U.S. Military Service Member Health Research Participation:

Research Trends, Recruitment Challenges, and Reasons for Research Participation

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Abstract

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Military-relevant health research often includes U.S. military service members as participants in studies of war-related conditions, such as traumatic brain injury (TBI) and post-traumatic stress disorder (PTSD). Service members' research participation contributes to advances that improve the wellbeing of all service members and supports military readiness. This dissertation explores current U.S. military service members' participation in health research including (1) trends in participation, (2) indications of recruitment challenges, and (3) service members' reasons for participation.

The first paper reports trends in service members' research participation. A review of ClinicalTrials.gov identified studies starting from 2005 to 2014 that included U.S. service members as participants, either exclusively or with other groups of participants. U.S. service members were participants in 512 studies. Service members participated together with other

groups in 392 studies, while 120 studies included only service members. The top five conditions of interest were PTSD, TBI, amputations, burns, and ocular injuries/disorders. The number of studies started each year peaked in 2011 and declined from 2012 to 2014.

The second paper identifies indications of difficulty recruiting service member research participants using data from ClinicalTrials.gov in 302 studies that included at least 25% U.S. service member research participants. Twelve percent of studies had been withdrawn, terminated, or suspended; enrollment and funding problems were the most common reasons. Only 44% of studies with all service member participants achieved 85% or more of enrollment goals. Findings support anecdotal reports suggesting difficulty recruiting service members as research participants, though findings did not differ significantly from a comparison group of studies with no or very few service members..

The third paper describes original research investigating the reasons current U.S. military service members decided to participate in health research. Fifteen service members with previous research participation experience were interviewed. Service members' research decisions spanned three categories: self-focused, others-focused, and fit-focused. Seven subcategories were identified: curiosity, quality of life, helping researchers, making things better for others, opening doors, fitting the bill, and "why not?" Appealing to the reasons for which service members decide to participate in research can improve recruitment and facilitate research that meets service members' needs.

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The author is a U.S. military service member. This work was prepared as part of her official duties. Title 17, USC, §105 provides that 'Copyright protection under this title is not available for any work of the U.S. Government.' Title 17, USC, §101 defines a U.S. Government work as a work prepared by a military service member or employee of the U.S. Government as part of that person's official duties.

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CHAPTER ONE

INTRODUCTION

Demand for Military-Relevant Health Research

Members of the U.S. armed forces sometimes participate in health research. Recent studies have focused on war-related injuries such as traumatic brain injury (TBI), traumatic amputation, multi-system trauma, and sequelae such as post-traumatic stress disorder (PTSD), depression, suicide, chronic pain, and substance abuse.[1-5]

It is important for military service members to be able to participate in health research. Their participation contributes to advances in health that promote a ready military force and that contribute to the wellbeing of all service members. These health advances are also important for society in general, as findings from military health research are often found to be relevant to civilian health care.[6,7] The recent wars in Iraq and Afghanistan have resulted in over 52,000 U.S. military service members wounded in action.[8] High rates of post-traumatic stress disorder and suicide among service members[8] have heightened society's demand[9-14] for investigation of prevention measures and treatment interventions to support this vulnerable population.

The U.S. Department of Defense's (DoD's) Military Health System reported 3,600 active research protocols in 2011.[15] The increased demand for war-related injuries research has also created a demand for military service members as research participants. As an example, the Army Study to Assess Risk and Resilience in Servicemembers (Army STARRS), supported by Executive Order No. 13625 "Improving Access to Mental Health Services for Veterans, Service Members, and Military Families"[16] had over 100,000 soldiers enrolled by the end of 2012. The executive order called for the establishment of a National Research Action Plan (NRAP) to

address needed research and development in the areas of TBI, PTSD, other mental health conditions, and suicide prevention.[17]

Military Service Members as Vulnerable Research Participants

Service members are vulnerable as research participants due to the superior-subordinate relationships inherent in the rank structure of the military. Such relationships may impede the conduct of ethical research. Other organizational and individual factors may also create power imbalances. Nearly half of service members are 18 to 25 years old.[18] Relative youth, along with military socialization may make some service members more likely to defer to authority.[19] Power imbalances can potentially lead to coercion or undue influence throughout the research process, and particularly during the recruitment and informed consent phases.[19-22]

The increased demand for research in this population may have further elevated service members' vulnerability as research participants. In addition, many service members are concurrently burdened by the experiences and injuries of war. Traumatic injuries may impair decision-making and slow thinking processes.[23] To continue achieving health care advances that enhance the health of military service members, it is important that service members be able to participate in ethically sound research. Further knowledge of the current research participation activities of this group is needed to ensure appropriate human subjects protections that do not unnecessarily impede recruitment of military research participants.[24]

U.S. Military Service Members' Health Research Participation: A Gap in Knowledge

A growing body of literature has explored reasons why various populations have participated in research about a variety of health problems. For example, reasons for pediatric research participation,[25,26] reasons for cancer research participation,[27,28] and reasons for participation in genetics research[29,30] have been explored. These examples from pediatric, cancer,

and genetics research substantiate the scientific community's recognition of the need to understand the reasons individuals decide to participate in specific types of research. Such knowledge contributes to improving recruitment and retention strategies that best support the needs of research participants and facilitates future research.

Empirical data evaluating current U.S. military service members' recent research participation experiences and information about their reasons for research participation could not be located. This suggests a gap in the literature. While it is critical for successful research on military health issues, recruiting and retaining military service members as research participants is reportedly challenging.[24,31,32] Researchers lack empirical evidence that would be useful for developing improved recruitment and retention strategies for research with service member participants.

Information regarding current service members' recent research participation activities and their reasons for participating in health research would be beneficial. The purpose of this dissertation is to explore and describe current U.S. military service members' recent activities related to health research participation including (1) trends in their research participation, (2) challenges in recruiting service members as research participants, and (3) their reasons for deciding to participate in research.

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CHAPTER TWO

TRENDS IN RESEARCH WITH U.S. MILITARY SERVICE MEMBER PARTICIPANTS: A CLINICALTRIALS.GOV REVIEW

ABSTRACT

The objective of this study was to identify trends in health care research from 2005 to 2014 in which U.S. military service members actively participated as research participants. A systematic review of the ClinicalTrials.gov clinical trial registry was performed to identify studies that included U.S. service members as participants, either exclusively or with other groups of participants. U.S. service members were identified as participants in 512 studies. Service members participated together with other groups in 392 studies, while 120 studies included only service members. The top five conditions of interest were PTSD, TBI, amputations, burns, and ocular injuries/disorders. The number of studies started each year peaked in 2011 and declined from 2012 to 2014. Twenty-five percent of studies exclusive to service members aimed to enroll 500 or more participants. Research exclusive to Guard and Reserve service members during this time period was limited. Service members participate in health research, and studies that enroll exclusively service members often seek at least 500 participants. To address the health needs of U.S. service members, it is important to ensure there is not a prolonged decline in research among this population.

INTRODUCTION

Investigators often include U.S. military service members as participants in health care research. For example, several recently published studies that included service members returning from deployments in Iraq and Afghanistan focused on war-related injuries such as traumatic brain injury (TBI)[1, 2] and post-traumatic stress disorder (PTSD).[3, 4] Studies such as these, in which military service members actively participated as research participants, providing the required informed consent, are different from studies[5-8] in which medical records, databases, and registries with U.S. service member health information are reviewed and analyzed. Understanding the types of studies in which U.S. military service members actively participate and identifying trends in such research can provide insights relevant to this population.

ClinicalTrials.gov is a Web-based clinical trials registry maintained by the National Library of Medicine.[9] Registry records contain detailed information about each study, such as the purpose, methods, participant eligibility, anticipated or actual enrollment, contact information, and locations. Information is provided by the study sponsor or principal investigator. ClinicalTrials.gov provides a robust, publicly available source of information about contemporary biomedical research worldwide.

Since the inauguration of ClinicalTrials.gov in February 2000, two important events have stimulated increased registration of studies. First, in 2004, the International Committee of Medical Journal Editors (ICMJE) announced that registration in a public clinical trial registry, such as ClinicalTrials.gov, would be a requirement for publication of a clinical trial in ICMJE member journals beginning in July 2005.[10] After an initial period of adjustment, this requirement was reportedly well received by the scientific community,[11] and it was continued in the most recent ICMJE guidelines.[12] Second, the U.S. Food and Drug Administration Amendments Act of

2007 required registration and results reporting for certain types of clinical trials,[13] thus expanding trial registration requirements that had first been established in the Food and Drug Administration Modernization Act of 1997.[14]

Recent reviews of ClinicalTrials.gov have evaluated trends, characteristics, and status of research in various fields, including pediatrics,[15] sports medicine,[16] rheumatology,[17] nephrology,[18] and oncology.[19] No similar published reviews related to military-relevant health care research or research involving U.S. military service members have been identified.

This study systematically reviewed studies registered in ClinicalTrials.gov that included U.S. military service members as research participants, either exclusively or with other groups of participants. The aim was to identify the trends in and extent of U.S. military service members' participation in health care research during the 10-year period from 2005 to 2014.

METHODS

Search Strategy

A search of ClinicalTrials.gov was performed using the registry's advanced search function, with the search terms and specifications described in Table I. Using the website's Download Search Results function, 5,159 studies, with all available data fields, were downloaded in extensible markup language (XML) format. The file was imported to Microsoft Excel.

No single search term proved to be adequate for broadly locating registered studies that were relevant to U.S. military service members as research participants. An extensive list of search terms was developed to identify a comprehensive and inclusive search in which each resulting item could then be reviewed for elimination or inclusion on a study-by-study basis.

Combining all search terms using the operator OR served to eliminate the duplication of studies that would have occurred in independent searches of unique search terms.[20]

Inclusion Criteria

Each study was evaluated for the following inclusion criteria: (a) The study start date was between 01/01/2005 and 12/31/2014 as specified in ClinicalTrials.gov. For studies with no start date provided, we used first received date between 01/01/2005 and 12/31/2014. (b) The study involved active participation. (c) Of the anticipated or actual number of participants sought for enrollment, at least 10% or at least 30 participants were U.S. military service members. U.S. military service members were defined as active duty, Reserve, or Guard members of any service. Studies were eliminated as reported in Figure I.

The 2005 to 2014 study start date timeframe was selected (a) to limit the search to a manageable volume of data while maintaining the ability to identify trends over time, (b) to correspond with studies that may have been initiated in response to increased military operations and casualties in Iraq and Afghanistan, and (c) because studies were not registered in ClinicalTrials.gov consistently prior to this time due to lack of formal guidelines[10] or regulations.[13]

ClinicalTrials.gov defines study start date as the date a study is first able to enroll participants in the study protocol.[21] Study start date was the most appropriate date to use for determining inclusion criteria in this review, due to the focus on service members' participation in health care research. However, the ClinicalTrials.gov advanced search function did not provide an option for searching by study start date.[20] Instead, we used first received date, with an expanded date range to select for review any eligible studies with actual study start dates in the target range.

Active participant involvement was required for a study to be included in this review. For example, retrospective chart reviews and safety surveillance studies were eliminated if the study did not involve contact with individuals and/or there was no direct data collection from individuals.

The thresholds of a minimum of 10%, or at least 30, U.S. military service member participants aimed to eliminate studies that did not involve a substantial proportion or number of service members. The intention was to avoid simply including all studies in which one or more service members could conceivably participate, and instead to examine studies that included U.S. military service member participants to an extent that was substantially meaningful.

The search was not limited to studies performed in the United States. Studies performed at overseas U.S. military installations that included U.S. military service members were also included.

Review Process

Studies outside the start date parameters were eliminated first. Next, the title of each study was reviewed to determine inclusion or exclusion. When a determination could not be made based on title alone, other data fields were evaluated, such as condition being investigated, lead sponsor, collaborators, or study location. Figure I shows the first reason found for determining a study ineligible for inclusion. (Many studies were excluded for more than one reason.)

One-third of the studies (n = 1,721, 33.4%) required further evaluation to determine if they met inclusion criteria. To accomplish this, the study hyperlink, a data field included in the downloaded search results, was used to review the complete registry entry on the ClinicalTrials.gov website. Each study record was reviewed with close attention to the reported

participant eligibility and participant inclusion and exclusion criteria to determine if the study met criteria for inclusion in this review.

Final Categorization

The studies meeting inclusion criteria were further categorized into three groups based on the proportion of U.S. military service member research participants compared to other study participants: (a) studies with approximately 10%–24%, or at least 30, service member participants; (b) studies with at least 25%, but not exclusively, service member participants; and (c) studies with exclusively U.S. military service member participants. For ease of reading, in this paper these groups will be discussed as including (a) few, (b) many, or (c) all U.S. military service member participants, respectively.

Individual study registry records were reviewed closely and information was manually collected to determine the types of participants and to categorize by proportions of participants. Items taken into consideration included but were not limited to lead sponsor, collaborators, location of the research, specific inclusion and exclusion criteria, number and types of civilian and military facilities for multi-location studies, anticipated or actual enrollment, condition being studied, and age groups most commonly affected by a given condition. Study methods or findings publications, recruitment materials, and study websites were reviewed when available.

Excluded Studies Comparison Group

A group of 512 studies identified in the initial search strategy but not meeting inclusion criteria were randomly selected to compare against the studies included in the review. They were limited to U.S. research with adult participants and study start dates from 2005 to 2014.

Data Analysis

Descriptive statistics, including frequencies and percentages of categorical variables, were performed using IBM SPSS Statistics Version 23. When appropriate, cross tabulations of two categorical variables were performed with weighted cases using 2-tailed Fisher's Exact Test to estimate *p*-value with level of significance $\alpha = 0.05$. Conditions of interest were ranked using Microsoft Excel.

RESULTS

As of August 1, 2015, ClinicalTrials.gov contained 196,305 registered studies from all U.S. states and 190 countries. A total of 512 studies were identified as including U.S. military service members, as defined by the inclusion criteria. These studies were further categorized into three groups to differentiate between the proportions of U.S. service members included as participants. Nearly a quarter of the studies (*n* = 120, 23.4%) had study inclusion criteria limiting participation exclusively to U.S. service members. The remaining 392 studies (76.6%) included U.S. service members and other participants such as Veterans, military retirees, military health care beneficiaries, U.S. Department of Defense employees, and other civilians. Of the total 512 studies, 182 (35.5%) included at least 25% but not exclusively U.S. service member participants, and 210 (41.0%) had at least 10% but less than 25%, or at least 30, U.S. service member participants (see Figure I and Table II).

Participant Type

Among all 512 included studies, 500 (97.7%) included active duty service members as participants, while only 168 studies (32.8%) included Guard or Reserve service members as participants (Table II). Among the studies that included 100% service members, more than half (*n* = 64, 53.3%) specifically limited participation to active duty service members, while 40.8% (*n*

= 49) permitted a combination of active duty and Reserve and/or Guard service members. Among studies exclusive to service members, significantly fewer studies (n = 7, 5.8%, $p < .001$) were specifically limited to Reserve or Guard service members compared to those limited to only active duty service members.

Roughly half of the studies also included military health care beneficiaries (n = 281, 54.9%) and military retirees (n = 249, 48.6%) in addition to service members. Approximately one-fifth of studies overall also included U.S. veterans (n = 117, 22.9%) and other civilians (n = 110, 21.5%).

Conditions of Interest

The top five conditions of interest among all 512 studies were post-traumatic stress disorder (PTSD; n = 100, 19.5%), traumatic brain injury (TBI; n = 56, 11.0%), amputation care (n = 22, 4.3%), burns (n = 22, 4.3%), and ocular injuries/disorders (n = 21, 4.1%). Studies had between one and six conditions of interest. Table III summarizes the top 20 conditions of interest for all included studies and Table IV summarizes the top 20 conditions of interest by study group.

PTSD was the top-ranking condition of interest overall for all included studies (n = 100, 19.5%), and for the study groups with many (n = 67, 36.8%) and all service member participants (n = 27, 22.5%). In contrast, in the study group with few service members, PTSD ranked only tenth in conditions of interest (n = 6, 2.9%), tied with back pain, dengue fever, glucose control, influenza, orthopedic trauma, obstructive sleep apnea, and wound research.

TBI was the second ranked condition of interest overall for all included studies (n = 56, 11.0%), and for the study groups with many (n = 29, 16.0%) and all service member participants

(*n* = 18, 15.0%). TBI was tied with cardiovascular disease as the fourth-ranked condition of interest for the study group with few military participants (*n* = 9, 4.3%).

Ocular injuries/disorders ranked in the top five conditions of interest when all 512 studies were combined but was not in the top five for any of the three study groups categorized by proportion of service members. The group with few service members had eight studies (3.8%) examining ocular injuries and disorders; the group with many service members had four studies (2.2%); and the group with all service members had nine studies (7.5%).

Ninety studies (17.6%) included pain as a condition of interest. Pain research was categorized as acute pain, chronic pain, back pain, postoperative pain, phantom limb pain, knee injuries/pain, leg/hip pain, shoulder/neck pain, and headache/migraine. Had all pain categories been combined in one group, pain would have been the second highest ranked condition of interest overall. Back pain research was the only pain-focused research in the top 20 conditions of interest for all study groups, and it ranked sixth for all studies overall. Chronic pain was among the top 20 conditions of interest for the groups with all and many service members (17th and 14th respectively). Acute pain was among the top 20 conditions only in the group with many service members, and was not in the top 20 overall.

Trends by Study Start Year

Figure II depicts study start dates by year over the 10-year period from 2005 to 2014. The number of studies by study start year peaked in 2011 for all included studies combined (*n* = 70), for the group with many service members (*n* = 35), and for the group with all service members (*n* = 19). For these groups, there was a decline in the number of studies started each year from 2012 to 2014. For the group with few military, 2014 was the year the greatest number of studies started (*n* = 31).

Study Type

Overall, most studies were interventional (n = 405, 79.1%) and fewer were observational (n = 107, 20.9%). This distribution did not differ significantly from the excluded comparison group (p = .433). The greatest difference between interventional and observational studies occurred in the group with many service members, with 84.6% (n = 154) interventional studies compared to 15.4% (n = 28) observational (Table V). There was a higher proportion of interventional studies in the many service member group than in the group with few service members (n = 160, 76.2%, p = .042), and in the group with all service members (n = 91, 75.8%, p = .071).

Anticipated Enrollment

Investigators often sought to enroll large numbers of participants (Table V). Significantly more studies among the included studies sought 500 or more participants compared to the excluded studies comparison group (n = 69, 13.5% vs. n = 45, 8.8%, p = .022). Among studies exclusive to military service members, 25% (n = 30) had a goal of 500 or more participants. This was a significantly higher proportion than for the groups with few service members and (n = 32, 15.2%, p = .040) and many service members (n = 7, 3.8%, p < .001) and for the excluded studies comparison group (p < .001).

Similarly, significantly more studies among the included studies sought 2,000 or more participants compared to the excluded studies comparison group (n = 21, 4.1% vs. n = 7, 1.4%, p = .011). Among studies exclusive to military service members, 13 (10.8%) had a goal of 2,000 or more participants. This was a significantly higher proportion than for the groups with few service members (n = 6, 2.9%, p = .005) and many service members (n = 2, 1.1%, p < .001) and for the excluded studies comparison group (p < .001).

Overall, more than half (n = 272, 53.1%) of the included studies had a goal of 100 or more participants, significantly more than in the comparison group (n = 218, 42.6%, $p < .001$). The group exclusive to service members had the highest proportion of studies seeking 100 or more participants (n = 83, 69.2%), while the group with many service members had the lowest proportion (n = 66, 36.3%). The group with many service members had significantly more studies enrolling less than 100 participants than both the groups with few and all service members ($p < .001$). However, the group with many service members did not differ significantly from the excluded comparison group in the number of studies enrolling less than 100 participants (p = .160).

DISCUSSION

A systematic review of ClinicalTrials.gov identified studies with U.S. military service member participants from 2005 to 2014 to identify and report the trends in and extent of their research participation. This study is unique among reviews of ClinicalTrials.gov in that it is the first we are aware of that focuses on research on military service members of any nationality.

Consistency of Studies' Top Conditions of Interest with Priority Clinical Needs

Nearly a quarter (22.5%) of the studies with exclusively military participants and over one-third (36.8%) of the studies in the group with many military participants had PTSD as a condition of interest. Overall, PTSD was the highest ranked condition of interest, accounting for 19.5% of all included studies. TBI was the only condition of interest represented in the top five conditions of interest across study groups, regardless of the proportion of service members included.

The top conditions of interest in the studies included in this review are consistent with many of the top health needs of service members given the wars and conflicts since the early

2000s. More than 52,000 U.S. service members have been wounded in action between 2001 and mid-2015; over 177,000 U.S. service members have been diagnosed with PTSD since 2000; there have been more than 327,000 cases of TBI among U.S. forces since 2000; and over 1,600 U.S. service members have suffered major limb amputations from battle injuries since 2001.[22] Based on this review, investigators are clearly making efforts to help address these priority clinical areas.

Trends in Numbers of Studies Started With Service Member Participants

From 2012 to 2014, there was a trend of decreasing numbers of studies started each year in the groups with many and all service member participants. This trend is inconsistent with other sources that have anticipated a continued increase in research relevant to and including military service members during this timeframe. For example, Executive Order No. 13625, "Improving Access to Mental Health Services for Veterans, Service Members, and Military Families,"[23] in 2012 called for the establishment of a National Research Action Plan (NRAP) to address needed research and development in the areas of TBI, PTSD, other mental health conditions, and suicide prevention. The NRAP is a wide-reaching collaboration developed by the U.S. Departments of Defense, Veterans Affairs, Health and Human Services, and Education.[24] The NRAP would lead one to anticipate an increase in the number of studies in these priority clinical areas following 2012, rather than the decrease identified in this review.

It is important to note that the comparison group of excluded studies also experienced a sharp decline in the number of studies started in 2014, after a peak in 2013. For the groups in which the number of studies started in 2014 declined from previous years, it is possible —yet unlikely—that this decline is due to studies not yet being registered in ClinicalTrials.gov: (a) studies are generally registered in advance of the study start date, as previously discussed; (b)

this review was conducted in the second half of 2015 to capture any late registries; and (c) the group with few military service members recorded its greatest number of study starts in 2014.

Trends in Research with Many Service Member Participants

The group of studies with many service members tended to be interventional studies with fewer participants. This group had significantly more studies with less than 100 participants compared to the groups with few and all service members. Additionally, significantly more studies in the group with many service members were interventional studies compared to the groups with few and all service members. This trend may be helpful for researchers to consider when designing interventional studies that will include mostly service members along with other groups of participants.

Trends in Research with Exclusively Service Member Participants

Studies with exclusively service member participants often sought large samples. Significantly more studies exclusive to service members sought to enroll 500 or more participants compared to the groups with few and many service members. When considering even larger studies of 2,000 or more participants, the group of studies with all service members remained with significantly more studies compared to the groups with few and many service members. Studies in which service members participate exclusively often seek significantly more participants than do studies with few or many service member participants. This trend may be important for investigators, institutional review boards, and funding agencies to consider when designing and reviewing studies that will include exclusively service member participants.

Research exclusive to Guard and Reserve service members was limited in comparison to the number of studies in which exclusively active duty service members participated. More research may be needed to support the unique needs of these service members, particularly in

relation to reintegration and transition to civilian environments following deployment. Guard and Reserve service members may have different challenges in post-deployment reintegration[25, 26] and access to care[27] as they may not have the extensive military community support and resources available to active duty service members.

Limitations

This review provides insight into one publicly available data source regarding research, completed and in progress, in which U.S. military service members participated. This study has several limitations. First, not all studies in which military service members participate are registered in ClinicalTrials.gov as not all studies are legally required to be registered.[9] This may explain why a smaller proportion of observational studies were identified in this review compared to interventional studies. A second limitation is the inability to determine whether there has been an increase in the overall number of studies in which service members participated or simply an increase in studies registered in ClinicalTrials.gov.

Data collection and study categorization were performed mainly by the primary author, who has nearly 20 years of full-time active military experience in the U.S. Military Health System. This approach provided consistency in the way studies were categorized. The time and attention to detail given to the data collection and organization was significant; it would not have been feasible for multiple authors to perform these tasks and it would not likely have added adequate value and improvement to the study overall to be worthwhile.

CONCLUSION

U.S. military service members participate in health care research both in exclusively military studies and along with other groups of participants, such as Veterans, military retirees, military health care beneficiaries, Department of Defense employees, and other civilians.

Investigators of studies that exclusively enroll service members often seek large numbers of participants. Research exclusive to Guard and Reserve service members during this time period was limited.

This review identified an overall decline in studies started each year from 2012 to 2014, following a peak in 2011, though the number of studies started in 2012, 2013, and 2014 still remained above the number started each year from 2005 to 2010. It is important to ensure that there is not a prolonged decline in research among this population. The top conditions of interest in the studies identified in this review were consistent with priority clinical needs of service members. U.S. military service members have acute and chronic health needs, often as a result of injuries or exposures during their service, which they experience during their service and long after leaving the military. Military-relevant health research must remain a priority.

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TABLE I. Search Strategy

Item	Specification
Registry	ClinicalTrials.gov
Search date	08/08/2015
Search type	Advanced
Search terms	Military
	"active duty"
	soldier
	sailor
	airman
	marine
	Guardsman
	Army
	Navy
	"Air Force"
	"Marine Corps"
	"Coast Guard"
	"National Guard"
	"service member"
	deployment
	combat
	war
	TBI
	PTSD
	reintegration
Age group	Adult (18–65)
First received	From 01/01/2003 to 08/01/2015

Notes: We tested and verified that for compound words in quotes (e.g., "Marine Corps," "active duty"), the use of capital versus lower-case letters did not change search results. Similarly, plural and singular search terms (e.g., soldiers vs. soldier) also provided identical results.

TABLE II. Participant Type by Study Group

		Participant type							
		Military participants			Other participants				
Group		Active duty only	Reserve or Guard only	Active duty with Reserve and/or Guard	Veterans	Military retirees	Military health care bene-ficiaries	DoD employees	Other civilians
Exclusively military participants (n = 120)	*n*	64	7	49	0	0	0	0	0
	%	53.3	5.8	40.8	0	0	0	0	0
At least 25% but not exclusively military participants (n = 182)	*n*	99	4	79	96	100	84	8	29
	%	54.4	2.2	43.4	52.7	54.0	46.2	4.4	16.0
10%–24% or at least 30 military participants (n = 210)	*n*	181	1	28	21	149	197	11	81
	%	86.2	0.48	13.3	10.0	71.0	93.8	5.5	38.6
All studies (N = 512)	*n*	344	12	156	117	249	281	19	110
	%	67.2	2.3	30.5	22.9	48.6	54.9	3.7	21.5

Note: DoD, Department of Defense.

TABLE III. Top 20 Conditions of Interest

All included studies ($N = 512$)			
Condition	*n*	% of total	Rank
PTSD	100	19.5	1
TBI	56	11.0	2
Amputation care	22	4.3	3
Burns	22	4.3	3
Ocular injuries/disorders	21	4.1	5
Back pain	20	3.9	6
Depression	19	3.7	7
Sleep	18	3.5	8
Malaria	17	3.3	9
Cognitive performance	15	2.9	10
Combat stress disorders	15	2.9	10
Nutrition status	15	2.9	10
Stress	15	2.9	10
Diabetes	14	2.7	14
Orthopedic trauma	14	2.7	14
Post-concussive syndrome	14	2.7	14
Post-op pain	14	2.7	14
Hemodynamic status	13	2.5	18
CV disease	12	2.3	19
Phantom limb pain	12	2.3	19

Notes: Studies may indicate more than one condition of interest. Studies are listed alphabetically in the same cell when there are ties within a rank. More than 20 conditions are listed when the 20th-listed condition was tied with other conditions. Abbreviations: CV, cardiovascular; Post-op, postoperative; PTSD, post-traumatic stress disorder; TBI, traumatic brain injury

TABLE IV. Top 20 Conditions of Interest by Study Group

10%–24% or at least 30 military participants (*n* = 210)				At least 25% but not exclusively military participants (*n* = 182)				Exclusively military participants (*n* = 120)			
Condition	*n*	% of total	Rank	Condition	*n*	% of total	Rank	Condition	*n*	% of total	Rank
Malaria	16	7.6	1	PTSD	67	36.8	1	PTSD	27	22.5	1
Diabetes	12	5.7	2	TBI	29	16.0	2	TBI	18	15.0	2
Cancer treatment	10	4.8	3	Burns	19	10.4	3	Stress	12	10.0	3
CV disease	9	4.3	4	Amputation care	14	7.7	4	Back pain	10	8.3	4
TBI	9	4.3	4	Combat stress disorders	9	4.9	5	Depression	10	8.3	4
Ocular injuries/ disorders	8	3.8	6	Sleep	9	4.9	5	Nutrition status	10	8.3	4
Post-op pain	8	3.8	6	Hemodynamic status	8	4.4	7	Ocular injuries/ disorders	9	7.5	7
Cancer screening	7	3.3	8	Phantom limb pain	8	4.4	7	Cognitive performance	8	6.7	8
Pregnancy	7	3.3	8	Post-concussive syndrome	7	3.8	9	Sleep	7	5.8	9
Back pain	6	2.9	10	Depression	6	3.3	10	Post-concussive syndrome	6	5.0	10
Dengue fever	6	2.9	10	Family functioning	6	3.3	10	Alcohol abuse	5	4.2	11
Glucose control	6	2.9	10	Post-op pain	6	3.3	10	Amputation care	5	4.2	11
Influenza	6	2.9	10	Suicide prevention	6	3.3	10	Anxiety disorders	5	4.2	11
Orthopedic trauma	6	2.9	10	Anxiety disorders	5	2.7	14	Combat stress disorders	5	4.2	11
OSA	6	2.9	10	Chronic pain	5	2.7	14	Muscle atrophy	5	4.2	11
PTSD	6	2.9	10	Hearing disorders	5	2.7	14	Suicide prevention	5	4.2	11
Wounds	6	2.9	10	Injury prevention	5	2.7	14	Chronic pain	4	3.3	17
Diarrhea prevention	5	2.4	18	Acute pain	4	2.2	18	Extreme environments	4	3.3	17
Health knowledge	5	2.4	18	Back pain	4	2.2	18	Injury prevention	4	3.3	17
Leg/hip pain	5	2.4	18	Cognitive performance	4	2.2	18	Orthopedic trauma	4	3.3	17
				Ocular injuries/ disorders	4	2.2	18	Smoking cessation	4	3.3	17
				Orthopedic trauma	4	2.2	18	Substance abuse	4	3.3	17

Notes: Studies may indicate more than one condition of interest. Studies are listed alphabetically in the same cell when there are ties within a rank. More than 20 conditions are listed when the 20th-listed condition was tied with other conditions. Abbreviations: CV, cardiovascular; Post-op, postoperative; PTSD, post-traumatic stress disorder; TBI, traumatic brain injury; OSA, obstructive sleep apnea.

TABLE V. Study Type and Anticipated Enrollment

Characteristic	All included studies (N = 512)	10%–24% or at least 30 military participants (n = 210)	At least 25% but not exclusively military participants (n = 182)	Exclusively military participants (n = 120)	Excluded comparison group (N = 512)
Study type, *n* (%)					
Observational	107 (20.9)	50 (23.8)	28 (15.4)	29 (24.2)	96 (18.8)
Interventional	405 (79.1)	160 (76.2)	154 (84.6)	91 (75.8)	416 (81.3)
Anticipated enrollment, *n* (%)					
<30	53 (10.4)	14 (6.7)	32 (17.6)	7 (5.8)	85 (16.6)
30–49	89 (17.4)	38 (18.1)	43 (23.6)	8 (6.7)	80 (15.6)
50–99	98 (19.1)	35 (16.7)	41 (22.5)	22 (18.3)	129 (25.2)
100–149	71 (13.9)	29 (13.8)	27 (14.8)	15 (12.5)	72 (14.1)
150–249	80 (15.6)	30 (14.3)	25 (13.7)	25 (20.8)	64 (12.5)
250–499	52 (10.2)	32 (15.2)	7 (3.8)	13 (10.8)	37 (7.2)
500–999	32 (6.3)	17 (8.1)	4 (2.2)	11 (9.2)	27 (5.3)
1000–1999	16 (3.1)	9 (4.3)	1 (0.5)	6 (5.0)	11 (2.1)
≥2000	21 (4.1)	6 (2.9)	2 (1.1)	13 (10.8)	7 (1.4)
<100	240 (46.9)	87 (41.4)	116 (63.7)	37 (30.8)	294 (57.4)
≥100	272 (53.1)	123 (58.6)	66 (36.3)	83 (69.2)	218 (42.6)
≥500	69 (13.5)	32 (15.2)	7 (3.8)	30 (25.0)	45 (8.8)

Note: Actual enrollment was used for 25 studies in the included group and 18 studies in the comparison group for which anticipated enrollment was not reported in the study records.

FIGURE I. Flow of studies through the review.

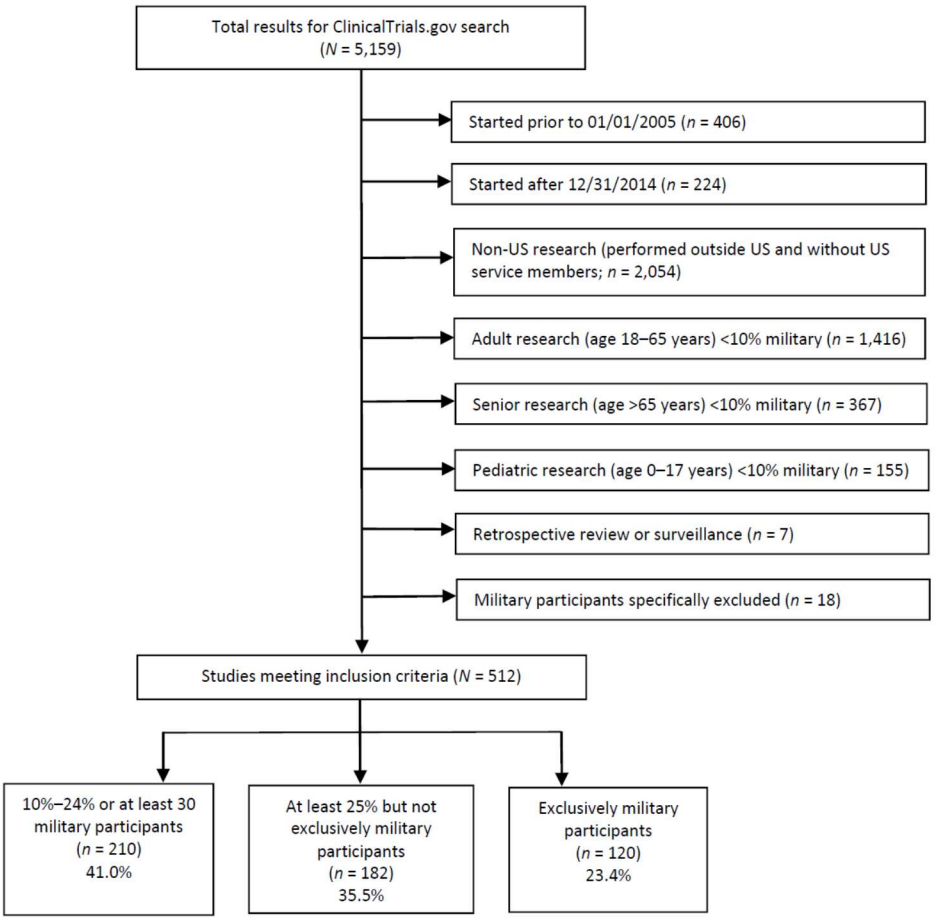
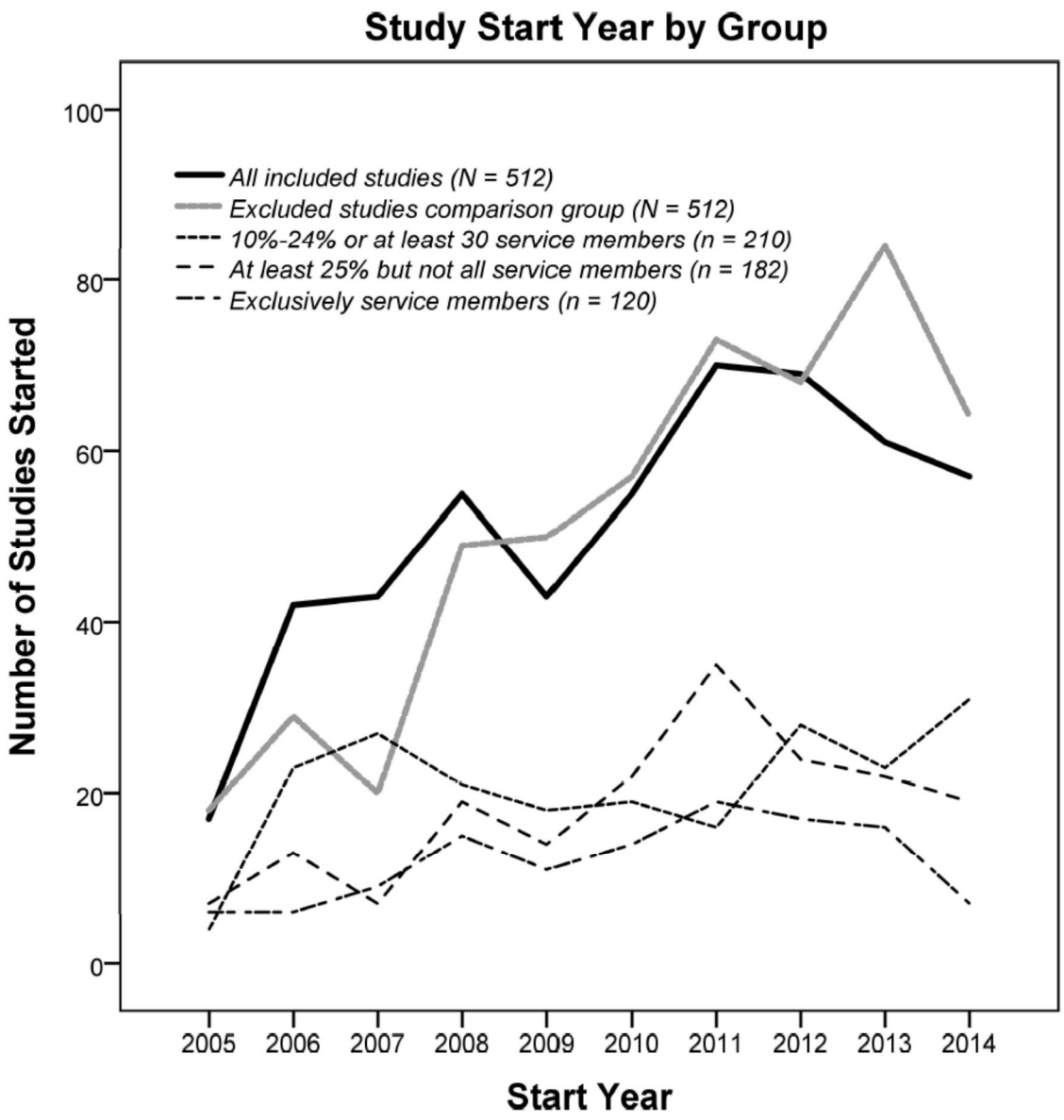


FIGURE II. Number of studies started per year, by study group. If study start date was not reported in ClinicalTrials.gov, then study first received date was used.



CHAPTER THREE

INDICATIONS OF RECRUITMENT CHALLENGES IN RESEARCH WITH U.S. MILITARY SERVICE MEMBERS: A CLINICALTRIALS.GOV REVIEW

ABSTRACT

The purpose of this study was to identify indications of difficulty recruiting U.S. military service members as research participants. Using data from ClinicalTrials.gov, 302 studies that included at least 25% U.S. military service member research participants were (1) compared to studies with no or very few service member participants and (2) compared by the proportion of service member participants. Studies were evaluated for recruitment status; reasons for study withdrawal, termination, or suspension; anticipated and actual enrollment; and changes in inclusion criteria. Twelve percent of military studies had been withdrawn, terminated, or suspended; enrollment and funding problems were the most common reasons. All study groups had indications of difficulty recruiting participants. There were no significant differences between the military and comparison groups. Only 44% of studies with all service member participants achieved 85% or more of enrollment goals. Although no significant differences were found between the military studies and a comparison group of studies, the findings support anecdotal reports suggesting difficulty recruiting U.S. military service members as research participants.

INTRODUCTION

Between 2001 and 2015, military operations in Iraq, Afghanistan, and surrounding locations resulted in over 52,350 U.S. service members wounded in action.[1] There is a need for military-relevant health research, and the success of such research often depends upon recruiting adequate numbers of military service members as volunteer research participants. U.S. military service members' participation in health care research is thus important to the development of health advances and interventions specific to this population.

In its 2012 MHS Stakeholders' Report, the U.S. Department of Defense's Military Health System reported 3,600 active research protocols in 2011.[2] The 2013 National Research Action Plan reflected to the need to enhance research and development in the areas of traumatic brain injury (TBI), post-traumatic stress disorder (PTSD), suicide prevention, and other mental health conditions for military service members.[3] The increased demand for war-related injuries research, as well as increased funding opportunities for military health research,[4] has created a demand for military service members as research participants, particularly those with war-related injuries and sequelae such as TBI, PTSD, and chronic pain.

Reports of Difficulty Recruiting Service Member Research Participants

While critical for successful research on military health issues, military researchers have recently reported difficulties in recruiting service members as research participants.[5-7] Bush and colleagues[5] described their own experiences of difficulties recruiting service members as research participants, while noting a lack of empirical data documenting such difficulties, despite anecdotal evidence. In their search of literature from 2001 to 2012, they identified only 24 published randomized controlled clinical trials that both included active duty service members

and reported recruitment or attrition data. Almost all of the 24 studies included attrition data but did not report enrollment rates (exact numbers not provided).[5]

Williams and colleagues[6] reported difficulties, particularly delays, in conducting military research and recommended reforms in military human subjects protections to alleviate some of the reported problems. They discussed their experiences of unnecessary delays in military ethical reviews, which led to increased difficulty in enrolling service members. For instance, delays had resulted in inadequate time to recruit participants for their study. They also reported that delays in getting approvals resulted in staff changeover, which hindered development of relationships with potential and enrolled participants.

Braun and colleagues[7] presented a review of literature that identified recruitment challenges in research with U.S. military women. Their findings indicated that there is limited literature regarding recruitment and retention challenges in research with service members as research participants, and specifically with female service members as research participants.

Use of the ClinicalTrials.gov Clinical Trial Registry

ClinicalTrials.gov is a publicly available, free, online clinical trial registry and results database of publicly and privately sponsored studies. The registry is maintained by the National Library of Medicine at the National Institutes of Health.[8] Principal investigators and study sponsors register their studies in ClinicalTrials.gov for several reasons, including to communicate transparently with the public,[9] to comply with Food and Drug Administration regulations,[10] and to meet journal recommendations.[11]

Recent reviews of ClinicalTrials.gov have identified challenges in participant recruitment, and barriers to study completion.[12-15] However, no reviews of ClinicalTrials.gov have explored such challenges in research with U.S. military service members. The purpose of

this current study was to identify indications of difficulty recruiting U.S. military service members as research participants based on data from study records in ClinicalTrials.gov. Records of studies starting between 2005 and 2014 and with at least 25% U.S. military service members as research participants were compared both within the group, according to the proportion of service member participants, and outside the group, to a similar group of studies with no or very few U.S. military service members.

METHODS

Identification of Studies

A search of the ClinicalTrials.gov registry was performed to broadly identify studies in which U.S. military service members may have participated. The search was limited to studies that were first received in ClinicalTrials.gov between 01/01/2003 and 08/01/2015 and included adult research participants (ages 18 to 65 years). Search terms included military, active duty, soldier, sailor, airman, marine, guardsman, Army, Navy, Air Force, Marine Corps, Coast Guard, National Guard, service member, deployment, combat, war, TBI, PTSD, and reintegration.

Each study was evaluated for three inclusion criteria: (1) The study started between 01/01/2005 and 12/31/2014. (2) The study required the active involvement of research participants. (3)At least 25% of the study's actual or intended participants were to be current members of any U.S. military service (Air Force, Army, Marine Corps, Navy) and of any duty status (active duty, Reserve, or Guard) at the time of enrollment.

After the initial group of studies was identified, the studies were further categorized according to the proportion of service member participants. Studies were categorized as having (1) *many* service member participants, if at least 25% but less than 100% of participants were estimated to be U.S. service members, or (2) *all* service member participants, when information

in a study's record specified that 100% of participants were U.S. service members. The combined group of studies with many and all service members will be referred to as the "military group."

A group of 302 U.S. studies with adult participants were randomly selected from the studies that had been excluded during the initial search. These studies were used as a comparison group of studies that shared characteristics with the included studies (since all studies were identified through the same search strategy), but whose participants were less than 10% service members. The comparison group was matched to the military group by study start year, to have an equal number of studies starting each year between 2005 and 2014, to account for research trends that may have occurred over this time frame, such as funding availability or public interest in research participation.

Data Collection

For each study in the military and comparison groups, the study record in ClinicalTrials.gov was reviewed for data elements that could indicate difficulty recruiting participants. Specific data elements are described below. Since a study's registry record is updated periodically by the principal investigator or sponsor, records were reviewed for updates throughout this review process, and any updated information was used in the analyses.

Recruitment status

Recruitment status of each study was assessed based on pertinent ClinicalTrials.gov categories of participant recruitment status: (1) Studies that are "not yet enrolling" have not begun to recruit or enroll participants. (2) Studies that are "recruiting" are enrolling new participants. (3) Studies that are "active, not recruiting" continue to involve participants but are no longer recruiting or enrolling new participants. Several recruitment status categories indicate

a study's progress: (4) "Withdrawn" studies were stopped early and did not enroll any participants. (5) "Terminated" studies are those which enrolled at least one participant, but stopped enrollment early, will not restart enrollment, and have ended all participant involvement. (6) "Suspended" studies stopped enrolling participants before meeting full enrollment but may start enrolling again at some point. And (7) "completed" studies reached their anticipated end and participants are no longer actively involved.[16-18]

Reason for withdrawal, termination, or suspension

For studies that were withdrawn, terminated, or suspended—in other words, stopped prior to reaching completion as planned—the reason was assessed. In ClinicalTrials.gov, the principal investigator or study sponsor may provide a short free-text description of up to 160 characters to explain the reason the study was stopped. However, providing a reason for stopping a study is not required by ClinicalTrials.gov or the Food and Drug Administration.[16] Reasons provided were grouped into 10 categories for analysis.

Anticipated and actual enrollment

Each study's record was reviewed to determine both anticipated enrollment and actual enrollment. This was accomplished by using the Study History feature in ClinicalTrials.gov, which provides access to all changes that have been made to a particular study record since its creation.[19] Actual enrollment data were not available for all studies, because some studies were still recruiting participants and some records of completed studies had not been updated with actual enrollment information. Some studies that were registered in ClinicalTrials.gov late (while already in progress or completed), and when the actual enrollment information was already known, the anticipated enrollment was not always provided.

Changes in inclusion criteria

Record archives for the studies in the military group were reviewed to identify changes in inclusion criteria over the course of a study's history. Particular attention was given to changes that expanded inclusion criteria from exclusively military service member participants to permitting and other groups of participants, such as civilians or military veterans, as well. (This analysis was not performed for the studies in the comparison group.)

Data Analysis

Descriptive statistics, including frequencies and percentages of categorical variables, were performed using IBM SPSS Statistics Version 23. Cross tabulations of two categorical variables were performed with weighted cases using 2-tailed Fisher's exact test to estimate *P* value with level of significance $\alpha = .05$. Student's independent samples parametric *t*-test was used to compare means using "equal variances not assumed" formula. The non-parametric Mann-Whitney test was performed to compare mean ranks of two groups reporting 2-tailed significance.

For studies in which both the actual and anticipated enrollment numbers were known, studies were categorized as having adequately met participant enrollment goals if the final enrollment was at least 85% of the anticipated enrollment. This metric was based on that used by Carlisle and colleagues[14] in their ClinicalTrials.gov review of studies that did not achieve adequate enrollment or were terminated. The authors argued that it was reasonable to conclude that studies that attained less than 85% of the anticipated number of participants were compromised.[14] Two more stringent metrics were also used in the current study to evaluate how close the actual enrollment was compared to the anticipated enrollment: (1) actual and

anticipated enrollment were equal, and (2) actual enrollment was within 5% of anticipated enrollment.

RESULTS

A total of 302 studies were identified that included current U.S. military service member participants as defined by the inclusion criteria. Of these studies, 182 (60.3%) included many U.S. service member participants (at least 25% but not all) and 120 (39.7%) included all service member participants.

Recruitment Status

Recruitment status is reported in Table I. In the military group, 84 studies (27.8%) were currently recruiting participants, compared to 93 studies (30.8%) in the comparison group. Within the military group, the group with many service member participants had 49 studies (27.0%) currently recruiting, and the group with all service members had 35 studies (29.2%) currently recruiting participants.

The only category of recruitment status that differed significantly between the military group and the comparison group was the category of studies "not yet enrolling"; there were significantly more studies in the military group that were "not yet enrolling" compared to the comparison group (n = 10, 3.3% and n = 0, 0%, respectively, p = .002). There was no significant difference among categories of recruitment status between the military subgroups with many or all service member participants.

Reasons for Withdrawal, Termination, or Suspension

In the military group, 36 studies (11.9%) were withdrawn, terminated, or suspended, compared to 33 studies (10.9%) in the comparison group (Table II). The two most common reasons reported in studies in the military group were enrollment problems (n = 11, 30.6%) and

funding problems (n = 10, 27.8%). In the comparison group, the most common reasons reported for study withdrawal, termination, or suspension were enrollment problems (n = 8, 24.2%) and sponsor decision (n = 5, 15.2%).

There were no significant differences in the number of studies withdrawn, terminated, or suspended for any particular reason between the military and comparison groups or between the groups with many service members and all service members. There was a trend toward a significantly higher number of study withdrawals, terminations, or suspensions attributed to funding problems in the military group compared to the comparison group (n = 10 , 27.8% and n = 3, 9.1% respectively, p = .066).

Anticipated and Actual Enrollment

Both anticipated and actual enrollment numbers were available for 140 studies (46.4%) in the military group and 143 studies (47.4%) in the comparison group (Tables III and IV). Sixty-seven military group studies (47.9% of the studies with known anticipated and actual enrollment numbers) achieved at least 85% of the anticipated enrollment, the metric suggested by Carlisle and colleagues[14] to determine adequate enrollment. In the comparison group, 72 studies (50.3% of the studies with known anticipated and actual enrollment) reported actual enrollment of at least 85% of anticipated enrollment (p = .722). There were no significant differences between the military and comparisons groups in actual compared to anticipated enrollment.

However, in comparing the military subgroups with many and all service member participants, significant differences were found in the median values for anticipated enrollment, actual enrollment, and differences between actual and anticipated enrollment (Table IV). The group with all service members had significantly higher median anticipated enrollment and actual enrollment numbers compared to the group with many service members (p = .001). The

median difference between actual and anticipated enrollment was significantly lower in the group with all service members compared to the group with many service members (p = .025). There was no significant difference in the median percent differences between actual and anticipated enrollment. Evaluations of mean values for anticipated enrollment, actual enrollment, difference between actual and anticipated enrollment, and percent difference between actual and anticipated enrollment were not significantly different between the groups with many and all service members.

Change in Inclusion Criteria

Four studies in this review changed their initial inclusion criteria of exclusively service members to later include additional groups of participants (Table V). One, a pilot study of the use of botulinum toxin type B for low-back pain, initially sought exclusively active duty participants, then expanded to include other military health care beneficiaries, and was eventually terminated. The reason provided for termination was enrollment failure: specifically, that no eligible participants had enrolled after two years of recruitment.

DISCUSSION

To evaluate indications of difficulty recruiting U.S. military service members for research, a systematic review of study records in ClinicalTrials.gov was performed for studies that included at least 25% service member participants. Findings provide additional evidence of the difficulty recruiting U.S. military service members as research participants. However, the indications of challenges in participant recruitment among studies with U.S. service member research participants were not significantly different from a comparison group of studies with no or very few service member participants. Findings also suggest that there is not a significant

difference in difficulty recruiting U.S. service member participants when studies include all service members or include many but not all service members.

Recruitment Status

Both military and comparison groups had similar proportions of studies withdrawn, terminated, and suspended; at 11.9% (military) and 10.9% (comparison), these numbers were higher than those reported in other reviews of ClinicalTrials.gov. For example, in their review of antimicrobial studies registered in ClinicalTrials.gov, Stockmann and colleagues reported that 8% of studies had been withdrawn, terminated, or suspended.[20] In a review of cardiovascular studies registered in ClinicalTrials.gov from 2007 to 2010, Califf and colleagues found that 4% of trials had been withdrawn, terminated, or suspended. Suspended studies were uncommon (≤1%) in both the current review and other reviews.[20, 21]

It is not clear why the studies in both the military and comparison groups would have higher proportions of withdrawn and terminated studies compared to other areas of research. A large proportion of studies in both groups were related to PTSD and TBI, so it is possible that one or both of these conditions may generally present more challenges in bringing a study to its planned completion. TBI was a condition of interest in a significantly smaller number of studies in the military group than in the comparison group (n = 47; 15.6% and n = 126, 41.7%, respectively, p = .001). Similarly, significantly fewer studies in the military group (n = 94, 31.1%) than in the comparison group (n = 120, 39.7, p = .033) had PTSD as a condition of interest.

Reasons for Study Withdrawal, Termination, or Suspension

Many studies in the military group that were withdrawn, terminated, or suspended did not provide a reason. This raises concern for two reasons. First, ClinicalTrials.gov provides a

platform for researchers to communicate with the public. Although providing a reason for study withdrawal, termination, or suspension is not required by ClinicalTrials.gov, by not doing so, the sponsor or principal investigator misses an opportunity for transparency. Secondly, enrollment and funding problems were the most commonly reported reasons for studies in the military group being stopped prior to reaching completion as planned, and it is reasonable to assume, were reasons for several of the withdrawals, terminations, or suspensions that had no reported reason in the database. Having such information documented would help researchers evaluate the challenges encountered in research with service members.

Difficulty with participant enrollment was the most common reason provided for withdrawal, termination, or suspension of studies regardless of study group. When considering only terminated studies, the military group had a slightly higher incidence of studies terminated due to enrollment difficulty (44.4%) than reported in other ClinicalTrials.gov reviews. In the Carlisle and colleagues[14] review of studies that did not achieve adequate enrollment or were terminated, 43% of terminated studies were due to poor accrual. The Williams and colleagues[15] review found that 39% of trial terminations were attributed to poor participant accrual. The current study's comparison group had a lower proportion of terminated studies attributed to problems with enrollment (25%). It is important to note that the other ClinicalTrials.gov reviews included a wide variety of conditions and participant populations. They are offered here to help show how the number of terminated studies in this review compares to those in other reviews of ClinicalTrials.gov.

Anticipated and Actual Enrollment

Overall, many studies in this review, in both the military and comparison group, did not adequately meet recruitment goals. Among the studies in each group for which anticipated and

actual enrollment numbers were known, only about half achieved at least 85% of the anticipated enrollment. Studies in both groups clearly had difficulty enrolling the anticipated number of participants, while the group with all service member participants performed the worst, with the lowest percentage of studies (44.2%) that achieved at least 85% of anticipated enrollment.

For comparison, in their review of unsuccessful participant accrual, Carlisle and colleagues[14] found that out of 2,214 trials registered in ClinicalTrials.gov that ended in 2011 and met their inclusion criteria, 1,889 (85.3%) enrolled at least 85% of the anticipated participants. Upon combining completed studies that achieved less than 85% of anticipated enrollment with studies in the same review than were terminated due to enrollment problems, 18.7% of the included studies were determined to not have met recruitment goals. Although the current study was not designed to replicate the Carlisle and colleagues study, and therefore the comparison is not exact, the studies included in this review were clearly less successful at achieving their recruitment goals.

In most ways the subgroups with many versus all service members did not differ significantly from each other in anticipate or actual enrollment metrics. When evaluating the median difference between actual and anticipated enrollment, the group with all service members had a significantly higher deficit in participant enrollment than did the group with many service members. However, when evaluating the percent difference between actual and anticipated enrollment, which would normalize for the disproportionately larger number of participants in studies in the group with all service members, no difference was found between the groups.

Changes in Inclusion Criteria

Four studies expanded their inclusion criteria to participants other than exclusively service members. The study on botulinum toxin type B for low-back pain was terminated due to

difficulty with enrollment; it is not known why the other three studies changed their inclusion criteria. It is reasonable to speculate that difficulty in enrolling exclusively service member participants could have been a reason for expanding the criteria to include other types of participants, but this cannot be confirmed within the scope of this review.

Limitations

This study has several limitations. First, ClinicalTrials.gov provides important publicly available information about ongoing and completed research, but not all existing studies that would otherwise meet the inclusion criteria are registered in ClinicalTrials.gov. This is a limitation for most, if not all, ClinicalTrials.gov reviews and reviews of other trial registries.[22] Second, despite vigilance in regularly reviewing the study records for both historical and updated information, due to the volume of studies in the review it is possible that some content changed by principal investigators or sponsors may have been overlooked. This type of oversight would result in the review including original or earlier record content rather than more recent record data. Third, recruitment status and enrollment data is provided by the principal investigator or study sponsor, if an update has not been provided, the data may not reflect the actual study status.[8] Many of the studies included in this review were still in progress and thus could not provide both anticipated and actual enrollment data for analysis. Of studies that were still in progress (n = 145, 48.0% in the military group, and n = 123, 40.7% in the comparison group), 37 (25.5%) studies in the military group and 27 (22.0%) studies in the comparison group had not been updated with new information between 12/31/14 and 01/31/16.

A fourth limitation of this review is that the studies in the comparison group may have been too similar to the studies in the military group to detect indications of differences in participant recruitment. For example, over one-quarter (27.8%) of the studies in the comparison

group recruited either exclusively veterans as participants or veterans along with other groups of participants. Veterans and current military service members may have similarities in terms of research participation, such as reasons for participating in research or ways in which they become aware of research opportunities. It is important to note that this study was not designed to compare military service members and veterans. The group of military studies thus may not have been as different from the group of comparison studies as in other ClinicalTrials.gov reviews with comparison groups, such as the Pasquali and colleagues review in which pediatric trials were compared to non-pediatric trials.[23]

CONCLUSION

Recruiting U.S. military service members as research participants has been reported to be challenging. This review supports, with empirical data, anecdotal reports of difficulty enrolling military service members as research participants. However, the findings also indicate that in many regards, there may not be much difference in the difficulties recruiting military service members versus non-service members as research participants.

There may be some difference in recruitment difficulty for studies that enroll exclusively U.S. service member participants compared to studies that include many but not all service members. Some findings in this study, such as the median difference between actual and anticipated enrollment and changes in inclusion criteria from exclusively service member participants to include other participants, indicate that there may be more difficulty in achieving enrollment goals for studies that restrict participation to only service members.

Findings in this study may be useful for those who are designing research that includes service members as research participants or for those who are apprehensive about including a large proportion of service members in their research. Findings suggest that it is often difficult to

recruit research participants regardless of the specific population, and that studies with either many or all service member participants have similar recruitment challenges. It would be beneficial to understand more about how to recruit participants for research in general, and specifically when conducting research with military service member participants.

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TABLE I. Recruitment Status by Study Group

	Military group (N = 302)	Comparison group (N = 302)	P value	Many military participants[a] (n = 182)	All military participants[b] (n = 120)	P value
Recruitment status *n* (% of total studies in group)						
Not yet enrolling	10 (3.3)	0	.002[c]	4 (2.2)	6 (5.0)	.203
Recruiting[d]	84 (27.8)	93 (30.8)	.475	49 (27.0)	35 (29.2)	.695
Active, not recruiting	45 (14.9)	30 (9.9)	.084	24 (13.2)	21 (17.5)	.325
Completed	127 (42.1)	146 (48.3)	.141	82 (45.1)	45 (37.5)	.234
Suspended	2 (0.66)	1 (0.33)	1.00	2 (1.1)	0	.519
Terminated	18 (6.0)	24 (7.9)	.424	9 (4.9)	9 (7.5)	.457
Withdrawn	16 (5.3)	8 (2.6)	.143	12 (6.6)	4 (3.3)	1.00

Notes:
[a] At least 25% but less than 100% military service member participants.
[b] 100% military service member participants.
[c] Significant at $P < .05$.
[d] This category includes studies "enrolling by invitation," a ClinicalTrials.gov recruitment status in which only participants from a predetermined population are invited to participate.

TABLE II. Reasons for Study Withdrawal, Termination, or Suspension by Study Group

	Military group (*N* = 302)	Comparison group (*N* = 302)	*P* value	Many military participants[a] (*n* = 182)	All military participants[b] (*n* = 120)	*P* value
Number of studies withdrawn, terminated, or suspended, *n* (% of total studies in group)	36 (11.9)	33 (10.9)	.798	23 (12.6)	13 (10.8)	.718
Reason for withdrawal, termination, or suspension[c] *n* (% of total withdrawn, terminated, or suspended studies in group)						
Enrollment problems	11 (30.6)	8 (24.2)	.642	7 (30.4)	4 (30.8)	1.00
Funding problems	10 (27.8)	3 (9.1)	.066	5 (21.7)	3 (23.1)	1.00
No reason provided	10 (27.8)	4 (12.1)	.139	6 (26.1)	4 (30.8)	1.00
Methods problems	2 (5.6)	1 (3.0)	1.00	2 (8.7)	0	.525
Product/device problems	2 (5.6)	1 (3.0)	1.00	2 (8.7)	0	.525
Administrative problems	1 (2.8)	3 (9.1)	.343	0	1 (7.7)	.361
PI left facility[d]	1 (2.8)	4 (12.1)	.186	0	1 (7.7)	.361
Sponsor decision	1 (2.8)	5 (15.2)	.097	1 (4.3)	0	1.00
Decided not to start study	0	2 (6.1)	.225	0	0	-
Futility	0	3 (9.1)	.104	0	0	-

Notes:

[a] At least 25% but less than 100% military service member participants.

[b] 100% military service member participants.

[c] For 3 studies (2 from the military group and 1 from the comparison group), 2 reasons for withdrawal or termination were provided, and both reasons are included in this table. For all 3 studies, funding problems was one of the 2 reasons.

[d] PI, principal investigator.

TABLE III. Comparison of Anticipated and Actual Enrollment Numbers by Study Group

	Military group (*N* = 140)	Comparison group (*N* = 143)	*P* value	Many military participants[a] (*n* = 88)	All military participants[b] (*n* =52)	*P* value
% of total studies in group with known anticipated and actual enrollment numbers[c]	46.4	47.4	.870	48.4	43.3	.411
Studies with actual enrollment meeting recruitment goals *n* (% of studies in group with anticipated and actual enrollment)						
Actual enrollment ≥ 85% of anticipated enrollment	67 (47.9)	72 (50.3)	.722	44 (50.0)	23 (44.2)	.600
Actual enrollment = anticipated enrollment	31 (22.1)	24 (16.8)	.294	22 (25.0)	9 (17.3)	.400
Actual enrollment ± 5% of anticipated enrollment	44 (31.4)	37 (25.9)	.357	31 (35.2)	13 (25.0)	.259
Studies with actual enrollment below anticipated enrollment *n* (% of studies in group with anticipated and actual enrollment)						
< 100% of anticipated enrollment	89 (63.6)	86 (60.1)	.625	52 (59.1)	37 (71.2)	.203
< 85% of anticipated enrollment	73 (52.1)	71 (49.7)	.722	44 (50.0)	29 (55.8)	.600
< 75% of anticipated enrollment	60 (42.9)	59 (38.6)	.810	37 (42.0)	23 (44.2)	.860
< 50% of anticipated enrollment	38 (27.1)	33 (23.1)	.493	25 (28.4)	13 (25.0)	.699
< 25% of anticipated enrollment	16 (11.4)	15 (10.5)	.851	12 (13.6)	4 (7.7)	.411
< 10% of anticipated enrollment	9 (6.4)	8 (5.6)	.807	7 (8.0)	2 (3.8)	.484
Studies with actual enrollment above anticipated enrollment *n* (% of studies in group with anticipated and actual enrollment)						
> anticipated enrollment	20 (14.3)	33 (23.1)	.068	14 (15.9)	6 (11.5)	.619
> 10% above anticipated enrollment	13 (9.3)	24 (16.8)	.077	9 (10.2)	4 (7.7)	.767
> 25% above anticipated enrollment	6 (4.3)	12 (8.4)	.223	5 (5.7)	1 (1.9)	.412
> 50% above anticipated enrollment	5 (3.6)	5 (3.5)	1.00	4 (4.5)	1 (1.9)	.651
> 100% above anticipated enrollment	2 (1.4)	3 (2.1)	1.00	2 (2.3)	0	.530
> 150% above anticipated enrollment	0	1 (0.7)	1.00	0	0	-

Notes:
[a] At least 25% but less than 100% military service member participants.
[b] 100% military service member participants.
[c] Withdrawn or terminated studies with known actual and anticipated enrollment numbers were included if the reason provided for withdrawal or termination was problems with enrollment. Terminated studies not providing a reason for termination were included because terminated studies must have enrolled at least one participant to be categorized as terminated. Withdrawn studies not providing a reason for withdrawal were not included because there was no way to verify that the study had ever been initiated (studies classified as withdrawn must not have enrolled participants).

TABLE IV. Descriptive Statistics for Studies With Anticipated and Actual Enrollment Numbers

Studies with anticipated and actual enrollment numbers						
	Military group (N = 140)	Comparison group (N = 143)	P value	Many military participants[a] (n = 88)	All military participants[b] (n =52)	P value
Anticipated enrollment						
mean (SD)	700.0 (3,704.6)	180.9 (302.3)	.101	115.4 (272.4)	1,689.4 (5,974.2)	.063
median	78.0	80.0	.848	51.0	171.0	.001[c]
range	5, 36,000)	(10, 2,000)	-	(5, 2,380)	(15,36,000)	-
Actual enrollment						
mean (SD)	417.4 (2,599.1)	154.2 (281.6)	.236	65.8 (96.3)	1,012.3 (4,221.5)	.112
median	51.0	64.0	.765	35.5	86.0	.001[c]
range	(0, 30,209)	(0, 2,011)	-	(0, 740)	(4, 30,209)	-
Difference between actual and anticipated enrollment						
mean (SD)	-282.7 (2,165.7)	-26.7 (92.6)	.165	-49.7 (224.0)	-677.0 (3,527.9)	.206
median	-9.5	-9.0	.135	-5.5	-17.0	.025[c]
range	(-24,859, 1,625)	(-360, 536)	-	(-2,066, 80)	(-24,859, 1,625)	-
Percent difference between actual and anticipated enrollment						
mean (SD)	-25.1 (40.8)	-19.9 (43.2)	.296	-23.8 (44.9)	-27.3 (32.9)	.605
median	-17.2	-15.0	.262	-15.9	-19.7	.641
range	(-100, 140)	(-100, 165)	-	(-100, 140)	(-99.4, 60.2)	-

Notes:
[a] At least 25% but less than 100% military service member participants.
[b] 100% military service member participants.
[c] Significant at $P < .05$.

TABLE V. Studies That Expanded Inclusion Criteria

Study Topic	Initial Participants	Additional Participants
Cognitive therapy for suicidal behaviors	Service members	Military health care beneficiaries [Veterans were expected to be added as well]
Hyperbaric oxygen therapy for TBI	Active duty service members	Veterans
Telephone-based smoking cessation intervention	Active duty Air Force personnel	Military health care beneficiaries
Botulinum toxin type B for low-back pain	Active duty service members	Retired military, military health care beneficiaries

CHAPTER FOUR

U.S. MILITARY SERVICE MEMBER RESEARCH PARTICIPANTS' REASONS FOR DECIDING TO PARTICIPATE IN HEALTH RESEARCH

ABSTRACT

Military-relevant health research often includes current U.S. military service members as research participants. Though potentially vulnerable as research participants due to military hierarchy, little is known about the reasons why service members decide to participate in health research. The purpose of this study is to explore the reasons why current U.S. military service members who have participated in health research decided to participate. Fifteen service members with previous research participation experience were interviewed in person or by telephone. Service members' decisions to participate in research spanned three main categories: self-focused, others-focused, and fit-focused. Within the three main categories, seven subcategories were identified: curiosity, quality of life, helping researchers, making things better for others, opening doors, fitting the bill, and "why not?" Findings from this study will inform researchers, sponsors, ethicists, and leaders seeking to better understand service members' reasons for participating in research. Appealing to these reasons can improve recruitment of U.S. service members as research participants and facilitate research designs that better meets their needs.

INTRODUCTION

Military-relevant health research often relies on current U.S. military service members as research participants, yet little is known about the reasons why service members decide to participate.[1, 2] The purpose of this study is to explore the reasons why current U.S. military service members decided to participate in health research.

A growing body of literature exists on why various populations have participated in research on various health issues. For example, literature explores reasons for participating in pediatric research,[3, 4] cancer research,[5, 6] and genetics research.[7, 8] This body of research has contributed to the scientific community's awareness of the variety of reasons involved in deciding whether to participate in research. Knowledge about participants' decision-making process can improve recruitment and retention strategies targeting specific types of research participants and facilitate high-quality research, with representative samples that are sufficient in size and diversity.

A review of the literature found no studies on the reasons why military service members participate in research. One study evaluated reasons for hypothetical participation in research among U.S. military veterans compared to non-veterans. In the study, veterans were defined as former U.S. military service members and non-veterans were defined as civilians without military experience. Individuals were approached in the Veterans Affairs (VA) Health Care System and university hospital primary care clinics. Sixty veterans and 75 non-veterans ranked a list of 10 possible reasons for participation in six hypothetical studies. Neither group was found to be more likely to participate overall; however, veterans were significantly more likely than non-veterans to participate in research for altruistic reasons and as a way to show gratitude to their health care providers.[9]

A limitation of the Campbell and colleagues study was that participants were limited to choosing from a list of possible reasons for research participation, and did not have an opportunity to propose additional reasons for participating in research. While the findings from this study provided some insight into possible motivations for research participation among former military service members, the researchers did not investigate the motivation of current service members. Nor did the investigators inquire whether individuals had previously participated in actual research.

Campbell and colleagues hypothesized that because veterans are inherently dutiful citizens willing to make sacrifices for their country, they are more inclined to participate in research from a similar sense of duty.[9] Their findings supported their hypothesis. Some researchers assume that current military service members participate in research primarily for altruistic reasons, because they are likely to hold similar values as former service members who reported altruistic reasons.[9, 10]

The absence of research exploring current military service members' decisions around participating in research suggests a gap in the literature. Bush and collegues[1] also reported an inability to locate studies on this topic. Successful research into military health issues relies on the participation of military service members, but recruiting them as research participants has been reported to be challenging.[1, 2, 11] Understanding and appealing to service members' motivation to participate in research may improve recruitment efforts and facilitate the design of research that better meets their needs.

METHODS

Recruitment

Ethical approval for this study was obtained from the institutional review boards of a large military medical center and a large state university. Current U.S. military service members (active duty, guard, and reserve) of the U.S. Armed Forces (Air Force, Army, Marine Corps, and Navy) at the time of screening were eligible. Participants were recruited through advertisements and word of mouth at two large military medical centers on the west coast of the United States. To be eligible to participate, service members were required to have experience as a research participant in at least one study within the past three years. Experiences could be any participation in health care–related research, including worker or student health. Research could be led by military or civilian investigators; a military-relevant study topic was not required.

A convenience sample of service members with a wide range of demographic characteristics (e.g. branch of service, rank, sex, age, race, and type of research experience) was enrolled for maximum demographic variation.[12] The anticipated number of participants was between 10 and 30. A sample large enough to achieve informational redundancy was sought, with the understanding that informational redundancy may not be possible to achieve.[12]

Data Collection

Study procedures were completed in person or by telephone based on participant preference. For each participant, demographic data were collected first, and the interview followed immediately. Interviews lasted approximately one hour and were audio recorded. All interviews were performed by a single interviewer, to maintain consistency of method.

Interviews focused on the service members' decisions regarding participation in research and any related experiences and insights. Interviews began with a standard opening question:

"Tell me about your previous experience(s) of being asked to participate in research." The opening question was followed by several additional topics and questions, including "What things did you consider when deciding if you would participate in the study?" and "Why did you decide to participate in the study?" All participants independently offered their reasons for deciding to participate in research; to avoid leading, no possible reasons for research participation were suggested by the interviewer.

Data Analysis

Interview audio recordings were professionally transcribed and the interviewer verified transcribed data for accuracy. Analysis began as the transcription of each interview was completed and verified. Data collection and data analysis occurred concurrently throughout the study. Data were managed using ATLAS.ti 7.5 (ATLAS.ti GmbH, Berlin, Germany) qualitative data management software.

Determinations of data included in the analysis were based on the study purpose to explore the reasons why service members decided to participate in research. The analysis focused on actual reasons mentioned by service members for deciding to participate in research, rather than speculations. Descriptive coding of interview data was used to identify key ideas, and in vivo coding was used when participants' exact words were unique or captured an idea particularly well.[13, 14] The goal of this content analysis was to identify similarities and differences in the participants' reasons for deciding to participate in research. Similar reasons were grouped by distinct, mutually exclusive categories and subcategories to improve understanding of service members' decision-making around participation in research. Each subcategory was defined and was named using the participants' most descriptive and fitting words.

For ease of analysis and reporting, each service member was assigned a male or female pseudonym in alphabetical order by their order of enrollment in the study. The primary author performed multiple rounds of coding and re-coding to ensure depth and accuracy of analysis. The authors developed matrices of the coded data detailing each category and pertinent quotations from participants to enable better analysis of the data through visualization.[13] Co-authors discussed and critiqued the matrices to validate the analysis of concepts and categorizations and to improve the rigor of the analysis.

RESULTS

Fifteen current service members with experience as research participants were enrolled in the study. Table I summarizes sample demographics and Table II reports participant characteristics. The interviewer conducted 11 interviews in person (73%) and 4 by telephone (27%). A total of 14 hours of interview data were obtained (average 55 minutes per interview, interviews ranged from 23 to 108 minutes). Six service members (40%) had participated in one study, four (27%) had participated in two studies, and five (33%) had participated in three studies. Of the 29 studies in which these service members had previously participated, 18 (62%) were interventional studies and 11 (38%) were observational studies. Four studies (14%) entailed greater than minimal levels of risk and 25 studies (86%) involved minimal risk.

The participating service members usually had more than one reason for deciding to participate in a particular study. The reasons given for deciding to participate in each study, including the current study, were categorized and are presented in Table III. After completing the analysis, it was noted that all subcategories were represented within the content of the first three service members' interviews, although informational redundancy was not obvious until many additional participants had enrolled in the study. Service members spoke in detail about their

reasons for deciding to participate in research. The reasons for participating in research spanned three main categories and seven subcategories:

- Self-focused
    - Curiosity
    - Quality of life
- Others-focused
    - Helping researchers
    - Making things better for others
    - Opening doors
- Fit-focused
    - Fitting the bill
    - "Why not?"

See Table IV for definitions and examples of the subcategories.

Self-Focused Category

One of the three main categories of reasons for deciding to participate in research was the *self-focused* category. Reasons in the self-focused category were based on the service member anticipating some degree of personal gain as a result of participation, such as fulfilling personal curiosity or improving their state of health. The self-focused category included two subcategories: (a) curiosity and (b) quality of life.

Curiosity

Some service members explained that their decisions to participate were due, at least in part, to a profound interest in the research topic. *Curiosity* was defined as interest in or appreciation for a particular topic or aspect of the research, as reasons for deciding to participate.

(See Table IV for further definition.) Service members usually found these topics inherently interesting, and not because they related directly to the individual's own health.

For instance, Jennifer explained that her decision to participate in a study about post-deployment reintegration experiences was due to her interest in the topic: "I was interested right away . . . I completed it right away because I was really interested in the topic." Later in the interview, Jennifer explained that she had participated in a study about health care worker fatigue for the same reason.

Curiosity about a new technology or device included in a study was sometimes a reason for a service member's decision to participate. The service members had participated in studies that used novel technologies such as hyperbaric oxygen therapy for traumatic brain injury (TBI), transcutaneous electrical nerve stimulation (TENS) for chronic back pain, virtual reality therapy for post-traumatic stress disorder (PTSD), a computerized mannequin for simulating cardiopulmonary resuscitation (CPR), and SurveyMonkey[15] for collecting survey data. David described his curiosity about a survey technology that he had not previously used: "I could maybe look at that survey and pattern my own research in the future using that kind of style or that kind of model, that kind of technology. Like SurveyMonkey was the first time I'd seen it . . . that fueled my curiosity."

In another example, Geraldine discussed her decision to participate in a study about preventing gall bladder complications during pregnancy:

> I liked the idea that early in pregnancy I'd get to see a picture of the baby. It's usually done in the middle of the pregnancy, and so I was able to get one very

> early because they wanted to see the gall bladder . . . I just thought it was kind of cool that you could see anything that early in the pregnancy.

This is an example of curiosity rather than quality of life (discussed below) because the service member was curious about the early ultrasound; it was not medically necessary at that point in her pregnancy and she was aware that an ultrasound would be performed as part of her usual care at an appropriate point in her pregnancy.

Quality of life

Concern for one's own quality of life was often mentioned as a reason for deciding to participate in research. *Quality of life* was defined as desire to improve one's own current state of health that substantially influences their decision to participate in research. This subcategory indicates the participant's hope that some aspect research will directly improve their health.

Several service members made quality of life decisions to participate in research that were based, at least in part, on desperation to change their current state of health. For example, when asked why he had decided to participate in a study about virtual reality therapy for PTSD described, Frank said, "At that point in my life, I was willing to try anything." Similarly, Larry described why he decided to participate in a study using meditation for chronic pain and PTSD symptom management: "At that point we had already exhausted all of the other alternatives. There was nothing left. I mean, I had been through everything I could do . . . What I was doing wasn't working."

Some service members explained that gaining access to medical technologies or interventions that they believed would improve their quality of life, but which they would not normally have access to otherwise, was a reason for deciding to participate in research. Examples

of such interventions included functional magnetic resonance imaging (MRI) to evaluate post-concussive symptoms, a TENS device for chronic back pain, hyperbaric oxygen therapy for TBI, virtual reality as therapy for PTSD, and complementary and alternative medicine therapies such as meditation and acupuncture. Brandon stated, "I wasn't going to get a functional MRI any other way other than through the study."

Several service members described their eagerness to participate in research related to complementary and alternative medicine therapies, usually to alleviate chronic conditions to avoid long-term use of pain medications or invasive procedures such as surgeries. Studies they had participated in included self-hypnosis for pain management, meditation for chronic pain and PTSD symptom management, a film-making workshop as group therapy for PTSD, and photography as therapy for PTSD. In an example of quality of life as it relates to accessing complementary and alternative therapies, Isaac stated, "My interest was looking for alternative means of therapy, pain relief. I was looking for something to help, versus taking a pharmaceutical."

Others-Focused Category

The second main category of reasons for deciding to participate in research was the *others-focused* category. In this category, reasons for participation were based on the service member anticipating some degree of benefit or gain for others. Subcategories were (a) helping researchers, (b) making things better for others, and (c) opening doors.

Helping researchers

Some service members described decisions to participate that were due, at least in part, to wanting to help researchers (see Table IV). *Helping researchers* was defined as participating in research specifically to support the researcher(s) performing the research. The motive is to assist

researchers to accomplish their research and to contribute to new knowledge. This subcategory is present-focused, with little or no emphasis on future benefits. The service member may express identifying with or relating to the researcher(s) in some way.

Helping researchers was a reason for Hailey's decision to participate in a study: "I know there's a lot of difficulties in finding people to participate and actually follow through. I think helping the researchers to get the information . . . is good." Service members also described helping researchers as an opportunity to contribute to new knowledge. Jennifer described why she decided to participate in a study about health care worker fatigue, "I knew it…would generate important information for our community… Knowledge that isn't out there."

The helping researchers subcategory did not include helping health care providers or those in the dual roles of provider and researcher. No service members reported helping health care providers or giving back to those who had cared for them as a reason for deciding to participate in research. Of the nine service members who had learned of the research in which they participated either directly from their health care provider or through an advertisement in their health care clinic, none mentioned reasons for participating related to helping or giving back to the health care providers who had treated or cared for them.

Making things better for others

Some service members explained that their decision to participate was due to a desire to help make things better for others. *Making things better for others* was defined as participating in research now with the long-term perspective that eventually others will benefit from the research findings. The making things better for others subcategory (see Table IV) is future-focused. The service member may express identifying with or relating to the research population in some way.

Service members' desire to make things better for others influenced their decisions to participate in research. For example, Brandon said, "I could provide data or information that could potentially help a larger category of folks than just me. It could be long term." Several service members described how hoping to make things better for others, specifically for other service members, had influenced their decisions. For example, Nathan stated, "I consider helping others . . . if they can benefit in any way, shape, or form from something I can do for them research-wise . . . to me that's worth it, just to help other soldiers."

Two service members explained that their decisions to participate in research were morally obligatory. Andrew said of his decision to participate: "To not help when I have the ability to, it's screwed up . . . To not help is just wrong." Andrew re-emphasized this belief several times throughout his interview. Kelley described her decision to participate stating, "I . . . felt it was my duty to do it." Kelley was the only service member in the study to use the term *duty* in the sense of an obligation. She did not emphasize this obligation as Andrew had in his interview.

It is noteworthy that the studies that Andrew and Kelley discussed were all civilian-led studies, in civilian institutions, on topics that were not specific to the military. No service members in this sample described their reasons for participation as deriving from a sense of duty linked to military service or military hierarchy. Additionally, no service members made normative claims that service members in general should participate in research.

Opening doors

Some service members explained that their decisions to participate in research were based on a desire to create opportunities, or to open doors, for improvement within the organization. *Opening doors* was defined as participating in research with the perspective that

participating could facilitate or encourage opportunities or improvements within the organization or for the organization's members. Role-modeling for other service members may be involved in the subcategory of opening doors.

Opening doors sometimes referred to participating in research so the organization could be improved. Emily decided to participate in a study that tested CPR mannequins because "it would be a way for the hospital or a way for the education staff to be able to purchase a piece of equipment that would help students." About her participation in different studies, Kelley stated, "I thought those were beneficial studies for my school, because they do need to understand what students are going through."

Opening doors sometimes referred to participating in research so the organization would consider making changes. Isaac explained that one reason for his participation was his hope for "convincing the Army medicine system to use alternative care." Oliver said, "I took part in a survey to talk about the kind of pain that I deal with on a daily basis and still go to work . . . I hope maybe that it will fix some things on the army medical side as far as pain management."

Some service members reported that through their participation in research, they were opening doors by serving as role models to support and encourage other service members who may be struggling with chronic conditions and the stigma that is sometimes associated with such conditions. Brandon explained:

> I'm trying to lead by example. I put my name out there. I put my rank out there. I put what I'm doing out there [participating in TBI and PTSD research]. I participate as somebody who is fully functioning, but also is suffering from the wounds [of war].

Fit-Focused Category

The third of the three main categories of reasons for participating in research was the *fit-focused* category. In this category, reasons for participation were based on how well the research met the service members' needs and vice versa. The fit-focused category included the subcategories of (a) fitting the bill and (b) "why not?"

Fitting the bill

Some service members explained that their decision to participate was based on how well they fit the requirements for the particular research (see Table IV). *Fitting the bill* was defined as an assessment of how well one met the requirements necessary to be a participant in a study. For some service members, simply meeting the criteria to participate in a study had influenced their decision to participate. In an example of fitting the bill, Hailey commented about meeting the inclusion criteria for a study about couples' post-deployment reintegration challenges: "I thought it looked like a study I could be in, because I'm married, we've both deployed, and it's something we could help if I fit in."

Why not?

Some service members explained that they decided to participate because there was no reason not to. *"Why not?"* was defined as a service member's assessment that there were insufficient reasons not to participate. This subcategory includes factors such as time, location, privacy, and research activities that a service member finds convenient or appropriate. Larry explained his reasoning: "What I was doing wasn't working. I figured, why not?" Convenience was often a focus of the reasons in the "why not?" subcategory. David described the importance of convenience in his decision to participate in research: "It was very, very convenient. . . . First and foremost is like time and convenience."

DISCUSSION

Service members in this study participated in research for reasons focused on self, others, and fit. Curiosity, quality of life, helping researchers, making things better for others, opening doors, fitting the bill, and "why not?" describe subcategories of reasons for service members' decisions to participate in health research. A discussion of the relevance of the three main categories follows.

Self-Focused Reasons

Interesting topics, new technologies, and complementary and alternative medicine therapies are appealing to service members deciding whether to participate in research. It is important to consider when designing research what service members will find interesting. Research topics that service members might consider dull could be made more appealing if a unique test, intervention, or data collection tool is used to stimulate their curiosity.

Some service members in this study participated in research to gain access to medical technologies to which they otherwise would not have access. It has been suggested by some researchers that because service members have access to comprehensive health care, they are unlikely to be motivated to participate in research to gain access to medical care or technologies[1] as is sometimes true for other populations.[16] However, this motivation may be a factor for research that includes medical technologies that are beyond the standard of care. During the ethical review process, it is important to consider how activities within the research protocol, such as access to medical technologies, may influence a potential participant's decision. This motivation may currently be underestimated in research involving service members.

Bush and colleagues surmised that due to their overall youth and healthiness, service members were less likely than others to be interested in participating in research that included

alternative medical technologies.[1] In this study, though nearly all service members were at least 30 years old, findings suggest the opposite. Service members, particularly those with chronic conditions, are interested in and readily participate in studies involving new medical technologies and complementary, alternative, and integrative therapies.

Service members may participate in studies of alternative therapies with the aim of reducing or eliminating chronic opioid medication usage. This was a concern for some participants in this study, and has been noted as a significant problem among service members.[17, 18] Many current service members have acute and chronic conditions such as PTSD, TBI,[19] and pain,[18] and therefore their desire for new technologies and alternative therapy options is an important consideration in future research with this population. Some have suggested an urgent need to research complementary and alternative approaches for service members,[20] and this study's findings suggest that service members are receptive to such research.

In the self-focused category, reasons for participating in research were based on self-interest rather than altruistic motives. This is not surprising as other researchers have found that decisions to participate in research are often based on a combination of altruistic and non-altruistic reasons.[21, 22] McCann and colleagues described "*conditional altruism*" as "the willingness to help others that may initially incline people to participate in a trial, but that is unlikely to lead to trial participation in practice unless people also recognize that participation will benefit them personally".[21, p. 1] All but one service member (Andrew) had both self-focused (non-altruistic) and others-focused (altruistic) reasons for participating in at least one of their past studies, indicating conditional altruism in service members' decisions to participate in research.

Others-Focused Reasons

The others-focused category consisted of altruistic reasons for participating in research. However, fewer service members than anticipated referred to a sense of duty as a reason for deciding to participate. Service members are often viewed as dutiful citizens, and their sense of duty has been assumed by some to be an important reason for their participation in research.[9] Also noteworthy is that no service members in this study described participating due to a sense of duty linked to military service or military hierarchy. These findings suggest that this population may not be as vulnerable, due to either altruism or military influence, as previously believed.

Service members in this study also did not report participating in research to help or give back to their health care providers; a reason ranked-highly by veterans in Campbell and colleagues' study.[9] This difference in findings may be attributed to study design—in this study, service members could freely describe their reasons for research participation, in contrast to the Campbell and colleagues study in which veterans were restricted to choosing from a predetermined list of reasons. From an ethical perspective, it is reassuring to find that service members did not report feeling compelled to participate in research just because their health care provider or clinic presented the opportunity, as there is sometimes concern for service members' potential vulnerability when recruiting them for participation in such settings.

The finding that service members, including both noncommissioned and commissioned officers, sometimes decide to participate in research to serve as role models for other service members is unique and unexpected. Role modeling has not previously been found in the literature as a reason for any group of participants to participate in research. The goal of serving as a role model may be unique to service member participants, particularly those who are more

senior or have more years of service. Further investigation of this concept of service members' participation in research as a form of role modeling is needed. Future research could potentially identify ways to leverage role modeling in an ethically appropriate manner to achieve better understanding and awareness of opportunities to participate in research among service members, while encouraging informed and voluntary participation.

Fit-Focused Reasons

Every service member in this study described a fit-focused reason for participating in at least one of the studies in which they had participated. This suggests that a study's fit is highly important in a service member's decision to participate. This is a significant and encouraging finding, because the factors that determine good fit are largely in the investigator's control. Good fit is primarily about inclusivity and convenience.

Service members in this study often participated in research simply because they met the inclusion criteria. Making criteria clear in study advertisements and announcements is important so that service members can understand exactly who the researchers are seeking. When service members see clearly how they fit in the research, they may be more likely to inquire about the study and to decide to participate.

Service members who did not meet criteria for studies expressed disappointment at being excluded. At a time when recruiting service member as research participants is notoriously difficult,[1,2,11] it is important to avoid turning away service members who actively inquire about their eligibility to participate in research. Avoiding unnecessarily restrictive criteria is recommended. When restrictive criteria cannot be avoided, investigators can identify ways in which they can include service members in some way. An investigator of a study with

particularly restrictive inclusion criteria could partner with investigators of studies with less restrictive criteria, and refer potential participants to the less restrictive studies.

Convenience played an important role in service members' decisions to participate in research. When service members in this study became aware of research opportunities, given the absence of adequate reasons to not participate, service members readily decided to participate. This is an important finding for researchers—service members are often willing to participate when they are made aware of research opportunities, as long as the research is convenient, appealing, and they meet the criteria. The main obstacle is ensuring that service members are aware of research opportunities. With appropriate permission, networking within the military organization to disseminate targeted advertisements, such as posters and group email messages, and collaboration with research coordinators and health care providers will help get the word out to appropriate potential participants about research opportunities.

Limitations

This study has several limitations. The service members included in this study were generally experienced senior noncommissioned and commissioned officers with high levels of education, some of whom were experienced researchers. Most were white, at least 30 years old, with 11 or more years of military service. Young, less experienced enlisted and officer service members, as well as those with less education, were not adequately represented in this sample, and their reasons for research participation may differ from the service members in this study. There were more officers than enlisted service members in this study, which does not represent the composition of the U.S. military. This limitation is tempered somewhat by the fact that four of the nine officers included in the study had served as enlisted service members prior to being

commissioned as officers and were asked to reflect upon their previous experiences as an enlisted service member.

Although service members from all services were sought for this study, none of the participants represented the Air Force or Marine Corps. This absence of Air Force and Marine Corps service members was probably due to the methods used to identify potential participants, which did not adequately reach individuals at Air Force and Marine Corps facilities. It is unknown if service members from the Air Force and Marine Corps would have different reasons for deciding to participate in health research. It is reasonable to speculate that their reasons would be similar to those of the Army and Navy service members participating in this study. While only one service member participant was from the guard or reserve forces, three active duty service members had previously served in the guard or reserve.

Service members who had previously declined to participate in health research were also sought for this study, though none enrolled. Identifying service members who had previously declined participation was expected to be difficult. Though logistically complicated, different recruitment approaches, such as collaborating with other investigators to approach research decliners at the time they decide to decline, may be necessary to identify such service members. It is important to understand service members' reasons for declining participation as well as their reasons for participating.

Many of the studies in which service members had previously participated involved minimal risk, and there may be different motivations for participating in studies involving higher risk. However, these service members had participated in a wide variety of health research studies, many had multiple experiences as research participants, and their detailed explanations for their reasons for deciding to participate in particular studies adds to the quality of the data.

CONCLUSION

Service members' reasons for previous participation in research are likely to be reasons for future participation. Service members in this study participated for reasons focused on self, others, and fit. It is likely that other service members would make decisions to participate in research based on similar reasons. Findings from this study provide a starting point for understanding why service members decide to participate in health research.

To our knowledge, this study is the first to provide empirical evidence regarding current U.S. military service members' reasons for having participated in health research. Findings from this study may help researchers, sponsors, bioethicists, and leaders better understand service members' reasons for deciding to participate in health research and could contribute to policy and research development. Appealing to these reasons may improve the recruitment of U.S. service members as research participants and facilitate the design of research that better meets their needs. The findings from this study serve as a foundation to build upon in the knowledge surrounding service members as research participants.

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TABLE I. Sample Demographics ($N = 15$)

Characteristic	*n*	%
Age		
18–29	1	6.7
30–39	4	26.7
40–49	7	46.7
≥ 50	3	20.0
Sex		
Male	9	60.0
Female	6	40.0
Race/ethnicity		
White, non-Hispanic	11	73.3
Hispanic	2	13.3
African American	1	6.7
Asian Pacific Islander	1	6.7
Other	0	0
Education level		
High school or some college	4	26.7
Bachelor's degree	1	6.7
Master's degree	4	26.7
Doctoral degree	6	40.0
Service		
Army	10	66.7
Navy	5	33.3
Air Force	0	0
Marine Corps	0	0
Status		
Active duty	14	93.3
Reserve or guard	1	6.7
Years of military service		
0–10	1	6.7
11–20	8	53.3
>20	6	40.0
Rank		
E-1 to E-4	0	0
E-5 to E-9	6	40.0
O-1 to O-4	2	13.3
O-5 to O-6	7	46.7

Note. Rank: E-1 to E-4, the first through fourth enlisted ranks for the respective service; E-5 to E-9, the fifth through ninth enlisted ranks for the respective service; O-1 to O-4, the first through fourth officer ranks for the respective service; O-5 to O-6, the fifth and sixth officer ranks for the respective service.

TABLE II. Participant Characteristics

Pseudonym	Service	Rank	Status	Service years	Age	Sex	Race/ ethnicity	Education level
Andrew	A	E-5 to E-9	AD	11–20	30–39	M	W	HC
Brandon	A	O-5 to O-6	AD	>20	40–49	M	W	M
Cynthia	N	O-5 to O-6	AD	>20	≥50	F	W	D
David	N	O-1 to O-4	AD	11–20	40–49	M	API	M
Emily	N	O-5 to O-6	AD	11–20	40–49	F	W	D
Frank	A	E-5 to E-9	GR	11–20	≥50	M	W	HC
Geraldine	A	O-5 to O-6	AD	11–20	40–49	F	W	D
Hailey	A	O-1 to O-4	AD	11–20	30–39	F	W	M
Isaac	A	O-5 to O-6	AD	>20	40–49	M	W	M
Jennifer	N	O-5 to O-6	AD	>20	40–49	F	W	D
Kelley	N	O-5 to O-6	AD	>20	40–49	F	AA	D
Larry	A	E-5 to E-9	AD	>20	≥50	M	WH	D
Michael	A	E-5 to E-9	AD	11–20	30–39	M	W	HC
Nathan	A	E-5 to E-9	AD	11–20	30–39	M	WH	B
Oliver	A	E-5 to E-9	AD	0–10	18–29	M	W	HC

Notes. Service: A = Army, N = Navy. Rank: E-5 to E-9, the fifth through ninth enlisted ranks for the respective service; O-1 to O-4, the first through fourth officer ranks for the respective service; O-5 to O-6, the fifth and sixth officer ranks for the respective service. Service years = range of total number of years of military service. Age = age range in years. Status: AD = active duty, GR = guard or reserve. Sex: F = female, M = male. Race/ethnicity: AA = African American, API = Asian Pacific Islander, W = white, WH = white Hispanic. Education level: B = bachelor's degree, D = doctoral degree, HC = high school or some college, M = master's degree.

TABLE III. Service Members' Reasons for Participating in Specific Studies

		Self-focused		Others-focused			Fit-focused	
Participant number and pseudonym	Focus of research study	Curiosity	Quality of life	Helping researchers	Making things better for others	Opening doors	Fitting the bill	Why not?
1 Andrew	Reducing psychological distress after ICU				X			X
	Hypnosis for pain				X			X
	Research participation				X		X	X
2 Brandon	Hyperbaric oxygen therapy for TBI		X		X	X		X
	TBI vestibular rehabilitation		X		X	X		X
	Film-making for PTSD		X		X	X		X
	Research participation			X			X	X
3 Cynthia	Deployment experiences	X		X		X	X	X
	Fatigue in health care workers	X		X				
	Research participation	X		X			X	
4 David	Stress in graduate students	X		X				X
	Research participation			X				
5 Emily	CPR mannequin testing	X		X		X		X
	Research participation	X		X				
6 Frank	Virtual reality for PTSD		X		X	X		X
	Symptom management		X		X	X		
	Telephone for PTSD		X		X			
	Research participation				X			
7 Geraldine	Gallbladder complications in pregnancy	X						X
	Balance in TBI	X		X	X			X
	Exercise and sleep on performance	X		X	X			X
	Research participation			X				
8 Hailey	Military couples reintegration experiences	X		X			X	X
	Research participation			X				
9 Isaac	TENS for back pain		X		X	X		X
	Symptom management		X		X	X		X
	Research participation			X	X			
10 Jennifer	Nurses' reintegration	X		X			X	X
	Fatigue in health care workers	X		X		X	X	X
	Women's' Health Study	X		X				X
	Research participation			X				
11 Kelley	Graduate student experiences	X		X		X	X	
	Graduate student stress	X		X		X	X	
	Military nurses shift-work	X		X		X		X
	Research participation			X				
12 Larry	Symptom management		X		X	X	X	X
	Research participation			X	X			
13 Michael	Symptom management		X		X			
	Photography for PTSD	X	X					X
	Research participation			X				
14 Nathan	Symptom management		X		X			X
	Research participation			X				
15 Oliver	Symptom management		X	X	X	X		X
	Research participation			X				X

Notes. X indicates that the service member described this subcategory, as interpreted by the researcher, as a reason for deciding to participate in the applicable study. In some cases, the study topic has been made less specific to avoid identifiability. Names are pseudonyms. "Research participation" refers to participation in the current study. CPR = cardiopulmonary resuscitation; ICU = intensive care unit; PTSD = post-traumatic stress disorder; TBI = traumatic brain injury; TENS = transcutaneous electrical nerve stimulation.

TABLE IV. Subcategory Definitions

Category	Subcategory	Definition	Exemplar	Is not
Self-focused	Curiosity	Interest in or appreciation for a particular topic or aspect of the research that substantially influences the decision to participate in research.	I was curious as to what kind of questions they would ask . . . I'm always kind of interested in research. (Jennifer)	Interest as a means to improve one's health.
	Quality of life	Desire to improve one's current state of health that substantially influences the decision to participate in research. The service member is hopeful that some aspect of the research will directly lead to improved health.	Number one was quality of life. I know that that's kind of a selfish point of view, but at the time, my quality of life had clearly and seriously deteriorated. (Brandon)	Interest in the topic or some aspect of the research.
Others-focused	Helping researchers	Participating specifically to support the researcher(s) performing the research. Helping to accomplish the research and to contribute to new knowledge. Present-focused. May express identifying with the researcher(s) in some way.	I wanted to make it easier on researchers to get their data . . . I feel for the researchers, how they choose subjects, how they reach out to them. It is really hard. (David)	Helping non-researchers, or helping people in the future who may benefit from the research.
	Making things better for others	Participating in research now with the perspective that eventually others will benefit from the research findings. Future-focused. May express identifying with or relating to the research population.	What I'm trying to do in the long run is make it better for the soldiers after me . . . in the long term, was it going to help another soldier? That's what I consider when I get involved in these studies. (Frank)	Helping the researcher. Helping the health care provider.
	Opening doors	Participating in research with the perspective that participating could facilitate or encourage opportunities or improvements within the organization or for its members. May involve role modeling.	I see that if someone in that position volunteers to do it, then that will open up the door for many of those below me. (Larry)	Helping make things better for others.
Fit-focused	Fitting the bill	Participating based on personal assessment of how well the service member meets the requirements necessary to be a participant in a study.	I fulfilled the requirements for the topic matter . . . because all the criteria were there…I think I fit that bill. (Cynthia)	Factors that are not attributes of the individual.
	Why not?	Participating based on personal assessment that there are insufficient reasons to not participate. May involve factors such as time, location, privacy, and research activities that the service member finds convenient and/or appropriate for his or her particular situation.	I was like, "Sure. Why not?" . . . It literally cost me nothing to do. There was no reason not to do it. (Andrew)	Arduous, time-intensive, burdensome to an extent that the service member finds unacceptable.

Notes. Names are pseudonyms. See Table III for a list of participants' past studies.

CHAPTER FIVE

CONCLUSION

This dissertation explored current U.S. military service members' recent health research participation activities including (1) trends in service members' research participation, (2) indications of challenges in recruiting U.S. military service members as research participants, and (3) U.S. military service members' reasons for deciding to participate in research. The overall goal of this research is to support future research participation for this potentially vulnerable group of research participants in order to continue making research-derived health care advances for U.S. military service members.

U.S. military service members participate in health care research both in exclusively military studies and along with other groups of participants. Investigators of studies that exclusively enroll service members often seek large numbers of participants. It is important to ensure that there is not a prolonged decline in research among this population. U.S. military service members have acute and chronic health needs, often as a result of injuries or exposures during their service, which they experience during their service and long after leaving the military. Military-relevant health research must remain a priority.

Recruiting U.S. military service members as research participants is reportedly challenging and findings in this dissertation support the anecdotal reports of difficulty in enrolling military service members as research participants. However, the findings also suggest that in many regards there may not be much difference in difficulty recruiting military service members as research participants compared to studies that do not include service members. Findings suggest that it is often difficult to recruit research participants regardless of the specific

population, and that studies with many and all service member participants have similar recruitment challenges.

Findings regarding current U.S. military service members' reasons for participating in health research may help researchers, sponsors, bioethicists, and leaders better understand service members' reasons for deciding to participate in health research. Appealing to these reasons may improve the recruitment of U.S. service members as research participants and facilitate the design of research that better meets their needs.

This dissertation serves as the foundation for a program of research in the topic areas surrounding U.S. military service members as research participation. Findings help guide future research focused on (1) identifying strategies that effectively promote service members' ability to participate in health research, (2) describing the experiences of military service members who have participated in health research, (3) supporting researchers in developing research that includes service members as participants, and (4) providing guidance to researchers and military leaders about policies that address the special needs of military service members as participants in health research.