

**AWARD NUMBER:** W81XWH-21-1-0050

**TITLE:** Addressing Post-Intensive Care Syndrome Among Survivors of COVID (APICS-COVID)

**PRINCIPAL INVESTIGATOR:** Samuel Brown, MD

**CONTRACTING ORGANIZATION:** IHC HEALTH SERVICES, INC., Salt Lake City, UT

**REPORT DATE:** February 2023

**TYPE OF REPORT:** Annual

**PREPARED FOR:** U.S. Army Medical Research and Development Command  
Fort Detrick, Maryland 21702-5012

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# REPORT DOCUMENTATION PAGE

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<b>4. TITLE AND SUBTITLE</b>  Addressing Post-Intensive Care Syndrome Among Survivors of COVID (APICS-COVID)				<b>5a. CONTRACT NUMBER</b> W81XWH-21-1-0050	
				<b>5b. GRANT NUMBER</b> PR202630	
				<b>5c. PROGRAM ELEMENT NUMBER</b>	
<b>6. AUTHOR(S)</b> Samuel M. Brown  E-Mail: Samuel.Brown@imail.org				<b>5d. PROJECT NUMBER</b>	
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<b>12. DISTRIBUTION / AVAILABILITY STATEMENT</b>  Approved for Public Release; Distribution Unlimited					
<b>13. SUPPLEMENTARY NOTES</b>					
<b>14. ABSTRACT</b> APICS-COVID seeks to address a key clinical and operational knowledge gap by defining patterns of unmet needs, resource utilization, readmissions, and long-term functional outcomes among ICU survivors in the age of COVID-19, allowing direct knowledge of COVID-19 patterns as well as comparison with the APICS-01 cohort, which completed enrollment with identical methodology, to allow comparisons. In the first year of award, APICS-COVID initiated enrollment and data collection ahead of schedule; in the second year, enrollment was completed ahead of schedule. In the coming period, the study team will complete the 6 months of patient follow-up, clean data, and report findings.					
<b>15. SUBJECT TERMS</b> Acute Lung Injury, Recovery after Clinical Illness, Cohort Study					
<b>16. SECURITY CLASSIFICATION OF:</b>			<b>17. LIMITATION OF ABSTRACT</b>	<b>18. NUMBER OF PAGES</b>	<b>19a. NAME OF RESPONSIBLE PERSON</b>
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Unclassified	Unclassified	Unclassified	Unclassified	12	<b>19b. TELEPHONE NUMBER (include area code)</b>

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### 1. INTRODUCTION:

The overall proposed approach is to generate an observational cohort and use pseudo-randomization (inverse probability of treatment weighting) to interrogate the relationship between unmet needs and hospital readmissions. This will occur in a multicenter cohort of patients with respiratory failure due to COVID-19 (as well as COVID-19 “bystanders,” patients who have acute respiratory failure during the pandemic not due to the SARS-CoV-2 virus) that we anticipate will usefully reflect the experience of service members and veterans.

### 2. KEYWORDS:

Acute Lung Injury, Long-term Outcomes, Intensive Care, Recovery from Illness/Injury

### 3. ACCOMPLISHMENTS:

#### What were the major goals of the project?

*Major Task 1: Prepare Study for Data Collection and Execution.* Major Task 1 has been completed ahead of schedule. All subtasks have been completed ahead of schedule.

*Major Task 2: Patient Enrollment and Data Collection.* We have reached our target enrollment of 200 patients ahead of schedule (note that due to a patient who withdrew after consent but before study procedures had been performed, a total of 201 patients were nominally enrolled). All the investigator meetings are happening on-time and consistently. All subtasks are being completed on time or ahead of schedule.

*Major Task 3: Data Analysis and Dissemination.* The work under this task will begin in year 3, once follow-up is completed.

#### What was accomplished under these goals?

Major Activities: Primary activities in this study period were enrollment and data collection. As indicated above, we have reached target enrollment and all goals are being achieved ahead of schedule. Data analysis and formal findings will be reported in year 3.

#### Enrollment Report – July 2022

	Total
BIDMC	21
IMC	54
JHU	100
VA	11
VUMC	15
<b>TOTAL</b>	201

**What opportunities for training and professional development has the project provided?**

Nothing to Report

**How were the results disseminated to communities of interest?**

Nothing to Report

**What do you plan to do during the next reporting period to accomplish the goals?**

For the next study period, we will continue patient follow ups and data collection.

**4. IMPACT:**

**What was the impact on the development of the principal discipline(s) of the project?**

Nothing to Report

**What was the impact on other disciplines?**

Nothing to Report

**What was the impact on technology transfer?**

Nothing to Report

**What was the impact on society beyond science and technology?**

Nothing to Report

**5. CHANGES/PROBLEMS:**

**Changes in approach and reasons for change**

Nothing to Report

**Actual or anticipated problems or delays and actions or plans to resolve them**

We are completing our milestones ahead of schedule. We do not anticipate problems at this stage.

**Changes that had a significant impact on expenditures**

Nothing to Report

**Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents**

**Significant changes in use or care of human subjects**

Nothing to Report

**Significant changes in use or care of vertebrate animals**

No animal use research will be performed to complete the Statement of Work

**Significant changes in use of biohazards and/or select agents**

Nothing to Report

**6. PRODUCTS:**

**• Publications, conference papers, and presentations**

**Journal publications.**

Nothing to Report

**Books or other non-periodical, one-time publications.**

Nothing to Report

**Other publications, conference papers and presentations.**

Nothing to Report

- **Website(s) or other Internet site(s)**

Nothing to Report

- **Technologies or techniques**

Nothing to Report

- **Inventions, patent applications, and/or licenses**

Nothing to Report

- **Other Products**

Nothing to Report

## **7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS**

### **What individuals have worked on the project?**

IHC Personnel:

Name: Samuel Brown

Contribution to Project: No change from semi-annual progress report.

Name: Harris Carmichael

Contribution to Project: No change from semi-annual progress report.

Name: Sarah Beesley

Contribution to Project: No change from semi-annual progress report.

Name: Valerie Aston

Contribution to Project: No change from semi-annual progress report.

Name: Danielle Groat

Contribution to Project: No change from semi-annual progress report.

Name: Jenna Lumpkin

Contribution to Project: No Change from semi-annual progress report.

JHU Personnel:

Name: Dale Needham

Contribution to Project: No change from semi-annual progress report.

Name: Naga Preethy Kadiri

Contribution to Project: No change from semi-annual progress report.

Name: Victor Dinglas

Contribution to Project: No Change from semi-annual progress report.

VA Personnel

Name: Mustafa Mir-Kasimov

Contribution to Project: No change from semi-annual progress report.

Name: Craig High

Contribution to Project: No Change from semi-annual progress report.

University of Utah Personnel:

Name: Tom Greene

Contribution to Project: No change from semi-annual progress report.

**Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?**

For Dr. Brown, the following funding is now providing effort:

5R01HL144624-03, "Study of Treatment's Echocardiographic Mechanisms – CLOVERS-STEM" (NHLBI, 5% effort)

3U01HL123009-07S1, "Investigate early interventions to improve outcomes in patients with early critical illness at risk for acute lung injury." (NHLBI, 12%)

1OT2HL156812-02, "PETAL Network International Coordinating Center for ACTIV-3b Trial Subaward" (NHLBI, 10%)

W81XWH-21-1-0050 "Addressing Post-Intensive Care Syndrome Among Survivors of COVID (APICS-COVID)" (DOD, 5%)

5UL1TR002538-05 "The Utah Center for Clinical and Translational Science Institute (CTSI)" (NIH, 5%)

1U01HL159878-01 "Implementation of Coordinated Spontaneous Awakening and Breathing Trials Using Telehealth-Enabled, Real-Time Audit and Feedback for Clinician Adherence: A Type II Hybrid Effectiveness-Implementation" (NHLBI, 2%)

UL1-TR002535-03S3 "Real world effectiveness and safety of nMAb treatment in high-risk COVID-19 Outpatients" (NCATS, 1%)

For Dr. Carmichael, only APICS-COVID funding is providing effort.

For Dr. Beesley, only APICS-COVID funding is providing effort.

For Dr. Needham, the following funding is now providing effort:

R01HL132887 "Nutrition and Exercise in Critical Illness (The NEXIS Trial): A Randomized Trial of Combined Cycle Ergometry and Amino Acids in the ICU" (NHLBI, 15%)

W81XWH-21-1-0050 "Addressing Post-Intensive Care Syndrome Among Survivors of COVID (APICS-COVID)" (DOD, 10%)

R01NR017433, “Symptoms Assessment and Screening for Laryngeal Injury Post-extubation in ICU” (NINR, 20%)

R01HL13288, “Effects of Exercise on Inflammation-Induced Lung and Muscle Injury in Critical Illness (NEXIS-FLAME)” (NHLBI, 2.5%)

R01AG061384 “Improving the statistical design and analysis of randomized controlled trials of delirium prevention and treatment for critically ill older adults” (NIA, 11.3%)

R42AG059451 “Novel Arm Restraint for Critically Ill Patients to Reduce Immobility, Sedation, Agitation and Cognitive Impairment” (NHLBI, 4.1%)

“A Pilot, feasibility randomized controlled trial of a behavioral activation and rehabilitation intervention to improve psychological and physical impairments in acute respiratory failure survivors.” (NHLBI, Time commitment: Mentor)

“Understanding Response Shift in Acute Respiratory Distress Syndrome (ARDS).” (NHLBI, Time commitment: Mentor)

For Dr. Greene, the following funding is now providing effort:

1R01AG074989-01 “Informing optimal first-line antihypertensive therapy: A rigorous comparative effectiveness analysis of ARBs vs. ACEIs on long-term risk of dementia, cancer, heart disease, and quality of life” (NIH, 10%)

1R01AG065805-01A1 “Guiding next steps for SPRINT-MIND implementation: Identifying high-benefit subgroups and comparative effects of ARB- vs. ACEI-based regimens” (NIA, 11%)

PCS-2017C2-7613 “Multi-Level Interventions for Increasing Tobacco Cessation at FQHCs” (PCORI, 8%)

UL1TR002538 “University of Utah Center for Clinical and Translational Science (CCTS)” (NCATS, 8%)

PT170087 “Optimizing Rehabilitation InterventiONs (ORION) for Cognition Following Complex Traumatic Brain Injury” (DOD, 8%)

R01DK118219 “Long-term metabolic effects of kidney events with intensive SBP control” (NIDDK, 8%)

5R01DK229079 “Dynamic Prediction of Renal Failure Using Longitudinal Prognostic Information among Patients with Chronic Kidney Disease and Kidney Transplant” (NIDDK, 4%)

5P30CA042014-32 “Cancer Center Support Grant – Biostatistics Center (CB)” (NCI, 6%)

W81XWH-21-1-0050 “Addressing Post Intensive Care Syndrome among Survivors of COVID (APICS- COVID)” (DOD, 5%)

5UH3AT009763-04 “SMART Stepped Care Management for Low Risk Pain in Military Health System” (NCCIH, 5% / 10%)

1R01DK126799-01A1 “Development of Prognostic Algorithms to Identify Subjects at High Risk of ESKD in Type 2 Diabetes” (NIH, 5%)

1R18DK123372 “Promoting Real World Implementation of an Evidence-Based Weight Management Intervention in Primary Care” (NIDDK, 4%)

1R01DK128640-01 “Sit Less, Interact and Move More (SLIMM) 2 Study” (NIH, 5%)

1R01AG074592-01 “Objectively Measured Sedentary Behavior and Physical Activity in PREVENTABLE Study” (NIH, 5%)

3UH3AT009763-04S1 “Nonpharmacologic Pain Management for Lumbar Surgery” (NIH, 5%)

4UH3NR019943-02 “Nonpharmacologic Pain Management in FQHC primary care clinics” (NIH, 7.5%)

For Dr. Mir-Kasimov, there is no change in other support.

**What other organizations were involved as partners?**

Nothing to Report

**8. SPECIAL REPORTING REQUIREMENTS**

**COLLABORATIVE AWARDS:** A collaborative award is present and an annual report for the collaborative report is being submitted.

**QUAD CHARTS:** Included in the Appendix.

**9. APPENDICES:** The Quad Chart and the Award Chart

# Addressing Post Intensive Care Syndrome among Survivors of COVID (APICS-COVID)

W81XWH2110050

PR202630



**PI:** Samuel Brown, MD

**Org:** Intermountain Healthcare

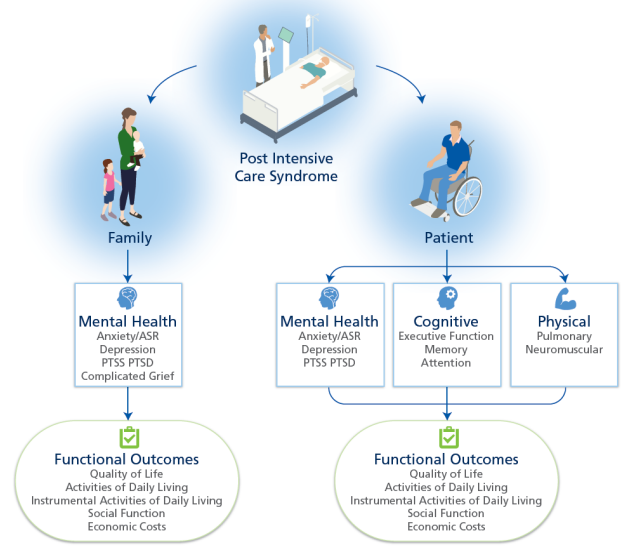
**Award Amount:** \$1,781,430

**Study/Product Aim(s)**

Aim 1: Assess the relationship between unmet needs after discharge and 3-month death or readmission, adjusting for the propensity to have unmet needs, among COVID-19 patients and COVID-19 bystanders. Secondly compare post-discharge outcomes among acute respiratory failure survivors during the COVID-19 pandemic to those of patients in the APICS-01 cohort.

**Approach**

The overall proposed approach is to generate an observational cohort and use pseudo-randomization (inverse probability of treatment weighting) to interrogate the relationship between unmet needs and hospital readmissions. This will occur in a multicenter cohort of patients with respiratory failure due to COVID-19 that we anticipate will usefully mimic the experience of service members and veterans. The population of patients treated at this facility is representative of the military.



**Timeline and Cost**

Activities	CY	21	22	23
Obtain IRB and HRPO Approval		█		
Site Education and Training		█		
Patient Enrollment and Data Collection		█		
Data Analysis and Dissemination				█
<b>Estimated Budget (\$K)</b>	<b>\$1781</b>	<b>\$609</b>	<b>\$594</b>	<b>\$578</b>

Updated: 15 January 2023

**Goals/Milestones**

**CY21 Goal – Study Initiation**

- Submit study for IRB and HRPO approval
- Standardize training and site education

**CY22 Goals – Patient Enrollment and Data Collection**

- Enroll patients
- Perform 6 month follow up visits

**CY23 Goal – Data Analysis and Dissemination**

- Perform primary and secondary data analysis
- Submit final report to the military
- Submit primary manuscript to peer-reviewed journal

**Budget Expenditure to Date**

Projected Expenditure: \$1,781,430  
Actual Expenditure: \$1,085,915

## W81XWH-18-1-0813: Addressing Post-Intensive Care Syndrome Among Survivors of COVID

PI: SAMUEL BROWN, IHC HEALTH SERVICES, INC.

Budget: \$1,781,430

Topic Area: COVID-19

Mechanism: CDMRP



Research Area(s): 1102, 1001

Award Status: 1/15/2021 - 1/14/2024

### **Study Goals:**

This study seeks to address this clinical and operational knowledge gap for ARDS survivors by defining patterns of unmet needs, resource utilization, readmissions, and long-term functional outcomes among ICU survivors particularly those with COVID-19. We will employ a prospective, multi-center, observational study of outcomes and healthcare utilization among ARDS survivors which are directly relevant to a military population.

### **Specific Aims:**

**Aim 1:** Assess the relationship between unmet needs after discharge and 3-month death or readmission, adjusting for the propensity to have unmet needs, among COVID-19 patients and COVID-19 bystanders. Secondarily compare post-discharge outcomes among acute respiratory failure survivors during the COVID-19 pandemic to those of patients in the APICS-01 cohort.

- **Hypothesis:** Unmet needs in the first 1-4 weeks after hospital discharge are associated with readmission or death after hospital discharge at 3 months, even after adjusting for the likelihood of having unmet needs, and we hypothesize that survivors of respiratory failure during COVID-19 pandemic will differ from those enrolled in the APICS-01 cohort.

### **Key Accomplishments and Outcomes:**

Study launched ahead of schedule. Enrollment (N=201/200) ahead of schedule.

Publications: none to date

Patents: none to date

Funding Obtained: \$1,781,430