

AWARD NUMBER: W81XWH-18-1-0813

TITLE: Addressing Post-Intensive Care Syndrome (PICS) Among Survivors of Acute Lung Injury

PRINCIPAL INVESTIGATOR: Samuel Brown

CONTRACTING ORGANIZATION: IHC HEALTH SERVICES, INC

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14. ABSTRACT APICS-01 seeks to address clinical and operational knowledge gap for acute lung injury (ALI) survivors by defining patterns of unmet needs, resource utilization, readmissions, and long-term functional outcomes among ICU survivors. We will employ a prospective, multi-center, observational study of outcomes and healthcare utilization among 200 ALI survivors which are directly relevant to a military population. In the third year of award, APICS-01 moved forward from the timely completion of enrollment to completion of follow-up, cleaning and locking of the dataset, and analysis of data. The first manuscript has been submitted to a peer-reviewed journal. The key findings are of an association between unmet medication needs and hospital readmission with a complex signal suggesting that patients with high risk of mortality may already receive extra attention to their medication needs. Secondary manuscripts, with their associated data cleaning and analysis are ongoing and will be the work of the fourth year (under no-cost extension).						
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1. INTRODUCTION:

APICS-01 seeks to address the clinical and operational knowledge gap for acute lung injury (ALI) survivors by defining patterns of unmet needs, resource utilization, readmissions, and long-term functional outcomes among ICU survivors. We will employ a prospective, multi-center, observational study of outcomes and healthcare utilization among ALI survivors which are directly relevant to a military population. The study will enroll 200 patients at multiple civilian and Veterans Administration hospitals centers. We hypothesize that unmet needs in the first 1-4 weeks after hospital discharge will be associated with readmission or death after hospital discharge at 3 months, even after adjusting for the likelihood of having unmet needs.

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 was entirely completed in study year 1, as outlined in the report for Year 1.

Major Task 2: Patient Enrollment and Data Collection. As of August 18, 2020 enrollment is complete at 200 patients, which comfortably exceeds our original milestone. Follow-up has now been completed.

Major Task 3: Data Analysis and Dissemination. Data lock has occurred for the primary manuscript, which has been submitted to a peer-reviewed journal. Secondary analyses and associated manuscripts are ongoing, and submission of those manuscripts will occur during the fourth year (during a no-cost extension). This work is in addition to manuscripts and abstracts that have already been published or presented.

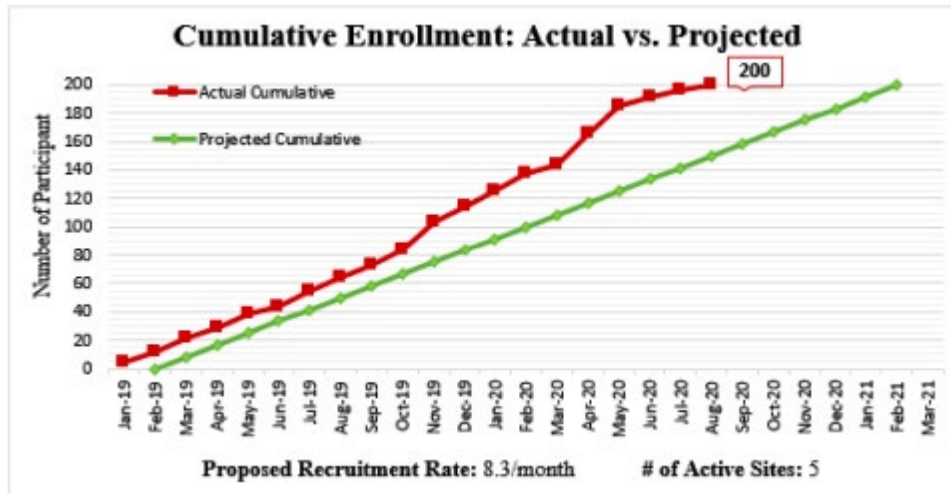
What was accomplished under these goals?

Major Activities: Primary activities in this study period were completion of follow-up, data cleaning, data analysis and dissemination of scientific research manuscripts. We published the protocol for this study in *BMJ Open* Journal. As indicated above, all goals were achieved ahead of schedule. The following figure demonstrates our enrollment status which was completed ahead of schedule. The first results manuscript has been submitted to a peer-reviewed journal.

Specific Objectives: Assess the relationship between unmet needs after discharge and 3-month

death or readmission, using inverse probability weighting to control for the propensity of having unmet needs.

Significant Results or Key Outcomes: All stated goals have been met.



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

Nothing to Report

How were the results disseminated to communities of interest?

We have published the rationale paper and protocol paper already; both are available for free. The primary results manuscript has been submitted for peer review. The study team also maintain an active social media presence to promote this research and also communicate the relevant findings as part of their existing Aftercare and Recovery Clinics for ICU survivors.

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

During the no-cost extension for the fourth year, we will work on data cleaning, 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 APICS-01 study. This will include additional analyses if requested during peer review for the primary manuscript as well as the work to support the secondary manuscripts which are planned.

4. IMPACT:

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

APICS-01 is the first study to our knowledge to carefully evaluate the first weeks after hospital discharge for ALI survivors. In that innovative setting, we are also studying the proportion of unmet needs as a marker of vulnerability and controlling—with innovative statistical techniques—for possible confounding. Our publications have advanced understanding in the field of this important area. Ongoing data analysis and results will inform both clinical practice and future interventional trials in the field.

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?

The publication of the framing paper (Brown et al, 2019) has advanced conversations in public about the importance of care coordination and attention to early unmet needs among ALI survivors. This helped advance the societal conversation about our obligations to patients through the entire arc of illness through recovery. The publication of the protocol paper helped inform future interventional trials in the field. We anticipate a similar effect from the results manuscripts, the first of which has now been submitted to a peer-reviewed journal.

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

Nothing to Report

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 use of vertebrate animals in this research.

Significant changes in use of biohazards and/or select agents

No use of biohazards and/or select agents.

6. PRODUCTS:

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

Journal publications.

Nothing to Report (the primary results manuscript has been submitted but not yet published, and the 2021MHSRS was canceled due to COVID19).

• **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**

The final data, including follow-up, has been collected and represents a substantial contribution to our understanding of the outcomes of survivors of acute lung injury.

7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

What individuals have worked on the project?

Name: Samuel Brown

Contribution to Project: No change from original submission

Name: Jennifer King

Researcher Identifier:

Project Role: Project Coordinator

Nearest person month worked: 1 CM

Contribution to Project: Jennifer King replaced Katherine Brown (previous research coordinator) and has worked on the study by consenting, enrolling patients and data entry.

Name: Dale Needham

Contribution to Project: No change from original submission

Name: Tejaswi Kalva

Contribution to Project: No change from original submission

Name: Victor Dinglas
Project Role: Data Manager for Data Coordinating Center
Researcher Identifier:
Nearest Person Month Worked: 6 CM
Contribution to Project: Works to maintain function of the data coordinating center including data processes oversight, communication with study team and related tasks.

Name: Mazin Ali Mahmoud
Project Role: Research Assistant
Researcher Identifier:
Nearest Person Month Worked: 3 CM
Contribution to Project: Study support, Telephone Follow-up, contacting study participants

Name: Darin Roberts
Project Role: Research Assistant
Researcher Identifier:
Nearest Person Month Worked: 3 CM
Contribution to Project: Study support, Telephone Follow-up, contacting study participants

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, 20% effort)
1OT2HL156812-01, “PETAL Network International Coordinating Center for ACTIV-3b Trial Subaward” (NHLBI, 20%)
1OT2HL156812-01, “PETAL Network International Coordinating Center for ACTIV-3 Trial Initiative Subaward” (NHLBI, 10%)
3U01HL123009-07S1, “Investigate early interventions to improve outcomes in patients with early critical illness at risk for acute lung injury.” (NHLBI, 11%)
W81XWH-21-1-0050 “Addressing Post-Intensive Care Syndrome Among Survivors of COVID (APICS-COVID)” (DOD, 15%)
UG3HL147011-01A1 “1/2 Ganciclovir to Prevent Reactivation of Cytomegalovirus in Patients with Acute Respiratory Failure and Sepsis” (NHLBI, 2% 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%)
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%)

RFTO #27 “Improving the statistical design and analysis of randomized controlled trials of delirium prevention and treatment for critically ill older adults” (NIA, 11.3%)
“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. 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*

W81XWH-18-1-0813: Addressing Post-Intensive Care Syndrome (PICS) Among Survivors of Acute Lung Injury

PI: SAMUEL BROWN, IHC HEALTH SERVICES, INC.

Budget: \$1,234,336

Topic Area: Acute Lung Injury

Mechanism: CDMRP



Research Area(s): 1102, 1001

Award Status: 9/30/2018 - 9/29/2021

Study Goals:

This study seeks to address the clinical and operational knowledge gap for acute lung injury (ALI) survivors by defining patterns of unmet needs, resource utilization, readmissions, and long-term functional outcomes among ICU survivors. We will employ a prospective, multi-center, observational study of outcomes and healthcare utilization among ALI 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, using inverse probability weighting to control for the propensity of having unmet needs.

- **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 propensity of having unmet needs.

Key Accomplishments and Outcomes:

Study launched ahead of schedule. Enrollment (N=200) ahead of schedule. Extremely high follow-up rates achieved.

Publications: 2 peer-reviewed manuscript and 3 abstracts; primary results manuscript has been submitted

Patents: none to date

Funding Obtained: \$1,234,336



Addressing Post Intensive Care Syndrome (PICS) among Survivors of Acute Lung Injury

Peer Reviewed Medical Research Program 2017

PR170552

PI: Samuel Brown, MD

Org: Intermountain Healthcare

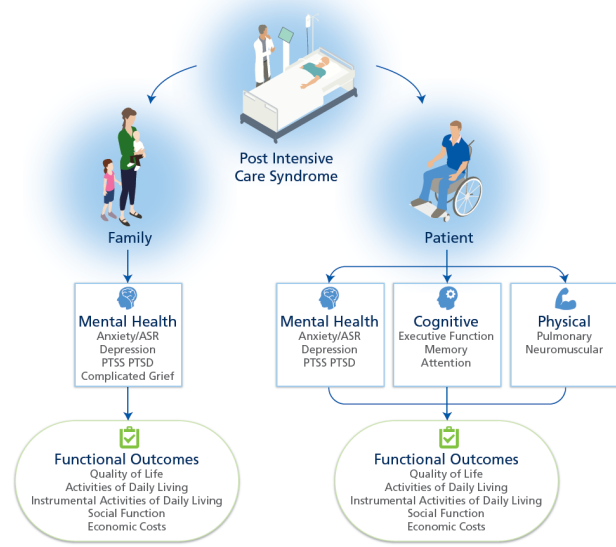
Award Amount: \$1,234,336

Study/Product Aim(s)

Aim 1: Assess the relationship between unmet needs (defined as less than 75% of items on the discharge plan being completed) after discharge and 3-month death or readmission, using inverse probability weighting to control for the likelihood of having unmet needs

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 that we anticipate will usefully mimic the experience of service members and veterans attempting to recover from ALI. The population of patients treated at this facility is representative of the military.



Timeline and Cost

Activities	CY	18	19	20	21
Obtain IRB and HRPO Approval		█			
Site Education and Training		█			
Patient Enrollment and Data Collection			█	█	
Data Analysis and Dissemination				█	█
Estimated Budget (\$K)	\$1234	\$440	\$428	\$134	\$232

Updated: 27 September 2021

Goals/Milestones

- CY18 Goals – Study Initiation**
- Submit study for local IRB and HRPO approval
 - Standardize training and site education
- CY19 Goals – Patient Enrollment and Data Collection**
- Enroll 100% of patients
 - Perform 6 month follow ups
- CY20 Goals – Data Analysis and Dissemination**
- Perform primary data analysis
 - Submit primary results manuscript
- CY21 Goals – No Cost Extension**
- Perform secondary data analysis
 - Submit final report to the military

Budget Expenditure to Date

Projected Expenditure: \$1,234,336
Actual Expenditure: \$1,002,410