Award Number: W81-XWH-11-2-0107

TITLE: Assessment of Chiropractic Treatment for Low Back Pain, Military Readiness and Smoking Cessation in Military Active Duty Personnel

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Fort Detrick, Maryland 21702-5012

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Assessment of Chiropractic Treatment for Low Back Pain, Military Readiness and Smoking Cessation in Military Active Duty Personnel

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**13. SUPPLEMENTARY NOTES**

**14. ABSTRACT**

This study is comprised of three trials, referred to as the Assessment of Chiropractic Treatment (ACT). The following accomplishments have been made in each study during the reporting period of February 15, 2016 through February 14, 2017. ACT 1 is a randomized controlled trial of chiropractic for low back pain with a nested smoking cessation component in 750 active duty military personnel. During this reporting period the study: Completed long-term follow up assessments, closed study sites; published the protocol manuscript. ACT 2 is a randomized controlled trial of response and reaction times in Special Operations Forces at Ft. Campbell, KY: We completed recruitment at 100% (N=120/120); completed data collection; and closed study sites. ACT 3 is a randomized controlled trial of strength, balance, and re-injury comparing standard care with standard care plus chiropractic treatment: We launched study at Naval Hospital Pensacola; recruited 13/110 targets; contracted a new study provider in the wake of the passing away of the original chiropractic doctor in October; Awaiting final site approvals for new study chiropractor in order to reinstate recruitment activities for ACT 3.

**15. SUBJECT TERMS**
Chiropractic, low back pain, tobacco cessation

| **16. SECURITY CLASSIFICATION OF:** | | | **17. LIMITATION OF ABSTRACT** | **18. NUMBER OF PAGES** | **19a. NAME OF RESPONSIBLE PERSON** |
|---|---|---|---|---|---|
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| U | U | U | UU | 47 | **19b. TELEPHONE NUMBER** *(include area code)* |

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**INTRODUCTION*:***

This annual report provides updates for the reporting period February 15, 2016 through February 14, 2017 on the study "Assessment of Chiropractic Treatment for Low Back Pain, Military Readiness and Smoking Cessation" (Grant Number W81XWH-11-2-0107). This program consists of three trials taking place at five military sites under the study. These trials have staggered start dates at multiple sites. Trial A is a randomized controlled trial of low back pain with nested smoking cessation for active duty personnel at Walter Reed National Military Medical Center (WRNMMC) in Bethesda, MD; Naval Hospital Pensacola (NHP), FL; Naval Medical Center San Diego (NMCSD), CA) which was the first study to be initiated. This study is followed by consecutively run Trials B and C. Trial B is a randomized controlled trial of response and reactions times in Special Operations Forces at Blanchfield Army Community Hospital, Fort Campbell, KY. Trial C is a randomized controlled trial evaluating the effects of chiropractic care on strength and balance, in active duty military personnel at Naval Hospital Pensacola, FL.

**BODY:**

***Clinical Trial A (ACT 1) Summary***

Assessment of Chiropractic Trials Study A (called "ACT 1") is a multi-site randomized controlled trial (RCT) for low back pain with nested tobacco cessation study at sites: Walter Reed National Military Medical Center in Bethesda, MD; Naval Hospital Pensacola, FL; Naval Medical Center San Diego, CA. The aim of ACT 1 is to conduct a multi-site, randomized controlled trial to test whether the combination of chiropractic treatment plus standard medical care is superior to standard medical care alone for relief of pain and the improvement in function in active duty military personnel (ages 18-50) with acute, sub-acute and/or chronic, non-surgical low back pain. A secondary aim is to assess success of tobacco cessation delivered by chiropractors. During this reporting period, 100% of the recruitment target has been met across all sites: a total of 750 participants have been recruited with 250 at Naval Medical Center San Diego (NMCSD), 250 at Naval Hospital Pensacola (NHP), and 250 at Walter Reed National Military Medical Center in Bethesda (WRNMMC), MD.

Recruitment Overview

Study recruitment for ACT 1 has been successful throughout the last reporting period. Recruitment ended at Naval Medical Center San Diego on January 27, 2015; at Naval Hospital Pensacola on April 22, 2015; and at Walter Reed National Military Medical Center on November 20, 2015. At the end of this reporting period, long-term assessment data collection was completed at the three sites (refer to Task 8). We conducted quarterly internal quality assurance visits at each site to maintain data integrity and ensure standardization of study procedures across all sites.

During the last reporting period, the ACT 1 protocol at Walter Reed National Military Medical Center in Bethesda and Naval Hospital Pensacola was amended to include long-term follow up. This includes 3 additional online assessments that will measure outcomes at months 6, 9, and 12 from allocation. In addition, we are collecting data on a weekly basis via Short Message Service (SMS) to capture LBP status in this subset of participants from week 7 to week 52 (1 year). The addition of these outcome measures will provide important information on the trajectory of LBP in military personnel. These items were not added at Naval Medical Center San Diego since enrollment was almost completed at the time of the amendment submission.

Personnel changes during this reporting period:

- Crystal Franklin, MPH, assumed the role of Associate Investigator February 26, 2016.
- Abigail Roots, BS, was removed from the role of Associate Investigator February 26, 2016.
- CAPT Michael Rosenthal, site PI at NMCSD, retired February 2016.
- CDR Joseph Penta was deployed May 18, 2016 after signing off on site closure documentation.

Task 1: Submit quarterly technical progress reports to project officers

- In compliance with reporting requirements, quarterly reports were submitted in this reporting period on the following dates: May 16, 2016, August 12, 2016, and November 8, 2016.

Task 2: Annual reports have been sent to Defense Technical Information Center

- In compliance with reporting requirements, annual reports were submitted on March 14, 2012, March 15, 2013, March 13, 2015, March 14, 2016, and March 14, 2017.

Task 3: Finalized protocol and sites

- No changes in sites since end of last reporting period.

Task 4: Convened advisory panel for review of all study matters

- Convened advisory panel meetings to report progress and challenges on May 3, 2011, May 1, 2012, March 17, 2014, August 10, 2015.
- Plans to convene another advisory panel meeting were postponed this reporting period due to waiting for the notification of the no cost extension which we received on February 15, 2017.

Task 5: Prepared data collection systems

- Kept data collection systems updated during reporting period.
- Maintained long-term follow up web assessments at months 6, 9, 12; updated associated reports and timelines to reflect these additions
- Maintained online module to track screen failures/reasons for exclusion
- Maintained online module to track participant care received for LBP during study (includes providers visits for LBP and medications prescribed)

Task 6: IRB approval processes and other regulatory requirements

- During this reporting period, IRB amendments were submitted for all changes in staff, to update recruitment materials, protocol changes to include refinement of the 'contextual component' procedures and addition of long-term follow up assessments as well as changes to the informed consent document resulting from these protocol changes. The amendments were routed through all active IRBs (RAND, Palmer, NHP, NMCSD, and WRNMMC) prior to site implementation. Samueli Institute has a Federalwide Assurance (FWA) that stipulates RAND as the IRB on record for this program.
- There were a series of IRB approvals in sequence that were obtained, including local military scientific and IRB reviews, RAND, Palmer College, and second level Human Research Protection Office (HRPO) approvals, as follows:

Walter Reed National Military Medical Center in Bethesda, MD

- Initial submission October 18, 2012
- Amendment 01 February 4, 2013
- Amendment 02 May 21, 2013
- Amendment 03 September 24, 2013
- Amendment 04 February 4, 2014
- Amendment 05 April 29, 2014
- Amendment 06 August 4, 2014
- Amendment 07 May 15, 2014
- Reportable event September 17,2014
- Amendment 08 September 18, 2014
- Amendment 09 November 10, 2014
- Amendment 10 March 24, 2015
- Amendment 11 August 17, 2015
- Reportable event October 9, 2015
- Amendment 12 February 26, 2016

Naval Hospital Pensacola, FL (IRB of record: Naval Medical Center Portsmouth)

*** Approval date indicates both Portsmouth approval as well as Commanding Officer of Naval Hospital Pensacola approval*

- Initial submission August 1, 2012
- Amendment 01 September, 17, 2012
- Amendment 02 January 31, 2013
- Amendment 03 April 12, 2013
- Amendment 04 September 6, 2013
- Data Sharing Agreement February 26, 2014 (renewal)
- Amendment 05 August 28, 2014
- Amendment 06 August 26, 2014
- Amendment 07 November 3, 2014
- Amendment 08 November 3, 2014
- Amendment 09 November 3, 2014
- Amendment 10 November 26, 2014
- Data Sharing Amendment July 24, 2015 (permission to use AHLTA data)
- Amendment 11 September 9, 2015
- Amendment 12 January 12, 2016
- Study Closure June 15, 2016

Naval Medical Center San Diego, CA

- Initial submission February 22, 2012
- Amendment 01 August 6, 2012
- Amendment 02 March 13, 2013
- Amendment 03 November 1, 2013
- Amendment 04 January 22, 2014
- Data Sharing Agreement February 26, 2014

- Amendment 05 April 14, 2014
- Amendment 06 July 21, 2015
- Data Sharing Amendment July 24, 2015 (permission to use AHLTA data)
- Study Closure August 19, 2015

RAND Corporation: ACT 1 gained initial approval on January 20, 2011 with continuing reviews and amendments to procedures approved on the following dates:

- Continuing reviews: Approved January 31, 2012, December 18, 2012, November 20, 2013, November 6, 2014, November 5, 2015, October 11, 2016.
- Amendment 01 July 28, 2011
- Amendment 02 August 9, 2011
- Amendment 03 January 31, 2012
- Amendment 04 April 12, 2012
- Amendment 05 May 15, 2012
- Amendment 06 September 16, 2012
- Amendment 07 January 2, 2012
- Amendment 08 August 21, 2013
- Amendment 09 November 7, 2013
- Amendment 10 April 3, 2014
- Amendment 11 September 15, 2014
- Amendment 12 October 21, 2014
- Amendment 13 December 16, 2014
- Amendment 14 August 12, 2016
- Event Report 01 March 4, 2013 - patient with gall bladder surgery that was deemed not connected to study
- Event Report 02 August 13, 2013 - an allocation algorithm error was corrected.
- Event report 03 October 3, 2014 – incorrect version of consent form utilized at WRNMMC, safety and welfare of participant was not compromised.
- Event report 04 December 11, 2015 – minor protocol deviation of mode of data collection

Palmer College of Chiropractic:

- Initial Submission January 18, 2011
- Amendment 01 March 9, 2011
- Amendment 02 March 16, 2011
- Amendment 03 June 6, 2011
- Amendment 04 December 7, 2011
- Amendment 05 February 7, 2012
- Amendment 06 March 19, 2012
- Amendment 07 May 4, 2012
- Amendment 08 May 11, 2012
- Amendment 09 July 26, 2012
- Amendment 10 January 11, 2013

- Amendment 11 November 15, 2013
- System Security Verification September 10, 2013
- Amendment 12 June 4, 2014
- Event report October 1, 2014
- Amendment 13 October 22, 2014
- Amendment 14 November 14, 2014
- System Security Verification November 26, 2014
- Amendment 15 August 12, 2015
- Event report October 7, 2015
- Amendment 16 December 10, 2015
- Study Closure January 4, 2017

Second Level Review at USAMRMC:

- During this reporting period, the U.S. Army Medical Research and Materiel Command (USAMRMC), Office of Research Protections (ORP), Human Research Protection Office (HRPO) provided official correspondence acknowledging HRPO receipt of continuing reviews for WRNMMC on January 23, 2017, Palmer on December 28, 2016, RAND on November 30, 2016, and NHP (closure report) on September, 28, 2016.

Task 7: Hired and trained study coordinators for each site

- Developed standard employment contract
- Trained study personnel in standardized methods, including data entry and management
- All study coordinators trained and certified for site-specific CITI
    - All human subject's protections certifications current through reporting period

- Obtained ID badges and security approvals for all on-site study personnel
    - Badges and security approvals current through reporting period

- Conducted administrative site visits to ensure all systems are in place and fully functional. Site visits for ACT 1 during this reporting period include:
    - *WRNMMC, Bethesda, MD* – No administrative site visits conducted during this reporting period. See quality assurance section.

    - *Naval Hospital Pensacola, FL* – No administrative site visits conducted during this reporting period. Study site closed.

    - *NMCSD, San Diego, CA* – No administrative site visits conducted during this reporting period. Study site closed.

Task 8: Study recruitment and data collection per site for reporting period:

- Tables and figures below display recruitment, accrual, retention and demographics for each site in ACT 1.

**Table 1. Recruitment, Accrual and Retention through 05 Dec 2016**

| | NMCSD: San Diego | NHP: Pensacola | WRNMMC: Bethesda | Total |
|---|---|---|---|---|
| **Baseline** | | | | |
| # excluded | 7 | 9 | 8 | 24 |
| # chose not to participate | 16 | 1 | 15 | 32 |
| **Allocated** | **250** | **250** | **250** | **750** |
| | | | | |
| **Week 2 Assessment** | | | | |
| # completed | 232 | 195 | 233 | 660 |
| # missed outcomes | 17 | 52 | 15 | 84 |
| *% missed outcomes* | *7* | *21* | *6* | *11* |
| # withdrawn | 1 | 3 | 2 | 6 |
| **Week 4 Assessment** | | | | |
| # completed | 221 | 183 | 222 | 626 |
| # missed outcomes | 27 | 64 | 24 | 115 |
| *% missed outcomes* | *11* | *26* | *10* | *16* |
| # withdrawn | 1 | 0 | 2 | 3 |
| **Week 6 Assessment** | | | | |
| # completed | 237 | 208 | 238 | 683 |
| # missed outcomes | 10 | 35 | 7 | 52 |
| *% missed outcomes* | *4* | *14* | *3* | *7* |
| # withdrawn | 1 | 4 | 1 | 6 |
| **Month 3 Assessment** | | | | |
| # completed | 221 | 189 | 215 | 623 |
| # missed outcomes | 25 | 51 | 29 | 105 |
| *% missed outcomes* | *10* | *21* | *12* | *14* |
| # withdrawn | 1 | 3 | 1 | 5 |
| **# consented for long-term follow-up** | N/A | 57 | 97 | 154 |
| | | | | |
| **Month 6 Assessment** | | | | |
| # completed | N/A | 25 | 67 | 92 |
| # missed outcomes | | 30 | 28 | 58 |
| *% missed outcomes* | | *55* | *29* | *39* |
| # withdrawn | | 0 | 0 | 0 |
| **Month 9 Assessment** | | | | |
| # completed | N/A | 31 | 75 | 106 |
| # missed outcomes | | 24 | 20 | 44 |
| *% missed outcomes* | | *44* | *21* | *29* |
| # withdrawn | | 0 | 0 | 0 |
| **Month 12 Assessment** | | | | |
| # completed | N/A | 38 | 79 | 117 |
| # missed outcomes | | 17 | 16 | 33 |
| *% missed outcomes* | | *31* | *17* | *22* |
| # withdrawn | | 0 | 0 | 0 |

## *Data for Walter Reed National Military Medical Center in Bethesda, MD*

**Table 2: Demographics for Annual Report of Project DoD ACT1***

**As of Feb 14 2016**

| Questions | Values | Treatment 1 (n=125) | | Treatment 2 (n=125) | | Total (n=250) | |
|---|---|---|---|---|---|---|---|
| | | n | % | n | % | n | % |
| **Ethnic** | Hispanic or Latino | 16 | 13 | 9 | 7 | 25 | 10 |
| | Not Hispanic or Latino | 95 | 76 | 108 | 86 | 203 | 81 |
| | Unspecified | 14 | 11 | 8 | 6 | 22 | 9 |
| **Sex** | Female | 39 | 31 | 40 | 32 | 79 | 32 |
| | Male | 86 | 69 | 85 | 68 | 171 | 68 |
| **Race** | American Indian or Alaska Native | 0 | 0 | 0 | 0 | 0 | 0 |
| | Asian | 6 | 5 | 3 | 2 | 9 | 4 |
| | Native Hawaiian or Other Pacific Islander | 1 | 1 | 5 | 4 | 6 | 2 |
| | Black or African American | 41 | 33 | 42 | 34 | 83 | 33 |
| | White | 62 | 50 | 62 | 50 | 124 | 50 |
| | Multi-racial | 3 | 2 | 3 | 2 | 6 | 2 |
| | Unspecified | 12 | 10 | 10 | 8 | 22 | 9 |
| **Age** | Mean SD | 34.4 | 8.4 | 34.7 | 8.6 | 34.6 | 8.4 |
| | Median | 34.0 | | 35.0 | | 35.0 | |
| | n | 125 | | 125 | | 250 | |

* this table is for **Walter Reed National Military Medical Center in Bethesda**

percentages may not add up to 100 due to rounding

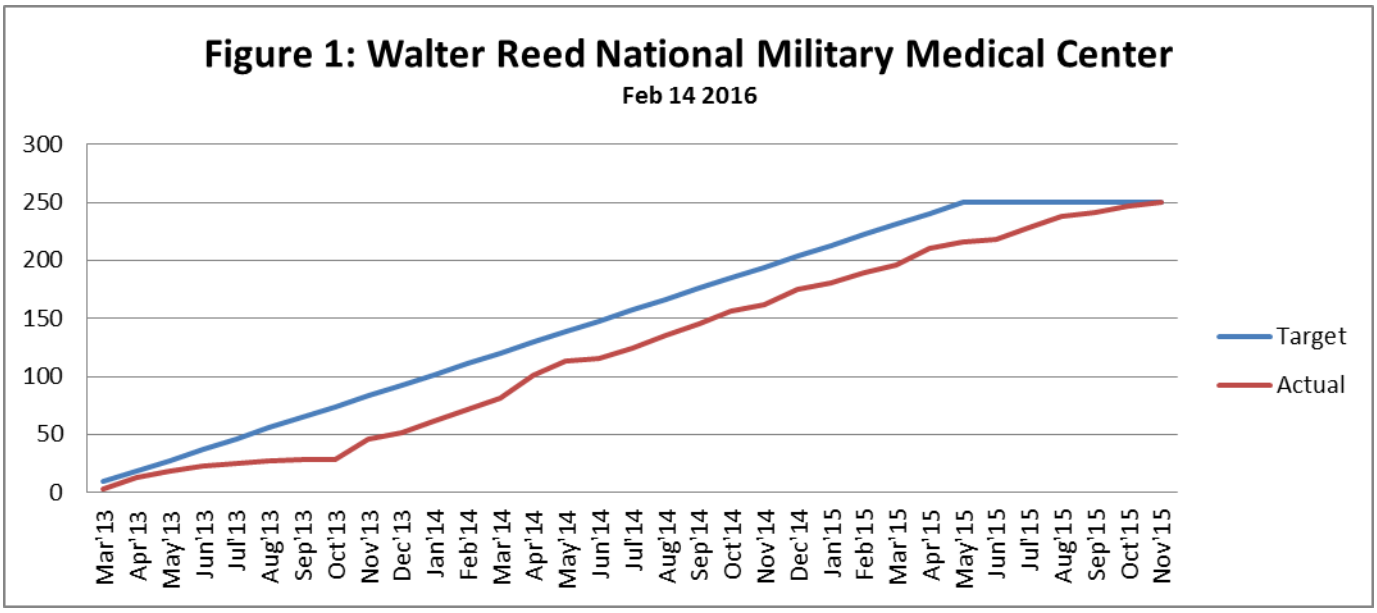
Figure 1: Walter Reed National Military Medical Center
Feb 14 2016
300
250
200
150
100
50
0
Mar'13
Apr'13
May'13
Jun'13
Jul'13
Aug'13
Sep'13
Oct'13
Nov'13
Dec'13
Jan'14
Feb'14
Mar'14
Apr'14
May'14
Jun'14
Jul'14
Aug'14
Sep'14
Oct'14
Nov'14
Dec'14
Jan'15
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May'15
Jun'15
Jul'15
Aug'15
Sep'15
Oct'15
Nov'15
Target
Actual

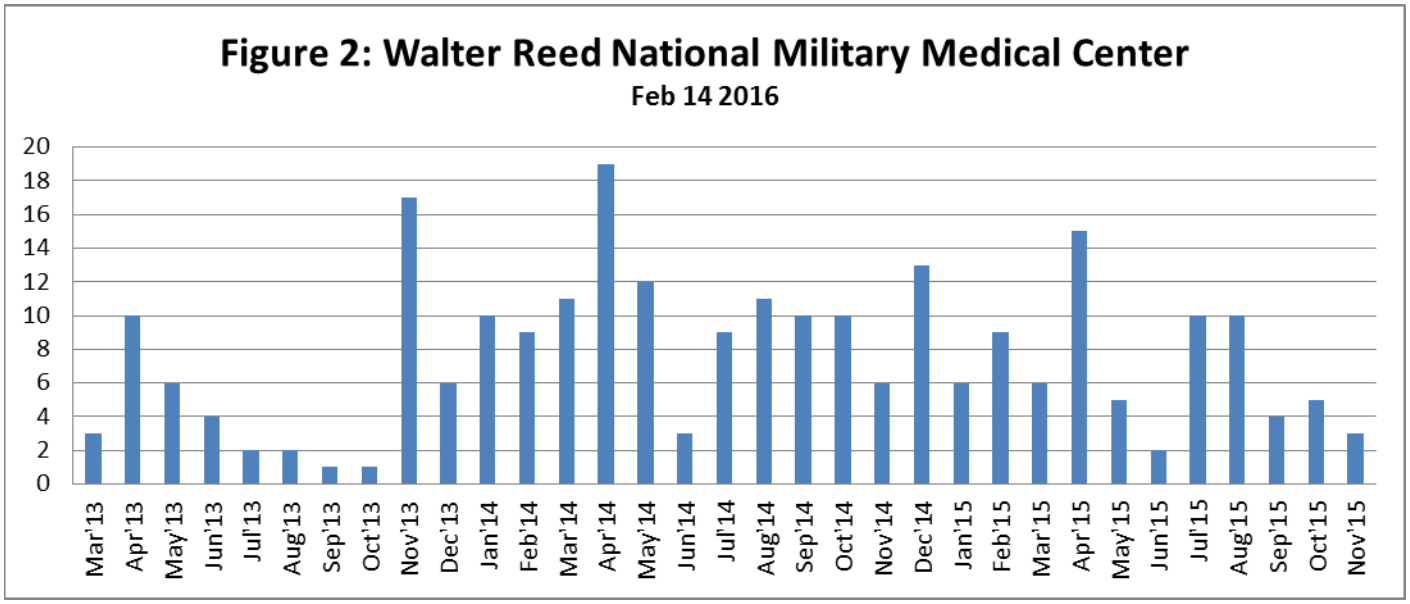
Figure 2: Walter Reed National Military Medical Center
Feb 14 2016
20
18
16
14
12
10
8
6
4
2
0
Mar'13
Apr'13
May'13
Jun'13
Jul'13
Aug'13
Sep'13
Oct'13
Nov'13
Dec'13
Jan'14
Feb'14
Mar'14
Apr'14
May'14
Jun'14
Jul'14
Aug'14
Sep'14
Oct'14
Nov'14
Dec'14
Jan'15
Feb'15
Mar'15
Apr'15
May'15
Jun'15
Jul'15
Aug'15
Sep'15
Oct'15
Nov'15

## *Data for Naval Hospital Pensacola*

**Table 3: Demographics for Annual Report of Project DoD ACT1***

**As of Feb 14 2016**

| Questions | Values | Treatment 1 (n=125) | | Treatment 2 (n=125) | | Total (n=250) | |
|---|---|---|---|---|---|---|---|
| | | n | % | n | % | n | % |
| **Ethnic** | Hispanic or Latino | 29 | 23 | 12 | 10 | 41 | 16 |
| | Not Hispanic or Latino | 94 | 75 | 112 | 90 | 206 | 82 |
| | Unspecified | 2 | 2 | 1 | 0.8 | 3 | 1 |
| **Sex** | Female | 19 | 15 | 18 | 14 | 37 | 15 |
| | Male | 106 | 85 | 107 | 86 | 213 | 85 |
| **Race** | American Indian or Alaska Native | 0 | 0 | 0 | 0 | 0 | 0 |
| | Asian | 3 | 2 | 1 | 1 | 4 | 2 |
| | Native Hawaiian or Other Pacific Islander | 0 | 0 | 0 | 0 | 0 | 0 |
| | Black or African American | 17 | 14 | 15 | 12 | 32 | 13 |
| | White | 102 | 82 | 106 | 85 | 208 | 83 |
| | Multi-racial | 1 | 1 | 0 | 0 | 1 | 0 |
| | Unspecified | 2 | 2 | 3 | 2 | 5 | 2 |
| **Age** | Mean SD | 25.5 | 7.9 | 25.7 | 7.5 | 25.6 | 7.7 |
| | Median | 22.0 | | 23.0 | | 23.0 | |
| | n | 125 | | 125 | | 250 | |

* this table is for **Naval Hospital in Pensacola**

percentages may not add up to 100 due to rounding

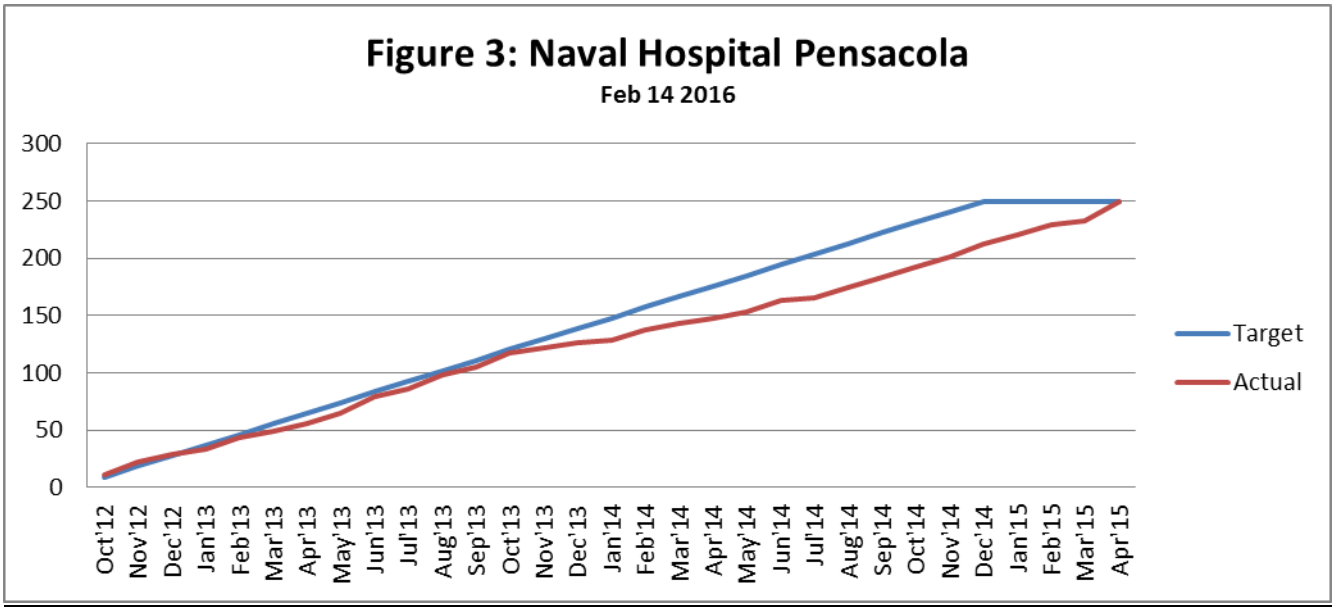
Figure 3: Naval Hospital Pensacola
Feb 14 2016
300
250
200
150
100
50
0
Oct'12
Nov'12
Dec'12
Jan'13
Feb'13
Mar'13
Apr'13
May'13
Jun'13
Jul'13
Aug'13
Sep'13
Oct'13
Nov'13
Dec'13
Jan'14
Feb'14
Mar'14
Apr'14
May'14
Jun'14
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Oct'14
Nov'14
Dec'14
Jan'15
Feb'15
Mar'15
Apr'15
Target
Actual

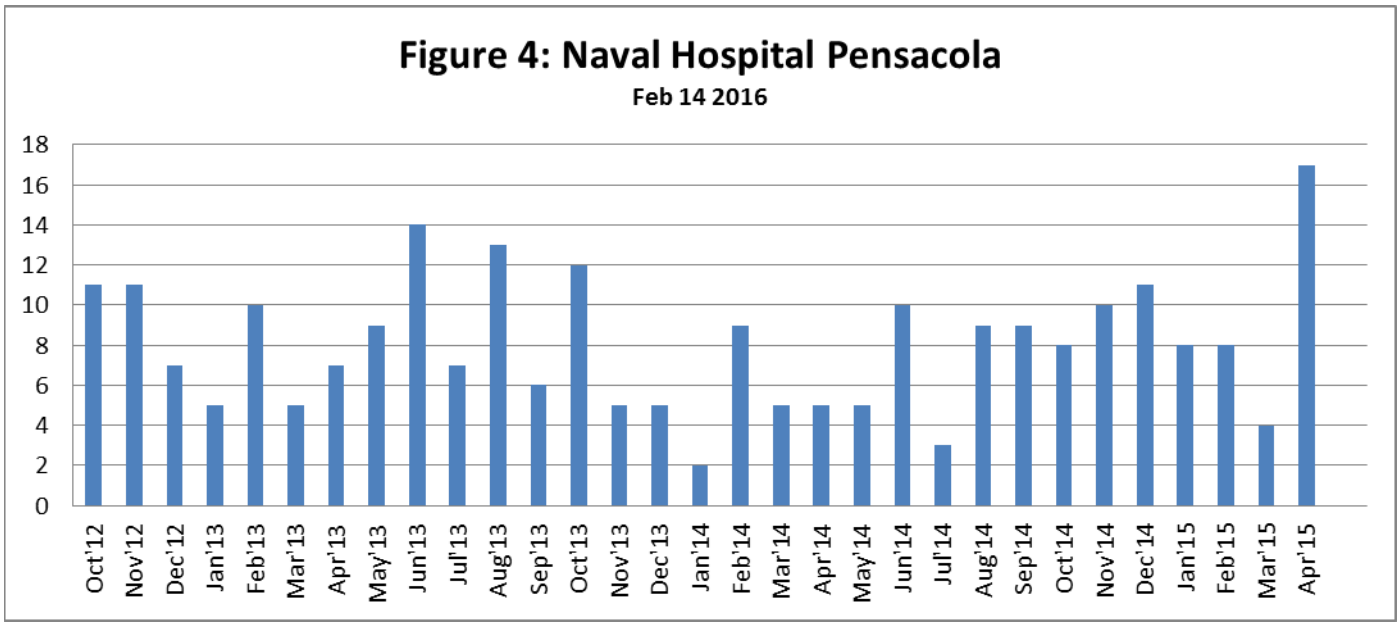


Figure 4: Naval Hospital Pensacola
Feb 14 2016
18
16
14
12
10
8
6
4
2
0
Oct'12
Nov'12
Dec'12
Jan'13
Feb'13
Mar'13
Apr'13
May'13
Jun'13
Jul'13
Aug'13
Sep'13
Oct'13
Nov'13
Dec'13
Jan'14
Feb'14
Mar'14
Apr'14
May'14
Jun'14
Jul'14
Aug'14
Sep'14
Oct'14
Nov'14
Dec'14
Jan'15
Feb'15
Mar'15
Apr'15

## *Data for Naval Medical Center San Diego, CA*

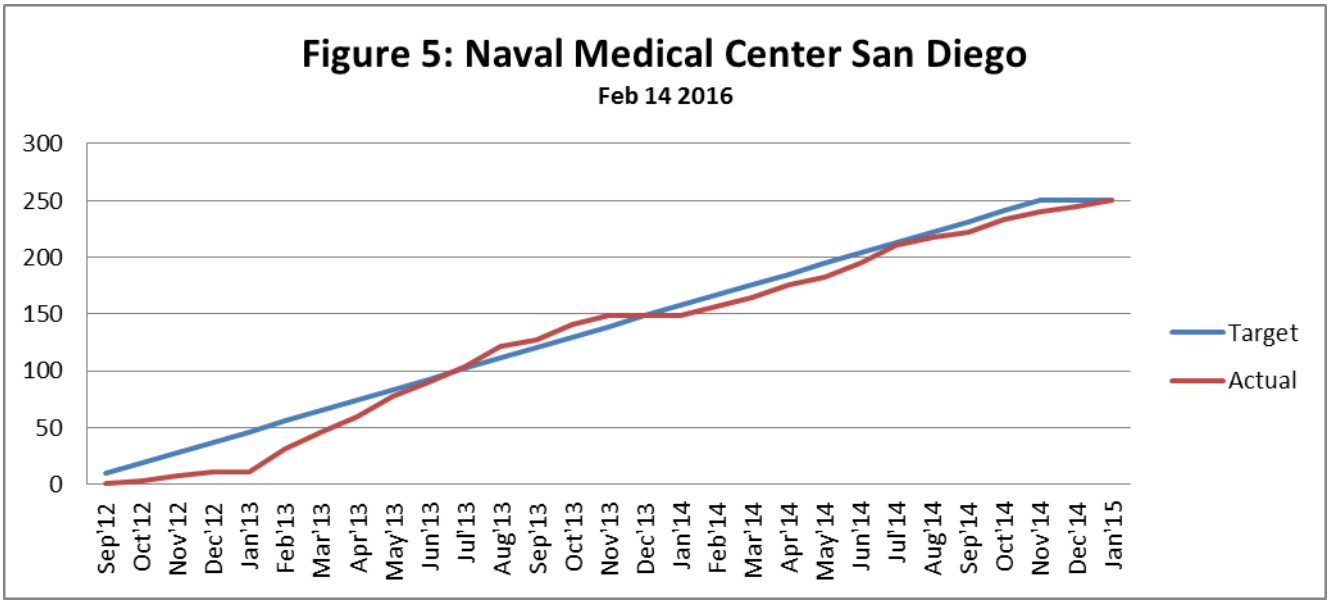
**Table 4: Demographics for Annual Report of Project DoD ACT1***

**As of Feb 14 2016**

| Questions | Values | Treatment 1 (n=125) | | Treatment 2 (n=125) | | Total (n=250) | |
|---|---|---|---|---|---|---|---|
| | | n | % | n | % | n | % |
| **Ethnic** | Hispanic or Latino | 21 | 17 | 31 | 25 | 52 | 21 |
| | Not Hispanic or Latino | 97 | 78 | 80 | 64 | 177 | 71 |
| | Unspecified | 7 | 6 | 14 | 11 | 21 | 8 |
| **Sex** | Female | 30 | 24 | 29 | 23 | 59 | 24 |
| | Male | 95 | 76 | 96 | 77 | 191 | 76 |
| **Race** | American Indian or Alaska Native | 2 | 2 | 0 | 0 | 2 | 1 |
| | Asian | 11 | 9 | 6 | 5 | 17 | 7 |
| | Native Hawaiian or Other Pacific Islander | 1 | 1 | 2 | 2 | 3 | 1 |
| | Black or African American | 14 | 11 | 20 | 16 | 34 | 14 |
| | White | 88 | 70 | 87 | 70 | 175 | 70 |
| | Multi-racial | 4 | 3 | 3 | 2 | 7 | 3 |
| | Unspecified | 5 | 4 | 7 | 6 | 12 | 5 |
| **Age** | Mean SD | 32.4 | 7.4 | 32.4 | 7.5 | 32.4 | 7.4 |
| | Median | 31.0 | | 32.0 | | 31.5 | |
| | n | 125 | | 125 | | 250 | |

* this table is for **Naval Medical Center in San Diego**

percentages may not add up to 100 due to rounding



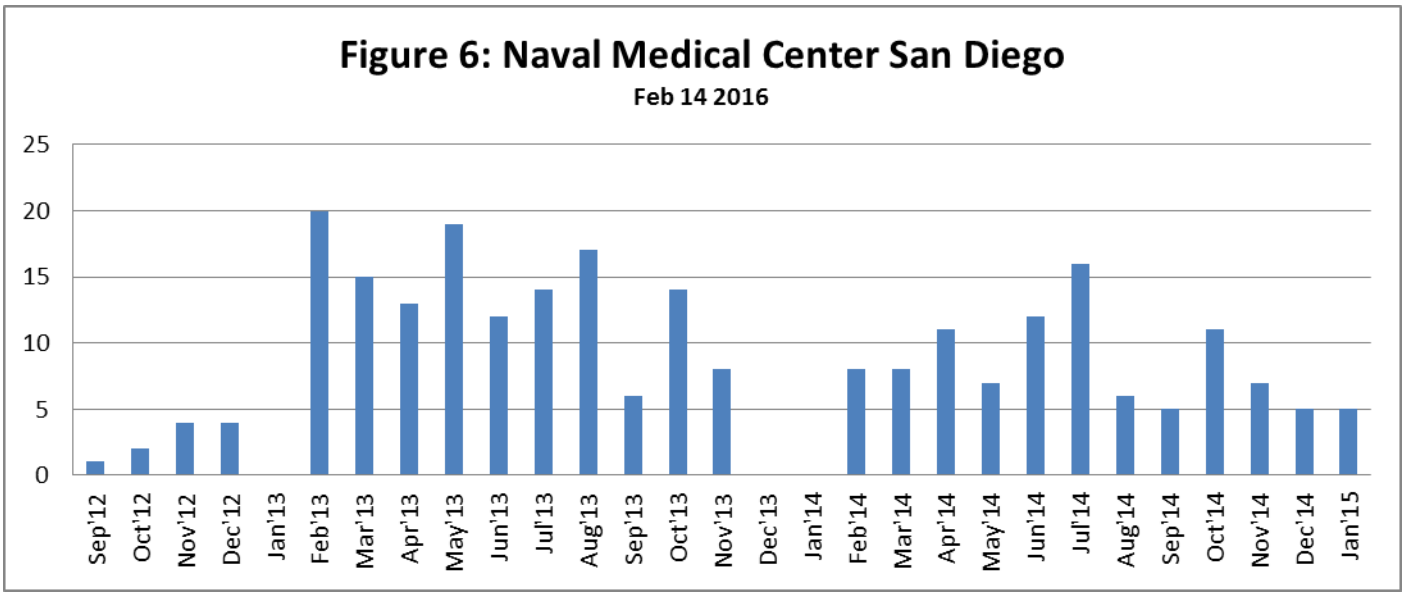



**Table 5. Recruitment Summary Table**

| | Time Period | | | | | |
|---|---|---|---|---|---|---|
| | 2/15/2013 to 2/14/2014 | | 2/15/2014 to 2/14/2015 | | 2/15/2015 to 2/14/2016 | |
| Site | # enrolled | Avg # per mth | # enrolled | Avg # per mth | # enrolled | Avg # per mth |
| WRNMMC | 67 | 5.6 | 119 | 9.9 | 64 | 5.3 |
| NHP | 94 | 7.8 | 96 | 8.0 | 22 | 1.8 |
| NMCSD | 129 | 10.8 | 96 | 8.0 | 0 | 0.0 |

Task 9: Quality assurance site visits conducted during this period included:

- Walter Reed National Military Medical Center in Bethesda, MD
    - *October 26, 2016* - Lead Project Manager, Julie Hartman, visited the site for a WRNMMC IRB initiated Quality Assurance Visit October 26, 2016. The visit included a review of the regulatory binder and storage of informed consent documents. Lead Project manager met with Site PI, LTC Keith Meyers and Ms. Barbara Bloomquist, WRNMMC Post Approval Compliance Monitor. Suggestions were given and responded to regarding organization and filing in regulatory binders. Ms. Bloomquist approved the submitted corrective action plan and no further actions were required or recommended.

- Naval Hospital Pensacola, FL
    - *No quality assurance site visits conducted during this reporting period. See administrative site visits section.*

- Naval Medical Center San Diego, CA

  *No quality assurance site visits conducted during this reporting period. See administrative site visits section.*

Task 10: Write methodology manuscript for submission

- ACT I methodology manuscript was published in *Trials*, http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4746780/

Task 11: Submit annual continuing review documents for IRB. The following IRB continuing reviews have been processed on these dates:

- Walter Reed National Military Medical Center in Bethesda, MD was due for continuing review on October 23, 2016. A lapse in IBR approval occurred, and was reported to all study IRBs. No participant activities occurred during this time. Continuing review approval was received on November 17, 2016 and will expire on November 16, 2017.
    - Continuing review approval documents were submitted to MRMC for WRNMMC (per MRMC request) on November 8, 2016. MRMC HRPO acknowledged receipt of the current continuing review documents for WRNMMC on January 23, 2017.
- Naval Hospital Pensacola, FL was granted approval for completion of protocol June 6, 2016.
    - HRPO closure documents were approved September 20, 2016.
- Naval Medical Center San Diego, CA was granted approval for completion of protocol August 19, 2015.
    - HRPO closure documents were approved February 9, 2016.
- RAND Corporation gained continuing review approvals
    - January 31, 2012, December 18, 2012, November 20, 2013, November 6, 2014, and for this reporting period: November 5, 2015, October 11, 2016.
    - MRMC HRPO acknowledged receipt of continuing review documents from RAND Corporation on December 14, 2015, December 28, 2016.
- Palmer College was granted approval for completion of protocol January 4, 2017.
    - Continuing review approval documents were submitted to MRMC for Palmer (per MRMC request) on January 14, 2016. MRMC HRPO acknowledged receipt of the current continuing review documents for WRNMMC on March 01, 2016.
    - Continuing review approval documents were submitted to MRMC for Palmer (per MRMC request) on December 13, 2016. MRMC HRPO acknowledged receipt of the current continuing review documents for WRNMMC on December 28, 2016.

Task 12: Convene advisory board at yearly intervals and as needed (Annually)

- Created advisory panel and kick off meeting May 3, 2011.
- Convened advisory panel on May 1, 2012, March 17, 2014, and August 10, 2015.
- Plans to convene another advisory panel meeting were postponed this reporting period due to waiting for the notification of the no cost extension which we received on February 15, 2017.

Task 13: Close study recruitment

- NMCSD completed study recruitment on January 27, 2015 after meeting target goals.
- NHP completed study recruitment on April 22, 2015 after meeting target goals.
- WRNMMC completed study recruitment on November 20, 2015 after meeting target goals.

Task 14: Analyze data

- The Publications Committee approved the proposal and outline for a contextual evaluation paper to be written for peer-reviewed publication. The manuscript is in draft mode at this time.

Task 15: Write final study reports and manuscript

- ACT 1 protocol paper published http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4746780/
- ACT 1 primary results paper in draft.

Task 16: Convene publications committee at Month 18 and as needed thereafter

- Recruited Publications Committee and initial meeting convened June 18, 2015
- Developed and approved charter and publication proposal form
- Convened publications quarterly: November 10, 2015, February 8, 2016, May 10, 2016, July 12, 2016, September 13, 2016.

***Clinical Trial A (ACT 1) Summary of Tobacco Cessation Trial***

The aim of this nested trial within Trial A is to measure changes in smoking and tobacco behavior between two treatment groups, in response to a tobacco cessation program delivered in the chiropractic arm of the study. Investigation of a smoking cessation program delivered by doctors of chiropractic will be imbedded in the low back pain trial. Those who wish to participate in the low back pain study but not the smoking cessation program will be allowed into the study.

Task 1: Finalized manual and other program materials
(Completed prior to this reporting period)

Task 2: Train chiropractors to deliver program in standardized fashion (Months 6-12) Palmer
(Completed prior to this reporting period)

Task 3: Finalized outcome parameters for tobacco cessation, loaded onto system
(Completed prior to this reporting period)

Task 4: Data Collection underway as follows:

**Table 6: Tobacco Enrollment Report**

| | Tobacco User | Consented | Enrolled | Withdrawn |
|---|---|---|---|---|
| Walter Reed National Military Medical Center | 24 | 14 | 8 | 1 |
| Naval Hospital Pensacola | 49 | 40 | 16 | 2 |
| Naval Medical Center San Diego | 52 | 28 | 11 | 1 |

Task 5: Data Analysis (Not applicable during this reporting period)

***Clinical Trial B (ACT 2) Summary***

The Assessment of Chiropractic Treatment using reaction and response times in members of the Special Operation Forces (ACT 2) is a randomized controlled trial designed to evaluate changes in reaction and response times following chiropractic treatment compared to controls in the Special Forces population.

During this reporting period, the ACT 2 protocol was amended to broaden our eligibility criteria to include soldiers from the 160th Special Operations Aviation Regimen (SOAR) (Night Stalkers) and eliminate the upper limit age restriction. The operational tempo of the 5th group Special Forces Qualified (SFQ) unit at Ft. Campbell is quite high and many soldiers in the 5th group are not on post. By including the approximately 1000 flight status members (pilots/crew) in 160th SOAR regiment we are confident we will accomplish our recruitment goals and have recruited 89/120 participants to date.

Personnel changes during this reporting period:

- Darla Freehart, BS, LPN, CCPR, completed her duties as Site PM on June 26, 2016.

Task 1: Make final selection of Special Forces site(s)

- Blanchfield Army Community Hospital, Fort Campbell, KY was identified as the single site for ACT 2.

Task 2: Finalized metrics for response and reaction times

- The protocols for the 5 different reaction time tests as well as the data collection forms were revised and finalized during a previous reporting period.
- Procedures for secure data transfer were finalized in previous reporting period.

Task 3: IRB approval process

- Worked through sequences of IRB approvals, including local military scientific and IRB reviews, RAND, Palmer College, and second level Human Research Protection Office (HRPO) approvals. As follows:

- Dwight D. Eisenhower Army Medical Center (Fort Campbell's IRB of record)
    - Initial submission — December 12, 2013 (contingent approval)
      Final approval received May 13, 2014
    - Amendment 01 — May 16, 2014
    - Amendment 02 — August 13, 2014
    - Amendment 03 — September 9, 2014
    - Continuing review — November 13, 2014
    - Amendment 04 — September 12, 2015
    - Continuing review — November 20, 2015
    - Closure report — September 26, 2016

- RAND Corporation
    - Initial submission December 6, 2012
    - Continuing reviews approved: May 31, 2013, May 19, 2014, May 8, 2015, April 11, 2016
    - Amendment 01 May 10, 2012 (Pilot approval)
    - Continuing review May 31, 2013
    - Amendment 02 August 21, 2013
    - Amendment 03 February 14, 2014 (re-design approved)
    - Amendment 04 June 9, 2014
    - Amendment 05 August 18, 2014
    - Amendment 06 September 15, 2014
    - Amendment 07 September 23, 2015
    - Protocol exception July 28, 2015 (Exception to increase age inclusion (currently 18-45) to allow 46 year old to participate in study.)

- Palmer College (Military study)
    - Initial submission February 2, 2012
    - Amendment 01 May 1, 2012
    - Amendment 02 June 14, 2012
    - Amendment 03 January 9, 2013
    - Continuing Review 01 January 23, 2013
    - Continuing Review 02 January 24, 2014
    - Amendment 04 June 9, 2014
    - Amendment 05 August 6, 2014
    - Amendment 06 August 18, 2014
    - Continuing review 03 December 8, 2014
    - Amendment 07 August 15, 2015
    - Amendment 08 September 22, 2015
    - Continuing review 04 November 30, 2015
    - Closure report October 10, 2016

- USAMRMC: The ACT 2 protocol received HRPO and CIRO approval on May 2, 2014. The CRADA was executed on May 15, 2014.
    - MRMC HRPO closure documents for Ft. Campbell (DDEAMC) were received on November 7, 2016.
    - Continuing review for Palmer was sent to MRMC HRPO on January 16, 2016 with acknowledgement received from MRMC April 26, 2016. Study closure for Palmer was accepted December 8, 2016.
- The ACT 2 protocol was selected for an audit during the Army Human Research Protections Office (HRPO) assessment. The audit took place via conference call on February 12, 2016 and was attended by site PI, Dr. Tom Jones, site PM, Ms. Darla Freehardt, and lead PM Dr. Julie Hartman. Auditors had no immediate concerns or recommendations for improvement regarding this study. Formal report cited no required or recommended follow-up action.

Task 4: Study recruitment and data collection

- Completed pilot study (previous reporting period)
- Launched main study September, 2014 at Blanchfield Army Community Hospital, Ft. Campbell, KY.
- Opened study enrollment to include pilots/crew from the 160th SOAR (Night Stalkers) September 2015.
- Completed study recruitment June, 2016.

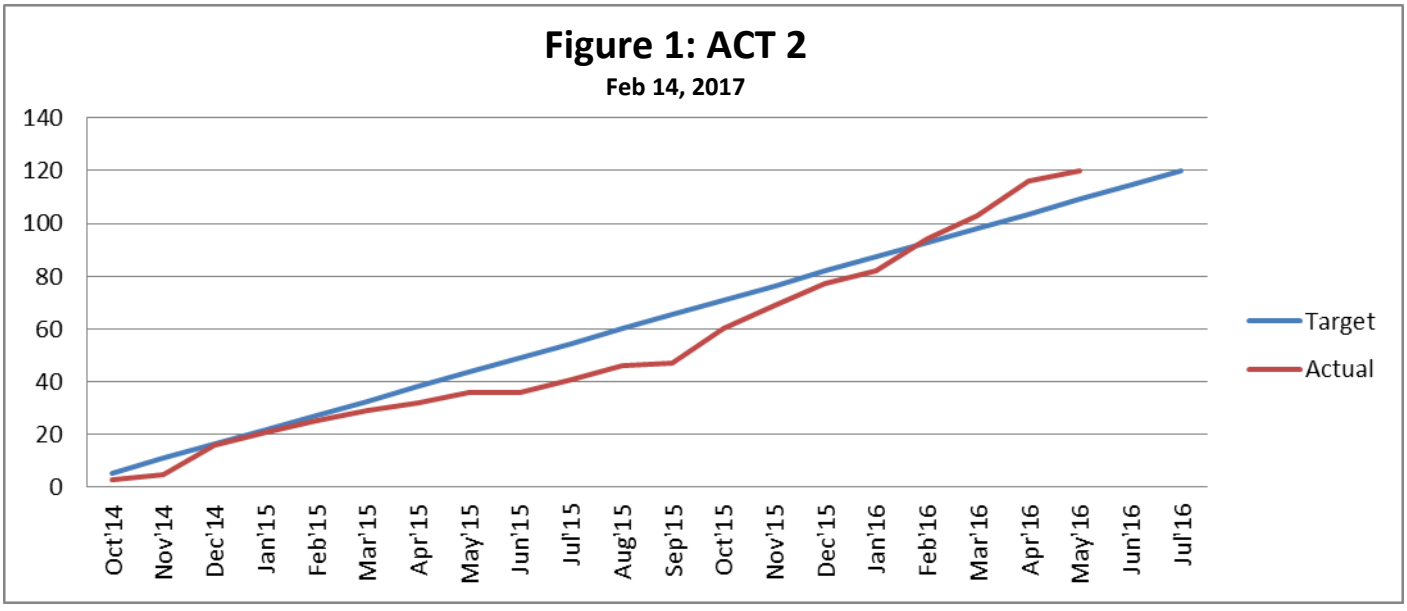
### *Data for Ft. Campbell, KY*

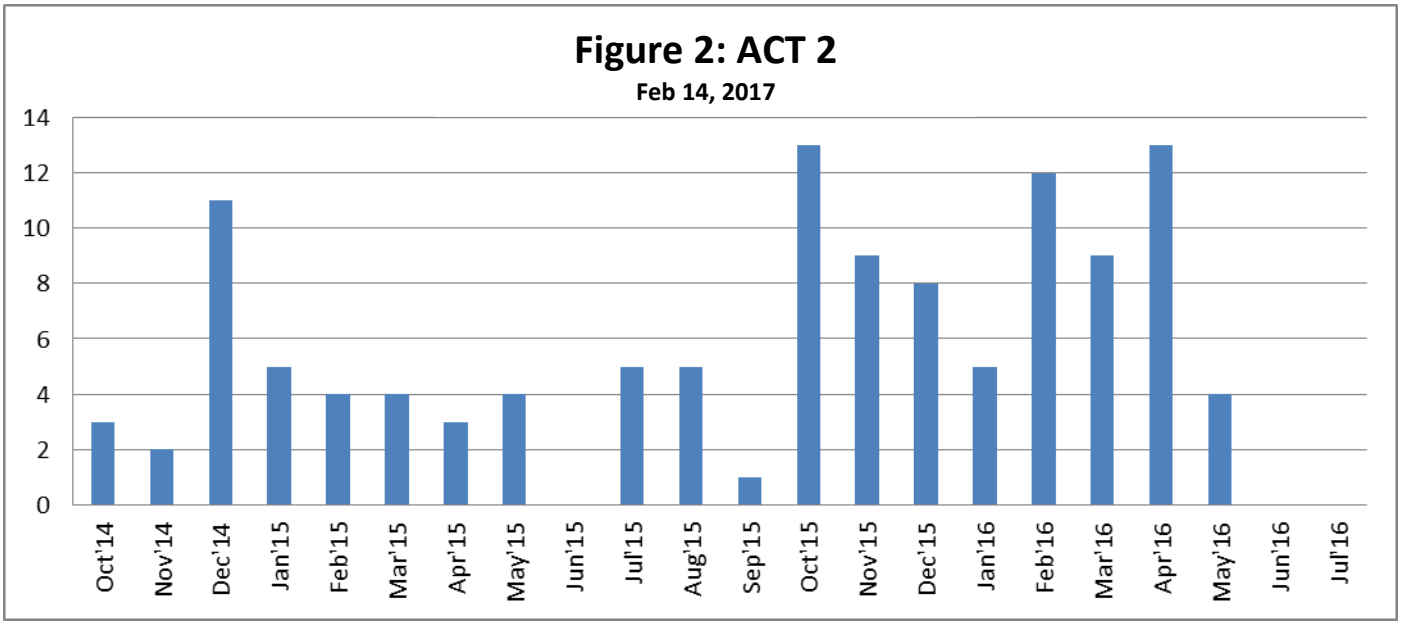
**Table 1. Recruitment, Accrual and Retention through 30 Sep 2016**

| | Total |
|---|---|
| **Screening** | |
| # Total screened | 175 |
| # Total excluded | 54 |
| **Baseline** | 121 |
| Excluded | 1 |
| **Allocated** | 120 |
| **Completed** | 117 |
| Lost to follow-up | 3 |

**Table 2. Participant Demographics through 30 Sep 2016**

| | | Treatment 1 (n=60) | | Treatment 2 (n=60) | | Total (n=120) | |
|---|---|---|---|---|---|---|---|
| | | n | % | n | % | n | % |
| **Ethnicity** | Hispanic or Latino | 5 | 8 | 3 | 5 | 8 | 7 |
| | Not Hispanic or Latino | 50 | 83 | 51 | 85 | 101 | 84 |
| | Unspecified | 5 | 8 | 6 | 10 | 11 | 9 |
| **Sex** | Female | 0 | 0 | 0 | 0 | 0 | 0 |
| | Male | 60 | 100 | 60 | 100 | 120 | 100 |
| **Race** | American Indian or Alaska Native | 0 | 0 | 0 | 0 | 0 | 0 |
| | Asian | 1 | 2 | 0 | 0 | 1 | 1 |
| | Native Hawaiian or Other Pacific Islander | 1 | 2 | 0 | 0 | 1 | 1 |
| | Black or African American | 3 | 5 | 2 | 3 | 5 | 4 |
| | White | 54 | 90 | 55 | 92 | 109 | 91 |
| | Multi-racial | 0 | 0 | 1 | 2 | 1 | 1 |
| | Unspecified | 1 | 2 | 2 | 3 | 3 | 3 |
| **Age** | Mean SD | 32.8 | 5.1 | 33.2 | 6.1 | 33.0 | 5.6 |
| | Median | 32.0 | | 31.5 | | 32.0 | |






Task 5: Quality assurance site visits

- *Blanchfield Army Community Hospital, Ft. Campbell, KY – February 29-March 1, 2016*
    - Lead Project Manager, Julie Hartman, conducted an internal quality assurance review February 29-March 1, 2016. All regulatory documents were reviewed and source documents were verified. During this visit, Lead PM met with site PI Dr. Thomas Jones and site PM Darla Freehart and discussed recruitment and study status.

- *Blanchfield Army Community Hospital, Ft. Campbell, KY – June 20-21, 2016*
    - Lead Project Manager, Julie Hartman, conducted an internal quality assurance review and site closure June 20-21, 2016. All regulatory documents were reviewed and source documents were verified. During this visit, Lead PM met with site PI Dr. Thomas Jones and site PM Darla Freehart and discussed study closure procedures. Dr. James DeVocht, study Co-Investigator, arrived June 21, 2016 to disassemble testing equipment and assist with site closure processes.

Task 6: Analyze pre-post data (Not applicable during this reporting period)

Task 7: Write final study reports and manuscript

- ACT 2 protocol paper published https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5029007/
- ACT 2 primary results paper in draft.

***Clinical Trial C (ACT 3) Summary***

The ACT 3 pilot study, designed to refine the strength and balance testing procedures in participants with low back pain, launched at the Palmer Center for Chiropractic Research April 30, 2014. A total of 15 participants were enrolled in this study. Since the goals of this pilot study were

accomplished prior to enrolling 20 participants (original study goal), the investigators closed this study in December, 2014. This feasibility study allowed us to finalize protocols for the strength and balance testing, ensure integrity of data collection software, and evaluate the safety of implementing these protocols.

Military study regulatory updates: During this reporting period, full military IRB approval was granted through the Portsmouth IRB April 6, 2016. Amendments were submitted to add a research administrator and statistician to the team and make slight alterations to study documents. The site PI was deployed in May 2016, and a new site PI was recruited and added to the project in June 2016. A compliance review was conducted in June 2016, and findings/actions to be taken were minimal and carried out per reviewing officer's request. The PI deployment caused a protocol deviation; study activities needed to be placed on hold, therefore, we finalized the active participants and collected the data we could at that time. Another protocol deviation was submitted after 2 participants' final study visits did not occur within the 35 day window specified. This was due to the fact that one was on vacation and the other was assigned to temporary additional duty. A third deviation occurred following the death of the study clinician on October 26, 2016. The participant was allocated just as the chiropractor fell ill, and the participant was not able to receive treatment. As a new clinician is in the hiring and credentialing process, study activities are currently on hold and will resume once the chiropractor is in position.

Personnel changes during this reporting period:

- Bridget Kane, MS, CCRC completed her duties as Project Consultant February, 2016.
- Shirley Callan assumed the role of associate investigator May, 2016.
- Qian Li, MS assumed the role of associate investigator May, 2016.
- Bruce Matchin, DO assumed the role of site PI, June 1016.
- Greg Lillie, DC was deceased and left the role of study clinician vacant, October 2016.

Task 1: Established metrics for strength, balance, re-injury

- Tested and refined programs and procedures for evaluating strength and balance during the pilot phase of the study
- Moved the long-term follow up assessments to ACT 1 (re-injury)

Task 2: IRB approval process

- Worked through sequences of IRB approvals, including local military scientific and IRB reviews, RAND, Palmer College, and second level Human Research Protection Office (HRPO) approvals. As follows:

- Madigan Army Medical Center IRB: (not applicable during this reporting period; no longer applicable)

- RAND Corporation:
    - Pilot approval March 19, 2013
    - Main study approval October 1, 2013
    - Continuing review approvals: February 14, 2014, February 13, 2015, February 11, 2016, February 3, 2017.
    - Amendment 01 June 3, 2013
    - Amendment 02 November 15, 2013
    - Amendment 03 December 5, 2013

- Amendment 04 March 7, 2014 withdrawn
- Amendment 05 April 4, 2014
- Amendment 06 September 22, 2014
- Amendment 07 July 22, 2015
- Amendment 08 November 13, 2015
- Amendment 09 April 22, 2016
- Event report July 26, 2016 (protocol deviation; military site PI deployed so study activity was required to halt, which denied two participants promised chiro visits.)

- Palmer College

  - Main study ** *Per the direction of the Palmer College IRB, since there have been multiple changes to the military study including site and study design, we will be submitting an entirely new protocol and closing out the study protocol listed below.*
    - Initial approval August 17, 2012
    - Amendment 01 January 10, 2013
    - Continuing review l August 19, 2013
    - Continuing review July 23, 2014
    - New protocol approval September 1, 2015
    - Amendment 01 October 21, 2015
    - Amendment 02 April 21, 2016
    - Continuing review April 21, 2016
    - Protocol Deviation 01 August 31, 2016
    - Protocol Deviation 02 November 16, 2016
    - Protocol Deviation 03 N/A; IRB recommended no further action

  - Pilot study
    - Initial approval January 11, 2013
    - Amendment 01 May 10, 2013
    - Amendment 02 June 24, 2013
    - Amendment 03 July 10, 2013
    - Amendment 04 October 7, 2013
    - Continuing review January 16, 2014
    - Amendment 05 April 2, 2014
    - Amendment 06 September 8, 2014
    - Study close out December 19, 2014

- Naval Hospital Pensacola, FL (IRB of record: Naval Medical Center Portsmouth)
    - Initial approval June 10, 2015
    - Amendment 01 September 8, 2015
    - Amendment 02 October 14, 2015
    - Amendment 03 May 27, 2016
    - Continuing review May 27, 2016
    - Amendment 04 June 22, 2016
    - Amendment 05 August 16, 2016

- Protocol Deviation 01 August 16, 2016
- Protocol Deviation 02 October 25, 2016
- Protocol Deviation 03 January 11, 2017

- Second level review at USAMRMC: As of initial study approval, Naval Medical Center Portsmouth IRB first informed the ACT team that the study did not require a HRPO review because the NMCP IRB only completes HRPO reports for protocols where CID funded contractors are conducting human subjects research. Upon further inquiry, our Science Officer at CDMRP/USAMRMC contacted HRPO and they recommended we proceed with HRPO review. We submitted all documentation on January 10, 2017 and as of February 15, 2017 the review is in process.

Task 3: Prepared data collection system:

- Updated web-based functional assessments and questionnaires
- Updated paper and web-based data collection forms

Task 4: Consulted advisory panel on validity/relevance of selected outcomes measures: Addressed issues with advisory panel last reporting period during convened panel on May 1, 2012.

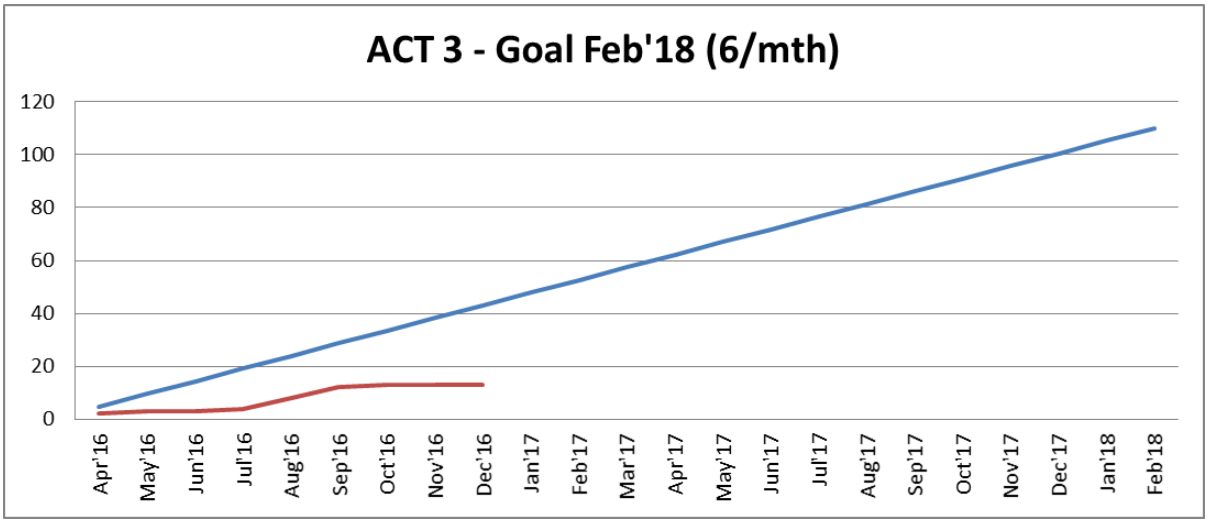
Task 5: Recruit and enroll subjects and collect data: Tables and figures below display recruitment, accrual, retention and demographics for ACT 3.

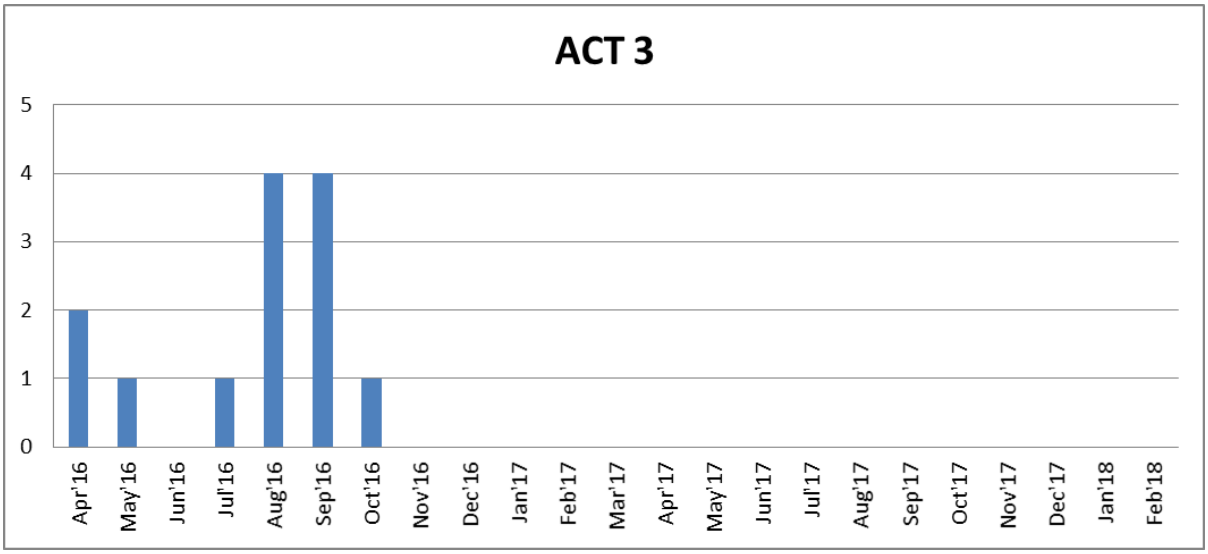
**Table 1. Recruitment, Accrual and Retention through 05 Dec 2016**

| | Total |
|---|---|
| **Screening** | |
| # Total screened | 35 |
| # Total excluded | 12 |
| **Baseline** | |
| # Total screened | 23 |
| # Total excluded | 10 |
| **Allocated** | 13 |
| **Completed** | 13 |
| Lost to follow-up | 0 |

**Table 5. Participant Demographics through 05 Dec 2016**

| | | Treatment 1 (n=7) | | Treatment 2 (n=6) | | Total (n=13) | |
|---|---|---|---|---|---|---|---|
| | | n | % | n | % | n | % |
| **Ethnicity** | Hispanic or Latino | 2 | 29 | 4 | 67 | 6 | 46 |
| | Not Hispanic or Latino | 5 | 71 | 2 | 33 | 7 | 54 |
| | Unspecified | | | | | | |
| **Sex** | Female | 1 | 14 | 0 | 0 | 1 | 8 |
| | Male | 6 | 86 | 6 | 100 | 12 | 92 |
| **Race** | American Indian or Alaska Native | 0 | 0 | 0 | 0 | 0 | 0 |
| | Asian | 0 | 0 | 0 | 0 | 0 | 0 |
| | Native Hawaiian or Other Pacific Islander | 0 | 0 | 0 | 0 | 0 | 0 |
| | Black or African American | 2 | 29 | 0 | 0 | 2 | 15 |
| | White | 4 | 57 | 4 | 67 | 8 | 62 |
| | Multi-racial | 0 | 0 | 1 | 17 | 1 | 8 |
| | Unspecified | 1 | 14 | 1 | 17 | 2 | 15 |
| **Age** | Mean SD | 30.7 | 6.5 | 27.8 | 9.7 | 29.4 | 7.9 |
| | Median | 31.0 | | 26.0 | | 31.0 | |






Task 6: Quality assurance site visiting and training

- Staff training
    - *August 3-14, 2015* – The new ACT 3 lead PM, Amy Minkalis, started on August 3, 2015 at the Palmer Center for Chiropractic Research, Davenport, IA. The lead PM was oriented and trained by outgoing lead PM, Bridget Kane. Ms. Kane then transitioned to the role of project consultant.
    - *September 28-October 9, 2015* – Crystal Franklin was hired as the ACT 3 on-site Clinical Project Manager for Naval Hospital Pensacola and started September 28, 2015. She was oriented to the protocol and trained at the PCCR in Davenport, IA by lead PM Amy Minkalis and research clinic staff.
- Study logistics
    - *February 24*-25, 2015 – Lead PM, Bridget Kane and Associate Investigator Dr. Robert Vining conducted a site visit to Naval Hospital Pensacola to meet with military site PI, CDR Joseph Penta and study DC, Dr. Greg Lillie, to review study logistics prior to protocol IRB submission. Lead PM also met with OIC and Senior Medical Officer of branch clinics to obtain support statements for the ACT 3 study.
    - *October 19-23, 2015* - Lead PM, Amy Minkalis, conducted a site visit with Associate Investigators Dr. Robert Vining and Dr. James Boysen. Visit activities included equipment assembly and testing as well as additional training for site project manager, study doctor of chiropractic and chiropractic assistant.
    - September 26-28, 2016 – Lead PM, Amy Minkalis, conducted a site visit and internal audit for quality. All participant records and data were reviewed and verified.

Task 7: Analyze data and write final study reports

- Evaluated feasibility and safety of functional testing protocols of following completion of pilot study.

**KEY RESEARCH ACCOMPLISHMENTS ACROSS ALL STUDIES:**

Key research accomplishments are as follows:

ACT 1:

- Achieved 100% of ACT 1 trial recruitment (N=750)
- Completed study recruitment at NMCSD, NHP, WRNMMC
- Completed contextual component of ACT 1 protocol
- Completed long-term follow up assessments at NHP and WRNMMC
- Published ACT 1 protocol manuscript

ACT 2:

- Expanded recruitment to broader Special Operation Forces with command support
- Achieved 100% (N=120) of recruitment goal
- Published ACT 2 protocol manuscript

ACT 3:

- Launched full study at the Naval Hospital Pensacola
- Recruited and initiated new site PI

**REPORTABLE OUTCOMES ACROSS ALL STUDIES:**

Not applicable during this reporting period.

**CONCLUSIONS:**

The significance of this research is high. Low back pain is a prevalent public health problem in both the military and civilian populations. Currently a clear “gold standard” medical treatment for low back pain does not exist and studies show that evidence-based guidelines are rarely used in general practice. Thus, there is a need to consider innovative treatment options for chronic diseases such as low back pain. Our preliminary data suggested that chiropractic treatment in addition to standard medical care may be superior to standard medical care alone in active duty service members. In addition, doctors of chiropractic are well positioned to provide information to support smoking cessation. The results from this set of trials will provide critical information regarding the health and mission-support benefits of chiropractic health care delivery for active duty service members.

**REFERENCES:** No references.

**APPENDICES:**
Appendix A. Newsletters from reporting period.
Appendix B. Published manuscript.

**SUPPORTING DATA:**
Not applicable during this reporting period.

DEFENSE HEALTH PROGRAM (DHP) CLINICAL TRIAL AWARD (W81XWH-11-1-0107)

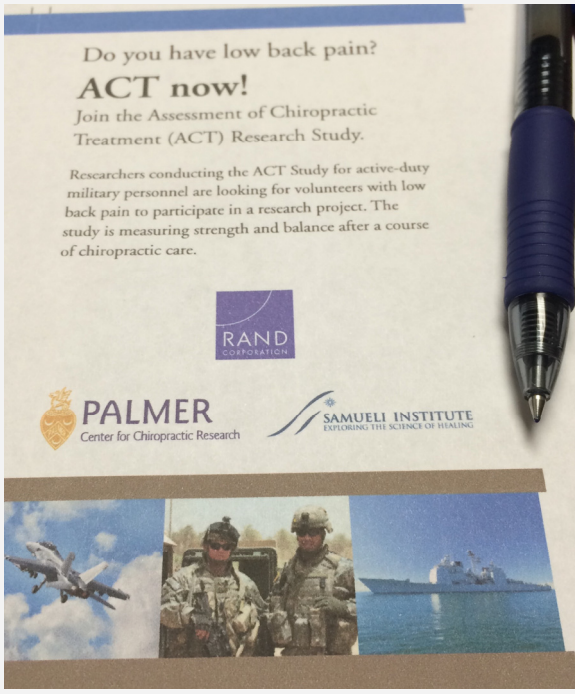
# Back to ACTion

Summer, 2016

## ACT 3 Study Launched!

The ACT 3 study at Naval Air Station Pensacola (NASP) has officially launched!

There are many tasks to accomplish prior to the launch of a study, but there are even more when the study is conducted off-site. The ACT 3 Lead Project Manager, Dr. Amy Minkalis, worked tirelessly from the PCCR to coordinate and execute all required agreements and contracts across multiple organizations, including: Palmer, RAND Corp, Samueli Institute, and the Navy.




Meanwhile, the ACT 3 Site Project Manager, Crystal Franklin, provided on-site launch support. Crystal began developing and fostering relationships throughout the clinic as we learned the importance of having reciprocal communication while conducting the successful ACT 1 study. Crystal routinely informs the clinic's administration, primary care providers, and other clinic staff of enrollment activities and recruitment efforts, and they continue to provide her with necessary updates. Participant enrollment began in April 2016, and currently three participants have been enrolled in the study.

Even with the best planning, unexpected delays can present themselves during research. About one month after the launch of ACT 3, the study team encountered an obstacle. The site Principal Investigator (PI), Commander (CDR) Joseph Penta, received deployment orders. A site PI is required to conduct study activities, so the ACT 3 team and CDR Penta worked diligently to quickly identify a replacement. Thankfully, Lieutenant Commander (LCDR) Bruce Matchin joined the ACT 3 team as the replacement site PI in May 2016.

The change in PI required updating of agreements and other IRB paperwork. These changes take time to be routed for approval, so ACT 3 was required to suspend enrollment and all other

*Continued on next page*

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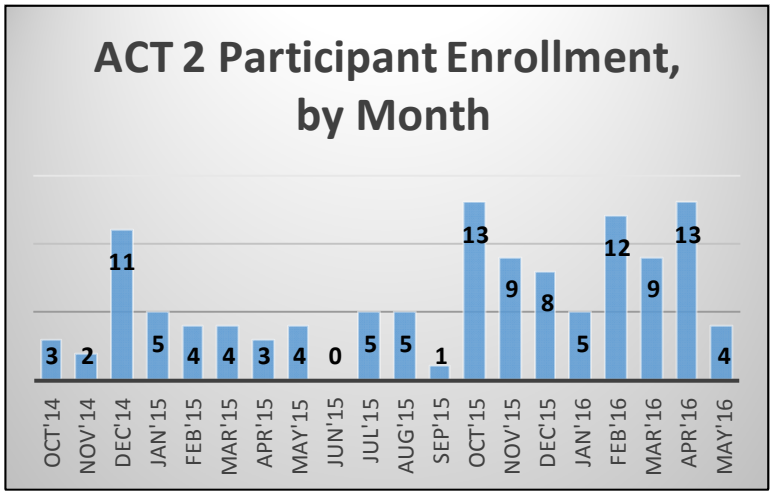
study activities until the personnel change was approved. Fortunately, all changes were approved by three separate IRBs, and the recruitment delay lasted only a few weeks. The study received all necessary approvals by mid-June, and recruitment efforts are back at full blast!

The ACT 3 team thanks the former site PI, CDR Penta, for his dedication and contributions to both the ACT 1 and ACT 3 studies. We also extend a warm welcome to LCDR Matchin, and look forward to the new collaboration.

***Stay tuned for exciting updates from the ACT 3 study in Pensacola!***

# ACT 2 Reaches 100% Enrollment!




**A Final Note from the ACT 2 Site Project Manager, Darla Freehardt, BS, LPN, CCRP**

"Begin with the end in mind" is a quote from Steven Covey. We started the ACT 2 study with an enrollment goal of 120 participants in October 2014. In May 2016 our final participant completed all study procedures and our goal was attained.

We want to highlight the teamwork and support that has been the driving force in the success of this study. The dedication of Dr. Haight and the site PI Dr. Jones has been outstanding. Their commitment to spinal health and the impact of wellness care on reaction and response times, as well as the entire Blanchfield Army Community Hospital (BACH) Chiropractic Clinic's unwavering commitment to research, has contributed to the achievement of the study goals. The successful collaboration with BACH Medical Command, members of 5th group, and SOAR also strengthened our study.

The military defines a team as "a group of people who function together to perform a mission or collective task." Recruitment has truly been a team effort. Our focus has been respect and open communication across Fort Campbell utilizing ACT 2 posters, emails, direct conversations, a PowerPoint presentation, pens, water bottles, and research study briefings given by the PI and Project Manager.


*Continued on next page*

***Continued from Page 2: A Final Note from the ACT 2 Site Project Manager***

We are extremely appreciative of the Special Operations Forces (SOF) members that came to our clinic and enthusiastically participated in this valuable research study. They have been interested in exploring the value of chiropractic adjustments to optimize their military performance. Even now that the study has been completed, SOF members are requesting chiropractic care because of the feedback they have received from their peers who were former ACT 2 study participants.

ACT 2 has been a remarkable journey and we look forward to the analysis of primary outcomes of the study.

## ACT 2 Metrics: Fast Facts!

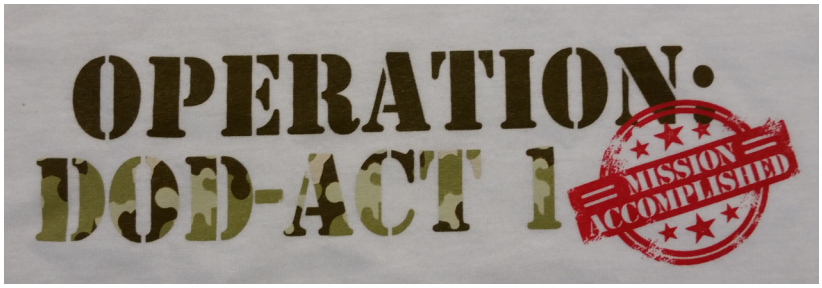
- 120 Special Operation Forces Participants
- 480 Data Time Points Collected
- 120 Eligibility Exams Conducted by DCs
- 240 Chiropractic Adjustments
- 360 Biomechanical Testing Visits
- 5,400 Biomechanical Tests Completed


Members of the ACT 2 Study Team pictured above, left to right: Dr. Michael Haight, Dr. Julie Hartman, Dr. Thomas Jones, Ms. Darla Freehardt, and Dr. James DeVocht.

## A Special 'Thank You' to the ACT 2 PM

Along with the excitement and sense of accomplishment that happens when completing the recruitment goals of a study comes the bittersweet realization that goodbyes will need to be said. While the PCCR will continue to collaborate with Dr. Jones on a regular basis regarding publications and future research, the ACT 2 Site Project Manager (PM), Darla Freehardt, will be leaving the team. To say 'Darla has fulfilled her duties as PM' is an understatement. Not only was she the link between the site PIs and the PCCR, but she also facilitated communication with the IRB and kept meticulous study records. In addition, Darla showed kindness and respect to everyone she interacted with at BACH and treated study participants as if they were members of her own family. We at the PCCR wanted to thank Darla for everything she has done for the ACT 2 study. Although she will be missed, we know Darla will be spending the summer with her family and welcoming another grandchild. We wish her and her family all the happiness for the future.

# ACT 1 Updates




Although recruitment has been completed for all 3 sites of ACT 1, there is still plenty of work to be done for the study. Naval Medical Center San Diego (NMCSD) has already finished data collection and has completed the site closure procedure through the IRB. However, Naval Hospital Pensacola (NHP) and Walter Reed National Military Medical Center (WRNMMC) participants had the option of being part of the long-term follow-up data collection portion of ACT 1. Happily, NHP has completed data collection and we are awaiting final IRB approval of site closure. WRNMMC is scheduled to complete data collection and site closure in December of 2016.

The ACT 1 study team is excited to have such a wealth of data to analyze, which translates into numerous opportunities to publish research papers to share study results. As reported in the last newsletter, the ACT 1 protocol paper has already been published in the journal *Trials* and work has begun on writing the primary results paper.

We will continue to share the progress of data collection and publication status in the next newsletter.

Members of the ACT 1 Study Team pictured above, left to right: Dr. Joan Walter, Dr. Cyndy Long, Dr. Ian Coulter, Dr. Christine Goertz, Ms. Lara Hilton, Dr. Julie Hartman, Dr. Amy Minkalis, and Dr. Katie Pohlman.

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DEFENSE HEALTH PROGRAM (DHP) CLINICAL TRIAL AWARD (W81XWH-11-1-0107)

# Back to ACTion

Winter, 2016 ACT 3 Special Edition

## Farewell to a Friend

The Palmer Center for Chiropractic Research (PCCR) has lost a treasured friend and colleague. Greg Lillie, DC, passed away on October 26, 2016 after a sudden and brief battle with cancer.

Greg served as the study chiropractor for both the ACT 1 and ACT 3 studies conducted at the Naval Air Station Pensacola site. Greg's involvement with the ACT studies was pivotal. He conducted all eligibility exams and provided all treatments to the ACT research participants. Greg's participation in research neither started nor stopped with the ACT studies; for more than six years he served as the Vice Chair on the Committee for Protection of Human Subjects at the Naval Hospital Pensacola (NHP).

Greg received his Doctor of Chiropractic degree in 1988 from Palmer College of Chiropractic in Davenport, Iowa. He continued on to pursue postgraduate work to become a Certified Chiropractic Sports Physician, and to obtain his Master of Science degree in Advanced Clinical Practice. Dr. Lillie joined NHP, based at the Naval Air Technical Training Center's (NATTC) Naval Branch Health Clinic (NHBC) on Naval Air Station, Pensacola, Florida in 2003 where he was the sole chiropractor on staff to treat active duty military personnel for more than 13 years. Throughout his professional career, Greg was the recipient of numerous awards, and was published in both chiropractic and medical journals.

Greg enjoyed so much in life, as was evidenced by his never-ending smile and his love for his dog Buoy. It was a pleasure to have worked with such a kind and passionate practitioner. The PCCR's condolences go out to Greg's wife, Jan, and his many family and friends.

*Continue to page 2 for ACT 3 Recruitment Update*

# ACT 3 Recruitment Update

## ACT 3 study accrual has surpassed 10 percent!

The ACT 3 study, which is being conducted at the Naval Air Technical Training Center's (NATTC) Naval Branch Health Clinic (NHBC) on Naval Air Station, Pensacola (NASP), has been successfully recruiting active duty military personnel. The study, which measures the effect of chiropractic care on the strength and balance of active duty military personnel with low back pain, has had 13 participants complete the study at the time of this publication.

Recruitment efforts were actively launched after the addition of the new site Principal Investigator (Lieutenant Commander [LCDR] Bruce Matchin) in June 2016. The ACT 3 site has deployed a multipronged approach to recruit new research participants. One of the most successful recruitment methods has been for the site project manager (Crystal Franklin) to work closely with NATTC NBHC physicians and other clinic staff to identify and recruit low back pain patients directly from the clinic.

In addition, Crystal has sought study referrals from clinicians outside of the NATTC NBHC. She has presented at the Naval Hospital Pensacola's Medical Staff Provider meeting, and has also worked directly with LCDR Matchin to provide study information to military clinicians all across the Pensacola area.

Flyers hung at public gathering places, such as coffee houses and gyms, have also proven to stir interest in the study, as has word of mouth. On occasion, special events on the base offer an opportunity for the site project manager to share study information with large groups of people. For example, in October 2016 Crystal attended a Breast Cancer Awareness 5K Run event hosted by the Radford Gym at NASP. An ACT 3 table was set up, and Crystal was able share study information with hundreds of active duty military personnel, military family members, veterans, and other community members.

*ACT 3 Site Project Manager, Crystal Franklin, at NASP's Radford Gym*

Currently, recruitment of new research participants has been put on hold. Sadly, the ACT 3 study unexpectedly lost a dear friend and the study chiropractor, Dr. Greg Lillie. A new study chiropractor is expected to come on board in the beginning of 2017, and participant recruitment will be relaunched at that time.

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**Look for future editions of Back to ACTion for updates on all the ACT studies!**

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Trials

STUDY PROTOCOL Open Access

# The effect of chiropractic treatment on the reaction and response times of special operation forces military personnel: study protocol for a randomized controlled trial

James W. DeVocht[1*], Dean L. Smith[2], Cynthia R. Long[1], Lance Corber[1], Bridget Kane[1], Thomas M. Jones[3] and Christine M. Goertz[1]

## Abstract

**Background:** Chiropractic care is commonly used to treat musculoskeletal conditions and has been endorsed by clinical practice guidelines as being evidence-based and cost-effective for the treatment of patients with low back pain. Gaps in the literature exist regarding the physiological outcomes of chiropractic treatment. Previous pilot work has indicated the possibility of improvements in response time following the application of chiropractic treatment. However, it is unknown whether or not chiropractic treatment is able to improve reaction and response times in specific populations of interest. One such population is the U.S. military special operation forces' (SOF) personnel.

**Methods:** This study is a randomized controlled trial of 120 asymptomatic volunteer SOF personnel. All participants are examined by a study doctor of chiropractic (DC) for eligibility prior to randomization. The participants are randomly allocated to either a treatment group receiving four treatments of chiropractic manipulative therapy (CMT) over 2 weeks or to a wait-list control group. The wait-list group does not receive any treatment but has assessments at the same time interval as the treatment group. The outcome measures are simple reaction times for dominant hand and dominant foot, choice reaction time with prompts calling for either hand or either foot, response time using Fitts' law tasks for small movements involving eye-hand coordination, and brief whole body movements using the t-wall, a commercially available product. At the first visit, all five tests are completed so that participants can familiarize themselves with the equipment and protocol. Assessments at the second and the final visits are used for data analysis.

**Discussion:** SOF personnel are highly motivated and extremely physically fit individuals whose occupation requires reaction times that are as quick as possible during the course of their assigned duties. A goal of CMT is to maximize the functionality and integration of the neuromusculoskeletal systems. Therefore, chiropractic treatment may be able to optimize the capacity of the numerous components of those systems, resulting in improved reaction time. The objective of this study is to test the hypothesis that CMT improves reaction and response times in asymptomatic SOF personnel.

**Trial registration:** ClinicalTrials.gov, NCT02168153. Registered on 12 June 2014.

**Keywords:** Chiropractic manipulative therapy, Reaction times, Response times, Special forces, Biomechanical assessments

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## Background

Chiropractic manipulative therapy (CMT) is generally used to treat musculoskeletal conditions, with a focus on spinal health. Spinal manipulation (SM) is the primary chiropractic intervention [1]. Multiple clinical practice guidelines have endorsed CMT as being evidence-based and cost-effective for the treatment of patients with acute, subacute, and chronic low back pain (LBP) [2–4]. These guidelines are based upon randomized controlled trials (RCTs) that demonstrate SM to be a conservative and effective approach for the treatment of LBP [5–8]. In the U.S., between 7 and 14 % of U.S. adults see a doctor of chiropractic (DC) annually, resulting in more than 190 million patient visits and there are more than 70,000 licensed DCs [9–12]. CMT receives high patient approval ratings in studies done to assess patient satisfaction [13–16]. In addition to private practice, DCs treat patients in a variety of settings including multidisciplinary health care organizations such as Veterans Health Affairs and military treatment facilities [17, 18]. Currently, DCs provide treatment in 65 military treatment facilities both within and outside the U.S. [19].

SM is used by professional sports teams to enhance player performance. Currently, there is some preliminary evidence that CMT may have a positive effect on both reaction time and movement time [20, 21]. Kelly et al. found that participants demonstrated a significant improvement in a complex reaction time task after receiving CMT [22]. Both Smith et al. [23] and Passmore et al. [24] reported that hand and head movements in response to visual stimuli were completed more quickly after participants had received CMT. Daligadu et al. reported that 10 volunteers with subclinical neck pain were able to complete specified sequences of button presses on a keypad more quickly after receiving CMT [25]. No adverse events (AEs) were reported in any of these studies.

One group that relies heavily on peak physical performance is special operation forces (SOF) of the U.S. military. Enhanced performance is critical for this population as they encounter dangerous situations. Split-second delays in response times to threats may mean the difference between life and death. It is for this reason that the Office of the Congressionally Directed Medical Research Programs issued a Program Announcement that led to the Defense Health Program Chiropractic Clinical Trial Award (W81XWH-11-2-0107) to, in part, "assess military readiness by evaluating pre-post differences in reflexes and reaction times following chiropractic treatment using a pre-post interventional cohort trial in members of Special Operation Forces." In response, the objective of this study is to test the hypothesis that CMT improves the reaction and response times of these highly motivated and extremely physically fit individuals.

## Methods

### Overview

This study is a RCT measuring reaction and response times in 120 volunteer SOF personnel at the Blanchfield Army Community Hospital, Fort Campbell, KY, USA. Following a first visit for screening and practicing the five biomechanical tests to be used in assessments, participants are randomly allocated to either a treatment group or to a wait-list control group. Beginning within a week of their first visit, those in the treatment group receive four CMTs over 2 weeks. The first of two assessments consisting of five biomechanical tests is made during their second visit, along with their first CMT. The second assessment is made during their final visit, along with their fourth CMT. In both of those visits with assessments, some of the biomechanical testing is performed before the CMT and some performed after. Participants in the wait-list control group do not receive any treatment but complete the two biomechanical assessments at the same time intervals as those in the treatment group. A flow chart of the study is shown in Fig. 1. Following their involvement in the study, those in the wait-list control group are offered the opportunity to receive four CMTs.

### Trial organization

This RCT is being conducted at Fort Campbell, KY because it has a population of SOF personnel as well as an established chiropractic clinic. The space to conduct the study, including the equipment used in the biomechanical tests, is housed within the facility used by the Chiropractic Clinic at Blanchfield Army Community Hospital. The CMT for this study is provided by two DCs, each with more than 10 years of clinical experience, practicing under the auspices of clinical guidelines established by the Department of Defense (DoD) and MedCom.

The investigators forming the research team for this study are from three collaborating institutions: the RAND Corporation, Palmer Center for Chiropractic Research (PCCR), and the Samueli Institute. Grants administration is managed by the RAND Corporation including the financial aspects and Institutional Review Board (IRB) issues of the grant award. It also ensures that the program officer at the DoD receives the required deliverables. The Samueli Institute ensures that the study complies with those entities that regulate the conduct of human subjects' clinical research within the DoD, which include the U.S. Army Medical Research and Material Command Human Research Protection Office and the Army's Clinical Investigation Regulatory Office. The Samueli Institute also provides advice concerning the general processes associated with the conduct of research within the military community.

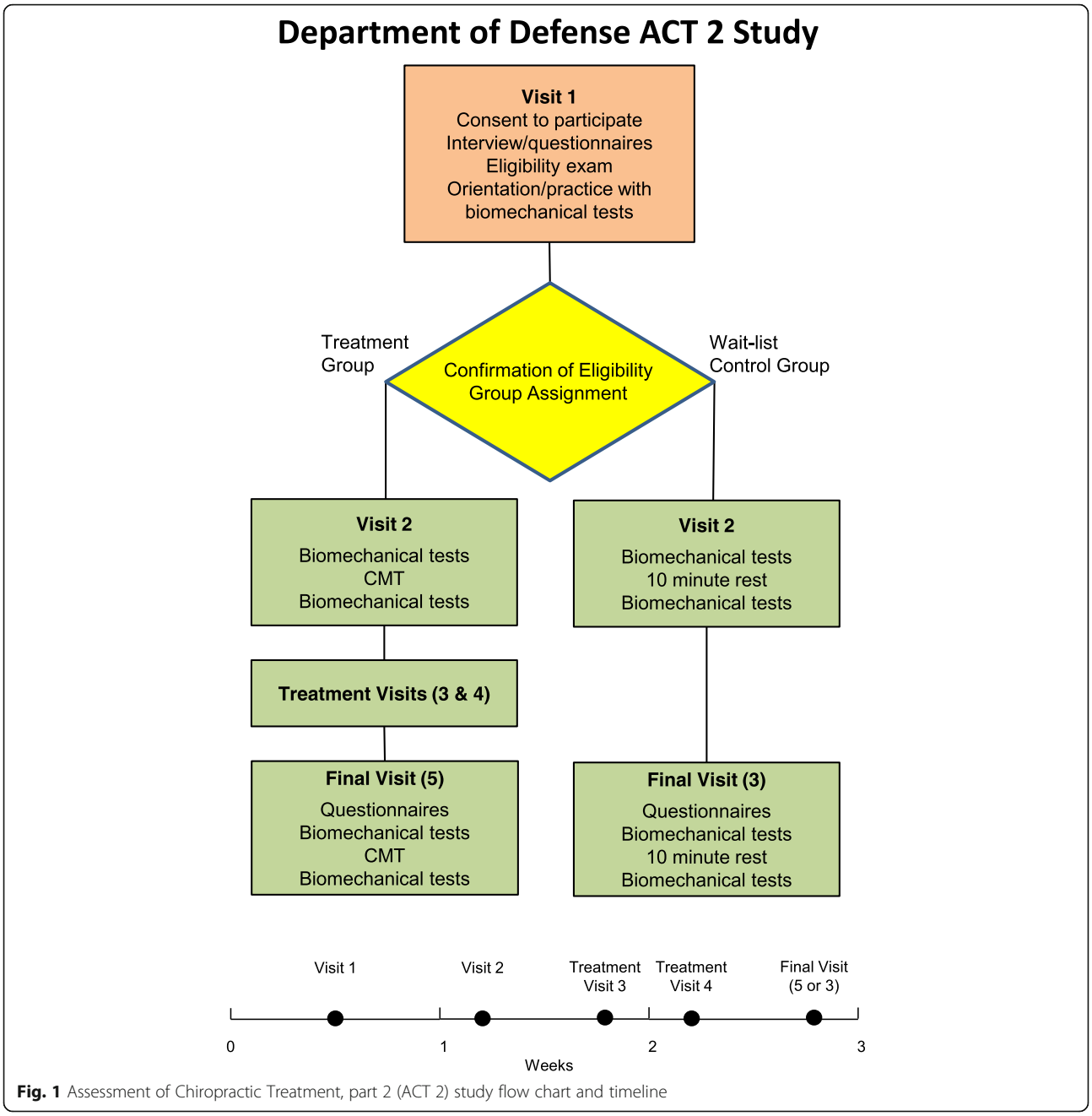


**Fig. 1** Assessment of Chiropractic Treatment, part 2 (ACT 2) study flow chart and timeline

Investigators from the PCCR are responsible for developing, implementing and managing the RCT at Fort Campbell. The investigators at Fort Campbell include: the site project manager (PM), two DCs (one of whom serves as site project investigator (PI)), and a physician medical monitor. The site PM is responsible for day-to-day trial implementation including recruitment and enrollment of trial participants, administration of a practice session and two biomechanical assessments of each participant, ensuring that each participant completes all phases of the study within the prescribed time windows, recording AEs, and maintaining all site-level trial documentation. The site PI oversees site administration including IRB issues, monitors study progress, conducts study evaluation and CMTs and ensures that all study procedures are conducted according to the protocol.

The lead PM at the PCCR oversees trial operations at Fort Campbell, acts as a liaison between trial coinvestigators, and ensures protocol adherence and fidelity. AEs are reviewed and monitored by a clinician at the PCCR. The project committee, consisting of all PCCR personnel involved in the study, meets weekly to review progress and resolve any issues that may arise. Any potential changes to the protocol are discussed in these meetings.

Action steps are determined for obtaining approval from the three IRBs and informing all relevant study personnel.

The Submission Tracking and Reporting System (STaRS) used in this RCT is a comprehensive web application developed by the PCCR with a dual purpose of collecting outcome assessments for study participants and serving as a secure electronic data capture and clinical trial management system. STaRS includes modules for confirmation of participant eligibility, biomechanical assessment file exchange, data collection of study participant's outcome assessments, and real-time reports for study management.

### Data and Safety Monitoring Committee

A Data and Safety Monitoring Committee (DSMC) provides oversight for this study. All DSMC members are independent of Palmer College of Chiropractic. Responsibilities of the DSMC are: (1) to ensure the overall safety of participants in clinical trials conducted by PCCR investigators by protecting participants from avoidable harm, and (2) to advise the DoD and the Expert Advisory Board regarding the scientific and ethical conduct of this RCT.

The DSMC reviews reports biannually. Should an AE occur, the DSMC evaluates the related data to protect the safety of study participants. If necessary, DSMC members make recommendations to the PIs and the DoD regarding continuation, termination, or other modifications of the RCT.

### Recruitment procedures

#### *Initial contact*

Flyers describing the study are placed in SOF facilities at Fort Campbell. SOF unit commanders and health care providers assigned to deliver care to SOF help to identify appropriate methods for dissemination of information concerning this study to their personnel. Quarterly presentations about the study are made in the language school on post as each new class begins. SOF soldiers who are interested contact the site PM by phone or email. The PM briefly describes the nature and extent of the study and asks basic screening questions. If the potential participant is still interested and appears to be eligible, the site PM arranges a preliminary visit to the study location for more extensive screening in a private setting.

### Visit 1

At the first visit, the site PM explains the study in detail utilizing the study flow chart and describing the specific activities of each visit. The site PM then goes over the Informed Consent Document with each participant and gives them a chance to read it and a Health Insurance Portability and Accountability Act (HIPAA) Compliance Document. The site PM is available to answer any questions they may have about either document or any aspect of the study. If the individual still desires to enroll in the study, the participant signs both documents and the site PM signs as a witness. The site PM then conducts an interview in which basic demographic information is obtained. The PM also screens the participant based on nonclinically obtained eligibility criteria. Those criteria are shown in Table 1 along with a rationale for why each was included. The PM enters the participant information directly into the STaRS system. Once preliminary eligibility is determined, the participant logs into the secure web application participant database

**Table 1** Eligibility criteria

| Inclusion criteria | Rationale |
|---|---|
| Minimum age of 20 years | Minimum age of SOF personnel |
| Written informed consent | Must be able to understand and agree to the requirements of the study |
| Active duty special operation forces' (SOF) personnel stationed at the Fort Campbell, KY military site | SOF personnel are the focus of this study. Fort Campbell is the study site |
| Exclusion criteria | |
| Pain intensity ≥4 (using the National Institutes of Health's PROMIS – question #29) at the initial visit | High pain levels have the potential to confound study results |
| Additional diagnostic procedure (other than X-ray) or referral required to determine a diagnosis, obtain a second opinion, or to manage a condition | Additional clinical diagnostic procedures are beyond the scope of this study |
| Bone and joint pathology contraindications for chiropractic manipulative therapy (CMT). Potential participants with conditions such as recent spinal fracture, concurrent spinal or paraspinal tumor(s), spinal or paraspinal infection(s), inflammatory arthropathies and significant osteoporosis | Participant safety. Care outside study scope needed |
| Other contraindications for CMT or suspicion of such contraindication requiring a consultation with another provider (i.e., unstable spinal segments, suspected cauda equina syndrome) | Participant safety. Care outside study scope needed |
| Currently being treated for traumatic brain injury | Potential to confound study results |
| No known or pending deployment, orders for a distant duty assignment or training site, or other absence from the current military site during the study participation period (2–4 weeks) | Compromises ability to adhere to study protocol |
| Received care from a doctor of chiropractic within the past 30 days | Prevent possibility of carryover effects from recent chiropractic care |

(STaRS) and completes a demographic information form, a health care utilization and medication use form, and the Patient Reported Outcomes Measurement Information System (PROMIS)-29 Health Survey. After the questionnaires are completed, one of the two DCs in the chiropractic clinic reviews the participant's medical records and conducts a physical examination. If no contraindications to chiropractic care are identified by the DC, the participant is referred back to the PM to complete the remainder of the visit. Participants with identified contraindications to CMT are ineligible to participate and referred to an appropriate provider if other care is needed. Those who are eligible are given an orientation of the five biomechanical tests. The orientation includes three videos, each approximately 2 or 3 min long, which demonstrate and narrate each of the five different tests..They show each test being performed and explain how the timing is measured for each one. Then the participant practices the five different biomechanical tests, repeating each one three times. The instructional videos were created to ensure that each study participant would receive standardized instructions. An appointment is then made for visit 2 within a week of visit 1.

There have been two changes in the eligibility criteria since this study began. Originally, the upper age limit was set at 45 years. However, as recruitment progressed it became apparent that SOF included members over the original age limit with an interest in the study. Consequently, it was decided to allow those who were still active in SOF to participate with no upper age limit. The second change allowed women to participate in the study. Initial study recruitment was limited to personnel who were not only in SOF, but were also special forces-qualified – a subset of SOF personnel who could not be female. In order to meet the required rate of recruitment, it was necessary to broaden the scope of eligibility to include members of the Special Operations Aviation Regiment who are on flight status, which includes female pilots. Both changes were approved by all IRBs involved in this study. The changes were made after 41 participants had been enrolled in the study.

### Between visit 1 and visit 2

The data from visit 1 is entered into STaRS. If all eligibility criteria are met, the participant is randomly allocated to either the treatment group or the wait-list control group. Group assignment is done using concealed allocation in a 1:1 ratio by a predetermined, computer-generated, restricted randomization scheme with random block sizes of 2, 4 or 6. The site PM has no knowledge of any details of the randomization process but accesses the group allocation module within STaRS to retrieve the participant ID and assigned group. The group assignment and date, time, and study participant ID are stored in the Structured Query Language (SQL) database. If the STaRS database is unable to be accessed when a participant needs to be allocated to a group, there is a backup allocation protocol consisting of predetermined sequentially numbered, opaque envelopes. Once allocation has been made to either the treatment group or the wait-list control group, the participant is called or sent a text message specifying their group assignment. Personnel at the PCCR who process the raw data are blinded to which group individual participants have been allocated to and will remain blinded until after completion of the study.

### Study interventions

The criteria for determining the clinical appropriateness for CMT are similar for the minimally symptomatic (current pain intensity no more than 4/10) and the totally asymptomatic participants of this study. The DCs perform a clinical evaluation, which may include standard orthopedic tests, spinal ranges-of-motion assessments, gross movement patterns, paraspinal muscular evaluation, and spine-related palpatory examinations to identify areas that may respond to CMT. Clinicians may use findings such as point tenderness over the spine, local muscular hypertonicity, asymmetry in posture, or pain/tenderness produced with orthopedic examination maneuvers to provide information regarding the appropriateness of spinal manipulation. In this manner, clinical evaluation can reveal musculoskeletal dysfunction in otherwise asymptomatic patients.

When applicable, the DCs decide which specific form of CMT to use based primarily upon the diagnosis and combination of comorbid or complicating diagnoses, if any. The participant's previous response to care (if known), flexibility and mobility, and general condition are also considered. The study chiropractor then makes a second decision regarding the application (location and direction) of CMT to the spine. This decision is based upon the diagnosis and other examination findings such as tenderness, hypertonicity, hypomobility, positions of relief and provocation, imaging findings (e.g., spinal curvatures, degeneration, spondylolisthesis) and other factors individual to the case. The care given to any individual participant consists of high-velocity low-amplitude (HVLA) spinal manipulative procedures. These procedures are typically associated with a quick manual thrust and an accompanying cavitation sound. For the cervical spine, the DCs use a cervical diversified technique. Thoracic manipulation occurs with unilateral or bimanual contacts in the prone or supine positions. Lumbar/pelvis manipulation is performed with a procedure referred to as side-lying or side-posture.

### Visit 2

At visit 2, the site PM shows the same instructional videos that were seen at visit 1 to the participant just before the participant performs the biomechanical tests. The participants are first asked to complete two repetitions of each of the five biomechanical tests. Following the two repetitions of the five tests, those in the treatment group receive their first CMT. Those in the wait-list control group wait for 10 min, the typical amount of time for a CMT to be given. Participants of both groups then complete one more repetition of each of the five biomechanical tests.

### Visits 3 and 4

Participants in the treatment group come in for two more visits and receive CMT over the next week with no biomechanical assessments. Participants in the wait-list control group do not attend these visits.

### Final visit

The final visit of the study is the fifth visit for those in the treatment group and the third visit for those in the wait-list control group. At the beginning of this visit, the participant logs into STaRS and completes the health care utilization and medication-use form and the PROMIS-29 questionnaire, as was also done during visit 1. The five biomechanical tests and CMT/break are conducted in the same manner as at visit 2, which marks the completion of an individual's participation in the study. Those who are in the wait-list control group are then offered the opportunity to receive CMT. If desired by the participant, the first of four CMTs is given at the final visit of their participation in the study after completion of the biomechanical tests.

### Missed visits

Due to the nature of SOF missions, unexpected deployments or local mission essential requirements can occur. Consequently, there are times when participants are not able to complete the study visits within the normal 2-week time window. However, participants must complete each of the visits for the study in the prescribed sequence. In the event of a missed appointment, the site PM contacts the participant to reschedule. It the study visits cannot be completed within 4 weeks, the PI and site PM discuss additional scheduling options on a case-by-case basis. If all visits are unable to be completed, the participant is considered as lost-to-follow-up.

### Outcome measures

Reaction times are typically very quick (less than 1 s). Subsequent changes in reaction time would be shorter still. Consequently, any tests to be used in this study must be very precise. Reaction time is the time from when a prompt is presented to the beginning of movement in response to that prompt. Response time is the time from when a prompt is given to the completion of a specified task. Three outcome measures are used that involve only a slight degree of movement, so the response time is essentially the same as the reaction time. Two additional outcome measures involve a higher degree of motion and require a longer period of time from the prompt to the response completion. Therefore, the length of time required to complete those tasks is more accurately referred to as response time. However, the movement required for these two outcome measures is still quite small – the response time for each event is still usually less than 1 s.

Before data collection was initiated at Fort Campbell, a pilot study was conducted at Palmer College of Chiropractic to develop and refine the specific procedures for each outcome measure. The three reaction time tests and two response time tests used in this study are described below. Due to the lack of information in the literature concerning these five biomechanical tests, no specific one of the five tests was selected as a primary outcome measure.

#### *Simple reaction time of the dominant hand*

Handedness of the participants is determined on the basis of self-report. The participant sits in front of a computer screen holding a button in their dominant hand and reacts to the appearance of visual prompts on the screen by pressing the button. A series of 11 prompts are shown in sequence. The time period between the response to one prompt and the appearance of the next prompt ranges from 0.5 to 4 s in a random although set sequence. The outcome variable for this test, the mean reaction time, is the average length of time between the appearance of each of the last 10 prompts and the button pressed in response to that prompt.

#### *Simple reaction time of the dominant foot*

This test is the same as the test with the dominant hand (previous paragraph), except that the participant's response to the visual prompt is made by pressing a pedal with the dominant foot.

#### *Choice reaction time*

This is a reaction time test involving both hands and both feet. The participant sits in front of a computer screen with a button in each hand and each foot resting on a pedal. A set of 41 prompts appear sequentially on the screen. The position of the prompt on the computer screen, as well as text within the prompt, indicates which hand or foot should be used in response to each prompt. If the prompt is in the upper left corner, the subject presses the button with their left thumb. If the

prompt is in the upper right corner, the subject presses the button with their right thumb. If the prompt is in the lower left corner, the subject presses the left foot pedal, and if the prompt is in the lower right corner, the subject presses the right foot pedal. There is a 1-s interval between the press of a button or pedal in response to a prompt and the appearance of the next prompt. If the wrong button or pedal is pressed, the software still goes on to the next prompt, but keeps track of how many incorrect responses were made and which ones were incorrect. The outcome variable for this test, the mean reaction time, is the average length of time between the appearance of each of the last 40 prompts and the press of a button or pedal in response to that prompt. However, the reaction times corresponding to incorrect choices are not included in the mean, in accordance with the protocol described by Whelan [26]. The number of incorrect choices is also provided.

#### *Response time involving the dominant hand (the Fitts' law test)*

In this test, participants perform a computerized, simple target-acquisition task (known as a Fitts' law task) to investigate their response times using a mouse with their dominant hand. The participant completes a block, a series of target selections on a computer screen, by working through 32 trials. That is, 32 pairs of "hits" – meaning the mouse is clicked when the cursor is inside each of two circles that make up a pair. When a pair is completed, the screen goes blank. The participant can then click the mouse with the cursor anywhere on the blank screen to begin the next of the 32 pairs in that block. This process continues until all 32 pairs of that block have been completed.

The two circles of any given pair are always of equal size, although the size varies in a random but set manner from pair to pair (W in Fig. 2) as does the orientation of the circles on the screen (the angle θ in Fig. 2). The distance between the centers of the two circles (D in Fig. 2) is always the same for every pair.

The participant is given a practice block of five trials before completing this task in order to become familiar with the process involved. The measured outcome from this task is the sum of the times required to complete each of trials (pairs) in a 32-trial block. The time elapsed between pairs is not counted.

#### *Response time involving whole body movement (t-wall)*

Participants stand in front of the t-wall, a commercially available device (Motion Fitness, Rolling Meadows, IL, USA) with a 4 × 8 bank of square buttons each of which is 8 cm per side (Fig. 3). When the test begins, one of the buttons will light. The participant hits that button with either hand. The light inside that button then goes

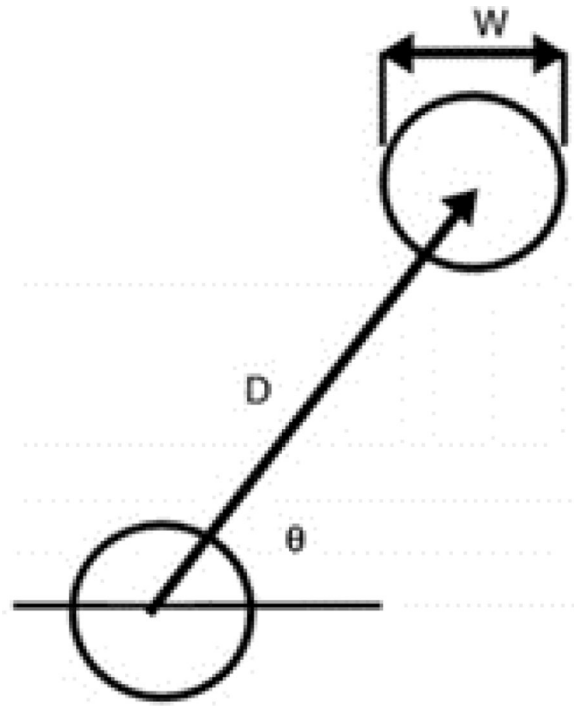


**Fig. 2** Computer screen used with the Fitts' law test. The participant moves the cursor from one circle to the other and back. The process is repeated for 32 pairs of circles of different size and orientation

out and another button lights until hit. This process continues for a random sequence of 100 buttons. When the last button is hit, all the buttons flash once to indicate that the test is complete. Participants are given a practice run on the t-wall to familiarize them with the process and the amount of force required in order to constitute a hit on any of the buttons. The starting position is standing an arm's length way from the center of the device. Initially, the first button of the 100 sequence is lit. However, the timing does not begin until the participant hits that first button. The measured

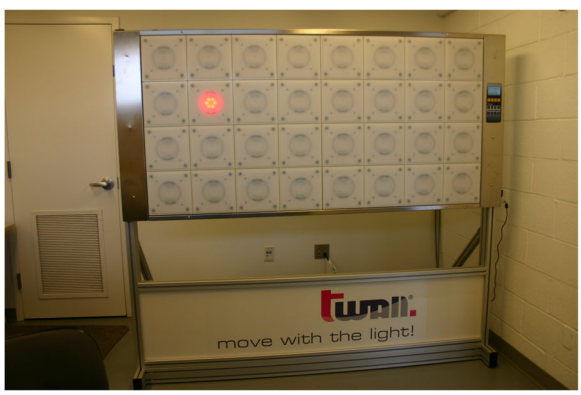


**Fig. 3** The t-wall. The participant goes through a random sequence of striking 100 lighted buttons, one immediately after the other

outcome from this test is the time from when the first button is hit to when the last button in the random but set sequence of 100 buttons is hit.

#### *Sequence of biomechanical testing*

The tests for each of the five reaction and response time outcome measures are given three times on each of the three different visits. Two different random but set sequences of prompts, designated A and B, are used for each of the five tests. This is done to prevent the participants from memorizing the sequence of prompts and, therefore, being able to anticipate the next prompt.

Although the five tests are all given at visit 1, it is only for practice – the data is not used in the analysis of the study. This allows the participants to become familiar with each test in preparation for the two assessment visits. The sequences of prompts as used at visit 1 are alternated for the three repetitions of each of the five tests using the pattern of A, B, A.

During visit 1, a video explaining the use of the t-wall is shown to the participant. The participant is then given the chance to hit a few buttons before actually beginning the test. This allows the participant to experience how much force is required when hitting a button in order to make the light go out. Once comfortable with this concept, the participant goes through three repetitions of the 100-button test. Next, the participant is shown a second video about performing the Fitts' law test, followed by a sample Fitts' law test of five pairs of circles. Once the participant feels able to do the test smoothly, three repetitions of that test are completed with 32 pairs of circles in each repetition of the test. After completion of the Fitts' law tests, a third video is shown that explains and demonstrates the hand and foot simple reaction time tests and the choice reaction time tests. The participant then performs three repetitions of each of those three tests. This denotes the completion of visit 1.

The first assessment is done during visit 2 and the second assessment is done 10 days later during the final visit. For each assessment, the five different biomechanical tests are given in the same sequence as they were practiced at visit 1. This includes showing the instructional videos before the relevant type of test but does not include doing the brief sample before performing the t-wall and Fitts' law tests. First, two repetitions of each test are performed. Then, the participant receives either a CMT or, for those in the wait-list control group, a 10-min break. After the CMT (or break), a third repetition of each type test is given – with the five tests being given in the same order. For these two assessment visits, the two sequences of prompts for each of the five tests and the CMT are given in the order of B, A, CMT/break, A. The videos are not shown again for the tests that are completed after the CMT or break.

### Software for the computer-based tests

The programs that are used for the computer-based tests were custom-developed using the Paradigm software package (Perception Research Systems, Inc.). The Fitts' law test uses the computer mouse for the participant to interact with the program. The reaction and response time tests use hand-held buttons and foot pedals for the participant interaction. The MP150 Data Acquisition System (BIOPAC Systems, Inc.) is used to interface the output of the buttons and pedals with the reaction time testing programs that were developed with Paradigm software.

### Data collection

Patient demographics are collected at visit 1. Health care and medication use and the PROMIS-29 are administered during both visit 1 and the final visit. A checklist is used that contains a list of each repetition of each of the five biomechanical tests in the order that they are to be given. Each test is checked off as it is completed.

Four of the five biomechanical tests that are administered to each participant are performed with the participant interacting with a computer: simple reaction time test with the hand, simple reaction time test with the foot, choice reaction time, and the Fitts' law test. A data file, in the form of a Microsoft Excel spreadsheet, is generated by the computer each time that one of those four tests is given. Since each of those four tests is given three times during each visit, there are 12 Excel files generated for each participant (visit 1 – just for practice, visit 2, and final visit). The name of each Excel data file contains the ID of the participant, a letter indicating when that data was taken: visit 1 – for practice only, visit 2, or the final visit. Also included is the date that the data was collected in the format of yy-mm-dd, as well as a letter and a number to indicate which of the five biomechanical tests, and which repetition of that test, generated the data.

The result from each repetition of the test using the t-wall is a single number representing the time in seconds (to two decimal places) that it took a participant to complete pressing the 100 buttons that constitute a repetition of that test. That number is shown in a digital display on the t-wall device. Immediately after a repetition of the t-wall test is completed, that number is written on the checklist. Consequently, there are three numbers for the t-wall that are hand-written on the hard copy checklist during the course of each visit.

### Data management and security

There are 12 Excel files that are generated during each visit in which data are collected. Those files are later combined into a single zip file. Consequently, there are three zip files created for each participant - each one

containing the 12 Excel files from one of the visits. Once a zip file is created following a visit, it is uploaded into the STaRS system.

At the PCCR, the zip file is downloaded from STaRS and stored on a secure file server on the PCCR network. All PCCR servers reside behind a state-of-the-art firewall with permissions determined by Active Directory. Through the use of a custom-developed macro in Excel, the individual data points are taken from each Excel data file and copied into a single large Excel file that acts as a database containing all of the data from all of the Excel data files. There is a separate sheet in the database file for the data of each type of test that generates an Excel data file: simple hand reaction time, simple foot reaction time, choice reaction time, and Fitts' law data. In addition, there is a fifth sheet that also contains the choice reaction time data, except that in that sheet there are blanks instead of data for those choices that were incorrect. For example, in the case when the test presented a prompt that called for a response with the left hand, but the participant used the left foot instead of the left hand. Generating a sheet of the choice reaction time data in this manner provides the opportunity for that data to be analyzed excluding times from incorrect choices, as described by Whelan [26].

There is one line created in the database file for each repetition of each type test with all of the data from that test. That line also contains the participant ID, visit number (1, 2, or 3), the type of test, which repetition of the test for that visit (1, 2, or 3), the date the test was given, and the name of the data file from which this particular set of data originated. In addition, the sheets for the choice reaction time test also include the number of incorrect choices that were made on that instance of the test.

A custom macro for Excel was developed to permit t-wall data for a given visit that had been hand-written on the hard copy checklist to be key-entered into an electronic form that has a field for each bit of data. The data thus entered consists of the participant ID, visit number, repetition number of the t-wall test on that visit, and the three times that were taken to complete the three repetitions of the t-wall test in that visit. The macro places the values on the electronic form into the correct places in an Excel file that serves as a database for all the t-wall data. In that database file there is one line for each participant. That line contains all of the t-wall data for that participant along with the participant ID and the date of each visit in which data was collected. Quarterly onsite audits are made by the PCCR project manager to ensure that the times of all repetitions of the t-wall tests, as manually written on the data collection forms, have been accurately entered into the computer.

Excel database files are backed up monthly and placed on two other hard drives. The data core manager writes programs in the SAS System for Windows (Release 9.4; SAS Institute Inc., Cary, NC, USA) using SAS ACCESS to create the analyzable datasets and creates the data dictionary. Only the data core manager and biostatisticians will have access to the datasets.

### Statistical methods

An intention-to-treat approach, in which participants will be analyzed according to their original treatment allocation, will be used. All observed data will be used in the analyses. Data analyses will be performed using SAS. The level of significance will be set at 0.05. Descriptive statistics of participant baseline characteristics, the reaction and response times and the PROMIS-29 scales at visit 1 will be presented for each treatment group.

The primary analyses compare the mean changes in reaction and response times from sequence A, performed before CMT/break at visit 2, to sequence A performed before CMT/break at the final visit between the treatment and wait-list control groups, using an analysis of covariance controlling for age, for each of the five biomechanical tests. Residual plots will be used to assess the validity of the model assumptions. If group variances are heterogeneous, we will use a mixed-effects regression model. If the data is non-normal, we will explore data transformations. Mean differences between groups, adjusted for age, will be reported with 95 % confidence intervals.

The secondary analyses will compare the immediate changes in sequence A before CMT/break to sequence A after CMT/break at both visit 2 and the final visit using the same methods described above.

Although we do not expect changes in the PROMIS-29 Health Survey scales or medication use in this short time frame, we will explore it by analyzing changes from visit 1 to the final visit.

### Sample size

A power analysis used the standard deviations of mean changes in response/reaction time over a 1-week period for each of the five biomechanical variables obtained in the pilot study. We estimated effect size as a 10 % change of the mean response/reaction time measured at visit 1 for each variable, assuming the control group would have no change. A total sample size of 100 participants, with 50 per group, gives at least 85 % power to detect a 10 % difference in mean change between groups at a 0.05 level of significance. We increased the sample size to 120, with 60 per group, to account for the possibility of up to 15 % loss-to-follow-up.

### Internal quality assurance process

The lead PM conducts an internal quality assurance audit on a quarterly basis for the purpose of

maintaining data integrity, ensuring study protocol fidelity and sustaining study operating procedures. During the audit, the lead PM reviews regulatory documentation and Informed Consent Documents. Electronic data is verified by comparing the paper source documents to the data entered into STaRS. Any errors discovered during the quarterly audits are documented, corrected by the site PM, and reported to the site PI, collaborating investigators, and appropriate regulatory bodies if applicable. During these site visits, the lead PM also meets with the site PM, PIs, DCs, and/or clinic command to facilitate communication about overall study status and discuss study timelines, as well as address site concerns or barriers interfering with study conduct. Information gathered during the site visits is conveyed to study coinvestigators. In addition, the PCCR PI has a monthly conference call with the lead PM and onsite PI and PM to monitor study progress.

#### Adverse events

For this study, an adverse event (AE) is defined as any untoward medical occurrence that may present itself during the conduct of the study and that may or may not have a causal relationship with the study procedures. AEs are monitored at two levels: (1) a participant self-report AE collected at all visits, and (2) serious adverse events (SAE) regardless of their attribution. Both are reported directly to the site PM, the site PI, and the medical monitor.

There is few rigorously collected data available reporting the risk of AEs following CMT. The lack of quantifiable information is in part the result of the inherent challenges presented by defining and identifying AEs in patients with musculoskeletal complaints with natural symptom variation, the large number of modifiable procedures available to DCs, and the combination of adaptable procedures in varying patient populations [27].

The scientific literature does contain case reports of SAEs such as fractures, serious neurological symptoms, and cauda equina syndrome following CMT. However, case reports are anecdotal in nature and lack definitive causal links. In addition, there are very few case reports of SAEs relative to the total number of chiropractic visits. Therefore, the risk for SAEs following chiropractic care is extremely small and implausible to estimate accurately [28]. The most recent systematic review on this subject failed to identify any reported SAEs resulting from chiropractic care in clinical trials [28].

AEs and the anticipated likelihood of each for this study are included below:

- Rare but serious (event rate <1 %)
  - Fracture to the ribs or hip
  - Nerve injury that may cause loss of bowel or bladder function, lower body sensation or leg paralysis
  - Strokes
- Less likely (1 % ≤ event rate < 5 %)
  - Inadvertent disclosure of data
- Likely (5 % ≤ event rate < 10 %)
  - Some individuals may also experience: neck pain; headache; radicular (radiating) pain; mid-back pain; hands or feet tingling, burning, pricking, or numbness; or dizziness following neck manipulation. These symptoms are usually self-limiting and short-lasting
- More likely (event rate ≥10 %)
  - Some participants may experience muscle and/or joint soreness associated with palpation and CMT, particularly at the beginning of the program

Oversight of the reported AEs is conducted by a designated study clinician who reviews a dynamic report of all information submitted by the site PM using the secure web module designed for event reporting for this study. The designated study clinician conveys classification of these events to the site PM for appropriate reporting to the IRBs and other required regulatory bodies. The study clinician may also ask the site PM to contact the participant if more information is needed regarding a reported adverse experience that is potentially serious, related to the study, appears to have no resolution date, or appears to require additional medical follow-up for safety purposes. Our goal is to ensure that we are following up any event that has the potential to affect participant safety and reporting AEs per all study IRB reporting guidelines.

For the second level of AE monitoring, we use the Food and Drug Administration (FDA) definition of a SAE. This is any adverse experience occurring during treatment that results in any of the following outcomes: death, a life-threatening adverse experience, inpatient hospitalization or prolongation of existing hospitalization, a persistent or significant disability/incapacity, or a congenital anomaly/birth defect.

Should any arise, all SAEs and unanticipated problems involving risk to subjects or others are reported to the involved IRBs (Dwight D. Eisenhower Army Medical Center, Palmer Center for Chiropractic Research, and the RAND Corporation), Medical Monitor, DSMC, and the U.S. Army Medical Research and Material Command Office of Research Protections according to the relative reporting guidelines for each entity. The site PM is responsible for reporting all AEs in STaRS and to the lead PM at the PCCR. The lead PM at the PCCR is responsible for ensuring all appropriate parties are informed about any SAEs.

All study protocol violations are reported to the Palmer DSMC. Protocol violations meeting study site's IRB criteria for reporting are reported per IRB guidelines.

### Study limitations

One limitation of this study is the use of a wait-list control group for comparison to the treatment group rather than a sham treatment group. A sham treatment would maximize the ability to compensate for the possibility of a placebo effect in the treatment group. However, it is very difficult to provide a sham treatment for HVLA active treatment, so the members of a sham group would likely suspect that they are not receiving an active treatment [29]. Furthermore, the outcome measures used in this study are objective in nature, potentially minimizing any placebo effect.

A limitation inherent in any study involving manual therapies is the variability of the treatment provided for each patient, and even each treatment of each patient. There are so many variables associated with virtually any form of manual therapy that it is impractical to try to quantify them. This is partly due to the fact that each patient's condition is certainly not constant from one visit to the next, and consequently the manual therapy given is typically modified by the treating clinician to address the specific needs of the patient during any particular visit. This study is intended to investigate the effects of actual clinical practice and, therefore, no attempt was made to restrict the manner in which the clinicians provide their treatment to participants of the study.

Similarly, despite the requirement for participants to meet the inclusion criteria established for the study, there will still be considerable variations within the exact physical condition, some of which are likely associated with age, of the participants in the study. This is also an inherent limitation in studies involving human participants.

Another limitation of the study involves blinding. Due to the setup for this study, it is not logistically feasible for the person administering the assessment tests to be blinded as to which group (treatment or wait-list control) each participant is in. Consequently, there is a possibility that the assessor's actions toward members of the treatment group might be somewhat more positive or encouraging than their actions toward members of the wait-list control group. This risk is minimized by having scripted dialog and prerecorded video presentations to explain how each assessment test is to be done. The objective nature of all five of the assessment tests reduces the ability for observer bias to impact the results of the tests.

One other limitation of the study is the low number of CMTs being given to each participant. It is currently unknown if CMTs of any quantity would induce a discernable reduction in the reaction time of SOF personnel. Three or four CMTs were chosen as feasible for busy SOF personnel to receive.

## Discussion

SOF personnel as a group are likely to be in need of reaction and response times that are as quick as possible during the course of their assigned duties. One goal of CMT is to maximize the integration and function of the neuromusculoskeletal systems. Therefore, this intervention is well-suited for attempting to optimize the capacity of the numerous components involved in the production of a minimal reaction and response time. This study is designed to show if CMT will result in quicker reaction and response times for those SOF personnel who receive it. The results of the study will be published following completion of data collection and analysis.

Two different random but set sequences of prompts for each of the five biomechanical tests were used to prevent participants from memorizing the sequence and anticipating prompts. However, different sequences can have different levels of difficulty. Consequently, whenever the results of two replications of the same test are to be compared with each other we wanted to have the same sequence of prompts used for those replications of that test. The only replications of each test that are to be used in the data analysis of this study are the ones taken immediately before and after the participant receives a CMT/break. Therefore, for visit 2 and the final visit, the order of prompt sequences and the CMT/break that is used is B, A, CMT/break, A. Having a replication of the test completed using sequence B just before the one with data that will be analyzed that uses sequence A has a double value. Not only does it prevent memorization of the prompt sequence, but it also provides an opportunity for the participant to get in the mode of doing that particular test after doing other, different tests before doing it for analysis.

Once the resulting manuscripts have been published, datasets will be provided for public access. Potential investigators can contact one of the co-PIs to present their hypothesis, study design, instruments and/or data on which to focus, and resources required. Depending upon the needs and desires of the requesting party, the data that is shared may include analytic tables or deidentified or limited datasets that are transmitted to the requesting parties for additional analyses. In addition, the trial is registered on ClinicalTrials.gov, making all key information about the trial freely available.

### Trial status

The first participant was enrolled on 30 September 2014. Data collection for the last of 120 participants was completed on 7 June 2016.

## Trial registration

The RCT discussed in this article was registered on ClinicalTrials.gov with the NCT02168153. The initial version sent to ClinicalTrials.gov was received on 12 June 2014.

### Abbreviations

ACT 2: Assessment of Chiropractic Treatment, part 2; AE: Adverse event; CMT: Chiropractic manipulative therapy; DC: Doctor of chiropractic; DSMC: Data and Safety Monitoring Committee; HVLA: High-velocity low-amplitude; IRB: Institutional Review Board; LBP: Low back pain; PCCR: Palmer Center for Chiropractic Research; PM: Project manager; PROMIS: Patient Reported Outcomes Measurement Information System; RCT: Randomized controlled trial; SAE: Serious adverse event; SOF: special operation forces; STaRS: Submission Tracking and Reporting System

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### Availability of data and materials

Not applicable.

### Authors' contributions

CG provided global oversight for the initiation and development of the entire trial. JD and DS developed the biomechanical assessments including processing the data that are used for the outcome measures. BK assumed responsibility for the development of the logistical portions of this trial after they had been initiated previously and then completed those aspects. CL developed the statistical analysis used in the trial. LC developed the mechanisms for capturing all administrative data and transferring all data from the collection site at Fort Campbell to the Palmer Center for Chiropractic Research, as well as handling all administrative data once it is received at Palmer. TJ developed the treatment protocol that is being used in the study, serves as the site principal investigator, and is one of two chiropractors who provide treatment in this study. JD made the first draft of the manuscript with input from other authors concerning their specific aspects of the protocol. All authors reviewed and commented on drafts of the manuscript, and eventually approved the final version before it was submitted.

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### Competing interests

The authors declare that they have no competing interests.

### Consent for publication

Not applicable.

### Ethics approval and consent to participate

Ethics approvals for the trial protocol were received from three Institutional Review Boards (IRBs): Palmer College of Chiropractic (#2012G143), the RAND Corporation (#2012-03520 AM02), and the Dwight D. Eisenhower Army Medical Center (#389611) which is the IRB of record for Blanchfield Army Community Hospital. An additional approval was given by the U.S. Army Medical Research and Material Command, the Human Research Protection Office, and the Clinical Investigation Regulatory Office. All changes to the protocol were submitted to and approved by all three IRBs. All study investigators have completed training in the protection of human subjects as required by the respective collaborating institutions.
A Cooperative Research and Development Agreement was established between the Clinical Investigation Regulatory Office and the Samueli Institute prior to study commencement. The Cooperative Research and Development Agreement was approved for the period of April 2014 through April 2017.
All aspects of the study are thoroughly explained to all potential participants and all participants in the study provide written informed consent.

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