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

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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, 2017 through February 14, 2018. 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. Study is complete and sites are closed. During this reporting period the study: Published primary results manuscript (in print), drafted secondary outcomes manuscripts. ACT 2 is a randomized controlled trial of response and reaction times in Special Operations Forces at Ft. Campbell, KY. The study is complete and sites are closed. We published the protocol manuscript and primary results paper is in draft. ACT 3 is a randomized controlled trial of strength, balance, and re-injury comparing standard care with standard care plus chiropractic treatment. During this study period: we have recruited 54/110 targets and drafted protocol manuscript.					
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INTRODUCTION:

This annual report provides updates for the reporting period February 15, 2017 through February 14, 2018 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 and end 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 (NMCS), 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 (NMCS), 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 was successful and 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 the last 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, ACT 1 data analysis was finalized and the primary manuscript was submitted for publication.

Personnel changes during this reporting period: N/A

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 15, 2017, August 21, 2017, and November 15, 2017.

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, 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 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 provider visits for LBP and medications prescribed).

Task 6: IRB approval processes and other regulatory requirements

- During this reporting period, there were no IRB amendments and continuing reviews at all sites were kept current (RAND, Palmer, NHP, NMCSO, and WRNMMC).
- 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 |

- Study Closure March 17, 2017

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; August 30, 2017 (Closure).
- 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.
- Study closed August 30, 2017

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:

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

	NMCSO: 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
% <i>missed outcomes</i>	7	21	6	11
# withdrawn	1	3	2	6
Week 4 Assessment				
# completed	221	183	222	626
# missed outcomes	27	64	24	115
% <i>missed outcomes</i>	11	26	10	16
# withdrawn	1	0	2	3
Week 6 Assessment				
# completed	237	208	238	683
# missed outcomes	10	35	7	52
% <i>missed outcomes</i>	4	14	3	7
# withdrawn	1	4	1	6
Month 3 Assessment				
# completed	221	189	215	623
# missed outcomes	25	51	29	105
% <i>missed outcomes</i>	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
% <i>missed outcomes</i>		55	29	39
# withdrawn		0	0	0
Month 9 Assessment				
# completed	N/A	31	75	106
# missed outcomes		24	20	44
% <i>missed outcomes</i>		44	21	29
# withdrawn		0	0	0
Month 12 Assessment				
# completed	N/A	38	79	117
# missed outcomes		17	16	33
% <i>missed outcomes</i>		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

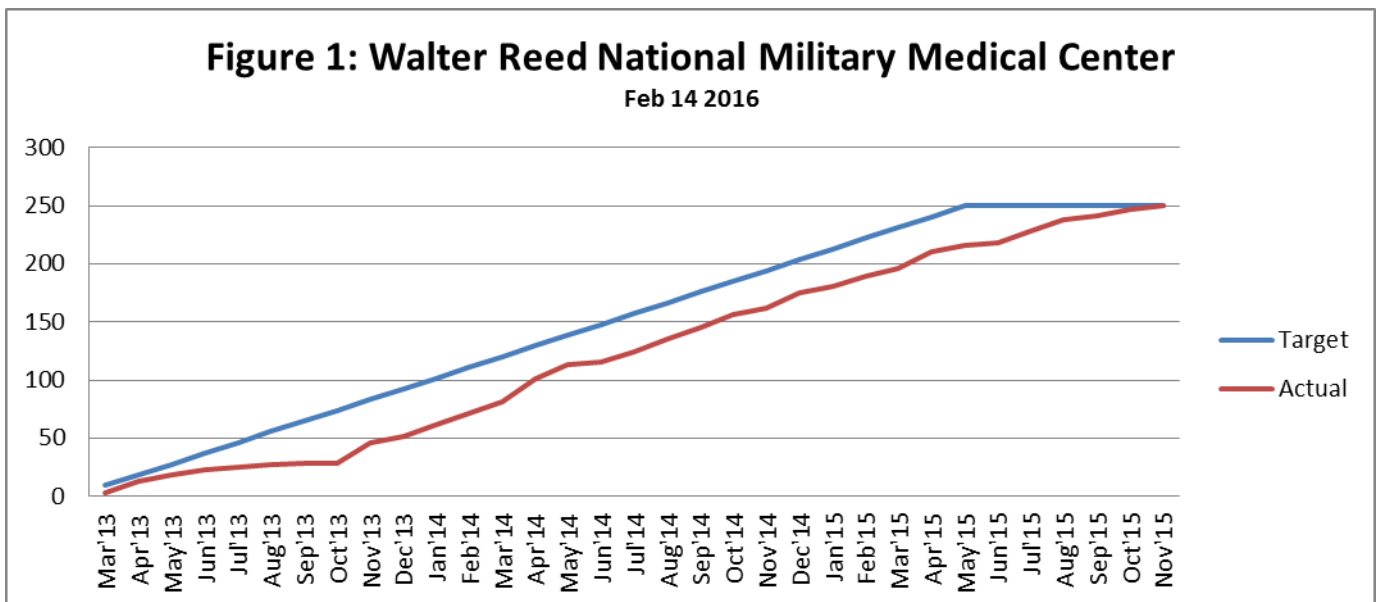
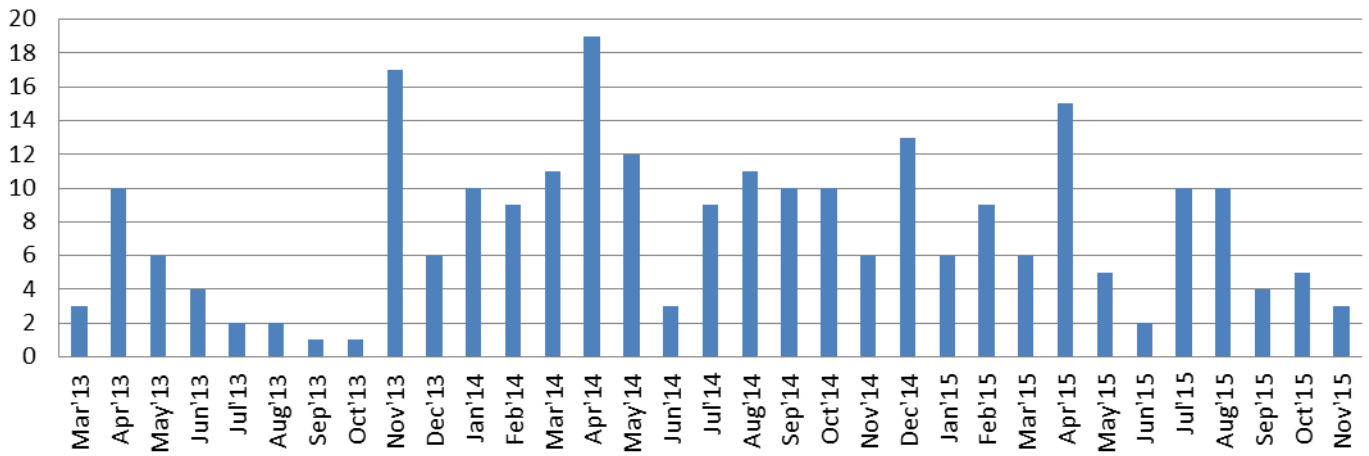


Figure 2: Walter Reed National Military Medical Center

Feb 14 2016



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

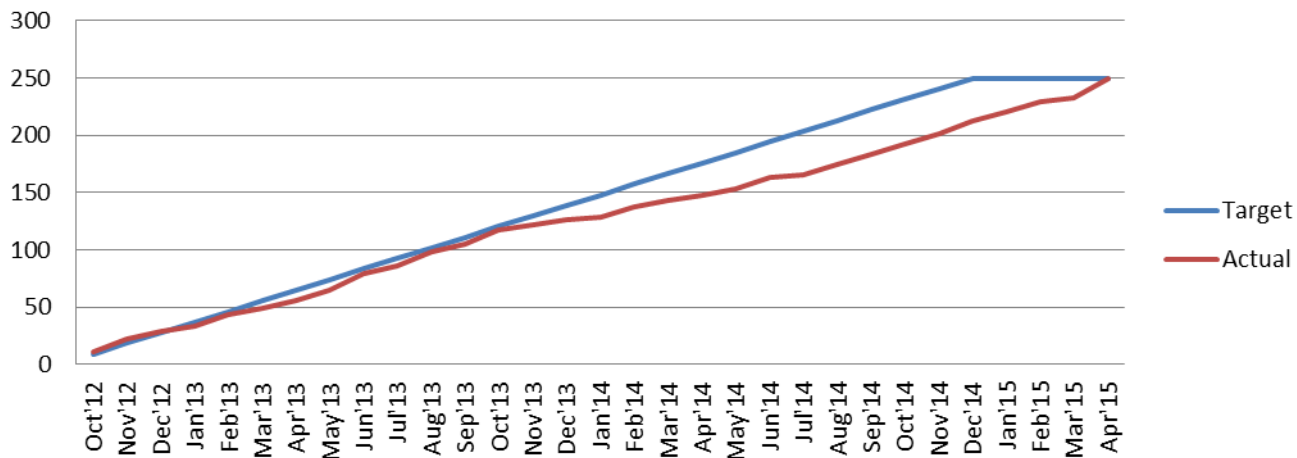
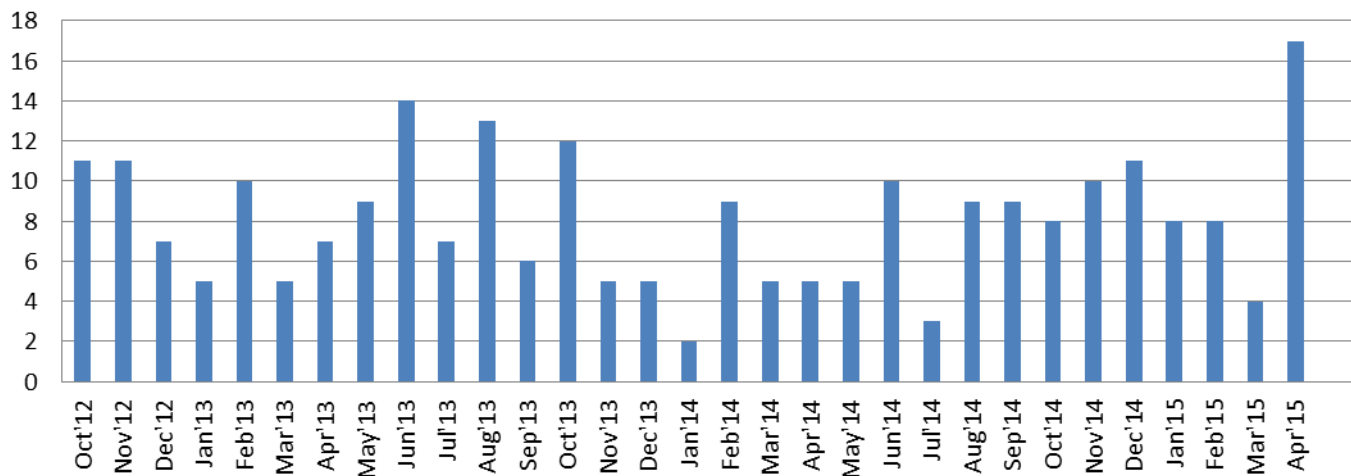


Figure 4: Naval Hospital Pensacola

Feb 14 2016



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

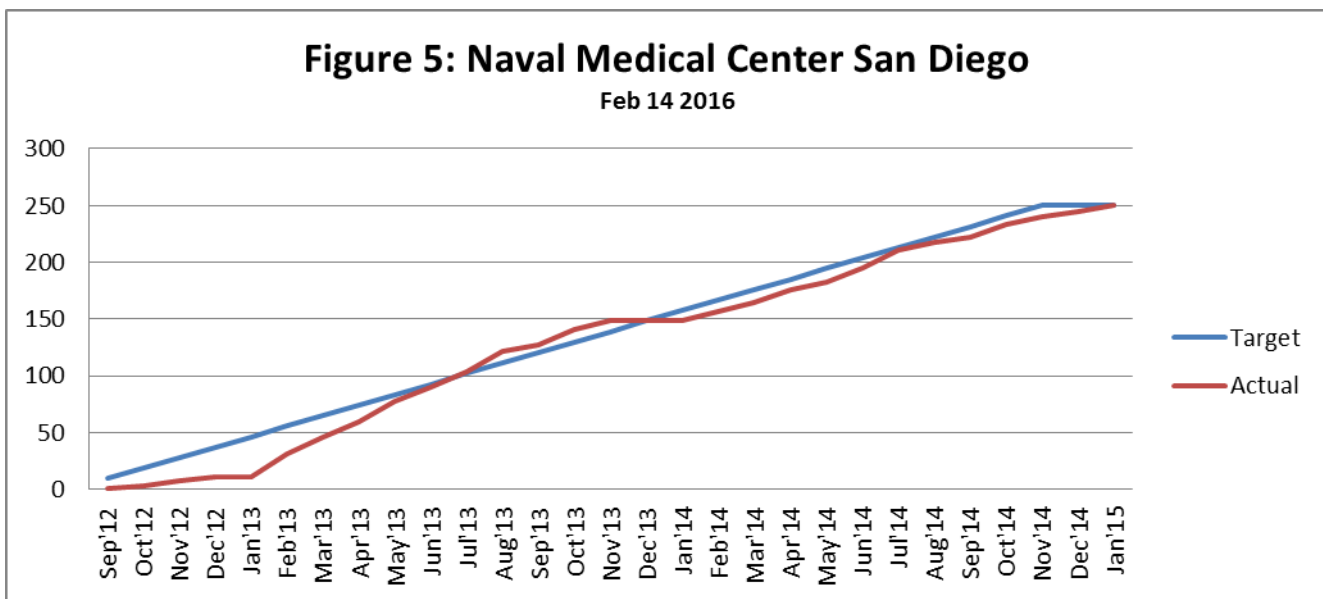
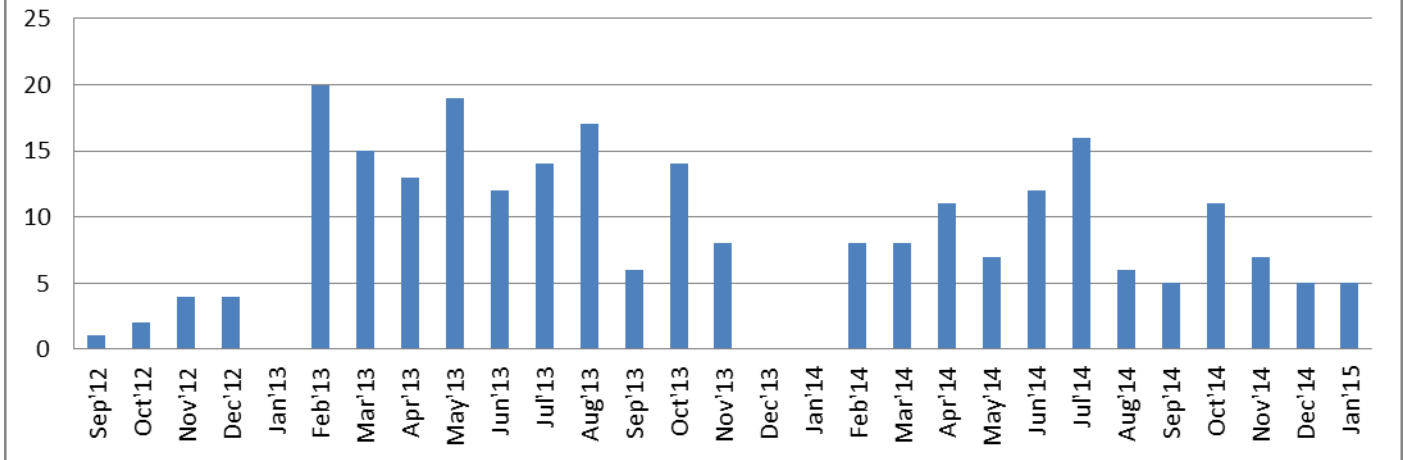


Figure 6: Naval Medical Center San Diego

Feb 14 2016



	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
NMCS D	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
 - *No quality assurance site visits conducted during this reporting period. See administrative site visits section.*
- 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 granted approval for completion of protocol March 17, 2017.
 - HRPO closed the site on November 27, 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, November 5, 2015, October 11, 2016, and closures on August 30, 2017.
 - MRMC HRPO acknowledged receipt of continuing review documents from RAND Corporation on December 14, 2015, December 28, 2016, and closure on November 27, 2017.
- Palmer College was granted approval for completion of protocol January 4, 2017.
 - HRPO closure documents were submitted November 8, 2017.

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, September 8, 2017.

Task 13: Close study recruitment

- NMCS D 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

- Analysis continues on the following topics: contextual evaluation, PROMIS-29; EMR data abstraction, and long term follow up data.

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 has been accepted for publication.

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 and then as part of biweekly team meetings thereafter.

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 completed as follows:

Table 6: Tobacco Enrollment Report	<u>Tobacco User</u>	<u>Consented</u>	<u>Enrolled</u>	<u>Withdrawn</u>
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

- Data analysis finalized and results are included in the primary manuscript.

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. The target of 120 participants have been recruited and allocated; recruitment was completed on May 23, 2016 and the study site was closed on September 25, 2016. Please see accrual plot below.

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 initial 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)
 - 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.)
- Closure approved March 23, 2017

- 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.
 - 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.
 - 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.
 - Closure for RAND Corporation was May 17, 2017.

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	

Figure 1: ACT 2

Feb 14, 2017

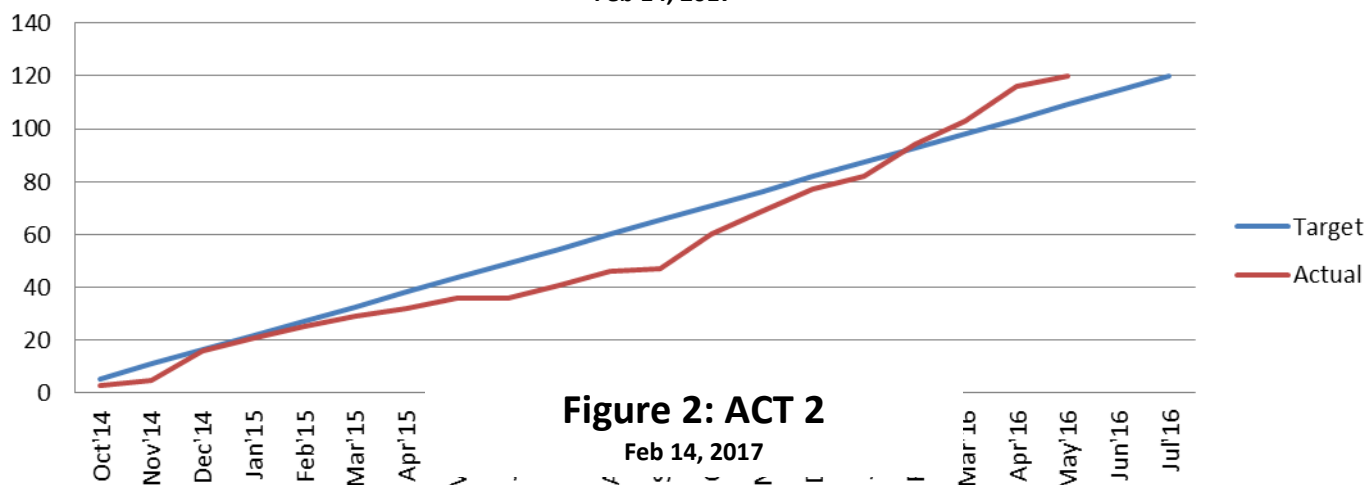
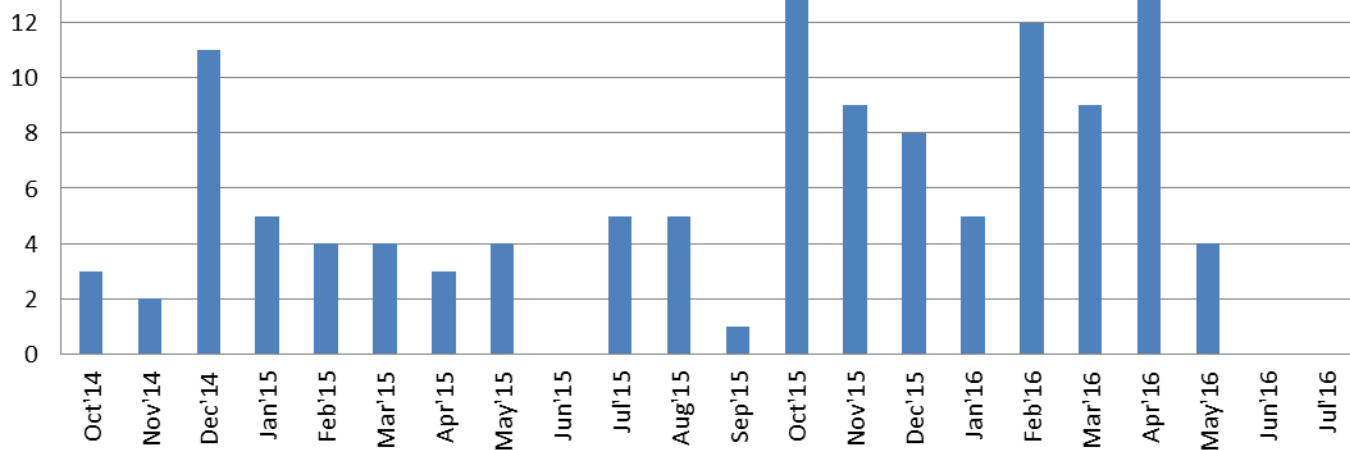


Figure 2: ACT 2

Feb 14, 2017



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 data

- Data analysis was finalized this reporting period. Primary manuscript is in draft form.

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.

Updates for this reporting period: In June 2017, the new study site chiropractor was approved and credentialed at the military site. Recruitment resumed and 54 of the targeted 110 participants have been enrolled in the study.

Personnel changes during this reporting period:

- Greg Lillie, DC was deceased and left the role of study clinician vacant, October 2016. In June 2017, Dr. James Boysen was approved and credentialed to treat at the military site, and his study role as chiropractor was updated. Allison Bush, Qian Li, Ram Gudavalli, Ting Xia, and Julie Hartman were removed from the project. LT Ryan Richmond was added to the project in the role of Research Monitor. LCDR Bruce Matchin was removed from the site PI role, and CDR John Biery was added as his replacement.

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:
 - 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 (site PI deployed requiring suspended study activity; 2 participants final visits occurred early)
 - Protocol Deviation 02 October 25, 2016 (participant final visits occurred out of window)
 - Protocol Deviation 03 January 11, 2017 (participant was allocated to receive chiropractic treatment but was not able due to death of study clinician)

- Amendment 06 May 11, 2017
- Continuing Review May 11, 2017
- Amendment 07 June 23, 2017
- Amendment 08 August 14, 2017
- Amendment 09 August 14, 2017
- Amendment 10 December 4, 2017
- Protocol Deviation 04 February 15, 2018 (participant final visits occurred out of window)

- 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 I 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 (deployment of site PI resulted in early final visits)
- Protocol Deviation 02 November 16, 2016 (final visits occurred out of window)
- Protocol Deviation 03 N/A; IRB recommended no further action
- Continuing review May 10, 2017
- Protocol Deviation 04 October 5, 2017 (final visit occurred out of window)

- 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

- 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, February 1, 2018.
- 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 and study activity was required to halt, resulting in early final visits for 2 participants).

- 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 it was approved June 10, 2017.

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.

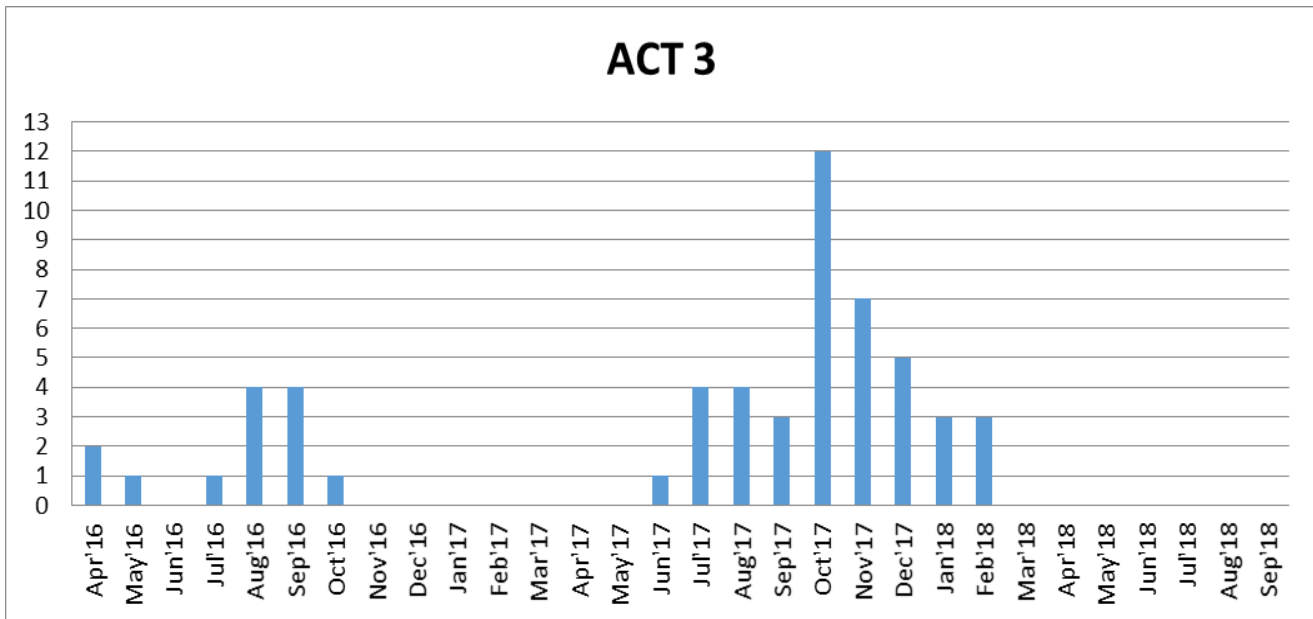
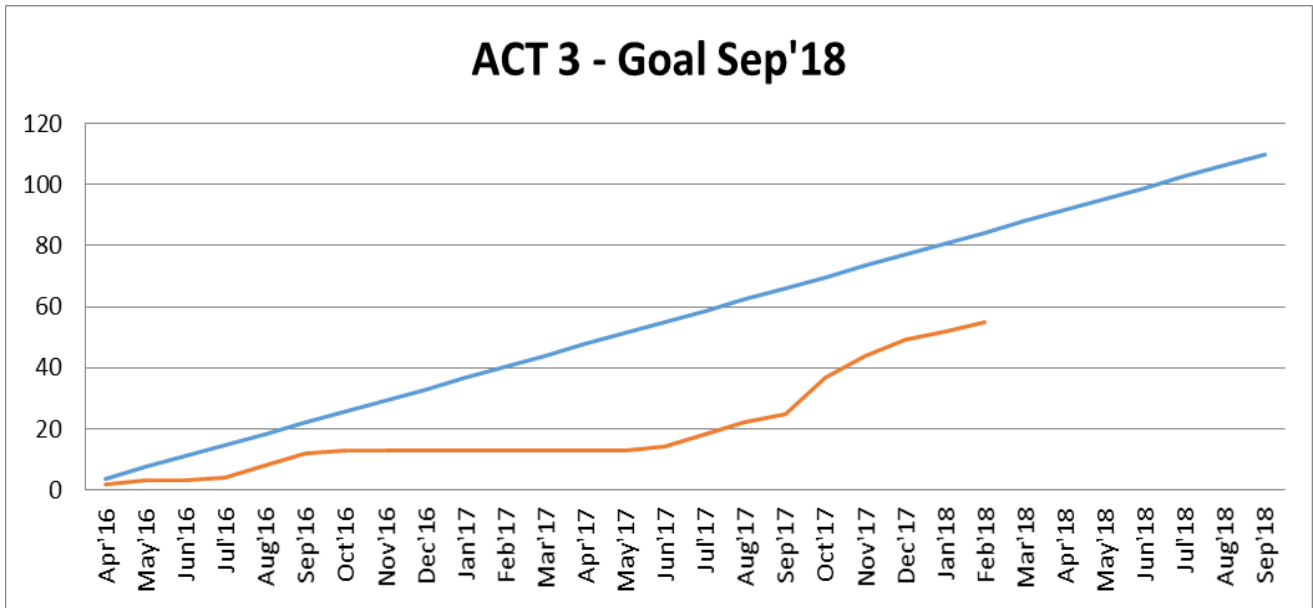
Table 1. Recruitment, Accrual and Retention through 14 Feb 2018

	Total
Screening	
# Total screened	113
# Total excluded	18
Baseline	
# Total screened	95
# Total excluded	39

Allocated	54
Completed	49
Withdrawal	1
Lost to Follow-up	1

Table 2. Participant Demographics through 14 Feb 2018

		Treatment 1 (n=27)		Treatment 2 (n=27)		Total (n=54)	
		n	%	n	%	n	%
Ethnicity	Hispanic or Latino	4	15	6	22	10	19
	Not Hispanic or Latino	21	78	21	78	42	78
	Unspecified	2	7	0	0	2	4
Sex	Female	2	7	2	7	4	7
	Male	25	93	25	93	50	93
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	1	4	0	0	1	2
	Black or African American	4	15	3	11	7	13
	White	19	70	21	78	40	74
	Multi-racial	1	4	1	4	2	4
	Unspecified	2	7	2	7	4	7
Age	Mean SD	31.6	5.8	30.4	6.6	31.0	6.0
	Median	30.5		32.0		31.5	



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. Other visit activities included site PM training as well as meetings with the site PI, command and study chiropractor.
 - *October 9-12, 2017* – Lead PM, Amy Minkalis, conducted a site visit and internal audit for quality. All participant records and data were reviewed and verified. Other visit activities included site PM training as well as meetings with the site PI, command and study chiropractor.
 - *February 20-22, 2018* - Lead PM, Amy Minkalis, conducted a site visit and internal audit for quality. All participant records and data were reviewed and verified. Other visit activities included site PM training as well as meeting with the study chiropractor.

Task 7: Analyze data and write final study reports

- Evaluated feasibility and safety of functional testing protocols of following completion of pilot study.
- Manuscript for study protocol in draft form.

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 NMCSO, 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 1 primary results paper has been accepted for publication

ACT 2:

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

ACT 3:

- Launched full study at the Naval Hospital Pensacola
- Recruited and initiated new site PI and new site study provider
- Reached 49% of target recruitment (54/110)

REPORTABLE OUTCOMES ACROSS ALL STUDIES:

Primary results paper for ACT 1 has been accepted for publication.

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:

No appendices.

SUPPORTING DATA:

Not applicable during this reporting period.