A PILOT FEASIBILITY STUDY COMPARING A NOVEL PHOTOTHERAPY KIOSK TO SUPPLEMENTATION TO PROMOTE VITAMIN D SUFFICIENCY

PROTOCOL # 217121

NCT04556136

27 JUNE 2017

MADIGAN
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Title Page

Study Title: A Pilot Feasibility Study Comparing a Novel Phototherapy Kiosk to Supplementation to Promote Vitamin D Sufficiency

Name of Product Tested: Solius, Photobiologic therapy kiosk

Indication Studied: Maintenance or repletion of serum 25(OH)D status

Study Description: This pilot feasibility study was designed to provide validation of the isolation of narrow spectrum ultraviolet B (UVB) rays delivered in a standing kiosk. A measured dose was administered under conditions of full body exposure every other week for 10 weeks. The stimulation of cutaneous vitamin D and subsequent 25(OH)D production from phototherapy was compared to the effect of an IOM determined RDA dose of 600 IU vitamin D3 supplement daily for 10 weeks. The primary outcome was serum 25(OH)D level.

Sponsor: BeneSol, Inc. dba SOLIUS

Protocol: Non-inferiority, feasibility, randomized, controlled trial with Institutional Review Board approval as a minimal risk human use protocol.

Phase of Development: Premarket

Study Initiation Date: 21 August 2017

Study Completion Date: 11 March 2019

Name of principal or coordinating investigator: Mary S. McCarthy, PhD, RN. Madigan Army Medical Center

DCP Statement: This study was performed in compliance with ICH Good Clinical Practice (GCP) including the archiving of essential documents.

1 List of Abbreviations & Definition of Terms

AD	Active duty
BIA	Bioelectrical impedance analysis
BMI	Body mass index
BMR	Basal metabolic rate
CAP	College of American Pathologists
CG	Comparison group
DXA	Dual energy xray absorptiometry
FST	Fitzpatrick skin type
IQR	Interquartile range
IRB	Institutional Review Board
JBLM	Joint Base Lewis-McChord
MAMC	Madigan Army Medical Center
MCAR	Missing completely at random
Mdn(mdn)	Median
Nm	Nanometer
Ng:	Nanogram
SM	Service member
SPK	Standing phototherapy kiosk
TG	Treatment group

2 Ethics and Regulatory Approval

2.1 Institutional Review Board (IRB) or Independent Ethics Committee (IEC) Approval

The study protocol and all its amendments were reviewed and approved by the IRB as detailed in table one below.

IRB Name	Regional Health Command – Pacific Institutional Review Board
Principal Investigator	Mary S. McCarthy, PhD, RN. MAMC
Date of approval of the final protocol	27 June 2017
Date of approval of amendment 1	5 October 2017
Date of approval of amendment 2	9 March 2018
Date of approval of amendment 3	11 May 2018

The study was performed in compliance with FDA 21 CFR 812. Since the product under investigation is low risk, IRB approval is sufficient.

2.2 Ethical Conduct of the Study

The study was performed in accordance with the current version of the declaration of Helsinki (52nd WMA General Assembly, Edinburgh, Scotland, October 2000). The trial was conducted in agreement with the International Conference on Harmonization (ICH) guidelines on Good Clinical Practice (GCP).

2.3 Patient Information and Consent

All patients provided written informed consent to participate in the study prior to being screened. The patient was given a copy of the signed consent form for their personal records. The original copy of the informed consent is kept in document control along with this test report. A sample of the consent form can be found along with the IRB-approved study protocol.

3 Investigators and Study Administrative Structure

The table below shows the principal study personnel involved in the study.

Title	Name and Affiliation
Principal Investigator	Mary S. McCarthy, PhD, RN, FAAN. MAMC
Sponsor	BeneSol, Inc. dba SOLIUS
Project Manager	Evelyn Elshaw, MS, RD, LD. MAMC
Clinical Research Associate(s)	Barbara Szekely, BSN, RN. MAMC
Biostatistician	Thomas A Beltran, MA. (Contractor)

4 Introduction

Low vitamin D status is common in individuals who regularly perform extreme physical exertion, particularly in combination with periods of psychological stress, inadequate nutrition, and sleep disruption.[1] This places military personnel in a high risk category with significant negative consequences to musculoskeletal, immune, and mental health, and thus, resilience. The large scope of this problem demands a multi-phased approach beginning with a self-care, easy access, safe biomedical device intended to stimulate cutaneous production of vitamin D. The pilot, or demonstration phase, involved installment of a standing phototherapy kiosk in an outpatient setting where we enrolled Active Duty (AD) and retired Service Members (SM), adult beneficiaries, and DA civilians to test the acceptability and feasibility of this health promotion concept. We anticipated that the phototherapy kiosk would be an inexpensive, convenient, and effective way to maintain or raise 25(OH)D levels to sustain Warfighter and beneficiary resilience.

Endogenous production of vitamin D comes from sun exposure, however concerns of skin cancer and heat injuries limits recommendations for even a safe level of exposure. The only alternative has been consumption of vitamin D supplements, yet there is a paucity of evidence for how often, how much, and for how long one should consume supplements. Unlike endogenous vitamin D, research shows that supplements do not bind completely to vitamin D binding protein and are not regulated in the body to prevent overdose.[32-35] Fat malabsorption conditions (cystic fibrosis, Crohn's disease, celiac, liver disease, etc.) can reduce the ability to absorb fat soluble vitamin D supplements yet endogenous vitamin D production from UVB light is uninhibited.[2,36-40] UVB radiation with a wavelength of 290-320 nm penetrates the exposed skin and converts cutaneous 7-dehydrocholesterol to pre-vitamin D3, which in turn becomes vitamin D3. Maximal immune system response occurs at a peak of 300 nm and vitamin D3 production at a peak of 298 nm.[3] Sunlight exposure provides 80-100% of the body's vitamin D requirements. Factors that influence UVB exposure and vitamin D synthesis include season, time of day, length of day, cloud cover, smog, skin melanin content, and sunscreen. However, a simple "prescription" for midday sun exposure under a cloudless sky with 90% skin exposure and no sunscreen in a non-urban, minimally polluted environment is a challenge for almost every American, and even more so for Service Members.

The current standard of care is 600 IUs oral vitamin D daily, which is the RDA established by the Institute of Medicine (IOM) who identified clinically significant levels of circulating 25(OH)D to be 20 ng/mL. The RDA for vitamin D represents a daily intake sufficient to maintain bone health and normal calcium

metabolism in 97.5% of the population.[20] While debate surrounds a sufficient range for 25(OH)D, there does seem to be a general acceptance that the optimum range is between 30 – 60 ng/mL.[5-7] The human body uses sunlight as the primary source of vitamin D and produces large quantities efficiently with limited UVB exposure.[12-15] Therefore, a rational way to determine the optimum vitamin D range is by studying natural cutaneous vitamin D synthesis. It has been demonstrated that a single session of full body exposure to solar radiation can produce a time-released equivalent of approximately 10,000 IU of oral vitamin D.[16] A safe upper limit for vitamin D is related to oral intake only. Cutaneous vitamin D production is automatically regulated by a photochemical reaction and pigmentation, preventing toxicity.[17-19] Consequently, hypervitaminosis D is not possible when the only vitamin D source is skin production following exposure to UVB light. For all these reasons, an innovative alternative to address low vitamin D status in adults, Warfighters included, is needed.

5 Study Objectives

The specific aims for this project were:

1. Determine acceptability and feasibility of a standing phototherapy kiosk designed as a self-care intervention for AD and retired service members, beneficiaries, and DA civilians;
2. Demonstrate that narrow spectrum UVB delivered by the SPK is at least equivalent to D3 oral intake to raise or maintain serum 25(OH)D levels over a 10-week intervention period;
3. Examine the relationship of demographic variables, including gender, age, body mass index, body fat, ethnicity, and sun exposure to serum 25(OH)D levels in both groups.

6 Investigational Plan

6.1 Overall Study Design and Plan

This non-inferiority study used a prospective, longitudinal, randomized design with repeated measures to address vitamin D sufficiency in AD, retiree, beneficiary, and DA civilian populations. It is important and necessary to conduct this study with adult humans, military personnel in particular, to determine acceptability and feasibility of this phototherapy kiosk as an addition to existing Warfighter resources to promote health and resilience. Following Madigan Army Medical Center (MAMC) Institutional Review Board Human Subjects and Ethics approval, the SPK will be installed in a location approved by the Radiation Safety Officer, the study team will be hired, and recruitment will begin for an anticipated 12-month project period. Approximately 120 volunteers will be approached from MAMC and Joint Base Lewis-McChord (JBLM), a large joint base in the Pacific Northwest, where over 25,000 Soldiers and Airmen train every day and regional beneficiaries' number ~98,000. Recruiting efforts will attempt to capture a representative sample of the population including both genders, diverse ethnicities, and a range of age (18-70 years) and body mass index (BMI), who have no contraindication for UVB exposure or oral vitamin D supplementation. In addition to walk-in volunteers, the research team will attend the JBLM Newcomer's Orientation. Using a computer-generated block design, volunteers will be randomized to one of two groups by the research pharmacist; 1) oral vitamin D supplementation, or 2) standing phototherapy kiosk with UVB exposure, for a 10-week period.

<u>Comparison Group (CG) – Supplement</u>
A MAMC research pharmacist will dispense a 70-day supply of the vitamin D3 600 IU oral supplement to subjects assigned to this group. The Project Director will work with the pharmacist to coordinate pick-up of supplement bottles for subjects or optimal in-person dispensing times.

Treatment Group (TG) – Phototherapy

The Project Director provides oversight for the phototherapy treatment. The kiosk will deliver the UVB dose under supervised conditions over a 1 – 10 minute interval based on the Fitzpatrick skin type with the subject wearing minimal or no clothing, preferably no more than a bathing suit, and protective eye-wear. The experience in the SPK was designed to be comfortable and user-friendly.

All eligible adult volunteers will be enrolled regardless of their baseline 25(OH)D level as it is important in this non-inferiority study to show there is no potential for harm from phototherapy, even if the baseline 25(OH)D level is above 30 ng/mL. If the goal is to develop a self-care kiosk, individuals will not have the ability to check their serum vitamin D status prior to use. We also want to learn the trajectory of vitamin D absorption and availability over a 3-4-month period in order to make evidence-based therapeutic recommendations. It is not possible to blind the subjects or research team to the group assignment given the two comparators.

Serum levels of 25(OH)D, calcium, and parathyroid hormone are drawn at baseline (T0), immediately following the intervention at 10 weeks (T6); at 14 weeks (T8), 25(OH)D is drawn to document sustainment of treatment effect. Remuneration in the form of $20 Amazon gift cards is provided to all volunteers after the baseline and final scheduled blood draw (as allowed by DoD Instruction 3216.02 Dated November 8, 2011).

A survey shall be completed at T1 and reviewed with participants again at the 10-week visit to capture relevant demographic, medical history, sun exposure, travel, daily activities, and dietary data. Active duty SMs shall report the number of days on profile (activity restriction) for the previous three months, at T1 and T6. A Device Usability Scale will be administered to the kiosk group participants upon protocol completion to address acceptability and feasibility of the treatment. With the assistance of a biostatistician, we will analyze data using repeated measures analysis of variance adjusting for significant covariates such as 25(OH)D level at baseline. Logistic regression analyses are used to predict outcomes and explain the interrelationships among variables, i.e. age, gender, BMI, body fat, ethnicity, and sun exposure relationship to 25(OH)D serum levels.

6.2 Discussion of the Study Design, Including the Choice of Control Groups

The objective of this non-inferiority study is to demonstrate the ability of the phototherapy kiosk to safely administer UVB radiation to participants with sufficient or insufficient levels of 25(OH)D and achieve comparable levels of serum 25(OH)D in a similar population of adults randomized to receive the RDA of 600 IU vitamin D oral supplementation once daily. As an experimental device, it is important to evaluate its equivalence to standard of care in the maintenance of sufficient levels of vitamin D in adults with all skin types between 18 and 69 years of age. In this study the supplement group (CG) was used as an active control.

6.3 Selection of Study Population

Inclusion and exclusion criteria are identical for both groups, supplementation (CG) and phototherapy (TG).

6.3.1 Inclusion Criteria

- Adults, age 18 - 69 years
- Ability to read and understand English
- Subjectively in good health

- Able to stand without assistance for ~10 minutes

6.3.2 Exclusion Criteria

- Any volunteer with relocation, deployment, or release from active duty in the next 4 months
- Pregnant, or currently breastfeeding, females
- Anyone with chronic health problems (e.g. kidney disease, liver disease, intestinal malabsorption)
- Any volunteer currently taking vitamin D supplementation
- Taking medications for an endocrine disorder, such as Synthroid or oral hypoglycemic agents
- Sarcoidosis
- Medications having a high potential for interaction with vitamin D:
  - anti-seizure medications, cyclosporine, indinavir (Crixivan)
- Adults diagnosed with light allergies:
  - Actinic prurigo, Polymorphous light eruption, Solar urticaria
- Adults diagnosed with light sensitivities:
  - Protoporphyria, Photodermatitis, Xeroderma pigmentosum, Lupus erythematosus, Actinic dermatitis, UV-sensitive syndrome

6.3.3 Removal of Patients from Therapy or Assessment

Participants enrolled in the study are free to withdraw at any time without repercussions; the study team requested to be informed in writing of their decision to withdraw.

Volunteers are reminded that the Principal Investigator of the research study may terminate their participation in the research study at any time if she determined this to be in their best interest, if they are unable to comply with the procedures required, or if they no longer meet eligibility criteria.

6.4 Treatments

6.4.1 Treatments Administered

<u>Comparison Group - Supplement</u>
Volunteers assigned to this group are provided with a 10-week supply (70 pills) of a vitamin D3 supplement. Consented participants are instructed to take one 600 IU pill by mouth each day for ten weeks. They are instructed to take this with a meal. This dose is the RDA for adults between 18 and 69 years old according to the Institute of Medicine Committee to Review Dietary Reference Intakes for Vitamin D and Calcium.[20]

<u>Treatment Group - Phototherapy</u>
Volunteers assigned to this group are administered phototherapy treatments once every other week, for 10 weeks. The treatment usually lasts no more than 10 minutes and is based on the Fitzpatrick skin type classification tool[19] which is self-assessed via the computer touch screen in the kiosk.

Table 1. Study Summary

Phase	Initial (T)	Time 1 (T+1wk)	Time 2 (T+3wk) Time 3 (T+5wk) Time 4 (T+7wk) Time 5 (T+9wk) Time 6 (T+11wk)	Time 7 (T+15wk)
Screening	X			
Informed Consent	X			
Submit Blood Tests	X		X (Time 6)	X
Randomization	X			
Demographics and Surveys		X	X (Time 6)	
Inbody		X		
Treatment -Phototherapy (every other week x6)		X	X (Time 6 = Final Exposure)	
Device Usability Scale - Phototherapy			X (Time 6)	
Treatment -Vit D Supplement (daily for 10 weeks)		X	X	

6.4.2 Identity Investigational Product

The Solius phototherapy device (SOLIUSOne, Serial# 00102) is intended for use in the stimulation of endogenous vitamin D. Solius is a freestanding booth designed to deliver a small amount of targeted UVB with an interactive user interface and cloud-based software that enables patient self-care. The treatment delivery mechanism uses a metal halide lamp with a series of filters and a lens to optimize full-body exposure to the narrow spectrum (293 – 303nm) of UVB light most efficient at producing vitamin D3. The device uses software to identify patients, establish individual skin types and determine dosage. The system has been designed to manage exposure time and frequency and deliver 60% of a skin-type-adjusted Minimal Erythemal Dose (MED). The expected result for users is a rise in blood levels of 25(OH)D via the endogenous pathway.[13]

6.4.3 Method of Assigning Patients to Treatment Groups

A computer-generated block design will be created by an onsite biostatistician and used by the research pharmacist to randomize participants. Upon meeting the inclusion criteria, the pharmacist will be notified of the new participant and she will relay the assigned group to the team. The study team will have had no knowledge of the group assignment in advance.

6.4.4 Selection of Doses in the Study

<u>Comparison Group - Oral Supplement Dosing</u>

For this non-inferiority study, the logical choice for a comparison arm was the Recommended Daily Allowance (RDA) of 600 IU vitamin D for adults in the age range of 18-70 years old. The RDA was established by the Institute of Medicine (IOM) who identified clinically significant levels of circulating 25(OH)D (20 ng/mL) and then estimated the amount of dietary vitamin D required to reach this circulating level with minimal sunlight exposure. The RDA for vitamin D represents a daily intake sufficient to maintain bone health and normal calcium metabolism in 97.5% the population.[20]

Treatment Group - Phototherapy Dosing
All patients shall be dosed at 0.6 MED at a distance of 12" from the light source for all treatments. This is consistent with dosing demonstrated to be effective at raising serum 25(OH)D without the risk of adverse events. [26, 27] Treatments shall occur on a 14-day interval (+/- 24 hours), for a total delivery of 6 doses.

To obtain dose, each participant will self-assess their skin type according to the Fitzpatrick skin typing scale using software inside the kiosk. The kiosk will determine the dose per patient, based on their answers. Erythemal response to the previous treatment dose is self-assessed. In the event erythema is self-reported via the kiosk, the participant's dose is reduced by the system for subsequent treatments.

6.4.5 Selection and Timing of Dose for Each Patient

Comparison Group
Each participant assigned to the comparison group will be instructed to take one vitamin D3 pill each day with a meal for 70 days. Participants will also be instructed not to take any additional vitamin D supplementation during the study period. This dosing frequency is consistent with the RDA recommendation.[20]

Treatment Group
Treatments shall occur on a 14-day interval (+/- 24 hours), for a total delivery of 6 doses. Each participant is informed of the need for consistency in the time of day for subsequent phototherapy treatments and every attempt will be made to ensure the participants return 14 days after each treatment for 10 weeks. This dosing frequency is consistent with the minimum recommended for Solius vitamin D therapy previously shown to be adequate in maintaining serum 25(OH)D levels.[26, 27]

6.4.6 Blinding

Due to the nature of the study, it is not possible to blind the subjects or research team to the group assignment.

6.4.7 Prior Concomitant Therapy

Other medications are allowed except those listed in the exclusion criteria (anti-seizure medications, cyclosporine, and idinavir). The research pharmacist will provide expertise for establishing screening criteria to eliminate any potential drug-drug or drug-nutrient interactions. No attempt will be made to control for sun exposure or dietary intake of vitamin D, however, all participants are instructed to refrain from taking any additional supplements containing vitamin D. Volunteers will be asked about vitamin D supplementation during screening and anyone taking a vitamin D supplement in the previous 2 months will not qualify for the study. Both amount of sun exposure and consumption of dietary vitamin D will be captured on surveys. Logistic regression analyses will be used to predict outcomes and explain the interrelationship among the two variables (i.e. sun exposure relationship to 25(OH)D serum levels).

6.4.8 Adherence

Comparison Group
Participants agree to oral administration of 600 IU vitamin D once per day. Participants must agree to abstain from ingesting oral vitamin D supplements. Participants must also have blood drawn at baseline , day 70, and at day 100.

Treatment Group
Participants must be exposed once every other week (14 days +/- 24 hours). Participants must agree to abstain from ingesting oral vitamin D supplements. Participants must also have blood drawn at baseline, day 70, and at day 100.

In this pilot feasibility study, one aim is to evaluate acceptability and adherence.

6.5 Efficacy and Safety Variables

6.5.1 Efficacy and Safety Measurements Assessed

To determine that phototherapy is at least equivalent to D3 oral intake to raise or maintain serum 25(OH)D levels over a 10-week intervention period baseline 25(OH)D levels are obtained. Blood draws will occur upon enrollment with two follow-up measurements, one at 10 weeks and a final level 4 weeks after completing the protocol to evaluate sustainment of the post-treatment level. Serum concentration of 25(OH)D is the best indicator of vitamin D status as it represents cutaneous production and consumption of food and supplements. Serum 25(OH)D has a circulating half-life of 15 days.[28] Serum 25(OH)D levels do not indicate the amount of vitamin D stored in body tissues.[10] All blood levels will be obtained by experienced phlebotomists in the hospital central laboratory. There will be no standardization of time of day for the blood draw. An Endocrine consultant will review all abnormal lab values [(25OH)D, PTH, Calcium] and recommended follow-up with the Primary Care Manager, if necessary.

To determine acceptability and feasibility of the standing phototherapy kiosk, a Device Usability Scale will be administered to the Kiosk Group upon completion of the study. This 12-item Likert-type scale was adapted from the Digital Equipment Corporation “System Usability Scale” (1986). Questions assessed cleanliness, ease of use, and comfort of the kiosk with a Likert-type scale where 1= Strongly disagree to 5 = Strongly agree.

The research team will meticulously track the number of potential participants screened, the number of enrolled subjects, completion of all study timepoints, and attrition from each arm.

To examine the relationship of demographic variables, including gender, age, body mass index, body fat, ethnicity, and sun exposure to serum 25(OH)D levels in both groups, several other measurements will be obtained including the following:

1. Body height (Ht) – Vertical height is measured at baseline using a Harpenden Stadiometer and recorded to the nearest 0.1 cm. The stadiometer is composed of a rigid vertical backboard with an attached rigid horizontal headboard which moves up and down the backboard. Final height was the average of two measurements taken by trained study staff.

2. Body weight (Wt), Body fat (BF)/lean mass (Fat free mass), Basal metabolic rate – weight in pounds, percent fat mass and % lean mass, and metabolic rate at rest. The study team will utilize bioelectrical impedance analysis (BIA) to obtain body composition measures. The InBody 230 lean and fat mass assessment device has been shown to be comparable to the gold standard, Dual-energy X-ray Absorptiometry (DXA). It is maintained in the office suite where the project team is located; all team members are trained in its use.

3. Demographic Questionnaire – Is administered at baseline and will be updated at 10 weeks. This tool was created specifically for the study to document relevant personal and family history related to diet, medical conditions, stress fracture history, alcohol and tobacco use, and exposure to sunlight. It is critical to know the presence of any of the following habits or conditions: current medications, age, gender, ethnicity, and race. The tool also covered physical activity and environmental exposures.

4. Vitamin D and Calcium Intake and Frequency Questionnaire[22] – This questionnaire is administered in-person by study team at baseline. It is used to record average daily and weekly servings of foods high in vitamin D and/or calcium. The tool has been validated for use in young adults. Permission was obtained from the author for its use. The tool is designed as an Excel worksheet with built-in calculations that total the amounts of vitamin D and calcium in foods that are consumed on a daily or weekly basis. The reference for the nutrient values is the Academy of Medicine. The tool was modified slightly to capture vitamin D and calcium-containing foods and quantities consumed from Northwest sources, such as salmon and ultraviolet irradiated mushrooms.

5. Serum biomarkers - Calcium and Parathyroid Hormone – standard blood tests performed at the same time as the 25(OH)D in order to provide a clinical interpretation in the setting of abnormal levels.

6.5.2 Appropriateness of Measurements

The Elecsys Vitamin D Total II assay is intended for the quantitative determination of total 25-hydroxyvitamin D in human serum and plasma. The electrochemiluminescence binding assay is intended for use on Elecsys and cobas e immunoassay analyzers.

Body composition measurements, biomarkers, and demographic questionnaires all represent valid and reliable methods to capture data relevant to a vitamin D investigation. All measures have been previously tested and used by this research team.

6.5.3 Primary Efficacy Variable(s)

Serum 25(OH)D level is the primary endpoint used to establish whether the treatment in the phototherapy kiosk group is equivalent to the oral vitamin D3 supplementation currently prescribed as the standard of care. It is expected that the serum 25(OH)D levels in both groups will rise over time and that the serum 25(OH)D levels will be equal to, or not less than, that of the oral supplementation group.

A Device Usability Scale will be administered to the Kiosk Group to assess acceptability and feasibility. This 12-item Likert-type scale was adapted from the Digital Equipment Corporation

"System Usability Scale" (1986) and it will be administered to the Kiosk Group upon completion of the study.

6.6 Statistical Methods Planned in the Protocol and Determination of Sample Size

6.6.1 Statistical and Analytical Plans

The original analysis plan will be carried out using all available subject data points. No interim analysis will be performed. Exploratory data analyses will be conducted on the serum vitamin D levels of participants assigned to either the oral vitamin D supplementation or kiosk group. The analysis will be restricted to participants with valid baseline serum vitamin D data and at least one follow-up blood draw. The Shapiro-Wilk test will be used to assess the normality of the data distribution. Measures of central tendency and dispersion are provided for continuous data as medians (mdn) with associated interquartile ranges (IQR). Summary statistics will be provided for categorical variables and include the number of participants as well as the prevalence within each group.

6.6.2 Determination of Sample Size

This is a pilot study therefore the appropriate sample size was estimated based on previous and current studies that achieved significance and involved this population and a similar approach to vitamin D supplementation.

We requested approval to enroll twice the number required, or 120 subjects, in order to overcome the potential for a higher than expected attrition (30%), or a particularly high level of enthusiasm for the study from beneficiaries and civilians working in the hospital.

Estimate Required Sample Size	60
Estimate Participant Drop Out / Withdrawal	30%
Total Enrollment Requirement	Minimum of 78, requesting 120

7.0 References

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