

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

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| 13. SUPPLEMENTARY NOTES | | | | | |
| 14. ABSTRACT 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. Most recently, our team completed the 6-month follow-up and data cleaning. In the final period, the study team will finalize the APICS-COVID manuscripts for submission and combine APICS-01/APICS-COVID data to derive further insights from the COVID-19 pandemic on Acute Respiratory Failure survivors and report insights from this linear analysis prior to, and during, COVID-19. | | | | | |
| 15. SUBJECT TERMS Acute Lung Injury, Recovery after Clinical Illness, Cohort Study | | | | | |
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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, with appropriate IRB approvals). All the investigator meetings are happening on-time and consistently. All subtasks are being completed on time.

Major Task 3: Data Analysis and Dissemination. The dataset is closed and data cleaning/validation is complete. Analysis of the primary and secondary aims has begun with one manuscript in the process of submission and a second manuscript drafted. Dissemination of findings will continue in the coming months with 2 planned manuscript submissions. A no-cost extension is requested to allow completion of additional analyses and manuscripts.

What was accomplished under these goals?

Major Activities: As indicated above, we have reached target enrollment and all goals are being achieved. Formal findings will be reported this coming year. A 1-year no cost extension was requested to allow completion of DCC activities and completion of all analyses and manuscript reporting. The DCC activities primarily relate to ad hoc data queries and data management to support ongoing analyses related to publication and dissemination of scientific research manuscripts for the primary and secondary objectives of the APICS-COVID study.

Enrollment Report – July 2022

| | Total |
|-------|-------|
| BIDMC | 21 |
| IMC | 54 |
| JHU | 100 |

| | |
|--------------|-----|
| VA | 11 |
| VUMC | 15 |
| TOTAL | 201 |

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

Junior researchers have taken the lead in first-authorship and are being supported by the senior team members in professional development of further researchers.

How were the results disseminated to communities of interest?

Formal manuscript submission will complete the goal of dissemination in the coming period.

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

Follow through with the formal reporting process via manuscript submission.

4. IMPACT:

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

Impact of the project is pending dissemination of our results.

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 or on 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

Name: Harris Carmichael

Contribution to Project: No change

Name: Sarah Beesley

Contribution to Project: No change

Name: Valerie Aston

Contribution to Project: No change

Name: Danielle Groat
Contribution to Project: No change

Name: Jenna Lumpkin
Contribution to Project: No Change

JHU Personnel:

Name: Dale Needham
Contribution to Project: No change

Name: Naga Preethy Kadiri
Contribution to Project: No change

Name: Victor Dinglas
Contribution to Project: No Change

VA Personnel

Name: Mustafa Mir-Kasimov
Contribution to Project: No change

Name: Craig High
Contribution to Project: No Change

University of Utah Personnel:

Name: Tom Greene
Contribution to Project: No change

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)

1U01HL168416-01, “The Intermountain West-Atlantic Center (InterACT) for the APS Phenotyping Consortium ” (NHLBI, 10%)

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

1UM1TR004409-01 “The Utah Center for Clinical and Translational Science Institute (CTSA UM1)” (NIH, 10%)

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%)

51-312-0217571-66994L “Strategies and Treatments for Respiratory Infections and Viral Emergencies – STRIVE ” (NHLBI, 2%)

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

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

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, 10%)

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

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

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

W81XWH-21-1-0050 “Addressing Post Intensive Care Syndrome Among Survivors of COVID (APICS COVID)” (DOD, 15%)

1UG3HL147011 “Ganciclovir to Prevent Reactivation of Cytomegalovirus in Patients with Acute Respiratory Failure and Sepsis-Cost Reimbursement” (NIH, 1%)

U01HL168416 “ARDS, Pneumonia, and Sepsis Phenotyping Consortium Clinical Centers (APS)” (NIH, 5%)

R01HD103811 “Clinical Effectiveness of the "PICU Up!" Multifaceted Early Mobility Intervention for Critically Ill Children: A pragmatic, stepped-wedge trial” (NIH, 13.75%)

R01HL164777 “Immune, hormonal, and muscle mitochondrial determinants of recovery in Acute Respiratory Distress Syndrome survivors” (NIH, 15%)

R01HL163660 “Health expectations after acute respiratory failure in survivor-care partner dyads” (NIH, 15%)

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

1UM1TR004409-01 “The Utah Center for Clinical and Translational Science Institute (CTSA UM1)” (NIH, 10%)

OTS-LBP-2017C1-6486 “SMART LBP Trial: Optimized Multidisciplinary Treatment Programs for Nonspecific Chronic Low Back Pain” (PCORI, 10%)

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

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

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

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%)

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

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%)
IU54CA280812-01 “Multi-sector; multi-level interventions for improving cancer prevention and control addressing persistent poverty” (NC, 5%)
1R01DK116790 “Improving Kidney Function Assessment in Health and Disease” (NIH, 2.8%)
IU54HD113169 ELEVATE Maternal Health Center of Excellence (NIH, 10%)

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

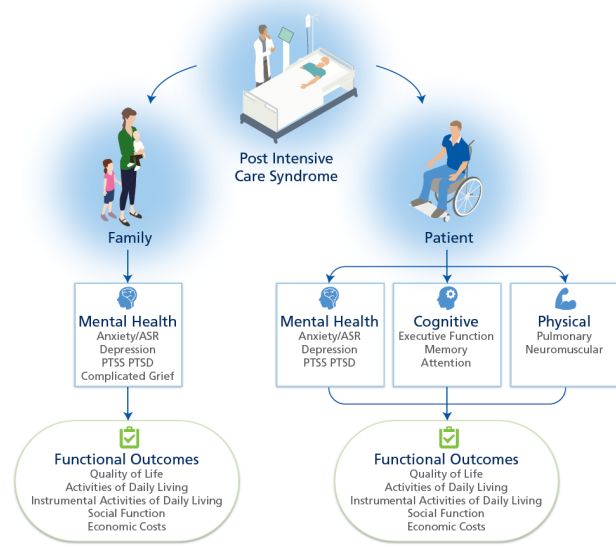
Award Amount: \$1,781,430

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. Secondarily 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 | | | | █ |
| Estimated Budget (\$K) | \$1781 | \$609 | \$594 | \$578 |

Updated: 5 January 2024

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**
 - Complete all 6-month follow-up visits and close dataset
 - 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: \$1,592,318

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 - 1/14/2025

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: