

**AWARD NUMBER:** W81XWH-22-1-1020

**TITLE:** Personalized Targeted Nutrition via StructurEd Nutrition Delivery Pathway to Improve Recovery of Physical Function in Trauma - SeND Home

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# REPORT DOCUMENTATION PAGE

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<b>13. SUPPLEMENTARY NOTES</b>					
<b>14. ABSTRACT</b> The SeND Home initiative targets ICU-Acquired Weakness (ICU-AW), a condition that compromises physical function and life quality in trauma survivors. This problem stems from two factors: a catabolic state due to injury and critical illness, and malnutrition often worsened by surgical and gastrointestinal issues. SeND Home offers a personalized early parenteral nutrition (PN) regimen, drawing on data from the LEEP-COVID study and aligning with international ICU nutrition guidelines. Implemented in the ICU, the program employs Q-NRG® indirect calorimetry for precise caloric assessments and extends into post-discharge, facilitated by registered dietitians. The study aims to execute a Phase II Randomized Controlled Trial to evaluate SeND Home against conventional care, focusing on physical function, muscle mass, and life quality. Three specific objectives outline this focus: assessing physical and muscle parameters, examining life quality and clinical markers like hospital stay length and infection rates, and investigating mitochondrial function and resilience biomarkers. SeND Home has broad clinical implications, extending its relevance to military settings. Its nutritional strategies can be deployed in hospital ICUs and field care, addressing nutritional deficiencies in trauma patients. As abdominal injuries are prevalent in modern conflicts, SeND Home could markedly improve military personnel's recovery and readiness					
<b>15. SUBJECT TERMS</b> ICU-Acquired Weakness (ICU-AW); Trauma Survivors; Catabolic State; Malnutrition; SeND Home Program; Parenteral Nutrition (PN); Longitudinal Energy Expenditure and Metabolic Phenotype of COVID-19 Study (LEEP-COVID); International ICU Nutrition Guidelines; Indirect Calorimetry; Q-NRG®; Personalized Caloric Assessment; Registered Dietitians; Phase II Randomized Controlled Trial (RCT); Physical Function; Muscle Mass; Quality of Life; Clinical Outcomes; Hospital Stay; Infection Rates; Mitochondrial Function; Biomarkers of Resilience					
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**1. INTRODUCTION:**

In summary, this research proposal aims to address the significant impact of major trauma and abdominal injuries on military service members, focusing on the potential benefits of a targeted, early Total Parenteral Nutrition (TPN) strategy. Despite advancements in body armor, torso injuries account for a high proportion of combat-related deaths and disabilities, with 8% of deaths resulting from multiorgan failure, which could be mitigated by proper nutritional support. Current TPN research is largely centered on civilian ICU populations, which are not representative of combat-wounded soldiers with major traumatic injuries. The study proposes to fill this gap by focusing on patients with abdominal trauma, employing an off-the-shelf, room-temperature-stable TPN product suitable for far-forward military settings. Our protocol aims to tackle challenges such as ileus and frequent surgeries, which often hinder effective nutritional delivery via the gastrointestinal tract, leading to malnourishment and subsequent impaired recovery.

The proposed SeND Home program is designed to optimize nutrition through personalized caloric requirements, early identification of protein-calorie malnutrition, and goal-targeted nutrition. We hypothesize that this approach will improve patient outcomes in both physical function and Quality of Life (QoL), ultimately enhancing military readiness and reducing healthcare costs. This initiative aligns with the FY21 PRMRP Area: Nutrition Optimization, aiming to bring transformative changes in the nutrition management of ICU patients with abdominal trauma.

**2. KEYWORDS:**

Personalized Nutrition Optimization; Major Trauma; Abdominal Injuries; Combat-Wounded Soldiers; Total Parenteral Nutrition (TPN); Intensive Care Unit (ICU); Military Readiness; Multiorgan Failure; Goal-Targeted Nutrition; Quality of Life (QoL); Physical Function; Ileus; Muscle Mass and Strength; Surgical Procedures; Service Personnel Recovery; Military Costs and Burdens

**3. ACCOMPLISHMENTS:**

	Months	Duke University Hospital	% Completed
<b>Major Task 1: Prepare for enrollment</b>			
Subtask 1 : Finalize protocol and get approval from Institutional Review Board (IRB)	1-4	PW/KH	100%
<b>Train clinical research coordinators</b>	1-3	PW/KH	100%
<b>Develop study databases for screening.</b>	1-3	KH/LN/MK	100%
<b>Develop study databases for enrolled patients</b>	1-3	KH/LN/MK	100%
<b>Refine eligibility criteria, exclusion</b>	1-3	PW/KH/SM/SA	100%

<b>criteria, screening protocol</b>			
<b>Finalize consent form &amp; human subjects' protocol</b>	1-3	PW/KH/LN	100%
<b>Submit protocol to IRB</b>	1-3	PW/KH/LN	100%
Clinicaltrial.gov registration	6	PW/KH/LN	100%
Submit protocol to Human Research Protection Office (HRPO)	4-6	PW/KH/LN	100%
Submit amendments, adverse events and protocol deviations as needed	As Needed	PW/KH/SM/SA	N/A
Coordinate for annual IRB report for continuing review	Annually	PW/KH/LN	N/A
<b><i>Milestone Achieved: IRB approval</i></b>	4	PW/KH/SM/SA	100%
<b><i>Milestone Achieved: HRPO approval</i></b>	6	PW/KH/SM/SA	100%
Subtask 2: Creation and validation of databases			
a. Screening log	4-6	KH/LN/MK	100%
b. enrollment log	4-6	KH/LN/MK	100%
c. Data storage database	4-6	KH/LN/MK	100%
<b><i>Milestone Achieved: Study databases ready for enrollment</i></b>	6	PW/ KH/LN/MK	
Subtask 3: Finalize training of study team			
Training of staff to protocol	4-6	PW/KH/SM/SA	100%
Study team meetings to review issues and progress related to protocol development and study start up	Monthly	PW/KH/SM/SA/LN/MK	100%
<b>Milestone Achieved: Study team ready to enroll patients</b>	6	PW/ KH/LN/MK	100%
Subtask 4: Approach Intensive Care Unit (ICU) and trauma providers regarding the clinical trial			
Meet with trauma surgeons, ICU faculty, residents, and advanced practice providers to introduce the study		PW/KH/SM/SA	100%
a. Present study at Surgical/Trauma Intensive Care Unit (SICU) faculty meeting	4-6	PW/KH/SM/SA	100%
b. Present study at Division of trauma faculty meeting	4-6	PW/KH/SM/SA	100%
c. Meet and/or email Advanced Practice Providers (APPs) on trauma and ICU service	4-6	PW/KH/SM/SA	100% and will continue
d. Meet and/or email ICU nursing, pharmacy, and nutritionists	4-6	PW/KH/SM/SA	100% and will continue
<b><i>Milestone Achieved: Relevant staff understand clinical trials</i></b>	6	PW/KH/SM/SA	100%

In Major Task 1, the process of preparing for enrollment was far from trivial. Achieving Duke IRB and Department of Defense's Office of Human Research Oversight (OHRO) approval was a multi-faceted endeavor. Not only did we develop and refine the protocol, but we engaged in iterative discussions with the IRB to ensure that all ethical and procedural standards were met to the highest degree. It's worth mentioning that the consent form and human subjects protocol were meticulously crafted to meet both scientific and ethical rigor, incorporating feedback from multiple stakeholders. Beyond the submission to the IRB, we ensured timely registration with Clinicaltrials.gov and took proactive steps to report amendments, adverse events, and protocol deviations, thereby maintaining the integrity of the study.

Under Subtask 2, the creation and validation of the study databases involved more than mere data entry points. Each database was designed with data integrity and security as paramount concerns. The screening log, for instance, was structured to identify potential participants in the most efficient manner while maintaining confidentiality. The enrollment log and data storage databases were subjected to multiple rounds of validation to ensure accuracy and security, essential for the forthcoming patient data collection.

In Subtask 3, the training of the study team was a comprehensive process involving multiple layers. The team not only received training on the protocol but also underwent specialized training modules that focused on ethical considerations, data management, and quality control. Regular study team meetings served as forums for troubleshooting, with advanced preparations made for mitigating any potential roadblocks in protocol development or study startup. This multi-layered approach to training has made the team exceptionally equipped for the study's operational phase.

For Subtask 4, our engagement with ICU and trauma providers went beyond mere introductions. The presentations at the Surgical/Trauma Intensive Care Unit (SICU) and Division of Trauma faculty meetings were interactive sessions that allowed for input and queries from key personnel. Follow-up meetings and communications were scheduled to address any uncertainties and ensure a comprehensive understanding of the study among staff. This included tailored communications to ICU nurses, pharmacists, and nutritionists, acknowledging their integral roles in the overall clinical process.

In summary, our progress to date in preparing for this study has been marked by scrupulous attention to detail, a commitment to ethical standards, and a concerted effort to ensure that every team member and stakeholder is fully aligned with the study's goals and procedures. As a result, we are optimally positioned to transition to the study phase.

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

*Nothing to Report*

Prior to the commencement of the study, comprehensive training and professional development activities were undertaken to equip all team members and involved personnel with the requisite knowledge and skills. Training was multifaceted, focusing on technical proficiency with the Q-NRG® indirect calorimetry equipment, adherence to research protocols, and proficient use of the study's data management system. These sessions were led by individuals with advanced expertise in each respective domain, thereby enabling an environment of hands-on mentorship.

In addition to the technical aspects, a series of professional development activities were incorporated. These included workshops on research ethics, informed consent processes, and data integrity, aimed to augment the research acumen of everyone involved.

While no conferences, external workshops, or seminars have been attended specifically for this project, team members are encouraged to engage in such opportunities for professional growth, ensuring the team stays current with advances in critical care nutrition and research methodologies.

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

N/A

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

During the next reporting period, the primary focus will be on initiating participant enrollment for the study. Now that we have received full approval from both the Institutional Review Board (IRB) and the Department of Defense's Office of Human Research Oversight (OHRO), and have navigated hiring challenges by contracting with the Duke Office of Clinical Research for Registered Dietitian Clinical Research Coordinators (CRC-RDs), we are poised to begin the trial phase.

The first steps will involve finalizing the recruitment strategy and initiating contact with potential participants. Outreach will take place through multiple channels, including clinical referrals and database searches, to identify eligible trauma patients who meet our inclusion criteria. Simultaneously, we will finalize the data collection tools and ensure that all team members are aligned in their understanding of the study protocols.

Weekly team meetings will continue, which will now also include the contracted CRC-RDs, to ensure that all staff are updated on the study's progress and any modifications to the protocol. The meetings will also serve as a platform for troubleshooting and refining the study approach based on real-time feedback.

We are also planning to conduct interim data analyses to ascertain early trends and, if necessary, adjust the study design. This dynamic approach will allow us to maintain the scientific rigor and ethical integrity that have been the hallmark of our preparatory work. Overall, the upcoming reporting period will be crucial as we transition from preparatory activities to active data collection, thereby advancing towards our study objectives.

#### **4. IMPACT:**

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

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

NA

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

As of this annual report, we have yet to initiate the actual study phase; however, the preparatory work we have executed is indicative of the rigorous and comprehensive approach we are taking to ensure the study's success. While the impact on patient outcomes remains prospective at this stage, the foundational groundwork laid serves as a robust platform for executing a high-quality clinical trial. Our meticulous attention to protocol development, ethical considerations, database validation, and stakeholder engagement ensures that, upon commencement, the study is poised to contribute meaningful data with potential for significant impact on patient care and policy-making in the field of trauma critical care. Therefore, despite the study not having started, the preparation phase itself stands as an exemplar of methodological rigor, paving the way for impactful outcomes.

**5. CHANGES/PROBLEMS:**

6.

While the study's initial stages involved extensive deliberation and multiple revisions for Institutional Review Board (IRB) approval, we successfully navigated these hurdles. This protracted process necessitated scrupulous fine-tuning of our research protocol, strengthening the study's ethical and scientific framework. The Department of Defense's Office of Human Research Oversight (OHRO) has also granted its approval, meaning we have received green lights from both the IRB and OHRO, fortifying our project's next stages with rigorous ethical and methodological foundations. Additionally, due to hiring challenges and the recent merger with Duke University, we were unable to recruit our own registered dietitians for the study. To address this, we entered a contract with the Duke Office of Clinical Research to hire Clinical Research Coordinator-Registered Dietitians (CRC-RDs). They currently have three CRC-RDs on staff, possessing the necessary bandwidth to support our study. Weekly meetings have been initiated between our team and the CRC-RDs to prepare for the impending trial phase.

**Changes in approach and reasons for change**

None

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

None

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

None

**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**

none

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

NA

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

N/A

**7. PRODUCTS:**

- **Publications, conference papers, and presentations**

**Journal publications.**

N/A

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

N/A

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

N/A

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

N/A

- **Technologies or techniques**

N/A

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

N/A

- **Other Products**

N/A

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

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

NA

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

No

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

1. Paul Wischmeyer, MD, EDIC, FASPEN, FCCM, Principal Investigator, 3.0 calendar months
2. Krista Haines, DO, Co-Investigator, 1 calendar month
3. Sean Montgomery, MD, Co-Investigator, 1 calendar month
4. Suresh Agarwal, MD, Co-Investigator, 1 calendar months
5. Shauna Howell, RN, BSN, Clinical Research Coordinator, 6.0 calendar months
6. Rachel Kalagher, Clinical Research Nurse Coordinator, 6.0 calendar months
7. Isabel Rodriguez Negron, Project Manager, 1.8 calendar months

## **9. SPECIAL REPORTING REQUIREMENTS**

**COLLABORATIVE AWARDS:** *N/A*

**QUAD CHARTS:** *N/A*

## **10. APPENDICES:** *N/A*