AWARD NUMBER: CDMRPL-17-0-DM170706

TITLE: Early Screening and Diagnosis for Low Bone Mineral Density Utilizing Opportunistic Screening, Serum Biomarkers, and Advanced Modeling

PRINCIPAL INVESTIGATOR: CAPT (sel) Scott M. Tintle, MC, USN

CONTRACTING ORGANIZATION: Uniformed Services University of the Health Sciences (USUHS), Bethesda, MD

REPORT DATE: April 2023

TYPE OF REPORT: Final

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

REPORT DOCUMENTATION PAGE

Form Approved
OMB No. 0704-0188

1. REPORT DATE	2. REPORT TYPE	3. DATES COVERED
April 2023	Final	15Mar2018-31Dec2022

4. TITLE

Early Screening and Diagnosis for Low Bone Mineral Density Utilizing Opportunistic Screening, Serum Biomarkers, and Advanced Modeling

5a. CONTRACT NUMBER

5b. GRANT NUMBER
CDMRPL-17-0-DM170706

5c. PROGRAM ELEMENT NUMBER

6. AUTHOR(S)
CAPT(sel) Scott M. Tintle, MC, USN

E-Mail: scott.m.tintle.mil@health.mil

5d. PROJECT NUMBER

5e. TASK NUMBER

5f. WORK UNIT NUMBER

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)

Uniformed Services University of the Health Sciences
(USUHS)
4301 Jones Bridge Road
Bethesda, MD 20814

8. PERFORMING ORGANIZATION REPORT NUMBER

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)

12. DISTRIBUTION / AVAILABILITY STATEMENT

Approved for Public Release; Distribution Unlimited

13. SUPPLEMENTARY NOTES

14. ABSTRACT

This is a 5-year, prospective cohort study of Hounsfield Unit (HU) and Fracture Risk, to determine whether HU obtained from existing CT scans is associated with BMD by DEXA, serum levels of bone turnover markers, and long-term risk fractures. Tow arms of this cohort will be recruited; a small cohort will receive a DEXA scan, serum biomarker testing, and prospective fracture monitoring, while a larger cohort will simply be enrolled for prospective fracture monitoring alone for two years. Patients in the second cohort will be categorized as osteoporotic, osteopenic, and normal BMD as determined by HU values as they are enrolled into the study. The study is being conducted at Walter Reed National Military Medical Center and the Uniformed Services University of the Health Sciences.

15. SUBJECT TERMS
osteoporosis, osteopenia, bone-health, fragility fracture, opportunistic screening, DEXA, serum repository, biomarkers, bone-breakdown products, Houndsfield units

16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT	18. NUMBER OF PAGES	19a. NAME OF RESPONSIBLE PERSON
a. REPORT	b. ABSTRACT	c. THIS PAGE			USAMRDC
Unclassified	Unclassified	Unclassified	Unclassified	19	19b. TELEPHONE NUMBER *(include area code)*

TABLE OF CONTENTS

1. INTRODUCTION:

Fragility fractures carry a significant risk of mortality, which has been shown to be up to 39% in women within 5 years of sustaining their first such fracture.4 Additionally, sustaining a fragility fracture is itself a strong risk factor for sustaining subsequent fractures in the future, each carrying additional cost to the patient and healthcare system as well as increased suffering and mortality. Efforts within the military healthcare system demonstrate poor correlation between bone mineral density screening guidelines and treatment. The objective of our proposal is to prevent fragility fractures through improved screening, diagnosis, and predictive modeling of low bone mineral density and fracture risk in the military population. This research will essentially involve two related projects. The first is to perform a prospective study to evaluate the value of the Hounsfield unit measurement from opportunistic CT scans to see how closely it is associated with Bone mineral density by DEXA Scan, serum biomarkers, and long term fracture risk. We will also evaluate serum biomarkers in an osteoporotic and non-osteoporotic cohort of patients over the adult lifetime of a female population utilizing the DOD Serum Repository.

2. KEYWORDS:

osteoporosis, osteopenia, bone-health, fragility fracture, opportunistic screening, DEXA, serum repository, biomarkers, bone-breakdown products, Houndsfield units

3. ACCOMPLISHMENTS:

What were the major goals of the project?

Specific Aim 1: Prospective cohort study of HU and fracture risk.

Specific Aim 2: Evaluate serum biomarkers as predictive factors for bone loss.

Specific Aim 3: Predictive modeling of fracture risk.

	Timeline (months) from 1/1/2020	Site 1	Site 2	Status

Protocol 1: CDMRP Bone Health- CT/DEXA/Serum				
Major Task 1: Prospective Correlation of HU and DEXA				
Subtask 1: Local IRB Approval Local IRB approval will be initiated and completed prior to the beginning of the period of performance of this award.	0-1	Dr. Tintle	Dr. Davis	completed
Subtask 2: Patient enrollment for Protocol 1 – Observation cohort Patients will be enrolled on a rolling basis until 462 patients are enrolled in each group (osteoporotic/osteopenic and normal BMD), and will be monitored prospectively for fracture	1-5	Dr. Tintle		Completed- total sample size increased to 2907
Subtask 3: HU and DEXA correlation performed HU values will be obtained and evaluated for correlation with DEXA scores.	1-12	Dr. Tintle		Completed
Protocol 1: CDMRP Bone Health- Fracture				
Subtask 1: Prospective monitoring of fractures Patients enrolled will have AHLTA record surveilled for incidence of fragility fracture, record review at end of surveillance period to inquire about fracture incidence.	5 - 29	Dr. Tintle		completed
Subtask 2: Analysis of relationship between HU and fracture risk	30-32	Dr. Tintle		completed

Milestone 1 Achieved: All Protocol 1 patients enrolled.	9	Dr. Tintle		completed
Milestone 2 Achieved: DEXA and HU correlated.	12	Dr. Tintle		completed
Milestone 3 Achieved: Fracture incidence of patients determined.	32	Dr. Tintle		completed
Protocol 2: Osteoporosis Serum Biomarkers				
Major Task 1: Serum sample acquisition from DoDSR				
Subtask 1: Formal request for samples from DoDSR from patients identified as osteoporotic or normal BMD on DEXA scan for 80 patients in each cohort	1	Dr. Tintle	Dr. Davis	completed
Subtask 1 amended: Formal request for samples from DoDSR from patients identified as osteoporotic or normal BMD on DEXA scan for additional 120 patients in each cohort	16	Dr. Tintle		completed
Subtask 2: DoDSR serum sample acquisition/transfer (80 patients in each cohort) Samples obtained and transferred from DoDSR to USUHS with appropriate handling/storage.	5 6	Dr. Tintle	Dr. Davis	Completed completed

Subtask 2 amended: DoDSR serum sample acquisition/transfer for additional 120 patient samples in each cohort Samples obtained and transferred from DoDSR to USUHS with appropriate handling/storage.	19 20	Dr. Tintle	Dr. Davis	completed
Major Task 2: Conduct immunoassay analysis of all				
Subtask 1: Immunoassay analysis of DoDSR serum samples (80 patients in each cohort)	6-11		Dr. Davis	completed
Subtask 1 amended: Immunoassay analysis of DoDSR serum samples (120 patient patients each cohort)	20-29	Dr. Tintle	Dr. Davis	completed
Milestone 4 Achieved: All serum samples analyzed (80 in each cohort)	12	Dr. Tintle	Dr. Davis	completed
Milestone 4 Amended: All serum samples analyzed (additional 120 samples in each cohort)	29	Dr. Tintle	Dr. Davis	completed
Major Task 1: Analysis of data and creation of a predictive model				
Subtask 1: Statistical analysis and modeling of data from Aim 1 & 2	13-36	Dr. Tintle		completed

Subtask 2: Predictive modeling analysis for Aim 3, including comparison to existing models	13-36	Dr. Tintle		completed
Subtask 3: Knowledge dissemination	15-36	Dr. Tintle	Dr. Davis	In progress
Milestone 5 Achieved: Statistical analyses complete	36	Dr. Tintle	Dr. Davis	completed
Milestone 6 Achieved: Predictive Model created	36	Dr. Tintle	Dr. Davis	completed

What was accomplished under these goals?

Protocol 1: CDMRP Bone Health- Fracture

Fragility Fracture Risk

The fragility fracture study looked at 2878 patients who had undergone computed tomography colonography (CTC) scans within the military health system (MHS). Of these 2878 patients, 142 experienced a fragility fracture over the course of the study. The study aimed to collect demographic information of these patients as well as their bone mineral density (BMD) data from previous dual energy x-ray absorptiometry (DXA) scans. Further, using the patient's CTC scans, we were able to obtain Hounsfield unit (HU) measurements at the left femoral neck and 5th lumbar spine vertebrae. Previous literature suggests these measurements can be used a proxy for evaluating a patient's BMD .

Results showed that HUs differed by sex ($p<0.001$) and race ($p<0.001$), pointing to an individualized diagnostic approach for low BMD. Data also indicated that longitudinal fracture risk differed by race ($p<0.0001$); there was a not statistically significant difference between sexes ($p=0.13$), but it is plausible this may become statistically significant at a 10 yr interval. Regardless, this reveals that a divergence in fragility fracture incidence occurs quickly with time; thus, it is clinically actionable and interventions can be taken early on in at-risk populations. Results also supported prior understanding that previous fracture is the strongest risk factor of subsequent fragility fracture ($p<0.001$).

We then evaluated the HU value and FRAX scores to see how they correlated with fragility fractures, respectively. HU was shown to have a higher correlation with fragility fracture incidence than a FRAX score, which is the current gold standard for a 10 year prediction of fragility fractures. Developing a model with combined spine/femur HU and a subsequent receiver operating characteristics (ROC) curve, the area under the curve (AUC) was found to be 69.9%. In an effort to find an HU screening value for low BMD/at-risk for fragility fracture, an 80% sensitivity cutoff was developed for both spine and femur HU. A screening value based on spine HU was 172.2 HU (AUC 72.4%, OR 3.6, PPV 7.4%, NPV 97.8%) and for femur HU was 136.8 (AUC 69.5%, OR 3.0, PPV 7.0%, NPV 97.6%). Over the 6.2yr study period, both of these values were shown to be predictive of fragility fractures longitudinally ($p<0.0001$), with the higher AUC percentage suggestive that the spine measurements may be slightly more optimal.

Table 1. Patient Demographics

	Overall	No Fracture	All Fragility Fractures	Hip Fracture	Distal Radius Fracture	Spine Fracture	Proximal Humerus Fracture	Rib Fracture	Pelvis Fracture	Femoral Shaft Fracture
No. of Patients (%)	2878	2736 (95.1)	142 (4.9)	15 (10.6)	41 (28.9)	18 (12.7)	12 (8.5)	41 (28.9)	14 (9.9)	1 (0.7)
Age (years)	63.3±9.5	63.0 ±9.3	68.2±10.4	73.2±10.2	64.2±9.2	73.4±10.0	65.7±6.7	65.9±10.9	76.4±7.8	71±0.0
Female Sex (%)	1301 (45.2)	1228 (44.8)	73 (51.4)	6 (40.0)	27 (65.9)	6 (33.3)	9 (75.0)	15 (36.6)	9 (64.3)	1 (100.0)
Race										
White (%)	1420 (49.3)	1322 (48.3)	98 (69.0)	12 (80.0)	26 (63.4)	14 (77.8)	8 (66.7)	27 (65.9)	11 (78.6)	0 (0.0)
Black (%)	647 (22.5)	632 (23.1)	15 (10.6)	2 (13.3)	5 (12.2)	0 (0.0)	1 (8.3)	6 (14.6)	1 (7.1)	0 (0.0)
Asian (%)	98 (3.4)	96 (3.5)	2 (1.4)	0 (0)	1 (2.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (100.0)
Other Race (%)	317 (11.0)	303 (11.1)	14 (9.9)	0 (0)	6 (14.6)	1 (5.6)	2 (16.7)	4 (9.8)	1 (7.1)	0 (0.0)
Unknown (%)	396 (13.8)	383 (14.0)	13 (9.2)	1 (6.7)	3 (7.3)	3 (16.7)	1 (8.3)	4 (9.8)	1 (7.1)	0 (0.0)
Mean Height (cm)	171.7±13.3	171.7±13.4	170.9±10.2	175.9±7.6	168.1±13.3	172.3±9.5	169.3±5.5	173.0±8.0	168.5±9.3	154.9±0.0
Mean Weight (kg)	84.9±20.6	85.2±20.6	81.1±18.6	89.9±20.3	79.8±20.4	77.4±18.3	93.2±13.0	80.5±17.7	71.7±12.1	72.0±0.0
Previous Fracture (%)	322 (11.2)	275 (10.1)	47 (33.1)	8 (53.3)	13 (31.7)	8 (44.4)	4 (33.3)	9 (22.0)	5 (35.7)	0 (0.0)
Parent with Hip Fracture (%)	63 (2.2)	56 (2.0)	7 (4.9)	2 (13.3)	0 (0.0)	1 (5.6)	1 (8.3)	2 (4.9)	1 (7.1)	0 (0.0)
Family History of Osteoporosis (%)	74 (2.6)	65 (2.4)	9 (6.3)	1 (6.7)	3 (7.3)	1 (5.6)	1 (8.3)	1 (2.4)	2 (14.3)	0 (0.0)
Teriparatide use (%)	9 (0.3)	6 (0.2)	3 (2.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (2.4)	2 (14.3)	0 (0.0)
DMARD use (%)	171 (5.9)	154 (5.6)	17 (12.0)	0 (0.0)	5 (12.2)	3 (16.7)	0 (0.0)	4 (9.8)	4 (28.6)	1 (100.0)
Secondary Osteoporosis or Metabolic Bone Disease (%)	100 (3.5)	87 (3.2)	13 (9.2)	1 (6.7)	5 (12.2)	3 (16.7)	0 (0.0)	1 (2.4)	3 (21.4)	0 (0.0)
Bone Mineral Density (BMD) Measures										
Mean HU, Spine	172.7±53.7	174.9±54.4	134.0±48.9	113.5±44.6	143.8±52.3	126.4±51.8	136.7±57.0	141.9±44.0	112.6±39.7	134.5±0.0
Mean HU, Femur	130.4±51.4	132.6±52.6	98.3±52.3	72.4±48.3	106.6±56.1	97.3±59.5	113.2±58.5	102.7±45.2	77.0±42.3	115.3±0.0

Table 2. Hounsfield units (HU) differences among sex and race

	Sex			Race					
	Female	Male	P value	White	Black	Asian	Other	Unknown	P value
Mean HU, Spine (SD)	168.6 (55.6)	176.0 (51.9)	<0.001	158.1 (48.4)	201.5 (56.4)	170.1 (48.9)	176.7 (50.2)	174.9 (51.4)	<0.001
95% CI	165.5-171.7	173.4-178.6		155.6-160.7	197.1-205.9	160.2-180.0	171.0-182.3	169.7-180.0	
Mean HU, Femur (SD)	124.9 (51.7)	135.0 (50.8)	<0.001	121.0 (48.2)	149.3 (54.7)	126.5 (43.6)	133.7 (52.5)	131.3 (49.0)	<0.001
95% CI	122.0-127.7	132.4-137.5		118.4-123.5	145.1-153.6	117.7-135.3	127.8-139.7	126.4-136.2	

Supplementary Table 1. Demographic predictors of fracture based on best multiple regression model

	Overall	Female	Male	White	Black	Asian	Other	Unknown
	P value							
Age	-	-	<0.001	-	-	-	-	-
Height	-	-	-	-	-	-	-	-
Weight	-	-	-	-	-	-	-	-
Previous Fracture	<0.001	<0.001	<0.001	<0.001	<0.001	-	-	-
Parent with Hip Fracture	-	-	-	-	-	-	<0.001	-
Family History of Osteoporosis	-	-	-	-	-	-	-	-
Teriparatide use	-	-	-	-	-	-	-	-
DMARD use	-	-	-	-	-	-	-	-
Secondary Osteoporosis or Metabolic Bone Disease	-	-	<0.01	-	-	-	-	-
Sex	-	-	-	-	-	-	-	-
Race	-	-	-	-	-	-	-	-

Protocol 2: Osteoporosis Serum Biomarkers

Serum samples from the Department of Defense Serum Repository were obtained from 205 women given the diagnosis of osteoporosis after age 46 years and 205 age-matched women with normal bone mineral density from 4 time points in their life (ages 25-31, 32-38, 39-45, and 46-60 years). Serum levels of bone turnover markers (propeptide of type I collagen, parathyroid hormone, bone-specific alkaline phosphatase, osteocalcin, C-terminal telopeptide of type I collagen, sclerostin, osteoprotegerin, osteopontin, and 25-OH vitamin D) were measured using commercially available arrays and kits.

We built logistic regressions using the diagnosis of osteoporosis as the response variable and the biomarkers as predictor variables at each time point. We built models with all possible combinations of biomarkers and a null model estimating their Akaike information criterion (AIC) value to choose the best model (lowest AIC value). Using the best model, we calculated ROC-AUC at each time point along with confidence intervals to estimate the predictive capability of our model. We also calculated the Brier score for the best model and additional metrics. Then, we ran a Student's t-test on the biomarkers that comprised the best model at each time point to determine if the control group and the osteoporotic group were different. Analyses were conducted in R. Timepoint 1 had 228 women's serum available for analysis, Timepoint 2 had 404, timepoint 3 had 406 women, and timepoint 4 had 314 women. At each time point, roughly half the participants went on to have osteoporosis with DEXA T-2.5, and the other half had normal bone mineral density

Time 1
At time point 1, we found that the biomarkers Leptin, OC, PTH, FGF-23, BSAP, and CTX-1 best fit our data. The ROC-AUC was 0.61 (95%CI=0.53-0.69) and a Brier score of 0.23 showing moderate predictive capabilities. We found differences in biomarker concentrations for FGF23 (t= -2.53, df=224.44, p=0.01) and PTH

Time 1 logistic regression output

	B	Standard error	Z-value	P-value
Intercept	-2.38	1.23	-1.93	0.05
Leptin	-0.10	0.13	-0.76	0.44

OC	0.33	0.17	1.88	0.06
PTH	-0.25	0.10	-2.43	0.01**
FGF23	0.28	0.12	2.31	0.02**
BSAP	-0.18	2.03	-0.09	0.92
CTX-1	0.002	0.22	0.01	0.99

** statistically significant differences

Time 2

At time point 2, we found that OC and Vitamin D were the biomarkers that best fit our data. The ROC-AUC was 0.57 (95%CI=0.52-0.63) with a Brier score of 0.25 demonstrating predictive capabilities. When comparing between the control group and the osteoporotic group, we found no difference in OC, however, Vitamin D was significantly higher in the osteoporotic group compared to the healthy population (t= -2.18, df=401.94, p=0.03).

Time 2 logistic regression output

	B	Standard error	Z-value	P-value
Intercept	-1.37	0.90	-1.52	0.12
OC	0.10	0.09	1.11	0.26
Vitamin D	0.01	0.007	2.06	0.03**

** statistically significant differences

Time 3

At time point 3, we found that DKK1, OPG, OC, SOST, PTH, and Vitamin D all contributed to the best model. We found an ROC-AUC of 0.60 (95%CI=0.53-0.65) and a Brier score of 0.24 indicating moderate predictive capabilities. A Student's t-test showed no difference between the healthy population and the osteoporotic population for DKK1 and PTH. However, we did find differences between the cohorts for OPG (t= 2.19, df=403.86, p=0.02) where the healthy population had higher concentrations, OC (t= -2.27, df=318.85, p=0.02) where they healthy population had lower concentrations, and SOST (t= 3.01, df=386.86, p=0.002) where the healthy population had higher concentrations.

Time 3 logistic regression output

	B	Standard error	Z-value	P-value
Intercept	0.53	2.31	0.23	0.81
DKK1	0.30	0.25	1.18	0.23
OPG	-0.60	0.27	-2.19	0.02**
OC	0.26	0.14	1.80	0.07
SOST	-0.35	0.11	-3.10	0.001**
PTH	0.14	0.08	1.67	0.09
Vitamin D	0.01	0.008	1.54	0.12

** statistically significant differences

Time 4

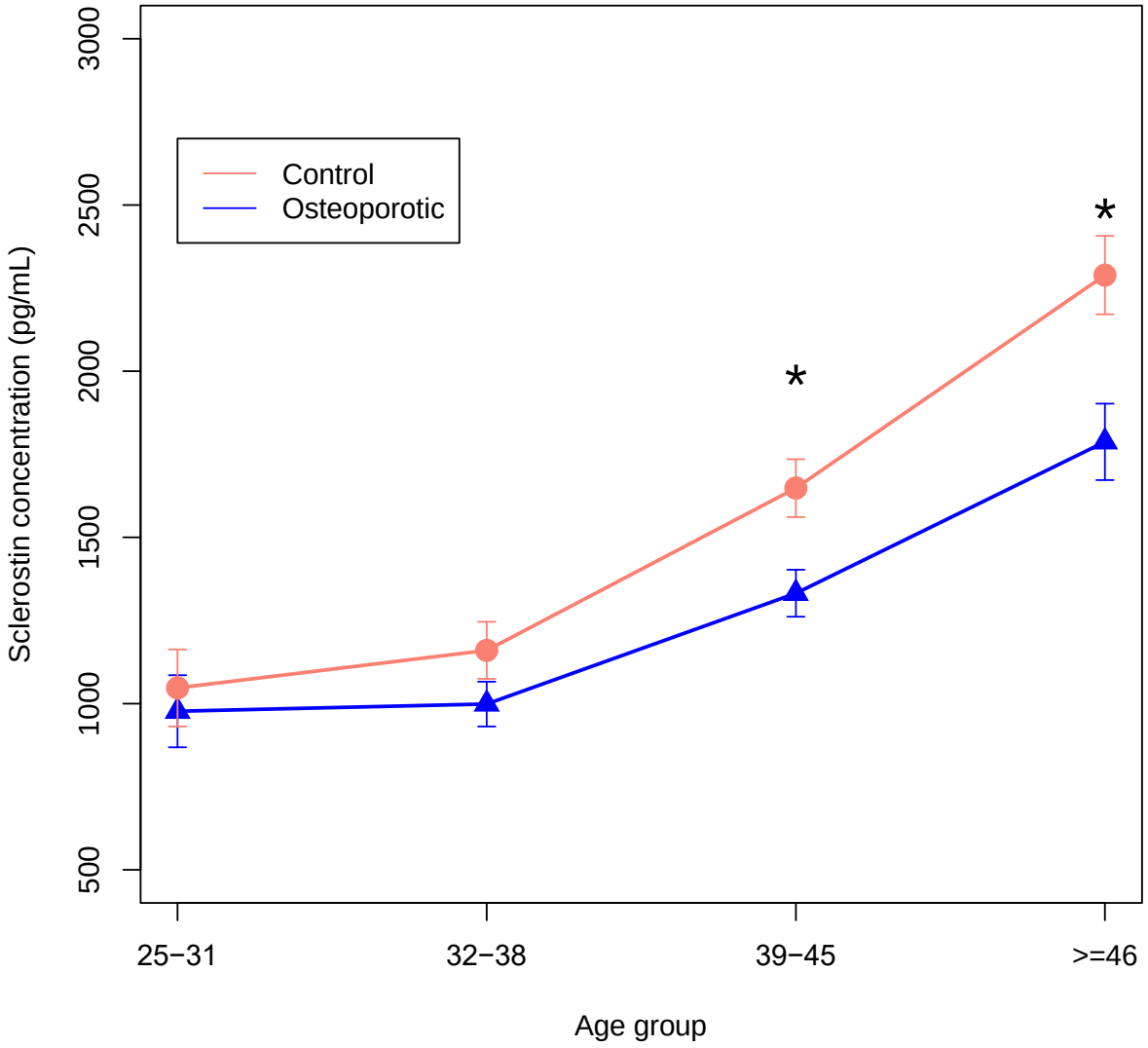
We found that SOST, OC, and TNFa best fit our data. The ORC-AUC was 0.70 (95%CI=0.58-0.73) and a Brier score of 0.21 demonstrating moderate predictive capabilities. At this time point, we found that TNFa was marginally different between the cohorts (p=0.06), but we did find differences in SOST (t= 3.15, df=308.08, p=0.001) where the healthy population had higher concentrations, and OC (t= -2.25, df=310.87, p=0.02) where the control group had lower concentrations.

Time 4 logistic regression output

	B	Standard error	Z-value	P-value
Intercept	-0.10	1.67	-0.06	0.94

SOST	-0.50	0.13	-3.59	0.0003**
OC	0.34	0.15	2.17	0.02**
TNFa	0.53	0.22	2.34	0.01**

** statistically significant differences



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

This year allowed for training in statistics. An intern and medical student have been involved in data analysis and in manuscript preparation.

How were the results disseminated to communities of interest?

At this time, there are three manuscripst currently in preparation with the above data. We have submitted for meeting presentations and will be presenting at the American Bone and Joint Society, The American Academy of orthopaedic Surgeons and the Society of Military Orthopaedic Surgeons.

Describe briefly what you plan to do during the next reporting period to accomplish the goals and objectives.

Nothing to report

4. **IMPACT:**

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

Protocol 1 Fracture Prediction

Our data demonstrates that opportunistic screening utilizing the HU measurements from the proximal femur and the lumbar spine is better at early prediction of fragility fractures than the standard FRAX tool in the same population. Additionally, we have demonstrated some unique differences amongst sex and race. The impact of this information will help to further demonstrate that opportunistic screening information obtained from CT scans can be very helpful in the early prediction of future fragility fracture. This will continue to challenge the existing paradigm of osteoporosis prediction at age 65 via use of a DEXA.

Protocol 2 Serum Biomarkers

Despite uncontrolled collection of serum samples, sclerostin level trended lower in the osteoporotic cohort of patients and was significantly different at time points three and four. Serum sclerostin level was found to be moderately predictive of the development of osteoporosis from ages 39-45, and from age 45-54 years old. This study we believe will have a dramatic impact on bone health. This study demonstrates that serum biomarkers and even just sclerostin is moderately predictive at the future development of osteoporosis.

What was the impact on other disciplines?

Eventually, the findings of these studies might help to lower the fragility fracture rate and lower orthopaedic fracture rates.

What was the impact on technology transfer?

Nothing to report yet at this time. We believe that with additional study, a serum sclerostin or biomarker panel test might eventually be able to be sold commercially to predict osteoporosis and fragility fractures.

What was the impact on society beyond science and technology?

Nothing to report yet at this time.

5. CHANGES/PROBLEMS:

We have modified the statement of work early on in the study because of COVID 19. This has previously been approved. Most recently, our lab work was delayed because of software that was necessary for the analysis of the serum samples. This was obtained and the study was completed.

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

No anticipated problems- we are preparing manuscripts for submission now.

Changes that had a significant impact on expenditures

No significant changes that had an impact.

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

No significant changes that had an impact.

Significant changes in use or care of vertebrate animals

Not applicable.

Significant changes in use of biohazards and/or select agents

Not applicable.

6. PRODUCTS:

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

Journal publications.

Early Screening for osteoporosis with serum biomarkers. American Bone and Joint Surgery Annual Conference- Best Paper Award Recipient. Prediction of Osteoporosis Development in Young Women Using Novel Biomarker Signatures, American Society for Surgery of the Hand Annual Meeting, Oct 2, 2021. *Top 5 Best Papers Longitudinal Analysis of Bone Turnover Biomarkers Across the Adult Life-Span of Osteoporotic Women. American Society for Surgery of the Hand Annual Meeting, Sep 2019. *Top 5 Best Papers 3 Manuscripts currently in preparation. Acknowledgement of Federal Support in all.

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

7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

What individuals have worked on the project?

Walter Reed National Military Medical Center (WR)

Name: CAPT(sel) Scott Tintle, MD
Project Role: Initiating PI at WR
ORCID ID: 0000-0003-0887-7600
Nearest person month worked: 1
Contribution to project: no change

Name: MAJ Sean Slaven, MD
Project Role: Co-Investigator
ORCID ID: 0000-0003-0395-9076
Nearest person month worked: 1
Contribution to project: no change

Name: Julio Rivera, PhD
Project Role: Data Scientist at WR
ORCID ID: 0000-0002-3197-1745
Nearest person month worked: 1
Contribution to project: no change

Uniformed Services University of the Health Sciences (USUHS)

Name: Thomas Davis, PhD
Project Role: Co-Investigator
ORCID ID: 0000-0003-0887-7600
Nearest person month worked: 1
Contribution to project: no change

Name: Andrea Dragon
Project Role: Research Assistant
ORCID ID: 0000-0002-3257-1567
Nearest person month worked: 1
Contribution to project: no change

Uniformed Services University of the Health Sciences (USUHS)

Name:	Elsa Ronzier
Project Role:	Cell Biologist
ORCID ID:	0000-0003-1008-4271
Nearest person month worked:	1
Contribution to project:	no change

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

Nothing to report.

What other organizations were involved as partners?

Nothing to report.