TASK ORDER NUMBER: W81XWH-19-9-0015
MTEC RESEARCH PROJECT NUMBER: MTEC-19-08-MULTI-0043
EGS NUMBER: MT19008.43

TITLE: Multicenter Implementation Trial of Targeted Normoxia Strategy to Define Oxygen Requirements for Major Burn Patients: An Approach to Reduce Warfighter Morbidity, Deployed Logistical Burden of Oxygen, and Readiness Costs

PRINCIPAL INVESTIGATOR: Adit Ginde, MD, MPH

PERFORMING ORGANIZATION: University of Colorado

CONTRACTING ORGANIZATION: Medical Technology Enterprise Consortium (MTEC)

REPORT DATE: January 28, 2022

TYPE OF REPORT: Annual Report Year 2

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

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1. REPORT DATE 1/26/2022	**2. REPORT TYPE Annual Report**	**3. DATES COVERED 1/30/2021-12/31/2021**

4. TITLE AND SUBTITLE	5a. CONTRACT NUMBER
Multicenter Implementation Trial of Targeted Normoxia Strategy to Define Oxygen Requirements for Major Burn Patients: An Approach to Reduce Warfighter Morbidity, Deployed Logistical Burden of Oxygen, and Readiness Costs	W81XWH-15-9-0001 **5b. GRANT NUMBER** N/A **5c. PROGRAM ELEMENT NUMBER** (Can be blank if don't know)
6. AUTHOR(S): Adit Ginde, MD, MPH E-Mail: adit.ginde@cuanschutz.edu	**5d. PROJECT NUMBER** MT19008.43 **5e. TASK NUMBER** W81XWH-15-9-0001 **5f. WORK UNIT NUMBER** N/A
7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES) University of Colorado **AND ADDRESS(ES)** Regents of the University of Colorado, 13001 E 17Th Place Aurora CO, 80045-2571	**8. PERFORMING ORGANIZATION REPORT NUMBER** 2019-632-001
9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES) U.S. Army Medical Research and Development Command Fort Detrick, Maryland 21702-5012	**10. SPONSOR/MONITOR'S ACRONYM(S)** **11. SPONSOR/MONITOR'S REPORT NUMBER(S)** N/A
12. DISTRIBUTION / AVAILABILITY STATEMENT Distribution Unlimited	
13. SUPPLEMENTARY NOTES	

14. ABSTRACT

Introduction/Background:
Oxygen therapy has undisputed importance in combat casualty care to treat/prevent morbidity associated with hypoxia. However, generous supplemental oxygen is routine, and often results in hyperoxia. Emerging evidence indicates that even modest hyperoxia can increases morbidity/mortality, however limited evidence exists specifically for trauma and burn patients.
In addition, oxygen is a limited resource that is challenging to obtain in austere settings—eg, prolonged field care and en route care, requiring substantial resources, space, weight, and logistics to procure. Therefore, it is critical to determine oxygen titration goals for combat injured to optimize care by reducing harm associated with hypoxia and hyperoxia and to conserve limited oxygen supply.

Scope/Project Objective:
Our objective is to determine the feasibility, safety, and effectiveness of the targeted normoxia approach to conserve oxygen and improve clinical outcomes in major burn patients. We hypothesize that more targeted use of oxygen therapy, to limit exposure to both hyperoxia and hypoxia, will safely reduce the needs for concentrated oxygen in the deployed, combat setting in the care of major burn patients.
We will conduct a prospective multicenter clinical trial in adult burn patients at 6 regional burn centers to achieve the following aims:
Aim 1. Measure the impact of targeted normoxia on oxygen requirements in major burn patients. We will define the oxygen requirements for major burn patients along with determining the proportion requiring high levels of supplemental oxygen (anticipated to be low). Specific to the resource-limited setting, we will estimate the potential reductions in oxygen consumption using the targeted normoxia approach.
Aim 2. Determine the safety of targeted normoxia, compared to conventional oxygenation. Specifically, we will determine the rate and duration of hypoxic and hyperoxic events for the targeted normoxia approach, compared to conventional oxygenation that relies on generous oxygen administration.

Aim 3. Determine the clinical effectiveness of the targeted normoxia approach. Specifically, we will compare hospital mortality, hospital-free days, ventilator-free days, and burn wound healing.

15. SUBJECT TERMS: Burn, ICU, Trauma, normoxia, hyperoxia

16. SECURITY CLASSIFICATION OF:			**17. LIMITATION OF ABSTRACT**	**18. NUMBER**	**19a. NAME OF RESPONSIBLE PERSON Adit Ginde, MD, MPH**
a. REPORT	**b. ABSTRACT**	**c. THIS PAGE**			**19b. TELEPHONE NUMBER** *(include area code)* 720-848-6777
Unclassified	Unclassified	Unclassified	Unclassified		

Standard Form 298 (Rev. 8-98)

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Annual Technical Status Report for

Multicenter Implementation Trial ofTargeted Normoxia Strategy to Define Oxygen Requirements for Major Burn Patients: An Approach to Reduce Warfighter Morbidity, Deployed Logistical Burden of Oxygen, and Readiness Costs

Research Project No. 2019-632-001
EGS# MT19008.43
Reporting Period: January 30, 2021- December 31, 2021

MTEC Research Project Awardee

University of Colorado

Principal Investigator: Adit Ginde, MD, MPH

Project Manager: Erin Anderson, RN

Data Analyst: John Rice, PhD Biostatistics

Research Project Technical POC: Erin Anderson, RN

E. 17th Place

Aurora, CO, 80045

Phone: 720-999-8760

Email: erin.l.anderson@cuanschutz.edu

1. Project Status

a. Accomplishments

1. Annual Report Year 1 Completed
2. Data Collection Instruments Implemented
3. Site Initiation Visits completed:
   Army Institute of Surgical Research – 01-MAR-2021
   University of Cincinnati – 08-JUL-2021
   University of Colorado Denver – 13-OCT-2021
4. Site Implementation launched:
   Army Institute of Surgical Research – 15-APR-2021
   University of Cincinnati – 15-JUL-2021
   University of Colorado Denver – 15-OCT-2021
5. Data Collection Infrastructure Implemented
6. Development and distribution of promotional materials to encourage site compliance
7. Quarterly Report 4 (January-March, Technical and Business Reports) completed
8. Quarterly Report 5 (April-June, Technical and Business Reports) completed
9. Quarterly Report 6 (July-September, Technical and Business Reports) completed

b. Reportable Outcomes

Abstracts submitted for presentation:

- Dylla L, Douin DJ, Anderson, EL, et al. Strategy to avoid excessive oxygen (SAVE-O2) in major burn patients: A multicenter cluster randomized, stepped wedge trial for targeted normoxia. [Submitted to Special Operations Medical Scientific Assembly (SOMSA), June 2022, awaiting approval]

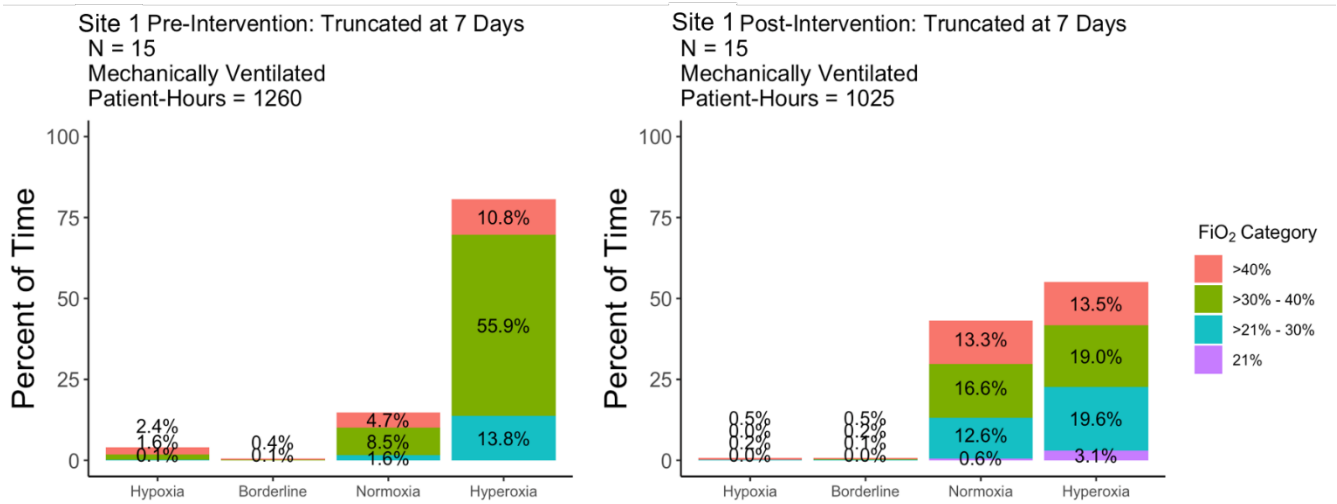
This may include development of a product, prototype, new methodology, or any other similar items that have resulted from this research. Write salient bullet points to highlight the requested information. Please also include a cumulative chronological list of written publications in technical journals, papers, or other presentations at meetings, conferences, seminars, etc.; New discoveries, inventions, or patent disclosures, and specific applications.

c. **Progress Detail:** Please see below for de-identified graphs; as of 12/31/2021, three of six sites have launched from preparatory to post-intervention phase.

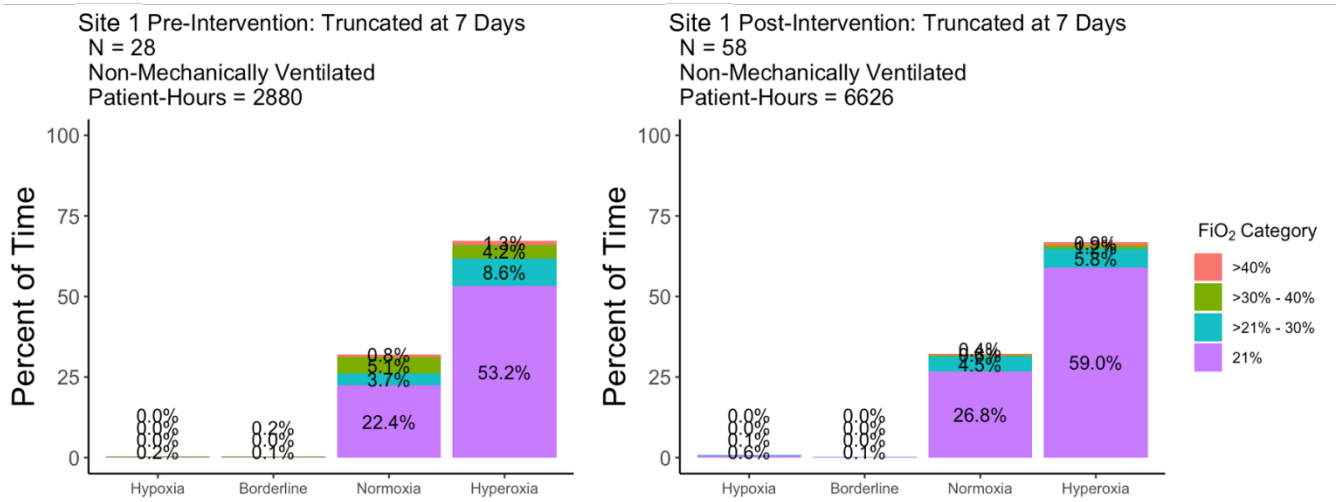
Major Task 2: Implementation	**Cumulative % Complete**
Randomized Implementation	50%
Site Monitoring	50%
Site Maintenance/Retraining	50%

Major Task 3: Data Collection/ Analysis	**Cumulative % Complete**
Data Collection	50%
Data Management/Cleaning	50%
Data Analysis	50%
Dissemination of Results	0%

Site 1:

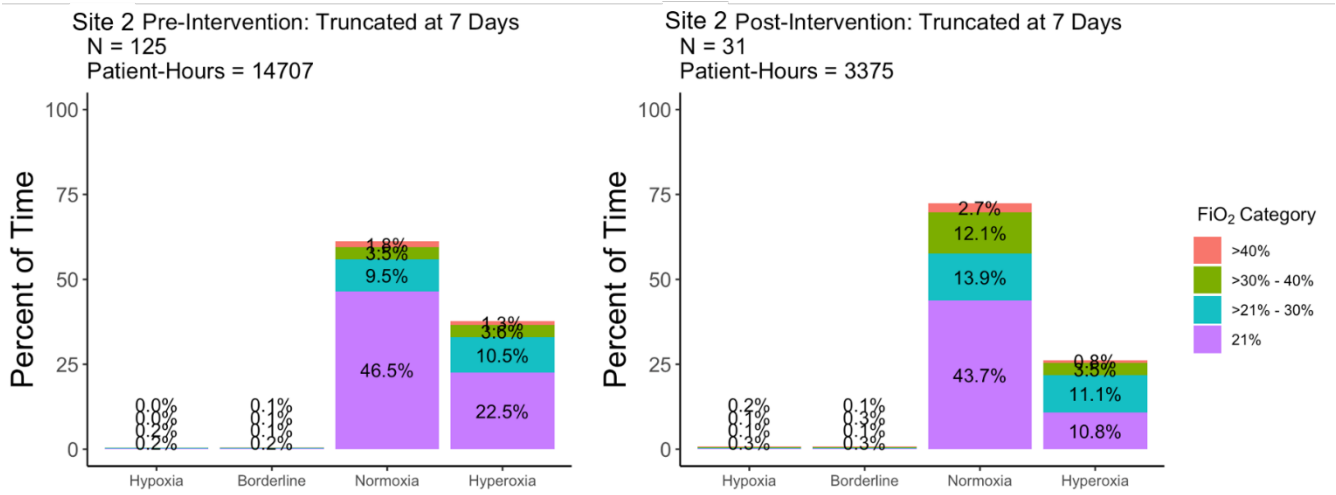


Graph 1: Pre/post-intervention comparison of mechanically ventilated patients at Site 1. There is a significant shift from hyperoxia to normoxia during the post-intervention phase of this trial.

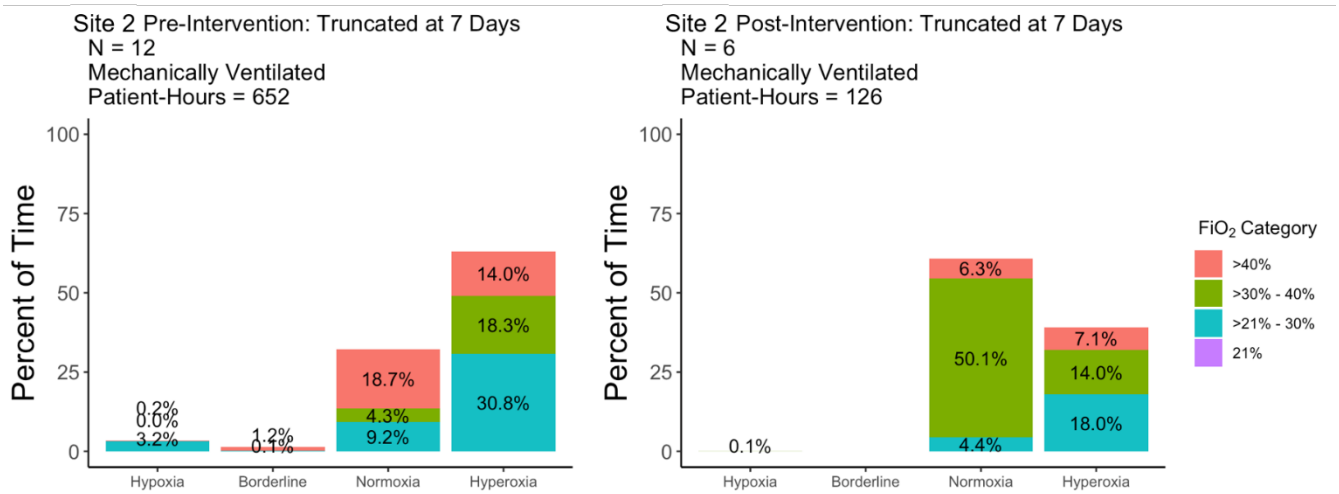


Graph 2: Pre/post-intervention comparison of non-mechanically ventilated patients at Site 1. There is a shift from hyperoxia to normoxia for patients FiO2 21%, as well as an increase in patients on FiO2 21% in hyperoxia during the post-intervention phase of this trial.

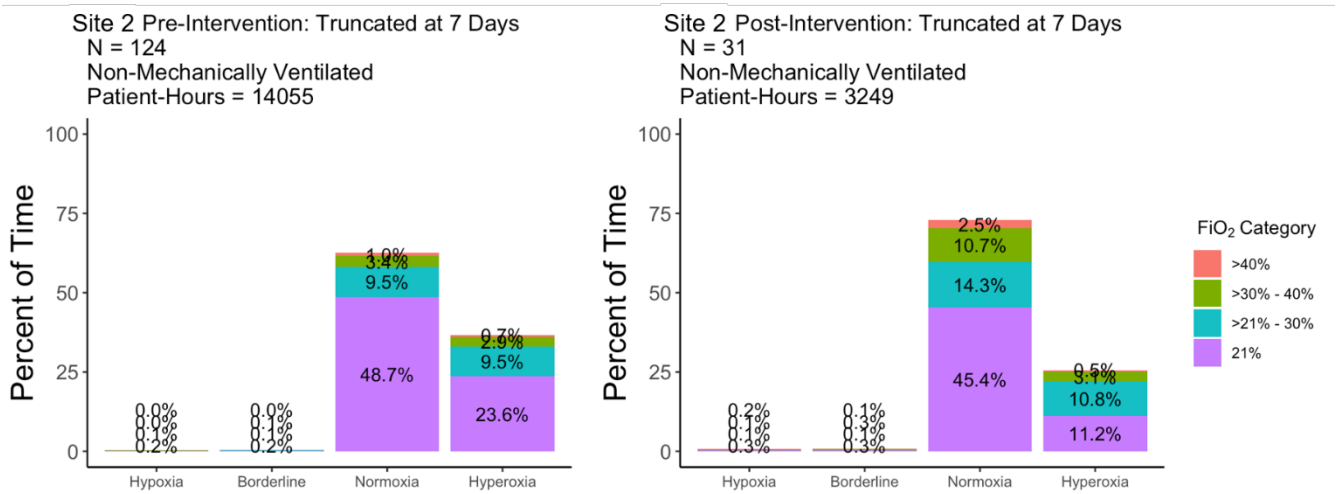
Site 2:



Graph 1: Pre/post-intervention comparison of all patients (mechanically ventilated and non-mechanically ventilated) patients at Site 2.



Graph 2: Pre/post-intervention comparison of mechanically ventilated patients at Site 2. There is a significant shift from hyperoxia to normoxia during the post-intervention phase of this trial.



Graph 3: Pre/post-intervention comparison of non-mechanically ventilated patients at Site 2. There is a shift from hyperoxia to normoxia for patients FiO2 21%, as well as an increase in patients on FiO2 21% in hyperoxia during the post-intervention phase of this trial.

Describe each Statement of Work (SOW) task or logical segment of work on which effort was expended during this quarterly reporting period only. Description shall include pertinent data and graphs in sufficient detail to explain any significant results achieved or problems encountered. A succinct description of the methodology used shall be provided.

For an award that includes the recruitment of human subjects for clinical research or a clinical trial:

i. **Enrollment:** Three of six sites have successfully launched into the post-intervention phase of the trial (see below), the remaining three sites (Vanderbilt, UAB, UPMC) are in pre-intervention . AISR and UCD have been successful in pushing deidentified data to the Data Coordinating Center at Vanderbilt University; the University of Cincinnati has had trouble accessing and uploading data from their Burn ICU/Ward, but we expect to see data from that site in Feb 2022. We are on track for ~1000 patients study wide which will still provide an adequate power to assess our primary endpoint at a reasonable effect size. *Please note:* enrollment milestones are time and institution-based and not specifically based on a previously estimated sample size.

Trial Enrollment	N	Pre-Intervention	Post-Intervention
Total Enrollment	103	42	61
AISR	95	34	61
Cincinnati*	Pending		
UCD	8	8	-

*There is a slight delay in data at this site due to data transfer issues at the local institution

ii. **Amendments:**
   a. 2021 COMIRB Continuing Review: approved 09-FEB-2021
   b. COMIRB Enrollment Number Amendment: approved 16-MAR-2021
   c. 2021 HRPO Continuing Review: approved 01-APR-2021
      i. This amendment accounts for accessing all patient's chart who are admitted to the burn ICU, which is predicted to exceed 1,000 charts. This enrollment change does not affect analysis.
   d. COMIRB Protocol Amendment Version 1.1 Dated 20-AUG-2021: submitted 17-DEC-2021, *pending approval as of 12/31/2021*
   e. COMIRB 2021 Continuing Review: submitted 17-DEC-2021, *pending approval as of 12/31/2021*

iii. **Adverse Events:** No AEs have been reported.

2. Future Plans

Milestones planned for the next year:

1. Site initiation visit 4- Vanderbilt University Medical Center- January 2022
2. Site 4 Implementation/Data Collection- January 2022
3. Site initiation visit 5- University of Alabama Birmingham- March 2022

4. Enrollment 60% complete- March 2022
5. Site 5 Implementation/Data Collection- April 2022
6. Quarterly report 7 (January-March, Technical and Business Reports)- April 2022
7. Site initiation visit 6- University of Pittsburgh Medical Center- July 2022
8. Site 6 Implementation/Data collection- July 2022
9. Enrollment 80% complete- July 2022
10. Quarterly report 8 (April-June, Technical and Business Reports)- July 2022
11. Enrollment 100% Completed- October 2022
12. Data Analysis Begins- October 2022
13. Quarterly report 9 (July-September, Technical and Business Reports)- October 2022
14. Primary Data Analysis Complete- December 2022

Present a brief statement of plans or milestones planned for the next year. If any of the plans deviate from the original approved SOW (e.g., new or modified tasks, objectives, experiments, etc), they will require review by the Sponsor Officer Technical Representative (SOTR) and final approval by USAMRAA Contracting through an award modification prior to initiating any changes. A change request must be submitted to MTEC.

3. Problems / Issues

Any change that is substantially different from the original approved SOW (e.g., new or modified tasks, objectives, experiments, etc.) will require review by the Sponsor Officer Technical Representative and final approval by USAMRAA Contracting through an award modification prior to initiating any changes. A change request must be submitted to MTEC.

a. Current Problems / Issues

Low enrollment numbers at the current sites that have launched. We are on track for ~1000 patients study wide which will still provide an adequate power to assess our primary endpoint at a reasonable effect size. *Please note:* enrollment milestones are time and institution-based and not specifically based on a previously estimated sample size. Data analysists are working on a recalculation of power for different enrollment numbers.

b. Anticipated Problems / Issues

Nothing to Report

Provide a description of anticipated problems or issues that have a potential to impede performance or progress. Also provide course of actions planned to mitigate problems or to take should the problem materialize.

4. Financial Health

The trial has remained financially stable throughout the last year and cumulatively for the completion as proposed by the period of performance.

Comment on the financial health of the study. Was the study financially on track during this year and cumulatively for completion as proposed within the period of performance? If not, describe the cause(s), whether this will have a short-term or long- term impact, the likelihood this can be overcome, and provide

remediation strategy. Provide amount expended this quarter and cumulatively. State if there was any major equipment procured, sub-award implemented, and/or travel conducted.

5. Personnel Effort

Provide names of current staff along with their roles and percent effort of each on this project. Add additional rows if necessary to list the complete team. If there is more than one project on this award, breakdown according to each project (one table per project).

Personnel	Role	Percent Effort
Adit Ginde, MD, MPH	Principal Investigator	5.711%
Vikhyat Bebarta, MD	Co- Investigator	0.735%
Arek Wiktor, MD	Co-Investigator	0.815%
Erin Anderson, RN	Project Manager	25.55%
John Rice, PhD	Data Analyst	8.781%
Conner Jackson, MS, MPH	Biostatistician	25%
Jessica Cwik	Research Coordinator	25%
Aimee Steinwand	Research Coordinator	29.8%

6. Protocol and Activity Status

For awards involving the use of human subjects, use of human cadavers, and/or use of animal subjects, prepare a summary in accordance with the following subsections. For all other awards, including those involving the use of human anatomical substances (such as tissue or cells or identifiable private information), mark as directed below.

a. Human Use Regulatory Protocols

TOTAL PROTOCOLS: State the total number of human use protocols required to complete this project (e.g., 5 human subject research protocols will be required to complete the Statement of Work."). If not applicable, write "No human subjects research will be performed to complete the Statement of Work."

PROTOCOLS: List all human use protocols to be performed to complete the project, an include approved target number for clinical significance, followed by type of submission and type of approval with associated dates, and performance status for each.

Protocol [HRPO Assigned Number]: E01218.1a
Title: Strategy to Avoid Excessive Oxygen (SAVE-O2) in Major Burn Patients
Target required for clinical significance: 2000
Target approved for clinical significance: 6000
Submitted to and Approved by:

- Protocol Development: 01-NOV-2019-27-FEB-2020
- Submitted to Colorado Multiple Institutional Review Board (COMIRB): 06-MAR-2020
- Approved by COMIRB: 13-MAR-2020
- Initial Review Received HRPO: 05-MAY-2020
- Amendment with HRPO recommendations Approved by COMIRB: 24-JUL-2020

- Approved by HRPO: 10-SEP-2020
- Continuing Review Submitted to COMIRB: 27-JAN-2021
- Continuing Review Approved by COMIRB: 09-FEB-2021
- Enrollment Number Amendment Submitted to COMIRB: 10-MAR-2021
- Enrollment Number Amendment Approved by COMIRB: 16-MAR-2021
  - This amendment accounts for accessing every patient's chart that is admitted to the burn ICU, which will exceed 1,000 charts per site. This enrollment change does not affect analysis. HRPO did not review the amendment, they determined this a non-significant event that didn't require review (see attached email).
- COMIRB Protocol Amendment Version 1.1 Dated 20-AUG-2021: *pending approval*
- HRPO Protocol Amendment Version 1.1 Dated 20-AUG-2021: *pending approval*

Provide bullet point list of protocol development, submission, amendments, and approvals (include IRB in addition to HRPO).

STATUS:

Three of the six sites have been launched into the intervention phase. Current enrollment is listed below:

Trial Enrollment	N	Pre-Intervention	Post-Intervention
Total Enrollment	103	42	61
AISR	95	34	61
Cincinnati	Pending		
UCD	8	8	-

Sites still in pre-intervention phase and launch dates:

- Vanderbilt University Medical Center – January 15th 2022
- University of Alabama Birmingham – April 15th 2022
- University of Pittsburgh Medical Center – July 15th 2022

**Low enrollment numbers at the current sites that have launched. We are on track for ~1000 patients study wide which will still provide an adequate power to assess our primary endpoint at a reasonable effect size. *Please note:* enrollment milestones are time and institution-based and not specifically based on a previously estimated sample size. Data analysists are working on a recalculation of power for different enrollment numbers.

b. Use of Human Cadavers for RDT&E, Education or Training

N/A

"Cadaver" is defined as a deceased person or portion thereof, and is synonymous with the terms "human cadaver" and "post-mortem human subject" or "PMHS." The term includes organs, tissue, eyes, bones, arteries or other specimens obtained from an individual upon or after death. The term "cadaver" does not include portions of an individual person, such as organs, tissue or blood, that were removed while the individual was alive (for example, if a living person donated tissue for use in

future research protocols, that tissue is not considered a "cadaver" under this policy, regardless of whether the donor is living or deceased at the time of tissue use).

TOTAL ACTIVITIES: State the total number of RDT&E, education or training activities that will involve cadavers. If not applicable, write "No RDT&E, education or training activities involving human cadavers will be performed to complete the Statement of Work (SOW)."

ACTIVITIES: Provide the following information in a bulleted list for all RDT&E, education or training activities involving human cadavers conducted or supported during the quarter:

- Title of the RDT&E, education or training activity
- SOW task/aim associated with the activity
- Date the activity was conducted
- Identification of the organization's responsible individual (e.g., PI or individual primarily responsible for the activity's conduct)
- Brief description of the use(s) of cadavers in the activity and the total number of cadavers used during the reporting period
- Brief description of the Department of Army organization's involvement in the activity
- Status of document submission and approvals
- Problems encountered in the procurement, inventory, use, storage, transfer, transportation and disposition of cadavers used for RDT&E, education or training. Examples of problems include but are not limited to: loss of confidentiality of cadaveric donors, breach of security, significant deviation from the approved protocol, failure to comply with state laws and/or institutional
  policies and public relations issues.

c. Animal Use Regulatory Protocols

N/A

TOTAL PROTOCOLS: State the total number of animal use protocols required to complete this project (e.g., 2 animal use research protocols will be required to complete the Statement of Work.). If not applicable, write "No animal use research will be performed to complete the Statement of Work."

PROTOCOLS: List all animal use protocols to be performed to complete the project, include approved target number for statistical significance, followed by type of submission and type of approval with associated dates, and performance status for each.

Protocol [ACURO Assigned Number]:
Title:
Target required for statistical significance:
Target approved for statistical significance:
Submitted to and Approved by:
Provide bullet point list of protocol development, submission, amendments, and approvals (include IACUC in addition to ACURO).

STATUS: Provide bullet point list of performance and/or progress status relating to the above protocol and discuss any administrative, technical, or logistical issues that may impact performance

or progress of the study (e.g. animal use protocol need revision to minimize animal suffering, animal protocol modification to include additional staff) for the above ACURO approved protocol.

Annual Business Status Report for

Multicenter Implementation Trial ofTargeted Normoxia Strategy to Define Oxygen Requirements for Major Burn Patients: An Approach to Reduce Warfighter Morbidity, Deployed Logistical Burden of Oxygen, and Readiness Costs

Research Project No. 2019-632-001
EGS# MT19008.43
Reporting Period: January 30, 2021- December 31, 2021

MTEC Research Project Awardee

University of Colorado

Principal Investigator: Adit Ginde, MD, MPH

Project Manager: Erin Anderson, RN

Data Analyst: John Rice, PhD Biostatistics

Research Project Technical POC: Erin Anderson, RN

13001 E. 17th Place

Aurora, CO, 80045

Phone: 720-999-8760

Email: erin.l.anderson@cuanschutz.edu

1. CURRENT STAFF

Personnel	Role	Percent Effort
Adit Ginde, MD, MPH	Principal Investigator	5.711%
Vikhyat Bebarta, MD	Co- Investigator	0.735%
Arek Wiktor, MD	Co-Investigator	0.815%
Erin Anderson, RN	Project Manager	25.55%
John Rice, PhD	Data Analyst	8.781%
Conner Jackson, MS, MPH	Biostatistician	25%
Jessica Cwik	Research Coordinator	25%
Aimee Steinwand	Research Coordinator	29.8%

2. CURRENT EXPENDITURES

DIRECTIONS: FILL OUT TABLE A OR B DEPENDING ON CONTRACT TYPE. TABLE A IS FOR COST REIMBURSBALE CONTRACTS AND TABLE B IS FOR FIX PRICED CONTRACTS.

A. Cost Reimbursable Contracts: Complete only if your contract is Cost Reimbursable or Cost Plus Fixed Fee.

Expenditures should be reflective of cost incurred to date, not exceeding awarded project ceiling. Expenditures should coincide with the latest invoice for the reporting period. For cost reimbursable contracts please use the table below.

Contract Expenditures	Current Annual Expenditures	*Cumulative To Date Expenditures*
Labor (Personnel and Fringe)	$ 146,950.21	$ 318,270.10
Supplies/Materials	$ 0.00	$196.00
Travel	$ 2,126.89	$ 2,126.89
Equipment	$	$
Subcontractors and Consultants	$ 109,534.81	$ 142,528.81
Other Direct Costs	$ 5,019.47	$ 32,818.08
Indirect Costs	$ 105,979.18	$ 234,910.45
Total	$ 369,610.56	$ 730,850.33

B. Fixed Priced Contracts: Complete only if your contract is Fixed Priced.

Expenditures should be reflective of milestones that are 100% complete and invoiced for. Milestones reported below should correspond to the Milestone Payment Schedule in the Project Award. **Milestones can only be invoiced for if they are 100% Complete**. Expenditures should coincide

with the latest invoice for the reporting period. For fixed priced contracts please use the table below.

MTEC Milestone Number	Milestone Description	Due Date	Government Funds
1		1/15/20	$1.00
2		2/15/20	$1.00
	Total Expenditures		$2.00 (Should reflect what has been invoiced for)

C. Cost Share Contributions: Complete only if you're reporting Cost Share:

Cost sharing includes any costs a reasonable person would incur to carry out (necessary to) proposed projects' statements of work not directly paid for by the Government. There are two types of cost sharing: **(1) Cash**: Outlays of funds to perform the proposed project. Cash includes labor, materials, new equipment, and relevant subcontractor efforts. Sources include new IR&D funds, profit or fee from another contract, overhead or capital equipment expense pool. **(2) In-Kind:** Reasonable value of in-place equipment, materials or other property used in performance of the proposed project. All cash or in-kind cost sharing availability must be clearly and convincingly demonstrated by the Offeror. The Offeror will be required to provide financial reporting with appropriate visibility into expenditures of Government funds vs. private funds.

Funding Source (Cash)	This Period	Cumulative to Date
Cash	$0.00	$0.00
Labor Dollars	$0.00	$0.00
Indirect Labor Rates (Overhead/Fringe Benefits)	$0.00	$0.00
Travel	$0.00	$0.00
General & Administrative Services	$0.00	$0.00
Equipment (New)	$0.00	$0.00
Material	$0.00	$0.00
Other Direct Costs	$0.00	$0.00
Other *	$0.00	$0.00
Sub-Total	$0.00	$0.00
Funding Source (In-Kind)	**This Period**	**Cumulative to Date**
Use of Existing Equipment (Estimated fair market value)	$0.00	$0.00
Use of Existing Software (Estimated fair market value)	$0.00	$0.00
Intellectual Property (Estimated fair market Value)	$0.00	$0.00

Space (Land or buildings)	$0.00	$0.00
Sub-Total	$0.00	$0.00
Cost Share Total	$0.00	$0.00

3. STATUS OF MILESTONES – FILL OUT FOR ALL CONTRACT TYPES (all project milestones are to be included)

All project milestones from the Milestone Payment Schedule, in the project award, should be accounted for below.

MTEC Milestone Payment Schedule					
MTEC Milestone Number	**Task Number**	**Significant Event/ Accomplishments**	**Due Date**	**Annual % Complete**	**Cumulative % Complete**
1	N/A	Project Kickoff	1/31/2020	N/A	100%
2	N/A	Quarterly Report 1 (January - March, Technical and Business Reports)	4/25/2020	N/A	100%
3	1	Local IRB Approval	5/31/2020	100%	100%
4	2	Data Collections Instruments Developed	5/31/2020	100%	100%
5	N/A	Quarterly Report 2 (April - June, Technical and Business Reports)	7/25/2020	N/A	N/A
6	3	HRPO Approval	7/31/2020	100%	100%
7	4	Site Implementation Materials Developed	7/31/2020	100%	100%
8	5	Data Collection Infrastructure Developed	12/31/2020	100%	100%
9	6	Site Initiation Visit #1	3/15/2021	100%	100%
10	7	Site Implementation/Data Collection Begins	4/15/2021	100%	100%
11	N/A	Quarterly Report 3 (July - September, Technical and Business Reports)	10/25/2020	N/A	N/A
12	8	Site Initiation Visit #2	6/15/2021	100%	100%
13	N/A	Annual Report 1	1/25/2021	N/A	N/A
14	9	Enrollment 20% Complete	9/15/2021	100%	100%
15	N/A	Quarterly Report 4 (January - March, Technical and Business Reports)	4/25/2021	N/A	N/A
16	10	Site Initiation Visit #3	9/15/2021	100%	100%
17	N/A	Quarterly Report 5 (April - June, Technical and Business Reports)	7/25/2021	N/A	N/A
18	11	Enrollment 40% Complete	12/15/2021	100%	100%
19	12	Site Initiation Visit #4	12/15/2021	0%	0%
20	N/A	Quarterly Report 6 (July - September, Technical and Business Reports)	10/25/2021	N/A	N/A
21	13	Site Initiation Visit #5	3/15/2022	0%	0%

22	14	Enrollment 60% Complete	3/15/2022	0%	0%
23	N/A	Annual Report 2	1/25/2022	N/A	N/A
24	N/A	Quarterly Report 7 (January - March, Technical and Business Reports)	4/25/2022	N/A	N/A
25	15	Site Initiation Visit #6	7/15/2022	0%	0%
26	16	Enrollment 80% Complete	7/15/2022	0%	0%
27	N/A	Quarterly Report 8 (April - June, Technical and Business Reports)	7/25/2022	N/A	N/A
28	17	Enrollment 100% Complete	10/15/2022	0%	0%
29	18	Data Analysis Begins	10/15/2022	0%	0%
30	N/A	Quarterly Report 9 (July - September, Technical and Business Reports)	10/25/2022	N/A	N/A
31	19	Primary Data Analysis Complete	12/15/2022	0%	0%
32	N/A	Final Report (Prior to the POP End)	1/31/2023	N/A	N/A
			Total		40%

Please name this annual report file as EGS#_Annual Report_Y# (For example MT160001.01_Annual Report_Y2)
Please submit as a PDF file.
Please make sure to fill in the page number on page 3 Table of Contents.
Don't forget to submit an updated Quad Chart as well. Please name the Quad chart file as EGS#_Quad Chart_Y#.

Multicenter Implementation Trial of Targeted Normoxia Strategy to Inform Oxygen Requirements for Combat Casualty Care in Major Burn Patients

PI: Adit Ginde, MD, MPH
Organization: University of Colorado Denver
Co-PI: MAJ Steven Schauer, DO
Organization: Army Institute of Surgical Research

Award Amount: 2,492,920

Objectives

Our **overall objective** is to determine oxygen titration goals for combat injured to optimize care by reducing harm associated with hypoxia and hyperoxia and to conserve limited oxygen supply

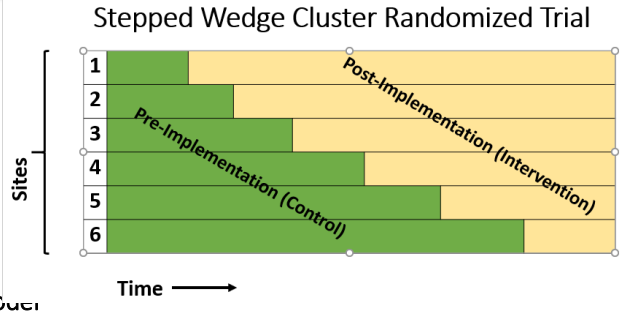
Aim 1. Measure the impact of targeted normoxia implementation on oxygen requirements in critically injured patients

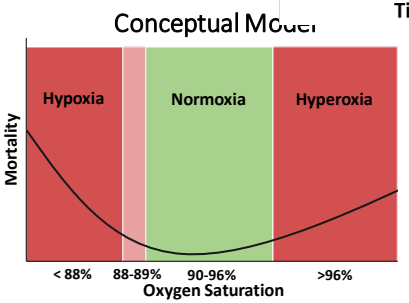
Aim 2. Determine the safety of targeted normoxia

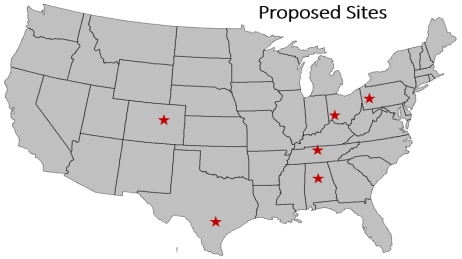
Aim 3. Determine the clinical effectiveness of targeted normoxia

Approach

Multicenter cluster randomized, stepped wedge implementation trial of the targeted normoxia approach (SpO2 90-96%). Efficiency will be greatly enhanced by a waiver of informed consent since protocol implementation is minimal risk (EFIC not required).







Timeline and Cost

Activities	Year 1	Year 2	Year 3
Preparatory Work			
Implementation			
Data Collection			
Analysis/Dissemination			
Estimated Budget ($K)	$1289	$1389	$1125

Updated: January 26, 2022

Goals/Milestones

Major Task 1: Preparatory Work
- ☒ Local IRB Reliance
- ☒ Finalize Protocol
- ☒ Central IRB Approval
- ☒ HRPO Approval
- ☒ Develop Data Collection Instruments
- ☒ Develop Site Implementation materials
- ☒ Develop Data Collection Infrastructure
- ☐ Site Initiation Visits/Training- ***50% complete***

Major Task 2: Implementation
- ☐ Randomized Implementation- ***50% complete***
- ☐ Site Monitoring- ***50% complete***
- ☐ Site Maintenance/Retraining- ***50% complete***

Major Task 3: Data Collection/Data Analysis
- ☐ Data Collection- ***50% complete***
- ☐ Data Analysis- ***50% complete (no interim analysis will occur)***
- ☐ Dissemination of Results
- ☐ Report Findings

Strategy to Avoid Excessive Oxygen (SAVE-O2) in Major Burn Patients: A Multicenter Cluster Randomized, Stepped Wedge Trial for Targeted Normoxia

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Word: 297/300 (includes disclaimer)

Background: Hyperoxia and hypoxia increase mortality in critically injured patients and may impact burn wound healing. Our objective is to determine the safety and effectiveness of targeting normoxia (pulse oximetry (SpO_2) of 90-96%) to conserve oxygen and improve clinical outcomes in major burn patients.

Methods: This multicenter cluster randomized, stepped wedge implementation trial will determine the effectiveness of a multimodal intervention to target normoxia in major burn patients (NCT04534972). Six hospitals are randomized to cross over from pre-implementation ("usual care") to post-implementation ("intervention") phases at three-month intervals. Starting with a one-month intervention run-in phase, we use a multimodal intervention tailored to individual sites to target normoxia and down-titrate supplemental oxygen in hyperoxic patients (SpO_2>96%). The primary outcome is supplemental-oxygen-free days.

Results: As of October 2021, the first site has undergone cross-over to the post-implementation phase and provides data from pre-implementation with 34 patients (4,141 patient-hours) and 46 patients (5,713 patient-hours) post-implementation. Pre-implementation, 60 (1.5%) patient-hours were spent in hypoxia (SpO2<88%), 1,107 (26.7%) patient-hours in normoxia, and 2,956 (71.4%) patient-hours in hyperoxia. In the post-implementation phase, 25 (0.4%) patient-hours were spent in hypoxia, 1,998 (35.0%) patient-hours in normoxia, and 3,670 (64.2%) patient-hours in hyperoxia.

Conclusions: Preliminary data from the SAVE-O2 Burn trial suggests a multimodal intervention to target normoxia in major burn patients can increase the proportion of patient-time spent in normoxia without increasing hypoxia. This has important implications for reduced supplemental oxygen use in the combat setting, including in remote and prolonged field care settings.

Acknowledgement: This effort was funded under MTEC solicitation MTEC-19-08-MuLTI and is funded by the USAMRDC under the Department of Defense. The views and conclusions contained herein are those of the authors and should not be interpreted as necessarily representing the official policies or endorsements, either expressed or implied, of the U.S. Government.