerative disorders

- Anosmia and Ageusia

- Acute Cerebrovascular Disease

- Infectious Toxic Encephalopathies (Hypoxia, metabolic disturbance and systemic inflammation)

Headache

- Common initial complaint in COVID-19 patients
- Variable prevalence, about 1/3 of patients
- Often accompanied by other symptoms (fever, cough, sore throat, shortness of breath)
- Possible mechanism may involve neuroinflammation
Anosmia: Loss of Smell

- Not usually accompanied by rhinitis or nasal swelling
- Mechanism unknown
- Olfactory nerve known to be involved in the sensation of smell
- COVID-19 virus may not be able to infect olfactory neurons but cells that “support” the neurons
Ageusia: Loss of Taste

- Pathogenesis from COVID-19 infection unknown
- In general, multiple causes of ageusia including:
  - taste pore damage
  - destruction of taste receptors
  - damage of nerve innervating taste buds
  - central lesions and neural disorders
  - medications
Impaired Consciousness

- Prevalence in hospitalized cohort is 37%
- Causes include
  - Direct infection
  - Hypoxia
  - Toxic-metabolic encephalopathy
  - Seizures
Stroke and Cerebrovascular Accidents

- Prevalence in hospitalized cohort 5%
- Various types of strokes (acute ischemic, cerebral sinus venous thrombosis, intracerebral hemorrhage)
- All ages (including those < 50) are vulnerable
- Multifactorial etiology including inflammation and hypercoagulability
- Strokes more likely in those with severe COVID-19
Neurological Implications of COVID-19

Non-immunological

- Hypotension
  - CBF
  - CPP

- Hypoxia

Immunological

- Adaptive Autoimmunity
- Microglial Activation
- Maladaptive Cytokine Profile

- Septic encephalopathy Delirium
- Micro- and macrovascular thrombosis
COVID-19 ICU Statistics for Indiana

As of June 6, 2020

- 6316 hospital admissions
- 1317 unique ICU admissions (3.6% of all ICU admissions)
- ICU Comorbidities
  - 23.31% hypertension
  - 15.64% type 2 diabetes mellitus
  - 11.85% COPD
  - 13.21% renal
  - 9.79% congestive heart failure
Pre-COVID-19 Facts about ICU Patients

- Over 50% of ICU admissions are patients 65+
- Patients 85+ are the fastest growing group of ICU admissions
- Over 70% of older adults develop delirium in the ICU
- Increasing survival rate over the past few decades
After ICU, Coronavirus Patients’ Ordeal Is Far From Over
Covid-19 puts the sickest people on ventilators. The experience can make for a tough recovery; like ‘being buried alive’

Long Road Ahead for Covid-19 Patient Back Home From ICU

Maury Hanks was in intensive care and on a ventilator. He survived, but like many Covid-19 patients, returning from the ICU, he could face cognitive, emotional and physical challenges.

By Mark Maremont and Jennifer Levitz
April 8, 2020 10:40 am ET
Delirium
Delirium: DSM-5 Criteria

A. Disturbance in *attention* (i.e., reduced ability to direct, focus, sustain, and shift attention) and *awareness* (reduced orientation to the environment)

B. The disturbance develops over a short period of time (usually hours to a few days), *represents an* acute change from baseline attention and awareness, and tends to fluctuate in severity during the course of a day
Delirium: DSM-5 Criteria

C. An additional disturbance in cognition (e.g. memory deficit, disorientation, language, visuospatial ability, or perception)

D. The disturbances in Criteria A and C are not better explained by a pre-existing, established or evolving neurocognitive disorder and do not occur in the context of a severely reduced level of arousal such as coma.
Delirium: DSM-5 Criteria

E. There is evidence from the history, physical examination or laboratory findings that the disturbance is a direct physiological consequence of another medical condition, substance intoxication or withdrawal (i.e. due to a drug of abuse or to a medication), or exposure to a toxin, or is due to multiple etiologies.
Cognitive dysfunction

Risk Factors
- Age
- Premorbid cognitive impairment
- Hospital-related risk factors
  - Hypoxia
  - Metabolic dysfunction
  - Organ dysfunction
  - Exposure to deliriogetic medications (e.g., benzodiazepines, opiates)

Delirium pathophysiology
- Pro-inflammatory cytokines
  - Interleukin-1 (IL-1)
  - IL-6
  - Tumor necrosis factor-α
  - Hypoxia

Long-term cognitive impairment

Cardiovascular system
- Reduced cardiac output
- SVR due to inflammation
- Hypotension and hypoperfusion
- Myocyte apoptosis and cardiac remodelling

Nervous system
- BBB permeability
- Direct cytokine mediated neuronal injury
- Activation of microglia
- Acute delirium and long-term cognitive dysfunction

Respiratory system
- Pulmonary vascular permeability and cellular infiltrate
- Impaired gas exchange
- ALI/ARDS with scarring

Hepatobiliary system
- Cholestasis
- Inflammatory response
- Impaired metabolic function
- Hepatocellular hypoxia

Intestinal system
- Reduced intestinal motility
- Villous necrosis and apoptosis
- Vascular permeability

Urinary system
- Renal perfusion
- GFR and oxygen delivery
- Leucocyte mediated damage

Cognitive dysfunction

- Affects 30-80% of ICU survivors
- Impairment in various domains including executive dysfunction, attention, memory, processing speed
- Trajectory: usually improves over the first year but deficits can still persist many years later
Mental Health Symptoms

- Symptoms include depression, anxiety and PTSD
- Risk factors include female gender, younger age, lower educational attainment, premorbid psychiatric disorders
- Median prevalence for depression 28%
PICS model

Post-intensive care syndrome

Patient

Cognitive impairment
- Executive function
- Memory
- Attention

Physical impairment
- Pulmonary
- Neuromuscular

Decreased quality of life

Family

Mental health
- Anxiety/ASR
- Depression
- PTSS, PTSD
- Complicated grief

Decreased quality of life
Post-intensive care syndrome–family (PICS-F)

Psychological symptoms that affect family members of a patient currently or recently hospitalized in the ICU
## Prevalence of PICS-F Symptoms

<table>
<thead>
<tr>
<th></th>
<th>Depression</th>
<th>Anxiety</th>
<th>Acute stress disorder and PTSD</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>70-90% during ICU stay</td>
<td>42-80% during ICU stay</td>
<td>32-33% during ICU stay</td>
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<tr>
<td></td>
<td>5-36% 6 months after ICU discharge</td>
<td>15-24% 6 months after ICU discharge</td>
<td>PTSD 30-42% 3 months after ICU discharge</td>
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<td></td>
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<td></td>
<td>PTSD 35-57% 6 months after discharge</td>
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</table>
Post-ICU Challenges for Caregivers

- Mostly family members who are untrained and unpaid
- Manage new impairments, particularly in older adults, after discharge
- Loss of income due to caregiver burden
<table>
<thead>
<tr>
<th>Pre-ICU</th>
<th>Intra-ICU</th>
<th>Post-ICU</th>
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<tbody>
<tr>
<td><strong>Caregiver</strong></td>
<td></td>
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<tr>
<td>Female</td>
<td>Sleep deprivation</td>
<td>High burden of caregiving (≥100 hours/month)</td>
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<tr>
<td>Spouse</td>
<td>Perception of patient being near death</td>
<td>Low sense of mastery</td>
</tr>
<tr>
<td>Low level of education</td>
<td>Perception of quality of care received</td>
<td>Expectations for post-ICU course</td>
</tr>
<tr>
<td>Mental or physical illness</td>
<td>Perception of decision-making responsibilities</td>
<td>Newly acquired physical illness</td>
</tr>
<tr>
<td>Family history of mental illness</td>
<td></td>
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<tr>
<td><strong>Age</strong></td>
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<tr>
<td></td>
<td></td>
<td>Perception of patient's post-ICU changes (cognitive, behavioral, physical)</td>
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<tr>
<td>High level of emotional expressivity</td>
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<td>Previous history of trauma</td>
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<tr>
<td>Resilience*</td>
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<tr>
<td><strong>Patient</strong></td>
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<tr>
<td><strong>Age</strong></td>
<td>Delirium including subtypes</td>
<td>Ability to make decisions about post-ICU care</td>
</tr>
<tr>
<td>MCI or ADRD</td>
<td>Behavioral disturbances</td>
<td>Ability to accept caregiver assistance and other services</td>
</tr>
<tr>
<td>Level of ADL assistance</td>
<td>Restraints</td>
<td>MCI or ADRD (new or worsening)</td>
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<td></td>
<td></td>
<td>Level of ADL assistance (new or worsening)</td>
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<tr>
<td><strong>Social network and resources</strong></td>
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<tr>
<td>Limitied social and professional support</td>
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<tr>
<td></td>
<td></td>
<td>Access to caregiving resources</td>
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<tr>
<td></td>
<td></td>
<td>Socioeconomic loss</td>
</tr>
<tr>
<td><strong>Healthcare system</strong></td>
<td></td>
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<td>Visitor restrictions</td>
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<tr>
<td>Quality of HCP communication about ICU care</td>
<td></td>
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<tr>
<td>Inclusion of caregiver in ICU care</td>
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<tr>
<td>Quality of HCP communication expectations about post-ICU course</td>
<td></td>
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</tbody>
</table>

* = Protective factor
HCP = Health care professional
Underlined = To be tested
Assessment

- Biopsychosocial aspects
  - Sense of caregiver mastery (sense of control)
  - Perception of their support network
  - Effect of caregiving on the caregivers’ lives
- Caregiver's perception of the health and functional status of the patient
Assessment

- Well-being of the caregiver
- Skills/abilities/knowledge to provide the patient with needed care
Intra-ICU prevention and management

- ABCDEF Bundle of ICU care
  F = family to involve families in the care.
- “Open” ICUs and redesign of units.
- Healthcare providers performing tasks in front of family
- ICU diaries
Intra-ICU prevention and management

- Engagement of family members in patients’ care
- Discuss the anticipated post-ICU trajectory
- Psychoeducation
Post-ICU prevention and management

- Access to appropriate resources (home health service).
- Web-based tools for caregivers are available from the SCCM and Healthtalk in the UK
Post-ICU prevention and management

- Referrals to mental health treatment
- Psychoeducation
- Skills training
- Emphasis on practices to improve the caregivers’ QoL, e.g. counseling, self-care, relaxation training, and respite
Aging and Postintensive Care Syndrome– Family: A Critical Need for Geriatric Psychiatry

Patricia Serrano M.D. a, You Na P. Kheir M.D. a, Sophia Wang M.D. a, b, c, g, Sikandar Khan D.O. d, e, Leslie Scheunemann M.D., M.P.H. f, g, Babar Khan M.D., M.S. c, d, e
The Vision of CCRC

Maximize the quality of life of acute critical illness survivors and their informal caregivers via a rapid translation of rehabilitation care discoveries into a routine clinical practice.
Clinic Assessment:
- Detect and treat
  - Physical disability
  - Psychological Disability
  - Cognitive Disability

Caregiver Focus:
- Problem solving skills
- Counseling
- Respite care
- Support group

Monitor, Coordinate & Deliver individualized protocols

Patient Focus:
- Individualized Care plan for cognitive, physical, psychological recovery
- Medication adherence and management support

Expert Team:
- Rehabilitation
- Pulmonary
- Psychology
- Geriatrics
- Psychiatry

Dynamic Feedback

Wang et al. AJGP 2017
A Typical CCRC Patient Encounter

- Care coordinators/case managers
- ICU Nurse Practitioner
- Contact with patient (physician/ CCRC nurse)
- Patient/ care giver informant questionnaire
- First visit: (physical/ psychological/ cognitive/ caregiver assessment)
- Second visit: (Individualized prescription)
- Follow up
Criteria

• Admitted to one of the local ICUs plus
• Mechanical ventilation for 2 days and/or
• Delirium for 2 days
<table>
<thead>
<tr>
<th>Activity</th>
<th>Not at all (0-1 day)</th>
<th>Several Days (2-6 days)</th>
<th>More than half the days (7-11 days)</th>
<th>Almost daily (12-14 days)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Judgment or decision-making</td>
<td></td>
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<tr>
<td>Repeating the same things over and over such as questions or stories</td>
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<tr>
<td>Forgetting the correct month or year</td>
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<tr>
<td>Handling complicated financial affairs such as balancing checkbook, income taxes &amp; paying bills</td>
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<tr>
<td>Remembering appointments</td>
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<tr>
<td>Thinking or memory</td>
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<tr>
<td>Learning how to use a tool, appliance or gadget</td>
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<tr>
<td>Planning, preparing, or serving meals</td>
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<tr>
<td>Taking medications in the right dose at the right</td>
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<tr>
<td>Walking or physical ambulation</td>
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<tr>
<td>Bathing</td>
<td></td>
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<tr>
<td>Shopping for personal items like groceries</td>
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<tr>
<td>Housework or household chores</td>
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<tr>
<td>Your safety</td>
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<tr>
<td>Your quality of life</td>
<td></td>
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<tr>
<td>Falling or tripping</td>
<td></td>
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<tr>
<td>Less interest or pleasure in doing things, hobbies or activities</td>
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<tr>
<td>Feeling down, depressed, or hopeless</td>
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<tr>
<td>Resisting help from others or getting agitated</td>
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<tr>
<td>Feeling anxious, nervous, tense, fearful or panic</td>
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<tr>
<td>Believing others are stealing from you or planning to harm you</td>
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<tr>
<td>Hearing voices, seeing things or talking to people who are not there</td>
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<tr>
<td>Poor appetite or overeating</td>
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<tr>
<td>Falling asleep, staying asleep, or sleeping too much</td>
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<tr>
<td>Acting impulsively, without thinking through the consequences of your actions</td>
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<tr>
<td>Wandering, pacing, or doing things repeatedly</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Place Sticker Here</th>
<th>COGNITIVE SUBSCALE</th>
<th>FUNCTIONAL SUBSCALE</th>
<th>BEHAVIORAL AND MOOD SUBSCALE</th>
<th>TOTAL SCORE</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>CCRC Population (n = 142)</td>
<td>Primary Care Population (n = 291)</td>
<td>P-value</td>
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<td>------------------</td>
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<tr>
<td></td>
<td>Mean (SD)</td>
<td>Mean (SD)</td>
<td></td>
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<tr>
<td>Cognitive</td>
<td>3.7 (4.1)</td>
<td>1.9 (2.9)</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>Psychological</td>
<td>6.4 (6.0)</td>
<td>3.2 (4.2)</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>Functional</td>
<td>6.3 (6.8)</td>
<td>3.2 (4.5)</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>16.3 (14.5)</td>
<td>8.3 (10.3)</td>
<td>&lt;0.001</td>
<td></td>
</tr>
</tbody>
</table>
Figure 2: Improvement in Post-Intensive Care Syndrome (PICS) symptoms over time

↓ scores mean improvement

Khan et al. AJN 2015
Psychiatric co-morbidities in ICU Survivors

Mean EQ-5D-3L Index or Mean EQ-5D-VAS Index Grouped by Psychiatric Comorbidities

Wang et al. JHM 2017
Psychiatric Symptoms and Sleep Disturbances

- 112 ICU Survivors (mean age 52 years, 85% with respiratory failure, 78% with delirium)

- Trauma-related symptoms and moderate to severe depressive symptoms

- Sleep Disturbances (insomnia, hypersomnia, difficulty with sleep onset, sleep maintenance, excessive daytime sleepiness)
<table>
<thead>
<tr>
<th>Psychiatric Symptoms and Sleep Disturbances</th>
<th>16.66 (2.89 - 96.00)</th>
<th>0.002</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trauma-related and depression symptoms</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trauma-related symptoms, no depression symptoms</td>
<td>4.59 (1.11 - 18.88)</td>
<td>0.035</td>
</tr>
<tr>
<td>Depression symptoms, no trauma-related symptoms</td>
<td>1.35 (0.23 - 7.83)</td>
<td>0.738</td>
</tr>
<tr>
<td>No trauma-related or depression symptoms, history of depression</td>
<td>0.95 (0.23 - 3.89)</td>
<td>0.946</td>
</tr>
<tr>
<td>No trauma-related or depression symptoms, no history of depression</td>
<td>1.00 (reference)</td>
<td></td>
</tr>
</tbody>
</table>
Summary

- COVID-19 has a number of unique neurological manifestations including delirium, anosmia, and prolonged loss of consciousness.

- ICU survivors, especially those who have had delirium, often suffer from post-intensive care syndrome (PICS).

- Mental health symptoms of family members of ICU survivors are common but frequently unrecognized.
Community Advisory Board

Dr. Andrew Saykin, PsyD, ABCN
Director, Indiana Alzheimer's Disease Research Center

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www.facebook.com/IndianaAlzheimersDiseaseResearchCenter
Questions?

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