FATIGUE AMONG MILITARY WOMEN WITH AND WITHOUT POLYCYSTIC OVARY SYNDROME

by

Dawnkimberly Y. Hopkins

Dissertation submitted to the Faculty of the
Daniel K. Inouye Graduate School of Nursing Graduate Program
Uniformed Services University of the Health Sciences
In partial fulfillment of the requirements for the degree of
Doctor of Philosophy in Nursing Science 2016

Distribution Statement

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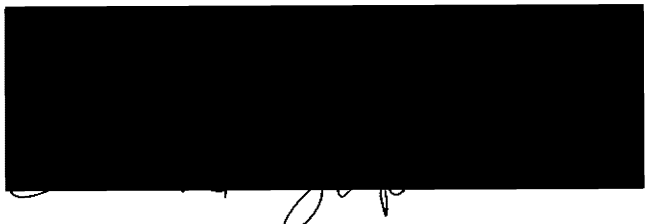

Dawnkimberly Y. Hopkins

November 1, 2016

ABSTRACT

Fatigue among Military Women with and without Polycystic Ovary Syndrome

Dawnkimberly Y. Hopkins, MSN, WHNP-BC, 2016

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Research Design/Methodology: This was a mixed-methods, between subjects, cross-sectional design study. A total of 96 military women with and without PCOS were recruited. An online website with self-report questionnaires administered through FluidSurveys™, was used to collect data on fatigue occurrence, severity, and dimensions, anxiety, depression, sleep quality and wakefulness. A demographic sheet (through FluidSurveys™) was used to collect data on age, BMI, social support, and fitness level. Semi-structured interviews were conducted for select participants who scored 60 or above on the PROMIS Fatigue Short Form 8a, to explore how a sample of military women with and without PCOS described their personal experiences related to various fatigue dimensions.

Results: *Quantitative*: There was no statistically significant difference between military

women with and without PCOS on fatigue occurrence χ^2 (1, n=96) = 0.00, p<0.98, phi = 0.01. However, when an independent t-test was applied, compared to women without PCOS, women with PCOS had significantly higher scores for general fatigue ($p < 0.001$, $d = 0.96$), physical fatigue ($p < 0.001$, $d = 0.80$), mental fatigue ($p < 0.001$, $d = 1.01$), reduced activity ($p < 0.001$, $d = 0.82$), reduced motivation ($p < 0.001$, $d = 0.92$), and fatigue severity ($p < 0.001$, $d = 0.98$). Controlling for covariates (age, BMI, anxiety, depression, sleep quality, wakefulness, social support, and fitness level) stepwise regression was applied. The effect size for the relationship between PCOS and fatigue dimension was large in four out of five models (physical fatigue and reduced activity were not statistically significant). Anxiety was a predictor of general fatigue ($\beta = 0.32$, $p < 0.001$); depression was a predictor for reduced motivation ($\beta = 0.19$, $p < 0.05$) and fatigue severity ($\beta = 0.45$, $p < 0.001$); and BMI was a predictor for general fatigue ($\beta = 0.19$, $p < 0.05$), mental fatigue ($\beta = 0.25$, $p < 0.01$), and reduced motivation ($\beta = 0.24$, $p < 0.05$). Interactions between PCOS and anxiety and depression resulted in an inverse relationship in general fatigue and anxiety ($\beta = -3.70$, $p < 0.01$) and reduced motivation and depression ($\beta = p < -0.71$). *Qualitative*: Although both groups of military women described fatigue as having a mental and physical component that impacts mind and body functioning, as well as activity and motivation levels; women with PCOS described fatigue as a persistent state, whereas women without PCOS described it as an overwhelming state. Both groups described mental fatigue as experiencing frequent mood variations with several mood states as well as experiencing decreased focusing, concentration and processing. However, women without PCOS additionally described mental fatigue as being similar to having attention deficit/hyperactivity disorder. Motivation of women with PCOS was described in regards to levels present (none, high, present, but…), yet women

without PCOS described motivation in regards to the impact to productivity.

Conclusion: Fatigue impacts military women with and without PCOS equally, and as such, should be addressed during clinical visits when providing care for this population. Although fatigue is present in both populations, women with PCOS experienced higher general fatigue, physical fatigue, mental fatigue, and fatigue severity and described fatigue as a persistent state; as opposed to women without PCOS who described fatigue as an overwhelming state. Women with PCOS also reported having lower activity levels and distinct motivation levels related to fatigue; whereas women without PCOS reported less about activity and motivational levels and more about the impact to productivity they experience related to fatigue. Functioning, work productivity, and quality of life have implications for mission readiness as they can decrease the military members' ability to be fit for duty. Understanding that fatigue impacts social and psychological functioning, work productivity, and quality of life, further research that focuses on reducing and managing fatigue are indicated.

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- *Fatigue among Military Women with and without Polycystic Ovary Syndrome*
  TriServices Nursing Research and EBP Dissemination Course, August, 2016, San Antonio, TX
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ACKNOWLEDGMENTS

I would like to thank the members of my committee for their extraordinary patience, guidance and wisdom. I would also like to thank Dr. Micah Hill for support through the Women's Health and Reproductive Clinic at Walter Reed National Military Medical Center and Maj Heather Ortiz for support and recruitment assistance. I would also like to thank Josh Krazman for specialized instruction in statistical support, and Sam Golenbock for the design and support of the web-based data collection program. Special thanks to the faculty and staff of the Uniformed Services University of the Health Sciences and the Daniel K. Inouye Graduate School of Nursing, administrative and other support and without whose help this research could not have been completed.

This investigation was supported by intramural funding from the Uniformed Services University of the Health Sciences through the Daniel K. Inouye Graduate School of Nursing.

DEDICATION

To Felix L. Hopkins, my husband, best friend, and inspiration; To Linda J. Hale, my mother, my biggest cheerleader; To my children, Anthony and Phoenix for your patience and understanding.

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CHAPTER 1: INTRODUCTION

BACKGROUND

Fatigue is a multidimensional condition that impacts 38% of community-based individuals, 42% of primary care patients, and occurs more frequently in women [1-3]. In America, fatigue-related drowsiness on the highways contributes to more than 1,500 fatalities, 100,000 motor vehicle accidents, and 76,000 injuries annually [4]. In 2007, the total cost of annual lost productive time (LPT) attributed specifically to fatigue in the U.S. workforce was estimated at $330 million with 83.9% of this LPT due to reduced work performance; not employee absenteeism [2]. In the military, 4% of U.S. Army accidents, 7.8% of U.S. Air Force Class A mishaps, and 12.2% of U.S. Navy Class A mishaps are directly related to fatigue [5]. Fatigue results not only in fatalities, injuries and monetary consequences; it also results in significant health consequences for individuals with chronic illnesses.

Fatigue is one of the most common complaints in chronic illnesses, and many patients describe it as one of the most debilitating symptoms experienced [6-10]. Fatigue is highly prevalent in chronic conditions such as multiple sclerosis (MS), systemic lupus erythematosus (SLE), rheumatoid arthritis (RA), Parkinson's disease (PD), sickle cell disease, and inflammatory bowel disease [9, 11-14] Polycystic ovary syndrome (PCOS) like other chronic illnesses includes a constellation of physiological, psychosocial and lifestyle factors that place these women at risk for fatigue.

Fatigue may reflect a combination of physiological factors (e.g. inflammation or central nervous system dysfunction), psychosocial factors (e.g. depression or anxiety),

and lifestyle factors (e.g. diet, exercise, alcohol use, tobacco use, or social role); and may not occur primarily due to lack of sleep or quality of sleep [15-19]. The physiological factor of chronic inflammation is common to many persistent conditions complicated by fatigue [9, 20, 21]. The fatigue experience of individuals with chronic conditions can be distinguished from *normal everyday tiredness* as being more frequent, unrelenting, unpredictable, and unresolved by rest [22, 23]. Patients are adamant that fatigue is different from tiredness; tiredness resolves but fatigue does not. Fatigue is also described as extreme fluctuations in lack of mental, physical, and cognitive energy from day to day and throughout each day. The uncertainty that fatigue presents in chronic illnesses marked by persistent inflammation increases the patient's experience of psychological, emotional, and social distress [24].

LITERATURE REVIEW

Definition of Fatigue. Although patients frequently complain of fatigue, one of the challenges of addressing this condition is the lack of consensus in a definition. Aaronson and colleagues [25] defined fatigue as "the self-recognized state in which an individual experiences an overwhelming sustained sense of exhaustion and decreased capacity for physical and mental work" (pg. 46). Ream and Richardson [26] defined fatigue as "a subjective, unpleasant symptom which incorporates total body feeling ranging from tiredness to exhaustion, creating an unrelenting overall condition which interferes with an individual's ability to function to their normal capacity" (pg. 527). Chaudhuri and Behan [16] proposed two definitions of fatigue; peripheral and central. Peripheral fatigue is the inability to sustain a specified force output or work rate because of physical limitations of the muscles, nerves or cardiovascular system, with little loss of endurance in mental tasks

(pg. 34). Central fatigue is defined as failure to initiate and/or sustain attentional tasks and physical activities requiring self-motivation, as opposed to external stimulation in the absence of clinically detected motor deficits or dementia (pg. 35). The Multiple Sclerosis Council for Clinical Practice Guidelines [27] defined fatigue in the context of chronic illness as a subjective lack of physical and/or mental energy perceived by an individual or their caregiver, which interferes with usual and desired activity. The National Comprehensive Cancer Network (NCCN) [28] defined fatigue as a distressing, persistent subjective sense of physical, emotional and/or cognitive tiredness or exhaustion related to cancer or cancer treatment that is not proportional to recent activity and that interferes with usual functioning. After thorough consideration of the literature and various disciplinary conceptualization of fatigue by the author, fatigue was defined as a distressing, unpleasant symptom perceived by an individual as a persistent lack of, or decrease in physical, emotional, and/or cognitive energy, not proportional to recent activity that interferes with usual functioning. Regardless of definition, decreases in cognitive processes, daily activities, work production, safety practices, quality of life (QoL), and emotional and social functioning are present with fatigue [17, 24, 29]. The impact and prevalence of fatigue mentioned above have been established in many chronic conditions [8, 30-34]; however, the etiology of fatigue remains elusive.

Theoretical Models of Fatigue. The theoretical models proposed to explain mechanisms of fatigue are derived from fatigue being characterized as either central or peripheral in origin. Models explaining central fatigue include immune system dysregulation, impaired nerve conduction, neuroendocrine and neurotransmitter dysregulation, and energy depletion [35]. Specific mechanisms proposed include the

disruptions of basal ganglia and frontal lobe function, hypothalamic-pituitary-adrenal (HPA) axis dysfunction, and enhanced proinflammatory cytokine release that affect neural metabolism [36]. Meeusen, Watson [37] proposed a central fatigue hypothesis and suggested that an increase in the brain ratio of serotonin to dopamine would be associated with feelings of tiredness and lethargy; where increased dopamine levels should favor improved performance through the maintenance of motivation and arousal. A neural model of central fatigue proposed by Chaudhuri and Behan [16] identified the basal ganglia as the primary neural structure for fatigue, specifically central fatigue. The basal ganglia comprise six extensively interconnected nuclei with close connections to the limbic system via amygdalostriatal projections; with afferent and efferent connections and feedback to the prefontal cortex, and links to the hypothalamic and limbic systems [35]. Disorders, such as (a) SLE, (b) PD, (c) MS, (d) Chronic Fatigue Syndrome (CFS), (e) postpolio syndrome, (f) stroke, and (g) depression with a strong association to basal ganglia disease or involving disconnections between the prefrontal cortex and the thalamus, are characterized by central fatigue [30, 38].

Disturbances in the HPA axis have been proposed as *influencers* of central fatigue [38]. The HPA axis is the key neuroendocrine system that helps the organism adapt to various challenges; including (a) emotional, (b) physical, (c) chemical, and (d) immune stressors [39]. A mild HPA axis suppression involving depressed adrenocorticotropic hormone (ACTH) production in response to psychosocial stress and increase potency of negative feedback of cortisol on the HPA axis [40, 41] have been noted in CFS patients. Dysregulation of HPA axis function may be causally associated with increased immune activation and inflammatory responses to potentially promote symptoms of fatigue,

malaise, somnolence, and myalgia [42, 43]. Additionally, abnormal release of central corticotrophin releasing hormone has been detected in chronic illnesses including SLE, MS, RA, and fibromyalgia [44].

Pro-inflammatory cytokines are important players in the inflammatory response and have been suggested as *initiators of fatigue:* they can act on the brain to affect neural metabolism [38]. Cytokines can impact the brain via four main pathways: (a) activation of the vagus and other afferent nerves with consequent signaling to the brain, (b) secretion by circumventricular organs, (c) active and passive transport across the blood brain barrier (BBB), or (d) active secretion by BBB cells [45]. The conceptualization of inflammation-induced fatigue requires an evolutionary perspective [46]. The seminal work of Miller [47] presented psychophysiological studies of motivation and the behavioral effects of illness, which helped establish the foundation for immune-initiated sickness and the concept of sickness behavior. Hart [48] extended Miller's work by presenting the role of fever, not as a maladaptive and undesirable effect of illness, but as a highly organized behavioral strategy/facilitator of a person's or an animal's ability to combat viral and bacterial infections, which at times is critical to the survival of that organism. This action was termed sickness behavior. Hart [48] presented an overview of the possible adaptive and functional values of the behavior typical of sick animals and people. The behavior associated with being sick centers around the body's physiological and psychological response to a fever. This idea is central to the immunologic perspective of sickness behavior. The discovery that a protein secreted by activated macrophages was responsible for causing sickness behavior was a critical advancement in understanding the neuroimmunologic contributions to fatigue [49-51]. The basic

elements of the frontostriatal network, including the basal ganglia and frontal cortex, have been found to be the targets of inflammatory mediators as well as the site where significant alterations in activity and function have been observed in chronic inflammatory conditions (e.g. MS, and PD) plagued by fatigue [46, 52, 53]. In addition to the multiple models postulated to explain fatigue through a central mechanism, peripheral mechanisms have also been considered.

Models explaining peripheral fatigue include the accumulation and exhaustion hypotheses. The accumulation theory hypothesizes that waste product collection outpaces the body's ability to dispose of them, whereas the exhaustion theory proposes that essential substances integral to muscle activity are not available or have been depleted [54, 55]. Peripheral models focus mainly on motor function and the neuromuscular contributions to fatigue; which involve the neuromuscular junction, muscle cell membrane activity, and peripheral nerves conduction [35, 55, 56]. Chronic illnesses such as (a) RA, (b) PD, (c) SLE, (d) MS, (e) and cancer are often associated with peripheral/physical fatigue; however, overwhelming reports of fatigue in conjunction with these chronic illnesses are categorized as mental fatigue and manifest as cognitive dysfunction, perception of increased effort to complete tasks, and mood changes [9, 21, 25, 57].

Fatigue is not simply a sense or perception of physical exhaustion; it also has an important cognitive component. In some patients, this component may be the most distressing aspect because they are limited in their ability to sustain concentration and endure mental tasks [30]. The search for foundational causes of fatigue continues because no one theory thoroughly explains the basis for fatigue in the patient with

chronic illness. Fatigue, like pain, in chronic conditions is not only explained by physiological mechanisms, but must be understood as a multicausal, multidimensional phenomenon that includes physical, psychological, and social aspects [54]. PCOS, a chronic syndrome with components associated with fatigue is a condition that necessitates studying to understand how fatigue displays and impacts this population.

Polycystic Ovary Syndrome. Polycystic ovary syndrome is a complex, chronic illness with reproductive, psychological, and metabolic implications across the reproductive lifespan. It is the *most common endocrinopathy of reproductive-age women of all ethnicities*, and affects up to 26% of this population [58-60]. PCOS was originally known as Stein-Leventhal syndrome; named after two gynecologists who described seven amenorrheic women with enlarged, polycystic ovaries, obesity, and infertility in 1935 [61]. The economic burden of PCOS in the U.S. is immense. Between 2005 and 2008, the mean yearly number of PCOS-related visits was 516,000. The estimated annual national health care cost associated with PCOS in 2010 dollars was $1.16 billion, with the greatest contributors being (a) Type 2 diabetes mellitus (T2DM), (b) obesity, (c) contraceptives, (d) initial evaluations, and (e) infertility treatment [62].

PCOS is a heterogeneous, inheritable endocrine disorder characterized by polycystic ovaries on ultrasound evaluation, hyperandrogenism (increased hair growth, acne, and male-pattern balding) and ovulatory dysfunction (oligomenorrhea or amenorrhea). Ovulatory dysfunction in PCOS puts these women at increased risk for endometrial cancer and infertility. [63, 64]. It is estimated that *33-38% of women with PCOS are overweight or obese* [65-67]. Also, an association between increased insulin resistance and PCOS is a consistent finding among all ethnic groups [68-70]. Women

with PCOS demonstrate a 5- to 10-fold increased risk of developing T2DM compared with age- and weight-matched women [71]. The metabolic component of insulin resistance also places women with PCOS at increased risk for CVD, which kills 1 in every 4 females in the U.S. [72]. In addition to the physiologic implications of PCOS, this condition has been linked with psychosocial impacts to include increased depressive and anxiety symptom severity [73-75]. The prevalence and risk of depression and depressive disorders in women with PCOS is 40-64%, and is much higher relative to healthy controls [76-78]. Anxiety has been found to be significantly higher in women with PCOS compared to controls as measured by the State-Trait Anxiety Inventory (STAI) [79-81]. Dysregulation of the HPA axis and various end organ systems has been implicated as the neuroendocrinological basis for many affective disorders such as bipolar disorder and major depression. However, the neurobiological correlates of emotional and cognitive dysregulation in persons with PCOS remain to be elucidated [82].

To assist in explicating the psychosocial dynamics of PCOS, researchers have used qualitative approaches to evaluate the life experiences of women with PCOS. Experiences included: (a) feelings of appearing less feminine, (b) wanting to be normal, (c) feelings of guilt due to infertility issues, (d) confusion related to information received and long processes leading to diagnosis, (e) frustration from lack of information and support, and (f) the desire to gain control over their condition [83-86]. One of the frequent complaints women with PCOS report is lack of support systems to adequately deal with their condition [85-87]. A decreased personal perception of womanhood directly related to the physical and physiological presentation of PCOS causes these

women to report feeling isolated and less than a *normal* woman [87, 88]. This condition can negatively impact every aspect of a woman's life and be a major source of health, body-image/cosmetic, and psychosocial concerns.

PCOS and Fatigue. As the name connotes PCOS is a syndrome. A syndrome is a cluster of symptoms that cannot be explained under the prism of a common etiologic factor or a unifying pathophysiological pathway [89]. The concept of symptom cluster was evaluated by Barsevick [90] who attempted to integrate and synthesize the literature on the definition and importance of the symptom cluster by considering the four symptoms of fatigue, insomnia, pain and depression. A symptom cluster was defined as a stable group of two or more concurrent symptoms that are related to one another and independent of other symptoms or symptom clusters [91]. It was concluded that a symptom cluster poses a clinically relevant problem to the individual who is impacted, it causes negative patient outcomes and clear and concise strategies need to be identified to alleviate a symptom cluster [90].

PCOS is a complex medical condition with symptom clusters that have significant physiological and psychological implications for women [65, 68, 73, 74], and may increase the experience of fatigue. The literature is sparse regarding the relationship between the symptom of fatigue and PCOS (See Figure 1) [92-94]. Interestingly, PCOS has many features in common with other chronic diseases where fatigue is an overwhelming symptom. For example, PCOS is associated with obesity, depression, and chronic inflammation. Another factor that may contribute to fatigue in PCOS is psychological status, to include anxiety and/or depression [17]. As previously noted, women with PCOS experience increased rates of psychological conditions including (a)

mood disturbances, (b) irritability, (c) anxiety and (d) depression [73, 81, 95], which may play a role in the presence of fatigue. Finally, lifestyle factors such as body mass index (BMI) and decreased physical activity show an association with fatigue [18, 96]. Obesity and increased BMI are prevalent in women with PCOS [97, 98]. Although the role of sleep quality in the occurrence of fatigue is inconsistent, the consideration of sleep quality as a lifestyle factor has been addressed in the study of fatigue [94, 99, 100].

PCOS has many of the markers suggestive of chronic inflammation [101-104]; thus inflammation could contribute to fatigue in PCOS. For example, increased levels of pro-inflammatory cytokines: (a) Interlukin-6 (IL-6), (b) Tumor Necrosis Factor-alpha (TNF-α), and (c) C-reactive protein (CRP) have been shown to be present in PCOS [94, 101-103], and are associated with new-onset of fatigue [105]. This pro-inflammatory process may initiate fatigue in PCOS.

Understanding that PCOS has factors in common with other chronic conditions plagued by fatigue, it is compelling to take the next step and study fatigue in women with PCOS. Fatigue has been mentioned as a *present* factor in studies considering health-related quality of life (HRQoL) and the experience of PCOS, but inquiry into the nature, quality, severity, and/or impact of fatigue has been limited [92, 93, 106]. Aaronson and colleagues established the Center for Biobehavioral Studies of Fatigue Management at the University Of Kansas School of Nursing in 1992 to systematically study fatigue in diverse populations. To build on the systematic study of fatigue in diverse populations, military women with PCOS have been chosen for the current proposed study. Polycystic ovary syndrome shares many features common to fatigue, but to date these commonalities have not been directly evaluated. Therefore, the author seeks to study the

impact of this symptom experience for the purpose of contributing new knowledge about fatigue under different circumstances and among women with a clinical condition that has not be considered with regards to fatigue. The author also seeks to shed light on the complicated and distressing problem of fatigue. The presence of fatigue in PCOS has significant implications for women and additional implications for military women serving in the United States Armed Forces.

Military Relevance. Fatigue is a symptom of great importance to the Department of Defense (DoD) [107]. Although fatigue exists in healthy populations, clinical populations, and males and females alike, the focus of this study is how fatigue impacts a population of women serving in the military. Women in the military are required to be ready for duty and *fit to fight*. High military demands and job responsibilities necessitate awareness and well-being. The climate of health and top personal performance dictate that both the individual and the healthcare providers work to ensure optimal well-being and health. Fitness plays a significant role in the DoD. Each service branch incorporates fitness into the professional profile of service members. Annual and semi-annual assessments of fitness levels seek to ensure members are capable of handling the physical demands of military life [108-111]. Being physically fit increases injury prevention, overall health, and mission performance. Military members who are physically fit are more resilient to operational stressors faced during operations [112, 113] Fatigue threatens readiness through decreasing the member's ability to perform at usual and optimal levels [107, 114]. Women in the military make tremendous contributions and serve critical roles in defense of the nation; 16% of officers and 15% of enlisted active duty members are females [115]. In light of recent policy changes, and as of January

2016, all military occupations, positions, and units have been opened to women [116]. It is imperative that the health status of women in the military is considered and high value placed on relevant research to address their needs. Although an analysis of the prevalence of PCOS over 10 years in the U.S. Armed Forces, from 2002 to 2012, revealed 1.3% of military women were affected [117], a recent Military Health System (MHS) report of outpatient visits by ICD-9 code of PCOS indicated that over a three year span (fiscal year (FY) 2012 – 2014) (a) 3, 998, (b) 4,022 and (c) 3,878 encounters respectively, were documented (FOIA report, 2015). These numbers do not indicate the count of individual patients per encounter, but the numbers do indicate this condition incurs medical attention. It is well established that PCOS is often underestimated as a result of under diagnosis [59], which makes it challenging to know the actual prevalence of this condition. Fatigue affects clinical and healthy populations, and the reporting rate of fatigue is also difficult to quantify. Researchers found that many who suffer from fatigue do not routinely report it unless specifically asked by the attending provider [1, 2, 118]. In the MHS, outpatient visits by active duty members over a three year span (FY 2012 – 2014) were documented as (a) 36,713, (b) 35,473, and (c) 42,166, respectively for fatigue. These numbers indicate that PCOS and fatigue impact the female military member, place a burden on the MHS as well as the units who must function with the affected member or compensate for the individual who needs time off for office visits for these conditions. This burden of fatigue is not new.

Evaluation of fatigue in the military began during WWII when researchers focused investigations on the impact of fatigue on the war effort such as the breakdown in skilled performance of aviators [119]. The evaluation of fatigue and its impact on

performance continues [120]. In the Australian Fatigue Management During Operations Manual, Murphy, [107] described many effects of fatigue on performance to include (a) reduced attention, (b) communication difficulties, (c) mood changes, (d) inability to concentrate, (e) increasing omission and carelessness, (f) decreased vigilance, (g) slowed comprehension and learning, (h) encoding/decoding difficulties, (i) hallucinations, (j) muddled thinking, (k) faulty short-term memory, (l) slowness in perception, (m) slow and uneven responsiveness, (n) and task complexity. Fatigue in the military has been considered in relation to deployments. Many injuries associated with deployments such as aviation mishaps, altered operational decision-making, musculoskeletal injury, as well as the stress of longer, and more frequent deployments, and decreased dwell time between deployments all play a role in deployment-related fatigue [4, 107, 121-123]. The effects of fatigue place members and their co-workers at risk during military operations, as well as when outside of military field operations. Although operation tempo has decreased due to the draw down in Iraq and Afghanistan, unique demands of military service members still remain overseas and in the United States.

Besides the impact of fatigue on military operations, fatigue is recognized as an occupational health and safety risk. Health professionals are expected to care for the warfighter and their families. Fatigue in health professionals has an adverse impact on patient safety. Fatigue has been associated with medical error, poor cognitive performance, and degradation of psychomotor skills [124-126]. Occupations that demand high alertness and vigilance such as munitions workers are at high risk for hazards in the presence of fatigue. The consequences of fatigue not only lead to impaired performance, but also have the potential to increase susceptibility to injury and illness,

decrease productivity, and place burdens on the healthcare system [123]. The prevalence rate of PCOS in the military and fatigue, which is reported more often in women with chronic conditions, may be an additional factor that jeopardizes productivity and safety in the DoD. There are vast collections of literature evaluating the occurrence and impact of fatigue in chronic conditions such as MS, SLE and RA. To date there is no literature available examining the occurrence, dimensions and severity of fatigue in the chronic condition of PCOS. Likewise, literature evaluating fatigue in military women is limited.

A literature search following the framework of Whittemore and Knafl [127] was conducted to identify articles that considered fatigue among military women. A search of PubMed, Cumulative Index to Nursing and Allied Health Literature (CINAHL), PsychINFO, and Web of Science was completed in collaboration with a medical librarian. Search terms included "fatigue," "military," "department of defense," "servicewomen," "women," "gender," and "difference." The search was limited to English-language research studies with no time range designated. There was moderate overlap in the results of the searches, which resulted in 156 titles and/or abstracts meeting inclusion criteria. Inclusion criteria included: title and/or abstract considering fatigue among a female population. The decision to not include "military-related" as a criteria for titles and/or abstracts was in the event an article considered fatigue in a civilian and military population where the military population was not the main focus, and as such not reflected in the title and/or abstract. This may have resulted in overlooking a potential article. Eight of the initial screened156 titles and abstracts were retained. A fuller review of the eight articles resulted in the elimination of three. Elimination criteria included

articles that were: (a) Non-military related, (b) editorials/commentaries, (c) Male only, (d) Gender not specified, or (e) Gender not differentiated out in statistical analysis.

The literature review process is diagramed in Figure 2. Researchers addressed fatigue (a) among military women in aviation, (b) in a Naval fitness program, (c) during perinatal and post-partum periods, and (d) during Marine Corps basic combat training [128-132]. Fatigue among military women impacts (a) performance, (b) pregnancy delivery outcomes, (c) route of birth, (d) degree of breastfeeding, (e) depression, (f) anxiety, (g) maternal sleep, and (h) infant mood [131, 132]. A relationship between fatigue and cholesterol panels has also been noted in the literature [130]. No literature was found addressing dimensions of fatigue, health conditions, nor the experience of fatigue.

CONCEPTUAL FRAMEWORK

The conceptual framework of this study is based on Lenz and associates' theory of unpleasant symptoms (TOUS) [133]. The TOUS was developed by nurse researchers who had a common interest in the nature and experience of different symptoms (specifically fatigue and dyspnea) [134]. The original version of TOUS considered each influencing factor as individually impacting symptom experience and with no interrelation among other influencing factors. This unidimensional, non-relational perspective has been replaced by a multidirectional, interrelated perspective [133]. The current TOUS has three major components: (a) symptoms, (b) influencing factors, and (c) performance outcomes.

The Symptoms. Symptoms, the central focus of TOUS, are the perceived indicators of change in normal functioning as experienced by patients [133]. A single

symptom can occur alone or multiple symptoms can occur simultaneously. Each symptom is conceptualized to be a multidimensional experience that can be measured separately or in combination with other symptoms. The common dimensions of the symptom experiences seen across symptoms and clinical assessments include intensity, quality, duration, and distress [133].

The first dimension of a symptom is intensity. Intensity refers to the severity or strength of a symptom and is the most frequently and easily assessed dimension of unpleasant symptoms. The assessment of a patient's pain during a medical appointment is an example of evaluating symptom intensity. This may be completed by the use of a numeric or visual pain scale instrument. The symptom intensity of fatigue can also be easily assessed with such instruments as the Fatigue Severity Scale, Fatigue Questionnaire, the Brief Fatigue Scale, and the Defense and Veterans Pain Rating Scale (DVPRS). In addition, these instruments evaluate how fatigue impacts a person's activities and lifestyle [135-138].

The second dimension of a symptom is quality. Quality refers to the nature of the symptom or the way in which it is manifested or experienced. This can be characterized as what it feels like to have the symptom. Describing and measuring the quality of specific symptoms depends on the patient's ability to articulate what they are experiencing. This may be a difficult task as symptom quality can be very personalized. Symptom quality is usually best addressed through qualitative studies when allowing individuals to describe in their own words the personal characteristics of a symptom [133, 139]. However, it is possible to quantify symptom quality of fatigue with measures such

as the Multidimensional Fatigue Inventory-20 (MFI-20), the Checklist Individual Strength, and the Fatigue Assessment Instrument and the DVPRS [138, 140-142].

The third dimension of a symptom in the TOUS model is duration. Duration refers to the time element of a symptom and includes both the frequency of a symptom as well as the amount of time that the symptoms persist. Unpleasant symptoms may be intermittent, constant, acute, or chronic in nature. The current study's goal is to describe the features of chronic fatigue.

Distress is the final dimension of the symptom experience. Distress refers to the degree to which a person is bothered by a symptom [133]. A symptom can be constant, and mild in nature, but is not perceived as bothersome; likewise, a symptom may be intermittent and severe, and is perceived as very bothersome. The degree of distress experienced may be directly related to intensity. Individuals with higher levels of fatigue report more distress as compared to individuals with lower levels of fatigue [11, 12, 17]. Like symptom quality, symptom distress is usually best addressed through qualitative studies that allow individuals to describe in their own words the personal characteristics of a symptom impact.

Influencing Factors of Symptoms. Influencing factors are the second component in the TOUS. Three categories comprise influencing factors: (a) physiologic, (b) psychologic, and (c) situational [133]. These categories display an interrelationship with each other (individually and/or in combination) to impact the symptom experience. The physiologic influencing factors include (a) normal systems and pathologic problems of anatomical/structural, (b) physiological, and (c) genetic variables. Examples of variables in this category include structural anomalies such as a ventricular septal defect, existence

of pathologic-like brain lesions, or disease states seen in multiple sclerosis or Alzheimer's disease. Inflammation due to infection or trauma, and Single Nucleotide Polymorphisms (SNPs) are other examples of physiological/genetic variables that influence the occurrence of a symptom and how it is, or might be, experienced.

Psychologic influencing factors include (a) the individual's mental state or mood, (b) affective reaction to illness, and (c) degree of uncertainty and knowledge about the symptoms and their possible meaning [133]. Lenz and colleagues [133] suggested that psychological factors play a significant role in the symptom experience. For example, the mental states of anxiety and depression, as well as one's perception of the illness as highly stressful, can cause the experience of symptoms to manifest as more severe than one who experiences less anxiety, depression, or negative illness perceptions [11].

Situational factors, the final influencing factor of symptoms in the theory, include the social and physical environment that may affect the individual's experience and reporting of symptoms. Social environments include (a) employment, (b) marital and family status, (c) lifestyle behaviors, and (d) social support. Physical environments can also include (a) place of employment, (b) residential dwelling, (c) sleep environment, and (d) availability of and access to health care resources. Individuals who are employed, have high work job demands, lack of support, and decreased activity levels, experience more fatigue [1, 118, 139, 143]. Individuals who are married, have higher academic degrees, and with high perceived support systems experience less fatigue than individuals who are not married [144, 145].

It is acknowledged that the three influencing factors interact synergistically with one another [133]. This interaction is an example of a moderating effect. Moderation is

present when the relationship between two variables (i.e., a situational factor and the intensity of a symptom) changes at different levels of a third variable (i.e., psychologic factor, such as depression). For example, the relationship between absenteeism at work and fatigue is stronger among ulcerative colitis patients with depression as compared to ulcerative colitis patients without depression [11].

The TOUS suggests that the relationship between and among the three influential factors may be reciprocal. The experience of unpleasant symptoms can change an individual's physiological, psychological, and situational status [133]. Findings from Cleare, Bearn [146] suggested that an association between stressful life events and the symptoms of depression is well established. Increasingly data illustrate how the neurobiological mechanism underlying the stress response, particularly the activation of the HPA, may be relevant to the pathophysiology of depression [7]. For example, an individual who experiences chronic stress, depression or fatigue may experience increased mood disturbances, social isolation, or increased inflammation on biomarker assessment.

Performance Outcomes. The final variable in TOUS is performance. Performance is conceptualized to include functional and cognitive activities. Functional performance is conceptualized broadly to include physical activity, activities of daily living, social activities and interactions, and role performance; including work and other role-related tasks [133]. The multiple dimensions of fatigue can work together to impact functional performance; however, physical fatigue is the primary influence on this outcome. As the inability to sustain a specified force or work rate increases, functional performance decreases. This is seen in conditions such as myasthenia gravis, congestive

heart failure, and PD [16]. Cognitive performance is conceptualized to include those processes involved in executive functioning such as concentrating, reasoning, decision-making, and problem-solving. Mental fatigue impacts the ability to endure sustained mental tasks required for executive functioning. Investigators suggests that patients with MS and T2DM show lower cognitive performance when mental fatigue is present than when not mentally fatigued [31, 35]. Performance outcomes represent the consequences of the symptom experience.

Applying the TOUS to PCOS. Through the TOUS, the three interrelated influencing factors (physiologic, psychologic, and situational) are postulated to impact a predisposition to and manifestation of a given symptom or multiple symptoms and the nature of the symptom experience. As a result, the symptom experience affects the individual's performance, which encompasses cognitive and physical performance [133]. In applying TOUS to this study (See figure 3), the physiologic factors of age, inflammatory markers, obesity, and insulin resistance are acknowledged as potential influencing factors that contribute to the symptom experience of fatigue and have an interactive relationship with psychologic and situational factors to influence the occurrence of fatigue. Literature linking physiologic factors of fatigue in PCOS is lacking; however literature linking the physiologic factors present in PCOS and other chronic conditions consistently report the presence of fatigue [34, 105, 147]. Psychological factors such as mood disturbances, anxiety, and depression can influence how fatigue presents and is experienced. The directionality between psychologic factors and fatigue is uncertain; however, researchers consistently report that fatigue and psychological factors are highly associated [11, 29, 34, 148]. For this reason, depressive

symptoms and anxiety were selected as variables of interest for this study. Finally, situational factors, such as lack of or presence of support systems, home and work environments, and sleep performance, contribute to the experience of fatigue [118, 149, 150]. Sleep quality and social support were chosen as variables for this study. As stated earlier, there are mixed results regarding the influence of sleep quality on fatigue in chronic condition. The influence of sleep quality on fatigue in the military has been evaluated in deployed setting, and has been shown to have a negative impact [151]; however, the influence of sleep quality on fatigue in non-combat situations has not been revealed. Social support in patients with chronic conditions such as MS, T2DM, and mild traumatic brain injury has been shown to positively impact fatigue levels [152-154]. Understanding the role of sleep quality and social support in the current study may help target effective interventions such as education on sleep hygiene practices, or ensuring support groups are established, identified and available for access.

The current study was proposed as a mixed methods, between groups, cross-sectional study to compare fatigue in military women with and without PCOS, examine differences between military women with and without PCOS on dimensions and severity of fatigue, identify predictors of fatigue among military women with and without PCOS, as well as explore how military women with and without PCOS describe various dimensions of fatigue. It does not seek to explore the etiology of fatigue. For this reason, biological markers indicative of physiological influencing factors of TOUS were not collected, but the physiological surrogates of age, BMI, and PCOS are used as a guide to explain the symptomology of fatigue presence, dimensions, and severity.

The situational factors of sleep quality and social support, and the psychological factors of anxiety and depressive symptoms were used to evaluate predictors of fatigue severity and dimensions. The symptom components of the TOUS were used to evaluate the severity, dimensions, and quality of fatigue described by military women with and without PCOS. Finally, performance outcomes of wakefulness and physical fitness level were not considered in this study for assessing performance but rather as predictors. As noted by the model, there is a bi-directionality of relationships between components. Physical fitness scores, which are used in the DoD to evaluate physical performance [108-111], and scores on the Epworth Sleepiness Scale (ESS), which is a surrogate measure for wakefulness, were both used to evaluate their influence on predicting fatigue severity and dimensions in military women with and without PCOS.

ASSUMPTIONS

The author assumed that subjective participant responses were valid at the time. The author assumed that participants understood the symptoms of PCOS. The investigator also assumed that the obtained sample was representative of the population desired to make inferences to.

ORGANIZATION OF THE DOCUMENT

Chapter 2 provides methods for the quantitative and qualitative portions of this mixed-methods study.

Chapter 3 is a manuscript submitted to Military Medicine documenting an integrative review underscoring the need for additional studies investigating fatigue in military women.

Chapter 4 is a manuscript submitted to Human Reproduction documenting investigation into fatigue occurrence, dimensions and severity level in military women with and without polycystic ovary syndrome.

Chapter 5 is a manuscript submitted to JOGNN documenting investigation into dimensions and impact of fatigue among military women with and without polycystic ovary syndrome.

Chapter 6 provides the mixed methods results of the quantitative and qualitative portions of this study.

Chapter 7 provides the unifying discussion of the study findings, implications of findings, strengths and limitations of the study and lastly the investigator provides recommendations for further research in the area of fatigue.

CHAPTER 2: METHODS

The long-term goal of this research is to establish relevant and efficient interventions that can be translated into clinical practice guidelines to improve functioning and performance, resulting in increased quality of life for military women with PCOS. The aims of this study were to (a) compare the occurrence, dimensions and severity of fatigue in military women with and without PCOS, (b) examine differences between military women with and without PCOS on dimensions and severity of fatigue, (c) identify predictors of fatigue among military women with and without PCOS, and (d) explore how military women with and without PCOS describe the various dimensions of fatigue.

STUDY DESIGN

A sequential mixed-method, between-groups, cross-sectional design with online questionnaires was utilized.

SAMPLE SIZE AND POPULATION

By a power analysis conducted in Gpower, a sample size of 51 per group was needed to detect a medium effect size (d = 0.50) with a power of 0.8 and alpha value of 0.05. Sample size for the qualitative portion of this study was determined when data saturation was achieved. Data saturation occurred when data became repetitive and no new themes, or new information was gained [155].

The population for this research included active duty military women (a) ages 19 – 45 (b) non-pregnant (c) perimenopausal and premenopausal (c) with and without the diagnosis of PCOS. Women were excluded if they had a diagnosis of (a) cancer or

receiving active cancer therapy, (b) rheumatoid arthritis, (c) multiple sclerosis, (e) systemic lupus erythematosus, or (f) a history of hysterectomy with singular or bilateral removal of ovary(ies).

PROTECTION OF HUMAN SUBJECTS

Approval from the Uniformed Services University (USU) IRB and concurrence from Walter-Reed National Military Medical Center (WRNMMC) IRB was obtained. A behavioral health resource handout (Appendix A) was given to all eligible participants with the explanation that if the study caused any anxiety, depression or other behavioral health issues there were resources available for assistance.

RECRUITING

A convenience sample of active duty military women with and without the diagnosis of PCOS who received health care at WRNMMC, Malcom Grow Medical Clinics and Surgery Centers (MGMCSC), or any Military Health System (MHS), attended USU, or had access to Facebook were recruited. When recruitment was in person, after eligibility was established, the primary investigator (PI) reviewed the requirements for participation in the study. Contact information was then obtained from interested individuals for the PI to email a weblink to FluidSurveys.com for study participation.

When recruitment was received through Facebook or email response to advertisement, the eligibility form was emailed to the interested individual. After eligibility was established the PI called the interested participant and reviewed the study requirements for participation in the study. Once the individual confirmed interest they were informed that a weblink to FluidSurveys.com would be emailed for completion of

the study, along with a behavioral health resource information sheet in the event the study caused any anxiety, depression or other mental health issues.

When recruitment was by phone call, eligibility was established at time of call. After eligibility was established, study requirements were reviewed and participant was informed that a weblink to FluidSurveys.com would be emailed for completion of the study, along with a behavioral health resource information sheet in the event the study caused any anxiety, depression or other mental health issues.

DATA COLLECTION

Quantitative

Participants accessed the study through FluidSurveys.com (Appendix B). Informed consent permission was encountered on the first page of the weblink (Appendix B). Participants gave consent before taking part in the study. After giving consent, page two of the weblink required participants to create a participant identification code and enter an email address. Participant identification code was created as follows: first two letters of their mother's maiden name, last four numbers of their cell phone, and last two letters of their father's first name. Email address and participant identification code were used to link study participant with study data. A notification for completion of the self-reported measures was sent to the PI by FluidSurvey™.

Study Instruments

An overview of the study variables, instruments, psychometrics, and study specific aims addressed are presented in Table 2. Depression and anxiety are correlates that require assessment in any study of fatigue. When measuring fatigue in a condition that has a high prevalence of depression or anxiety, it is difficult to differentiate which

variable is being analyzed. It is important that studies have a standard measure for mood disturbance to factor in or control for the effect of depression and anxiety on measures of fatigue. For this reason, psychological factors of depression and anxiety were measured in the current study. From the State –Trait Anxiety Inventory (STAI) (Appendix C) only the trait anxiety portion was used to measure anxiety and the Center for Epidemiological Studies-Depression scale (CES-D) (Appendix D) measured depression. Sleep quality is also an important factor of concern when evaluating fatigue. Researchers have found that chronic fatigue, unlike acute fatigue, is not relieved by sleep, and is not the result of lack of sleep. However, to ensure this potential confounder was accounted for, sleep quality was measured by using the Pittsburg Sleep Quality Index (PSQI) (Appendix E) and wakefulness was measured by the Epworth Sleepiness Scale (ESS) (Appendix F).

A demographic questionnaire (Appendix G) was used to collect the following data: Age, weight, height, current medical diagnoses, medical history, branch of service, pay grade, duty title, education level, marital status, physical fitness score, profile status, social support, ethnicity, number of pregnancies, age at diagnosis of PCOS, medication use, and supplement use. The quantity of social support was analyzed as counts: for example the number of support personnel chosen were calculated to indicate the amount of social support present. The quality of social support was analyzed in the context of women expressing the type of support present, not sufficiency of support present. Physical fitness score were analyzed by category (excellent, satisfactory, and unsatisfactory) to reveal current level of fitness.

PROMIS Fatigue Short Form 8a. The PROMIS Fatigue Short Form 8a (Appendix H) is an instrument that measures a range of self-reported symptoms of fatigue from mild

subjective feelings of tiredness to an overwhelming, debilitating, and sustained sense of exhaustion that decreases the ability to execute daily activities and function normally in family or social roles [156]. It consists of 8 items from a 95-item bank, with each on a 5-point Likert scale, ranging from 1 to 5. Fatigue scores are reported as a T-score. A score of 50 is the average for the United States general population with a standard deviation of 10. A higher PROMIS T-score represents a higher level of fatigue [157]. Although the reliability and precision of the short forms within a domain are highly similar, the short form 8a is the most precise of the short forms [158]. The short form has reliability greater than 0.9 in both healthy control and clinical patient populations [159]. Fatigue is divided into the experience of fatigue (frequency, duration, and intensity) and the impact of fatigue on physical, mental, and social activities. The fatigue short form is universal rather than disease-specific and it assesses fatigue over the past seven days [160]. It has been validated against the Functional Assessment of Chronic Illness Therapy-F ($r = 0.95$) and the SF-36v2 ($r = 0.91$) [143]. The occurrence was evaluated with item analysis of question 1 responses [I feel fatigued…]. The severity of fatigue was evaluated by the T-score given.

State-Trait Anxiety Inventory(STAI). The STAI State & Trait is a 40-item self-report questionnaire that is among the most widely researched and used measures for general anxiety [161]. It comprises two 20-item scales designed to measure state and trait anxiety. State anxiety (A-State) measures the intensity of feelings or anxiety at a particular moment in time. Trait anxiety (A-Trait) measures a person's general tendency to perceive a wide range of situations as threatening [162]. Respondents are asked to rate each item on a 4-point Likert scale, ranging from 1 (almost never) to 4 (almost always).

The total score ranges from 20 to 80, with higher scores indicating greater state and trait anxiety. The STAI has shown good internal consistency with a Cronbach's alpha < 0.90 on both scales [163]. Test-retest reliability ranges from 0.73 to 0.86 on the Trait scale and 0.16 to 0.62 on the State scales [164]. Content validity has been established with Taylor Manifest Anxiety Scale (0.73) and Scheier's Anxiety Scale Questionnaire (0.85) [161]. Only the STAI-Trait was used for this study, because the participant's general disposition related to anxiety was sought versus a particular moment in time as the STAI-State assesses.

Center for Epidemiologic Studies Depression Scale (CES-D). The CES-D is designed to assess current frequency of depressive symptoms, with emphasis on depressed affect or mood, and was originally intended for use with cross-sectional samples in survey research. In contrast to other commonly used measures of depression such as the Beck Depression Inventory (BDI), the CES-D is not designed for use as a clinical intake measure for the evaluation of illness severity over the course of psychiatric treatment. The CES-D's 20 items reflect the major components identified by [165] using both factor analysis and clinical literature. Specific items were selected to reflect the following six components: depressed mood, feelings of guilt and worthlessness; feelings of helplessness and hopelessness, psychomotor retardation, loss of appetite, and sleep disturbance. Patients are asked how frequently they experienced a given symptom in the past week. Responses include: "rarely or none of the time (less than 1 day)," "some or a little of the time (1-2 days)," "occasionally or a moderate amount of time (3-4 days)," "most of the time (5-7 days)." Each of the frequency levels is assigned a numerical score from 0 (rarely or none of the time) to 3 (most or all of the time). Four of the items (#4,

#8, #12, and #16) are worded in a positive (non-depressed direction) to help avoid response set and to assess positive affect (or its absence). Scores range from 0 to 60, with higher scores indicating a higher degree of symptomatology. The CES-D has been validated in both household surveys and in psychiatric settings, with test-retest reliabilities ranging from 0.32 for 12 months to 0.67 for 4 weeks. Internal consistency of the measure has been good. Split-half correlations are reported as 0.85 for patient groups and 0.77 for normal groups. Cronbach's alpha and Spearman-Brown coefficients are 0.90 or above for both the normal volunteers as well as the patients [165, 166].

Multidimensional Fatigue Inventory-20 (MFI-20). The MFI-20 is a 20-item self-report questionnaire that uses a 5-point Likert scale; it has five subscales: general fatigue, physical fatigue, mental fatigue, reduced motivation and reduced activity. It is a widely used measure and has been validated extensively in many populations, including a military population [141]. The score on each item ranges from 1 (no fatigue) to 5 (very fatigued), the score in each dimension ranges from 4 (no fatigue) to 20 (highest possible fatigue). The general and physical fatigue subscales measure the physical domain of fatigue. The reduced activity measures the behavioral, the reduced motivation measures emotional, and the mental fatigue measures cognitive. The MFI-20 is used as a composite measure of the overall subjective fatigue experience. It has shown good internal consistency with a Cronbach's alpha of 0.84. The convergent validity was established by comparison of MFI-20 with the VAS. The correlations of between and within group comparisons are generally acceptable $0.22 < r < 0.78$ [167].

Pittsburg Sleep Quality Index (PSQI). The PSQI is a 24-item scale with 19 questions by self-report and the remaining 5 answered by the subject's sleeping partner.

The self-reported questions are subjected to evaluation while those answered by sleep partners provide data on sleep apnea. The five sleep partner questions were not administered during this study. The 19 self-reported questions evaluate seven subscales, to include subjective sleep quality, sleep latency, duration of sleep, routine sleep activity, sleep disorders, the use of drugs for sleeping, and daytime dysfunction. Each item in the scale is scored between 0 and 3 (no difficulty to severe difficulty). The sum of the seven subscale scores gives the overall PSQI score. The score of each subscale varies between 0 and 3. The range of overall PSQI score varies between 0 and 21. Sleep quality is evaluated as disturbed in those with an overall score above 5 [168]. The 7 component scores have good internal consistency with a Cronbach's alpha of 0.83. The reliability of the global PSQI scores was 0.85 and the component scores ranging from 0.65 to 0.84. The validity of global PSQI scores is supported by its ability to discriminate patients from controls. The PSQI has a sensitivity of 89.6% and specificity of 86.5% for identifying cases with sleep disorder using a cutoff score of 5 [169].

Epworth Sleepiness Scale (ESS). The ESS is an 8-item self-report questionnaire on a 4-point Likert scale that assesses wakefulness in adults. The ESS is based on eight situations in which an individual may fall asleep. The questionnaire evaluates the individual's potential frequency of falling asleep under these eight situations. The ESS was developed as an alternative for the gold-standard, but cumbersome, Multiple Sleep Latency Test (MSLT). Each item is scored between 0 = would *never* doze to 3 = *high* chance of dozing. The total score ranges from 0-24 [170]. The 8-items have good internal consistency with a Cronbach's alpha ranging from 0.73 to 0.88. Construct validity with Maintenance of Wakefulness Test (MWT) ranges from -0.48 and -0.40, and

-0.27 to -0.42 with the MSLT. Values >10 are considered to indicate significant sleepiness [169, 171]. The use of the PSQI and ESS together is a common practice. Support for the effectiveness of the two questionnaires to evaluate distinct dimensions of sleep and reflect sleep health status and sleep quality has been presented in clinical and community populations [169, 172].

Table 1. Specific aims and research questions

Specific Aims	Research Questions
1. To compare the occurrence, dimensions and severity of fatigue in a sample of military women with and without PCOS.	1. What is the occurrence of fatigue, dimensions and severity of fatigue in a sample of military women with and without PCOS?
2. To examine differences between women with and without PCOS on dimensions and severity of fatigue,	2. Is there a difference in dimensions and severity of fatigue between military with and without PCOS?
3. To identify predictors of fatigue among military women with and without PCOS.	3. What are predictors of fatigue in military women with and without PCOS? a. Does PCOS moderate the relationship between predictor variables and dimensions and severity of fatigue?

4. To explore how women with and without PCOS describe the various dimensions of fatigue.	4. What words or themes will a sample of military women with and without PCOS use to describe the various dimensions of fatigue?

Table 2: Overview of study variables, quantitative instrument psychometrics, and study specific aims

Study Variable	Instrument and possible range	Reliability & Validity	Number of items	Study specific aim addressed
Fatigue	Multidimensional Fatigue Inventory-20 (MFI-20) Possible range: 4-20 per subscale	R = 0.84 V = 0.78 (VAS)	20 items 5 subscales	Specific aim 1, 2, 3 & 4
Fatigue	Patient Reported Outcomes Information System (PROMIS Fatigue Short Form 8a) Possible range: 8-40	R = 0.90 V = 0.95 (FACIT-F) 0.91(SF-36v2)	8-items	Specific aim 1, 2, & 3
Depression	Center for Epidemiologic Studies Depression Scale Possible range: 0 -60	R = 0 .85 (Non-psych pop) 0 .90 (Pysch pop)	20-items	Specific aim 1, 2, & 3

Anxiety	State and Trait Anxiety Inventory (STAI) Possible range: 20-80 per scale	R (Trait) = 0.73 to 0.86 (Taylor Manifest) 0.85 (Scheiers Anxiety)	20-items for Trait	Specific aim 1, 2 & 3t
Sleep Quality	Pittsburg Sleep Quality Inventory (PSQI) Possible range: 0-21	R = 0.83 V = 0.89 sensitivity, 0.86 specificity for identifying sleep disorders	19-items	Specific aim 2, &3
Wakefulness	Epworth Sleepiness Scale (ESS) Possible range: 0-24	R = 0.73 to 0.88 V = -0.48 to -0.40	8-items	Specific aim 2 & 3

Qualitative

The semi-structured interview was conducted to elicit descriptions of fatigue in women with and without PCOS. To fully answer the qualitative research questions, the interview explored the experiences, perceptions and perspectives of each individual. The interview was also used to expand on quantitative data received from self-report questionnaires to provide a deeper understanding of the impact of fatigue. The advantage of the semi-structured interview was that participants had the freedom to describe the impact of fatigue in their own words, and any confusion or misunderstandings were

clarified by the PI. Upon notification of study completion the PI reviewed answers to the CES-D, STAI-T, and PROMIS Fatigue short form 8a to evaluate depression, anxiety and fatigue scores. Participants who scored 60 or above on the PROMIS Short Form 8a were contacted for a follow-up semi-structured qualitative interview. The score of 60 or above was chosen because 50 is the average fatigue score of the US general population with a standard deviation (SD) of 10 [156]

Interview. Nine out of forty six women with PCOS scored 60 or above on the PROMIS Fatigue Short Form 8a and nine out of fifty women without PCOS scored 60 or above; these women were considered for the qualitative portion of the study. All nine of the women with PCOS were contacted and interviewed. Seven of the women without PCOS were contacted and interviewed. Two of the women without PCOS were away at military training and were unable to be contacted for interviews.

Trustworthiness of the data. To ensure trustworthiness of data for the qualitative portion, criteria guided by Guba et al. [173, 174] and Lincoln et al. [158] for credibility, dependability, confirmability, and transferability were met.

Credibility involves processes that increase the probability that credible findings will be produced, such as including diverse populations and selecting methods that will achieve the most accurate data. *Dependability* involves ensuring data collection was performed in a consistent manner as not to influence participants differently. *Confirmability* involves creating an audit trail (clearly detailed steps) so that the study may be replicated by other researchers. *Transferability* refers to the ability of other researchers to view the study findings as meaningful enough to transfer findings to other similar groups or settings. The study investigator can assist with transferability by

providing clear and distinct information about the context of the topic, descriptions of the population, setting, and data collection.

Credibility. Dimensions explored through the semi-structured interviews were developed from the MFI-20 [141] (Table 3). The composition of questions was reviewed by qualitative nurse-experts to ensure the "essence" of fatigue would be achieved through accurate questioning.

Table 3. MFI-20 Guided questions

Fatigue Dimensions	Semi-structured interview (Qualitative)
General	In your own words describe what the word fatigue means to you
Physical	Can you describe how your physical activity level is affected when you are fatigued?
Mental	1. Can you describe how your emotions, and/or mood are affected when you are fatigued? 2. Can you describe how your concentration is affected when you are fatigued?
Reduced Activity	Can you describe any personal or professional activities that you stop doing or decrease doing when you are fatigued?
Reduced Motivation	Can you describe how your motivation is affected when you are fatigued?

Dependability. An interview guide containing eight open-ended questions (Appendix I) for women without PCOS, and nine open-ended questions (Appendix J) for

women with PCOS was developed with the collaboration of two qualitative research experts. The semi-structured interview guide included open-ended questions such as "In as much detail as possible, in your own words can you describe what the word "fatigue" means to you" and "In as much detail as possible, can you describe how your physical activity level is affected when you are fatigued?" A closing question of "Is there anything else that you would like to tell me about your experience of fatigue?" was included in the questions of women without PCOS as well as a closing questions of "Is there anything else that you would like to tell me about your experience of fatigue or PCOS?" was included in the questions of women with PCOS. After several interviews with women with PCOS a pattern was noticed of women expressing why they chose to participate in the study and expressing their opinions of why military women were choosing not to participate in the current study. The PI returned to USU IRB for the addition of one question: "It has been a challenge recruiting women with PCOS, did you have reservations about participating? Would have any insight into why military women with PCOS would choose not to participate in this study?"

To provide participants with adequate privacy, interviews were conducted in a quiet study room in the campus library for the local participants. For participants out of the local area, interview was conducted over the phone in a quiet area chosen by the participant. Field notes were taken to annotate nuances by participants when answering questions. With participants' permission, all interviews were recorded by audio-recorder and then transcribed to ensure accuracy of each report. Interviews ranged from 7 to 20 minutes.

DATA ANALYSIS

The application of mixed-methods combines elements of quantitative and qualitative research, which provides breadth and depth of understanding and corroboration of findings [175]. This study used an explanatory sequential design, where quantitative data was collected first, followed by qualitative data. It was determined a priori that qualitative would inform quantitative.

Quantitative

Power Analysis

The present study was powered to detect statistically significant differences between women with and without PCOS across several outcome variables (general fatigue, physical fatigue, mental fatigue, reduced activity, reduced motivation, and fatigue severity). By a power analysis conducted in Gpower, a sample size of 51 per group was needed to detect a medium effect size (d = 0.50) with a power of 0.8 and alpha value of 0.05. To detect a large effect size (d = 0.80), a sample size of 21 per group was needed. Statistical analyses were conducted using SPSS version 22 (SPSS, Inc. Chicago). Multiple studies in a variety of populations have evaluated or used the primary outcomes of this study; however no studies have used these primary outcomes in a PCOS population. Therefore the predictions of primary outcomes were established from previous studies comparing fatigue among populations with chronic conditions such as myocardial infarction, diabetes, and SLE against controls. In those studies general fatigue had an effect size ranging from small d = 0.18 to large d = 1.7; physical fatigue ranged from d = 0.44 to d = 1.8; mental fatigue ranged from d = 0.21 to d = 1.8; reduced activity ranged from d = 0.17 to d = 1.5; and reduced motivation ranged from d = 0.06 to d = 1.1 [31, 176, 177].

Statistical plan

Fatigue was assessed first as a categorical variable by χ^2 in order to indicate whether or not it was present and, second, as a continuous variable by independent *t*-tests to compare the level of fatigue between groups. Comparisons between PCOS and non-PCOS groups were also performed by independent t-test for continuous variables of age, BMI, anxiety, depression, sleep quality, wakefulness, and social support. Data were presented as mean values and standard deviation. A $p < 0.05$ was used to indicate statistical significance.

To evaluate if statistically significant differences remained between groups while controlling for covariates, stepwise regression was used with PCOS as the independent variable entered in the first block and forward entry of covariates age, BMI, anxiety, depression, social support, sleep quality, wakefulness and fitness level in the next block. To assess which variables were statistically significant predictors of fatigue dimensions and fatigue severity, multiple regression models were evaluated. Finally interaction terms were created with PCOS and statistically significant predictors from the stepwise regression to evaluate if moderation was present. Standardized beta coefficients (β) were used to interpret effect size (< 0.10 = small; 0.10 to 0.25 = medium; > 0.25 = large; [178]; models were summarized by using R^2 for sample size and predictors.

Qualitative

Analysis Plan

Audio recordings were transcribed by the PI. Transcripts were compared with their audio recording to ensure accuracy. The PI and three qualitative nurse scientist experts used transcribed data for manual analysis by constant comparative analysis. This

iterative process of comparing responses from each incoming interview with previous responses enabled the PI and team members to compare elements identified from the responses in one data source with those identified in another. This process continued until the content of all data sources had been compared and commonalities in the responses were identified [155]. Participants' words, phrases, or sentences were grouped into categories that best conceptualized or represented specific experiences, thoughts, feelings or descriptions. The groupings in the categories were referred to as "meaning units." The different meaning units were then organized into themes and subthemes. Once data analyses were completed on all participants by each team member, they were collected by the PI. To ensure inter-rater reliability, the collected analyses were then re-distributed to different team members so each member received another team member's completed analysis for confirmation of themes and subthemes. The intent was not to have team members conform to the same themes and subthemes, but to have a discussion among members to ensure the themes and subthemes created gave an accurate depiction of descriptions from the participants. Finally the team of investigators came together to confirm and edit the final list of subthemes and themes created from each participant's responses. Analysis of the participants' transcribed responses revealed that each group had similar, yet slight, differences in descriptions of the various dimensions of fatigue. Sight differences were in the dimensions of general fatigue, mental fatigue and reduce motivation (Table 16).

CHAPTER 3: An Integrative Review: Fatigue among Military Women

CHAPTER 4: Fatigue and Polycystic Ovary Syndrome in the Military

CHAPTER 5: Dimensions and Impact of Fatigue among Military Women with and without Polycystic Ovary Syndrome

CHAPTER 6: Results of mixed-methods

The current study applied a mixed-methods approach to capture a complete picture of fatigue in military women with and without PCOS. Each fatigue dimension was assess through the combining of quantitative and qualitative measures (Table 4). The following section provides results of the study, where the qualitative data informed the quantitative data. Additional qualitative results are provided that extend beyond the stated specific aims.

Table 4. Overview of mixed-methods

Fatigue Dimensions	Instruments (Quantitative)	Semi-structured interview (Qualitative)
General	MFI-2- General & Physical subscale	In your own words describe what the word fatigue means to you
Physical	MFI-20 General & Physical subscale, Physical fitness score	Can you describe how your physical activity level is affected when you are fatigued?
Mental	MFI-20 Mental subscale	1. Can you describe how your emotions, and/or mood are affected when you are fatigued? 2. Can you describe how your concentration is affected when you are fatigued?
Reduced Activity	MFI-20 Reduced Activity subscale	Can you describe any personal or professional activities that you stop doing or decrease doing when you are fatigued?
Reduced Motivation	MFI-30 Reduced Motivation subscale	Can you describe how your motivation is affected when you are fatigued?

SAMPLE CHARACTERISTICS

There were 46 military women with PCOS and 50 military controls without PCOS, with an average age of 33.5 ± 5.3 yrs. BMI differed significantly between the two groups (PCOS 27.7 ± 3.5 vs. no-PCOS 25.6 ± 3.6, $p < 0.05$). No other significant differences were noted between the two groups across other demographic characteristics. The sample was diverse, with women in the Army, Navy and Air Force, enlisted and officers all represented in the study (Table 5).

SPECIFIC AIM 1 AND 2

Table 6 outlines the occurrence of fatigue and mean scores for the dimensions within the sample and between groups. Fatigue was present in 89.1% of women with PCOS and 88.0% of women without PCOS, which was not significantly different based on univariate analysis, for fatigue occurrence ($\chi 2$ (1, n = 96) = 0.00, $p < 0.98$, phi = 0.01). However, women with PCOS had significantly higher scores for general fatigue ($p < 0.001$, d = 0.96), physical fatigue ($p < 0.001$, d = 0.80), mental fatigue ($p < 0.001$, d = 1.01), reduced activity ($p < 0.001$, d = 0.82), reduced motivation ($p < 0.001$, d = 0.92), and fatigue severity ($p < 0.001$, d = 0.98) compared to women without PCOS. When asked to describe the various dimensions of fatigue both groups of women described physical fatigue as a decrease in physical activity; reduced activity as a decrease in social and physical involvement; and described using professional practice modification; but when women with PCOS described general fatigue they reported it as *persistent* mental and physical *tiredness*, whereas women without PCOS described general fatigue as an *overwhelming state* of mental and physical involvement and energy imbalance, not solely tiredness. Likewise, both women described mental fatigue as experiencing frequent

mood variations with several mood states, and decreased focusing, concentration and processing, in addition women without PCOS described mental fatigue as having attention deficit/hyperactivity disorder. Finally, women with PCOS described reduced motivation in regards to levels of motivation experiences (no motivation, high motivation, motivation, but…) in contrast; women without PCOS described how productivity was impacted due to reduced motivation.

None of the outcomes correlated with social support or fitness level for either group. No outcomes correlated with BMI in the PCOS group. Reduced activity and fatigue severity were weakly related to wakefulness in the PCOS group only. Many of the outcomes were weakly correlated with depression, anxiety and sleep quality for both groups (Table 7 & 8). In particular, trait anxiety was significantly associated with general fatigue, reduced activity, and fatigue severity in the No PCOS group, but not the PCOS group.

SPECIFIC AIM 3

There was a large effect size when the relationship between PCOS and fatigue dimension was examined in four out of five models on fatigue dimensions (physical fatigue and reduced activity were not statistically significant) (Tables 9, 10 and 11).

General fatigue.

PCOS, anxiety, and BMI explained 35% of the variance in general fatigue score of military women. A large effect size was noted for the relationship between PCOS and general fatigue score ($\beta = 0.54$), when controlling for anxiety and BMI. Likewise, a large effect size for trait anxiety ($\beta = 0.32$), and a medium effect for BMI ($\beta = 0.15$) (Table11) were noted for general fatigue. Despite that there was a large effect size for the

relationship between PCOS and general fatigue, the most frequent word used to describe fatigue by women with and without PCOS was tired (5 out of 9, and 5 out of 7 respectively)

Mental fatigue.

PCOS and BMI explained 44% of the variance in mental fatigue score of military women. A large effect size was seen for the relationship between PCOS and mental fatigue score ($\beta = 0.44$), when controlling for BMI. Likewise, a large effect size for BMI and mental fatigue score ($\beta = 0.25$) was noted (Table 9).

Reduced motivation.

PCOS, BMI and depression explained 31% of the variance in reduced motivation score of military women. A large effect size was seen for the relationship between PCOS and reduced motivation score ($\beta = 0.40$), when controlling for BMI and depression. A 26 y.o. Army Officer with PCOS reported "My desire to do anything plummets. When I'm fatigued my motivation is almost non-existent." When BMI and depression were considered, there was a medium effect size ($\beta = 0.24$ and $\beta = 0.19$, respectively) between the relationship of BMI and depression, and reduced motivation score (Table 10) A 29 y.o. Army NCO with PCOS reported "I think fatigue also comes with depression, because you just want to be to yourself," in regards to weight issues, military standards and the impact fatigue can place on motivation.

Fatigue severity.

PCOS and depression explained 44% of the variance in fatigue severity of military women. A large effect size was noted for the relationship between PCOS and

fatigue severity (β = 0.50), while controlling for depression. Also a large effect of depression (β = 0.45), on fatigue severity was noted (Table 9). These results support the idea that having PCOS impacts the dimensions of fatigue and fatigue severity experienced.

Interactions between PCOS and the three statistically significant predictors (anxiety, depression and BMI) from the stepwise regression were assessed for all four models to evaluate if PCOS moderated any relationships between outcome variables and covariates. Significant interactions were noted between PCOS and depression on reduced motivation (β = -0.71), and between PCOS and anxiety for general fatigue (β = -3.69), respectively (Table 12 and 13). Over 40% of the variance in general fatigue score was explained by the interaction between PCOS and anxiety, while 43% of the variance in reduced motivation score was explained by the interaction between PCOS and depression. Because interactions for general fatigue and anxiety (Table 12), and reduced motivation and depression (Table 13) were noted, additional regressions were conducted separately on women with and without PCOS by using stepwise regression analysis. Among women with PCOS, anxiety was excluded in the regression model for analysis as this variable did not contribute significantly to the explained variance in general fatigue (Beta In 0.16, $p < 0.44$). In contrast, for general fatigue among women without PCOS, anxiety (β=0.37, $p < 0.01$) explained an additional 26% of the variance in general fatigue for a total explained variance of 40% of the variance ($p < 0.001$) (Table 14). Likewise, among women with PCOS, depression was excluded from the regression model for analysis because it did not contribute significantly to the variance in predicting reduced motivation score (Beta In =-0.16, $p < 0.41$). Among women without PCOS depression

(β=0.64, p<0.001)) explained an additional 34% of the variance in reduced motivation score for a total explained variance of 55% of the variance (p <0.001) (Table 15). The negative beta coefficients in the original analyses (-0.71 and -3.69) indicate that the large effect sizes relating anxiety to general fatigue and depression to reduced motivation in women without PCOS were significantly weakened in women with PCOS The correlation between anxiety and general fatigue was strong and positive (r = 0.549, $p <$ 0.001), and depression and reduced motivation was strong and negative (r = -0.690, $p <$ 0.05) for women without PCOS (Table 7), whereas the correlation between anxiety and general fatigue was weak and positive (r = 0.095) and depression and reduced motivation was weak and negative (r = -0235) and not significant for women without PCOS (Table 8). No other interactions were significant.

Table 5. Descriptive characteristics of the sample

	Total (n = 96)	PCOS (n = 46)	No PCOS (n = 50)
Demographics	n (%)	n (%)	n (%)
Age	33.5 ± 5.3	33.5 ± 4.4	33.3 ± 6.1
Race			
African-American/Black	31 (32.3)	15 (32.6)	16 (32.0)
American Indian/Alaska Native	7 (7.3)	7 (15.2)	0
Asian	9 (9.4)	7 (15.2)	2 (4.0)
Latina	4 (4.2)	3 (6.5)	1 (2.0)
Native Hawaiian/Other Pacific Islander	1 (1.0)	1 (2.8)	0

White	41 (45.8)	13 (28.3)	31 (62.0)
Marital Status			
Single	19 (19.8)	6 (13.0)	13 (26.0)
Married	62 (64.6)	36 (78.3)	26 (52.0)
In a relationship, but not legally married	12 (12.5)	3 (6.5)	9 (18.0)
Divorced	3 (3.1)	1 (2.2)	2 (4.0)
Education level			
Associates Degree	9 (9.4)	7 (15.2)	2 (4.0)
Some College but not a 4-year Degree	8 (8.3)	5 (10.9)	3 (6.0)
4-year college degree	34 (35.4)	14 (30.4)	20 (40.0)
Post-Bachelor's Degree	45 (46.9)	20 (43.5)	25 (50.0)
Branch of Service			
Army	30 (31.3)	17 (37.0)	13 (26.0)
Navy	18 (18.8)	10 (21.7)	8 (16.0)
Air Force	46 (47.9)	18 (39.1)	28 56.0)
Other	2 (2.1)	1 (2.2)	2 (2.0)
Pay Grade			
E-5 to E-9	24 (25.0)	16 (34.8)	8 (16.0)
0-1 to 0-3	44 (45.8)	13 (28.3)	31 (62.0)
0-4 to 0-6	28 (29.2)	17 (37.0)	11 (22.6)
BMI*	26.6 ± 3.7	27.7 ± 3.5	25.6 ± 3.6

< 18.5	1 (1.0)	0	1 (1.9)
18.5 - 24.9	30 (31.3)	9 (19.5)	21 (42.0)
25.0 - 29.9	49 (51.0)	26 (56.5)	23 (46.0)
≥ 30.0	16 (16.7)	11 (23.9)	5 (10.0)
Fitness level	272.0 ± 23.2	278.1 ± 17.33	266.3 ± 26.5
Excellent	67 (69.8)	38 (82.6)	29 (58.0)
Satisfactory	26 (27.1)	7 (15.2)	19 (38.0)
Unsatisfactory	3 (3.1)	1 (2.2)	2 (4.0)
Health Conditions			
High Blood Pressure	0	0	0
High Cholesterol	3 (3.0)	1 (2.2)	2 (4.0)
Infertility	4 (4.0)	2 (4.3)	2 (4.0)
Depression	32 (32.0)	27 (58.7)	5 (10.0)
Anxiety	14 (14.4)	5 (10.9)	8 (16.0)

*$p < 0.05$

Table 6. Fatigue occurrence, mean dimension scores, and PROMIS[a] fatigue severity scores within sample & between groups

	Total n (%)	PCOS n (%)	No PCOS n (%)	Effect size (d)
Fatigue Occurrence	89 (89)	42 (89.4)	47 (88.7)	-
Fatigue Dimensions (range 4 – 20)				
General Fatigue	13.46 ± 4.25	15.57 ± 3.21	11.52 ± 4.20	0.96
Physical Fatigue	9.99 ± 3.90	11.67 ± 3.22	8.44 ± 3.87	0.80

Mental Fatigue	12.74 ± 4.60	15.15 ± 4.13	10.52 ± 3.80	0.82
Reduced Activity	9.67 ± 3.34	11.13 ± 3.32	8.32 ± 2.80	0.92
Reduced Motivation	10.34 ± 3.95	12.22 ± 3.83	8.62 ± 3.24	1.01
Fatigue severity	55.92 ± 9.27	60.58 ± 7.60	51.63 ± 8.61	0.98

a-PROMIS score of 50 is the average for the U.S. general population with a standard deviation of 10. Higher score indicates worse fatigue

Table 7. Pearson correlations between fatigue dimensions and potential predictors for No PCOS group (n = 50)

	General Fatigue	Physical Fatigue	Mental Fatigue	Reduced Activity	Reduced Motivation	Fatigue Severity
Age	0.107	0.091	0.211	0.080	-0.029	-0.072
BMI	0.228	-0.026	0.399*	0.119	0.333	0.159
CES-D	0.522**	0.346*	0.436*	0.382*	0.690**	0.615**
STAI-T	0.549**	0.266	0.515**	0.404**	0.530**	0.520**
PSQI	0.252	0.111	0.322*	0.342*	0.351*	0.187
ESS	0.101	0.013	0.104	-0.14	0.104	0.160
Social Support	-0.029	0.090	-0.081	-0.074	-0.168	0.010
Physical Fitness Level	-0.084	-0.155	0.104	0.135	0.156	0.157

*p < 0.05, **P < 0.001

Table 8. Pearson correlations between fatigue dimensions and potential predictors for PCOS group (n = 46)

	General Fatigue	Physical Fatigue	Mental Fatigue	Reduced Activity	Reduced Motivation	Fatigue Severity
Age	-0.287	-0.160	-0.414**	-0.264	-0.185	-0.000
BMI	0.153	0.201	0.150	0.171	0.137	-0.201
CES-D	0.089	-0.234	-0.211	-0.89	-.0235	0.417*
STAI-T	0.095	-0.071	-0.312*	-0.237	-0.331*	0.247
PSQI	-0.001	0.000	-0.448*	-0.436*	-0.334*	0.332*
ESS	0.172	0.049	-0.141*	-0.298*	-0.003	0.386
Social Support	-0.149	0.184	-0.063	-0.048	-0.043	0.064
Physical Fitness Level	-0.002	-0.094	0.107	0.159	0.204	0.088
*p < 0.05, **P < 0.001						

Table 9. Multiple regression analysis of associations with Mental Fatigue and Fatigue Severity: Main Effects (n = 96)

	Mental Fatigue	**Fatigue Severity**

Variables	B (SE)	β	B (SE)	β
PCOS	4.01 (0.81)**	0.44	9.29 (1.43)**	0.50
BMI	0.31 (0.11)**	0.25	-	-
CES-D	-	-	0.63 (0.11)**	0.45
	R^2 0.315*	R^2 adj 0.300	R^2 0.439**	R^2adj 0.427

*p< 0.05, **p < 0.001

Table 10. Multiple regression analysis of associations with Reduced Motivation: Main Effects (n = 96)

	Reduced Motivation	
Variables	B (SE)	β
PCOS	3.13 (0.72)**	0.40
BMI	0.26 (0.10)*	0.24
CES-D	0.11 (0.05)*	0.19
	R^2 0.315*	R^2 adj 0.264

*p< 0.05, **p < 0.001

Table 11. Multiple regression analysis of associations with General Fatigue: Main Effects (n = 96)

	General Fatigue	
Variable	B (SE)	β
PCOS	4.53 (0.78)**	0.54

STAI-T	0.43 (0.12)**	0.32
BMI	0.22 (0.10)*	0.19
	R^2 0.351*	R^2 adj 0.330

*p < 0.05, **p < 0.001

Table 12. Multiple regression analysis of associations with General Fatigue: Interactions (n = 96)

	General Fatigue	
Variable	B (SE)	β
PCOS	36.50 (11.43)**	4.31
STAI-T	0.80 (0.17)**	0.60
PCOS X STAI-T	-0.66 (0.24)**	-3.69
	R^2 0.403**	R^2 adj 0.376

*p < 0.05, **p < 0.001

Table 13. Multiple regression analysis of associations with Reduced Motivation: Interactions (n = 96)

	Reduced Motivation	
Variable	B (SE)	β
PCOS	7.03 (1.08)**	0.89
CES-D	0.35 (0.07)**	0.58
PCOS X CES-D	-0.44 (0.09)**	-0.71

	R^2 0.427**	R^2 adj 0.392

*p < 0.05, **p < 0.001

Table 14. Multiple regression analysis of associations with General Fatigue: No PCOS group Main Effects (n = 50)

	General Fatigue	
Variable	B (SE)	β
STAI-T	0.80 (0.19)**	0.53
	R^2 0.396**	R^2 adj 0.295

*p < 0.05, **p < 0.001

Table 15. Multiple regression analysis of associations with Reduced Motivation: No PCOS group Main Effects (n = 50)

	Reduced Motivation	
Variable	B (SE)	β
CES-D	0.33 (0.06)**	0.64
	R^2 0.612**	R^2 adj 0.548

*p < 0.05, **p < 0.001

SPECIFIC AIM 4

Analysis of the participants' responses revealed that each group had similar, yet slight differences in descriptions of the various dimensions of fatigue (Table 16).

Table 16. Similarities and differences in themes between groups

Dimensions of fatigue	**Themes in PCOS group**	**Themes in No PCOS group**
General Fatigue	▪ **Persistent** mental & physical tiredness	▪ **Mental & physical involvement** ▪ **Fatigue as an overwhelming state** ▪ **Energy imbalance**
Physical Fatigue	▪ Decrease in physical activity	▪ Decrease in physical activity
Mental Fatigue	▪ Frequent mood variations with several mood states ▪ Decreased focusing, concentration and processing	▪ Frequent mood variations with several mood states ▪ Decreased focusing, concentration and processing ▪ **ADHD-like symptoms**
Reduced Activity	▪ Decrease in social and physical involvement ▪ Isolation ▪ Professional practice modification	▪ Decrease in social and physical involvement ▪ Isolation ▪ Professional practice modification
Reduced Motivation	▪ No motivation ▪ High motivation ▪ Motivation, but…	▪ **Productivity impacted**
Red indicates differences in themes between the groups		

General fatigue

Although many definitions of fatigue have been proposed, for this study, fatigue was defined as a distressing, unpleasant symptom perceived by an individual as a persistent lack of, or decrease in physical, emotional, and/or cognitive energy, not proportional to recent activity that interferes with usual functioning [179]. Both groups

of women with and without PCOS described general fatigue as such a state. The most common words used to describe general fatigue were "tired" "exhaustion" and "overwhelmed/ overwhelming." Both groups spoke of how fatigue was persistently present and impacted their functioning.

> 34 y.o. Air Force officer with PCOS - Having no energy, being tired all the time mentally, spiritually and especially physically.
>
> 25 y.o. Air Force officer without PCOS - Being extremely tired and feeling overwhelmed either in your body and/or in your mind so that you don't really function well at all.

Physical Fatigue

Both women with and without PCOS reported having low energy, loss of vitality and perceiving an impact to performance. From these reports a theme of decreased or cessation of physical activity was used to describe physical fatigue; However, whereas only one of the seven women without PCOS reported coping mechanism to combat the physical fatigue she experienced, four of the nine women with PCOS reported coping mechanisms.

> 42 y.o. Air Force officer without PCOS - I don't do my full workout, or I don't work as hard. I also have found that sometimes once I get started, in spite of fatigue, and I do my morning workout, it turns me around and sort of makes me feel better.
>
> 26 y.o. Army Officer with PCOS - My physical activity levels are dramatically decreased. I can maintain physical levels if I'm in a situation

where I absolutely have to. I have decreased the distance I run when I do distance runs.

Mental Fatigue

Just as there are many definitions of fatigue, there are many dimensions of fatigue. For this study, mental fatigue was conceptualized as emotional and cognitive symptoms [141, 180]. Both groups described multiple emotional and psychological symptoms related to the impact of fatigue on their personal and professional life. The overarching theme from the responses was that mental fatigue caused frequent mood variations with several mood states.

> 26 y.o. Army officer with PCOS - I can become irritable and short-tempered. Whereas I'm usually upbeat and no-nonsense, I become easy to anger and a bit more harsh with my peers. I also notice that I feel more depressed for no apparent reason. My emotions are all over the place. I cry more often and I don't normally cry, and that gets on my nerves.
>
> 30 y.o. Air Force officer without PCOS - When I'm fatigued my emotions and my mood are altered often towards inward negative standpoints; however, I have found the necessity of keeping a positive frame of mind even when I'm fatigued. The state of fatigue can be so draining and emotionally hardening that it's probably an adapting process that I've learned over the years. But I really try to avoid how incredibly negative fatigue can make you.

In contrast to the frequent mood variations with several mood states, two women reported a detached, void-type of feeling with mental fatigue.

45 y.o. Army enlisted NCO with PCOS - My mood is somewhat kind of not really bad, but not too happy, just kind of in between. It's like maybe I become numb? Yes, I think that's it, not happy or sad…just void.

42 y.o. Air Force officer without PCOS - It's not so much sadness at all, I think part of it is the mental tiredness because it's hard to be excited or joyful or upbeat, but it's not like it's the opposite of that either. It's the absence of those highs. It's sometimes frustrating, because you want to just go on with life and not think about it. That frustration comes because you feel your body's letting you down with fatigue.

Investigations of how mental fatigue impacts cognitive performance have revealed that processing and concentration are altered, and attention-span, and vigilance are decreased [107, 181]. Mental fatigue was described as decreased focus, concentration and processing in both groups. In addition, for women without PCOS described mental fatigue as having attention deficit hyperactivity disorder (ADHD), and one woman with PCOS described mental fatigue as having attention deficit disorder (ADD). It is interesting that when speaking of the impact of fatigue, hyperactivity was considered as accurately describing fatigue's impact.

45 y.o. Navy officer without PCOS - When I am fatigued the symptoms closely mirror what I know as ADHD. It's harder to concentrate, read and write. It's harder to remember things that I have written. It's harder to maintain my concentration and train of thought.

30 y.o. Army officer without PCOS - My concentration is definitely impacted. It's more difficult to stay focused. It's almost like you have

ADHD. Your thoughts are all over the place. It can really affect how you work.

Many of the women (three out of nine with PCOS, and four out of seven without PCOS) spoke of how they compensated or combated the cognitive impact of mental fatigue. Methods consisted of: (a) Making checklists, (b) setting small goals, (c) walking away from tasks or work area when slowing or difficulty of processing noted , (d) planning extra time in schedule to account for decreased processing, (e) alerting staff, and employing staff's assistance, (f) modifying activities, and (g) making frequent self-checks.

Reduced Activity

Reduced activity refers to not only physical fitness-type activities, but also the act of simply being involved and participating in various activities. Both groups described decrements in physical and social areas due to fatigue. Physical decrements included reduced participation in aerobic, and yoga classes, or high intensity training programs. Social decrements included withdraw from marital relations, friends, and off-sight work functions. Professional activities were also negatively impacted with productivity, and efficiency decrements being the common complaint due to fatigue.

34 y.o. Air Force Officer with PCOS - When I'm fatigued the very first thing to suffer is my marriage. I withdraw from social activities. I don't want to go out with people. I don't want to be bothered. On the job, I am a talker but when I'm fatigued and I'm scatterbrained, and I'm irritable, I withdraw. That makes my co-workers uncomfortable because they're trying to figure out what's wrong. I'm like nothing, but really it's because I'm tired.

29 y.o. Army enlisted NCO with PCOS - I stop doing a lot of my aerobics classes. I used to be really big on High Intensity Interval Training and warrior runs. If it's not running for work, I don't do it. I don't do as good a job at work because I'm just too drained. I resent being at work. I resent doing anything and just want to go home.

30 y.o. Army officer without PCOS - Personally, I don't really do many things physical. I'll cancel on friends, or not make many plans because I just want to veg out or relax at home. Not really sleep, because I'm not sleepy, I'm just tired. I've stopped socializing as much.

Although a common theme of decreased physical and social involvement emerged; some women with PCOS described their activity levels as the same or higher, specifically relating to professional performance. Perseverance seemed to connote the attitude of these women.

39 y.o. Air Force officer with PCOS - My activity does not decrease. I just press through fatigue.

38 y.o. Air Force officer with PCOS - I still try to stay active.

38 y.o. Air Force officer with PCOS - Professionally, I think I do more. I'm constantly replaying the day to self-check.

34 y.o. Navy officer with PCOS - With work, it's hard to stop things because it's not just you.

A 42 y.o. Air Force officer without PCOS described the activity level of her work performance as 100%; in fact she stated "I try not to let fatigue affect my work life. I give 100% during that time and after that with family or what have you may suffer a bit."

Reduced Motivation

Chaudhuri and Behan [16] noted that fatigue may be defined as the failure to initiate and/or sustain attentional tasks (mental fatigue) and physical activities (physical fatigue) requiring self-motivation (as opposed to external stimulation). Motivation has been investigated in sick animals, and sick and healthy humans to explore fatigue's role in motivation [47, 182]. Motivation is influenced by effort/reward calculation. Effort will be put forward when fatigue is present, if the reward is seen as impactful or significant to the person engaged in the activity [181, 183]. Although effort/reward ratio was not evaluated, to assess its impact on the presence or absence of motivation; presence of motivation was assessed to understand how the women described this dimension of fatigue. It appeared that for women without PCOS, across the board motivation was decreased, and productivity was highly impacted by the lack of motivation.

For women with PCOS there was a distinct division between motivation levels. These levels included: (a) no motivation, (b) high motivation, and (c) motivation, but…

No motivation.

Women who reported no motivation (four out of nine) described motivation as plummeted, and nonexistent. Mental struggles to accomplish tasks, and physical strength to push past no motivation were expressed.

High motivation.

For women who reported high motivation (two out of nine) the presence of fatigue appeared to be a challenge to the participant to not succumb to the influence of fatigue on motivation levels

38 y.o. Air Force officer with PCOS 38 y.o. Air Force officer with PCOS - Motivation? I'm always motivated…well, maybe not always, but sometimes the fatigue actually makes me motivated, because I feel like my body and mind are turning on me and I have to fight past that, so I'm motivated to win against…me, and not let this state get to me completely. So my motivation when I'm fatigued can either be very high, because I'm trying to continue with my life, or it can be low, where I'm like I give up, I just want to sit here and stare out into space. But the "I give up" motivation part is less than the "I'm going to do this" part!

39 y.o. Air Force officer with PCOS - With my motivation, I stay involved in programs, in my professional life, I can't say that my level of motivation goes down, because I'm very driven. I'd say that's one of the pluses of military structure is that it keeps you driven towards goals.

Motivation but…

For women who described motivation, but…, they expressed how motivation (mental thoughts) was present, however, the ability (physical capability) to act on that motivation with actual follow-through on the motivation was affected when fatigue was present.

45 y.o. Army enlisted NCO with PCOS - I have lots of things I would like to do, but when I'm tired or when I'm feeling down, or feeling a little slow, it's almost impossible to do the things that you want to do and you start to get behind, because there is not motivation.

28 y.o. Air Force enlisted NCO with PCOS - I'm motivated to do a lot of things, but for me to actually do it, either start or once I do start it's really hard for me to finish things because I get really exhausted because I'm trying to concentrate and it just gets, it's overwhelming.

34 y.o. Navy officer with PCOS - I'm always motivated to do things…I just don't have the energy to do most of it. I don't think my actual motivation decreases, it's like I said earlier, my mind will WANT to do it, but it's so foggy, or tired, that my body say's 'nahh, sit down, you don't need to do anything right now."

Additional Results

In an attempt to solicit the full expression of the fatigue experience in both groups of women; participants were encouraged to speak of any additional topics related to fatigue. For women with PCOS, in addition to speaking about additional topics related to fatigue, they were also asked about additional topics related to PCOS. Furthermore, participants were asked about who/what provided support to them and how/what type of support did the indicated person/thing provide.

Additional fatigue information. When additional responses regarding the experience of fatigue were solicited, two of the seven women without PCOS had a response. A 30 y.o. Army officer without PCOS relayed that although she suffers from the impact of fatigue, the impact does not completely disable her. A 42 y.o. Air force officer without PCOS wanted to ensure that it was understood that while fatigue is very present and impactful, the focus should be on how to live with it and manage it effectively. She stated "I think the point I would want to make sure that

gets captured is the journey of figuring out how to work with fatigue or being tired and how do I mange that well? Do I treat it like oh this is terrible, poor me, or do I treat it like something terrible has happened and don't get stressed about it? I feel like I've sort of taken the approach of it is what it is and I need to find a way to manage it that works for me."

When eight out of nine women with PCOS expressed additional comments regarding fatigue, fatigue was seen as a comorbid condition interwoven with PCOS. A 29 y.o. Army enlisted NCO with PCOS explained "As females in the military we are about physical appearance. We are supposed to be slim and trim, not overweight. So, a lot of times the depression comes from lack of nutrients because you're too busy trying to starve yourself to lose weight. So, I think fatigue also comes with depression, because you just want to be to yourself. A 34 y.o. Navy officer with PCOS spoke of the burden of suffering from fatigue and having PCOS as a military member. She stated "Fatigue sucks, and so does PCOS. Both really make it difficult to stay on top of things especially in the military. It's really hard being tired and having to always be at work, like not being able to call in like civilians can, even when you really, really need a break. Or it's really hard also when you have to lead Sailors, and you just want to go somewhere and be left alone.

Polycystic ovary syndrome and the military. Women with PCOS spoke more to PCOS-specific issues and military life versus fatigue-specific issues and military life. Themes included: a) perceived and actual negative career impact b) lack of education, and c) lack of awareness of PCOS in the military.

38 y.o. AF officer with PCOS: I have also worked with women with PCOS and they struggle with the diagnosis and fight being put on medication because they feel it will flag them for a medical condition. Education about this condition is paramount, for ALL, not just the patients.

34 y.o Navy officer with PCOS: It's kind of embarrassing having all this extra weight, when I really work hard to get thinner, and I know PCOS and insulin resistance are causing me to have extra fat, and my waistline is thicker than it should be no matter what I seem to do. That really makes me angry and frustrated for the PFA (physical fitness assessment) because I can do the run, push-ups and sit-ups with no problem, but when it comes to the weigh-in, I always get penalized. It just seems unfair, but what do you do?"

45 y.o. Navy enlisted with: I've never even seen anyone talk about PCOS, I thought it was something that I was sharing alone. I notice that no one really understands it.

Polycystic ovary syndrome and relationships. The impact of PCOS on relationships was reported. Participants spoke of how living with PCOS negatively influenced some of their social relationships. Symptoms from PCOS such as overweight, obesity, increased acne, and facial hair caused the participants to feel isolated, unattractive, embarrassed, and frustrated. Although participants reported negative influences of PCOS on their relationship, five of nine women reported that receiving the diagnosis of PCOS helped improve their relationship.

39 y.o. AF officer with PCOS: My husband is more understanding and supportive when I am trying to control my weight

26 y.o. AF officer with PCOS: Now that I know it's the PCOS that is causing my hairiness, weight gain, and probably fatigue, it has changed the way I interact sometimes with friends and family.

Social support. All participants reported receiving social support (Table 17). The average amount of social support was 2, with a minimum of 1 and a maximum of 5. The types of support received by women with PCOS included: a) instrumental/practical, b) emotional, c) spiritual, d) passive, and e) informational. The types of support received by women without PCOS included: a) instrumental/practical, b) emotional, c) spiritual, and d) passive.

Table 17. Social support received by groups

Type of social support	PCOS group	No PCOS group
Instrumental/practical	• My husband helps me keep focused and calm. • Husband keeps me motivated. • Husband helps with logistic of getting care	• When I'm sick my family cooks for me and comfort me. • My mom helps watch children, provides transportation, emotional support. • Husband splits duties to take care of our household and our pets. • Friend invites me to dinner with her family once a week. • My parents give me financial support.
Emotional	• Friends, provider, and infertility support group help me to not feel so alone and confused • Husband helps me stay grounded and in a good state of mind • Husband always remind me that I am beautiful	• Family members help by talking, listening, and offering advice • Kids give me motivation to keep going. • I can talk to mother and sisters about anything and I know they would come here in a heartbeat.

	• Mother has always been a great foundation and support • I have girlfriends who are the same way	
Spiritual	• God lets me know all things are possible • God helps me remember I can do all things with Him • Mindful meditation • My belief in God keep me grounded and hopeful • Regularly attends church and praying together • God reminds me I can get through anything	• My faith gives me a bigger picture of the meaning of life. • Constant conversation, reassurance and prayer. • Pastor gives emotional and spiritual support • Religious affiliation-helps me to have faith through hard times and place trust in God
Passive	• Husband supports me unconditionally • Husband having an open ear • Family allows me to vent when I don't want to burden my husband all the time • Husband, provider and pastor are willing to sit and simply listen to me explain how I am feeling	• Mom and friends are back up, non-judgmental support. • I can vent my frustrations. • Family would be supportive, if I reach out. Most often I do not reach out
Informational	• Provider, support group and family give time and advice • Husband helps with life decisions • My provider helps me understand certain medical issues that make me feel overwhelmed • I call my mom about medical issues I have. I trust her with my information	• None reported

CHAPTER 7: DISCUSSION

DISCUSSION

Fatigue is an overwhelming state as it impacts (a) physical, (b) mental, (c) personal, (d) social, and (e) professional functioning, as well as activity and motivation levels of military women with and without PCOS. This mixed-methods study investigated fatigue among 46 military women with and 50 military women without PCOS. This is the first study to examine PCOS in a military population, and the first study to consider fatigue in an all-female military population, independent of perinatal status. Semi-structured interviews were conducted with nine military women with PCOS and seven military women without PCOS. Through use of the TOUS as a guiding framework, the symptom of fatigue in a military population was revealed to be influenced by PCOS, anxiety, depressive symptom, and BMI; the symptom of fatigue was not influenced by age, sleep quality, wakefulness, fitness level, or social support.

In this sample, anxiety, depressive symptoms, and BMI were predictors of fatigue, whereas age, social support, sleep quality, wakefulness, and fitness level were not. These results are similar to those found by Fritschi, et al (2012) who considered predictors of fatigue in patients with T2DM, and found depressive symptoms and BMI were significant predictors. The presence of PCOS was associated with increases in the level of fatigue experienced in some dimensions; however, its presence was also associated with decreases in levels of fatigue experienced in other dimensions. In studies where chronic conditions and fatigue were considered, the presence of that chronic condition (SLE, inflammatory bowel disease, Parkinson's disease) has been associated with an increase in the level of fatigue [184-186]. No investigation of fatigue in chronic

conditions has resulted in the decrease in levels of fatigue as was found in the current study.

No statistically significant difference in fatigue occurrence was noted between military women with and without PCOS ($\chi 2$ (1, n = 0.98) = 0.00, p < 0.001, phi = 0.01) fatigue occurred in both groups similarly. Having knowledge regarding the occurrence rate of fatigue in military women is important because of the potential impact of fatigue on military-specific situations, such as deployment, and occupational specialty, which may be negatively impacted by fatigue. Both military women with and without PCOS spoke of their decrease in physical activity due to fatigue, and how it is not an option to choose not to work-out, as physical assessment tests are given to evaluate the fitness and readiness of military members. Although both groups of women reported decreased physical activity, and how fatigue impacts their ability to initiate and maintain physical activity; women with PCOS on average had higher fitness levels (278/300) than women without PCOS (266/300), and these levels were statistically significantly different between groups (t (94) = -2.55, p = .01). Mission readiness depends on the functionality of members and the negative consequences of fatigue reported, jeopardize the effectiveness and efficiency of these military women and the Department of Defense.

Some military occupations demand high vigilance and alertness to ensure the safety of this nation. Many women reported how concentration, focus, and processing are all altered when fatigue is present. Not only are the cognitive disruptions (decreased concentration and mental processing time) of fatigue impactful, the psychological disruptions of frequent variations in mood with several mood states also impact the productivity, and quality of life in these women. Women in the military have

responsibilities and roles that demand commitment, focus and motivation. The military environment is a microcosm where members persevere in spite of fatigue. Core values across the Army, Navy, Air Force and Marines remind members that service before self, selfless service and commitment are values that military members embody. Snider et al., [187] defined military culture as a deep structure of organization drawn from past successes and from its current interactions with the environment. Military culture is rooted in the prevailing assumptions, values, and traditions that collectively, over time, have created shared individual expectations among the members. During the semi-structured interviews a sense of pride in service and an almost hesitancy to speak negatively toward the military or reveal the full impact of fatigue were experienced. For example, although anxiety, depression and BMI were predictors of fatigue in both women with and without PCOS, when anxiety was present in women with PCOS the relationship between general fatigue and anxiety was weakened. This may mean that PCOS acted as a moderator and decreased the impact of anxiety on general fatigue. This was also the case with reduced motivation when depression was present in women with PCOS. These results may seem counter-intuitive in that as anxiety increased, general fatigue decreased and as depression increased, motivation increased, and no literature corroborates these puzzling findings. Investigators have shown how anxiety increases general fatigue and depression decreases motivation levels in those with SLE, myocardial infarctions, and type 2 diabetes [167, 176, 184]. It can be suggested from the data of the current study, that the embodiment of military culture may have influenced how these women reported and dealt with fatigue. It is almost as if women with PCOS felt the need to suppress the influence of fatigue and PCOS on their existence to be a good service member.

Although fatigue was present in military women, in the current study, when military women had PCOS combined with anxiety or depression, it appeared that they tried to overcome their fatigue and enhance their motivation. This same military culture they embraced and believed in may also explain how fitness level, sleep quality, and wakefulness failed to predict fatigue in this population. These are assumptions, as no investigations have been conducted to evaluate the impact of comorbid conditions on outcomes.

In some cases it appeared that the military was a motivating factor and helped some in both groups push beyond fatigue and find ways to function, in spite of fatigue. Many factors may speak to this phenomenon. As mentioned earlier, military culture often affects the way members perceive themselves and their situations: these women may feel the need to push beyond or even overcompensate for having concomitant conditions to show their selflessness, committed nature and consideration of their comrades. Other factors that may explain why more women with PCOS chose to persevere in spite of are (a) the ethos of each service branch, (b) leadership role and/or position, or (c) occupational status.

The description of fatigue dimensions was common for physical fatigue and reduced activity in both groups of women (Table 16). It is interesting to note that on mental fatigue there were also similar descriptions, however, there was an additional theme for women without PCOS where they described mental fatigue as mimicking attention deficit hyperactivity disorder. This hyperactivity component was strictly a mental aspect, as women without PCOS reported decreases in social and physical involvement when questioned about activity levels. Women without PCOS also

described how reduced motivation levels negatively impacted their professional and personal productivity. The disruption of mental processes and impact to productivity by fatigue has been reported from previous authors investigating the impact of fatigue on military members and operations [107, 123, 131]. The description of fatigue dimensions by both groups added depth and insight into the nature and experience this symptom.

IMPLICATIONS

Fatigue is a phenomenon experienced by all individuals at one time or another in their life; it has a healthy, restorative purpose in that it serves to decrease unnecessary activity and encourage rest. Eidelman et al. [188] postulated that fatigue is the mechanism by which slow-down and/or cessation of function is initiated to allow for regeneration and rejuvenation; it is also the mechanism that prevents overuse of individual tissues or organs within the overall physiologic framework of the body. When fatigue becomes chronic, it becomes unhealthy and problematic. The results of this study were consistent with investigations of fatigue in populations with a chronic condition where fatigue is increased compared to controls [31, 189, 190].

Military

Fatigue was present in both women with and without PCOS which indicates it should be considered clinically in military women, despite the presence of a chronic condition, and definitely in women with PCOS. According to the PROMIS [160], a T-score of 50 represents the average fatigue level of the general U.S. population. A T-score of 60 is one SD worse than average. By comparison, a fatigue T-score of 40 is one SD better than average. The average score of women without PCOS was consistent with the general U.S. population scores (T-score 50.81), whereas women with PCOS on average

scored one SD worse (T-score 60.89). Although a significant difference in fatigue severity between groups was noted, both groups described general fatigue as an overwhelming feeling of constant exhaustion and tiredness of body and mind.

One of the objectives of this study was to find predictors of fatigue. Anxiety, depression and BMI were significant predictors of fatigue for both women with and without PCOS. However, the interaction between PCOS and depression and anxiety raises multiple questions. First, the prevalence and risk of depression and depressive disorders in women with PCOS is 40-64% and much higher than healthy controls [76-78]. Furthermore, anxiety has been found to be significantly higher in women with PCOS compared to controls as measured by the State-Trait Anxiety Inventory (STAI) [79-81]. In this study the interaction between PCOS and the psychological variables - depression and anxiety -showed a decrease in the impact of fatigue. Further investigation into this phenomenon should be sought to understand the mechanisms at work. A 26 y.o. Army Officer with PCOS spoke of her motivation level stating, "Ultimately we fake it til we make it, which is something I feel I'm doing more frequently, but it's a mental struggle to get anything accomplished." This potential overcompensation or inverse reaction may reflect excessive stress and strain on the member to maintain the appearance of normal functioning in the presence of fatigue. Lastly, as BMI increased fatigue increased. It is estimated that 33-38% of women with PCOS are overweight or obese [65-67]. Finding interventions that help decrease BMI, could serve a two-fold advantage: military woman need to meet weight standards, be physically fit, as well as meet appearance standards. Creating effective exercise programs to decrease and manage

weight will assist in 1) being successful at achieving and maintaining fitness and appearance standards and 2) mitigating the impact of BMI on fatigue occurrence.

Nursing

Both women with and without PCOS spoke of the impact of fatigue, such as slowed reaction times & mental processes, decreased physical, social and professional activities, as well as the psychological factors of fatigue. Nurses and Advanced Practice Nurses (APNs) have an opportunity to make a positive impact related to fatigue and PCOS. These opportunities include (a) having an awareness of fatigue and PCOS, so early assessment can be conducted, (b) educating on fatigue and PCOS, and (c) collaborating management of physical, and psychological symptoms of fatigue to include self-care practices.

Nurses are the first point of contact when patients attend clinical appointments. A heightened sense of awareness would be important to ascertain which patients may be at an increased risk for fatigue, so an immediate assessment is conducted and collaborations can be formed. Having said that, this requires nurses and APNs to be aware and informed on the symptom of fatigue and the condition of PCOS. It is not the sole responsibility of nurses to assess, care for and consider this condition; ultimately it should be a multi-disciplinary collaborative approach. However, nurses are in a prime position to ensure and encourage initial awareness even occurs.

STRENGTHS AND LIMITATIONS

One strength of this study was the use of a mixed-methods approach. This method allowed the qualitative interviews to inform the quantitative data, which resulted in a complete picture of fatigue impact and experience. Reviewing the quantitative data

alone leaves many questions regarding the interpretation of the obtained results. Simply viewing the predictors of fatigue and observing that as anxiety and depression increase, fatigue decreases and motivation increases in women with PCOS calls into question the validity and reliability of the measures used. However, when the qualitative interviews are connected, a picture emerges, and it can be seen that women reported that they persevered in spite of fatigue or even felt more motivated to overcome the obstacle of fatigue. This is the first study to demonstrate a positive outcome of a burdensome symptom. As such, it raises questions: (a) are there positive outcomes as a result of fatigue? and (b) what are the implications of these outcomes to the member's fitness status and mission readiness?

Another strength was the use of an all military population, independent of the perinatal period. Of the five studies completed in a military population regarding fatigue, two were investigations of women during the perinatal period, and none considered a chronic health condition. Polycystic ovary syndrome is the most common reproductive endocrinopathy in women of childbearing age, yet no studies regarding the impact of this condition are with military women. This study is the first to consider military women with PCOS, which adds to the much needed knowledge and understanding of the condition.

A limitation to this study, although it was also an advantage, was the use of an all military population. The use of a military population is viewed as a limitation in that a phenomenon developed as the study progressed, which this investigator termed *risk of disclosure*. A pattern was noted from participant's responses during the semi-structured interviews: women with PCOS were reluctant to be identified as having PCOS. This

noted pattern prompted the PI to return to the IRB to add a question inquiring about reluctance to participate. Reponses to this question revealed a fear or concern that having PCOS and being identified as such may initiate inquiry and led to discharge from the military or restriction from certain occupations. This concern with repercussions or consequences of coming forward may have limited participant recruitment as well as full disclosure of the impact of fatigue.

A second limitation was the use of self-reported information versus a review of medical records for concomitant conditions and/or verification of psychological diagnoses. Participants were screened for exclusionary conditions that increase the risk of fatigue, and were also asked about any clinical diagnoses of anxiety or depression. It is difficult to know if any conditions existed that may have inflated the occurrence and severity of fatigue.

An additional limitation was the size of the sample. Although significant differences were achieved between groups, it would be valuable to repeat the study with a larger sample size and with lower enlisted member ranks of E-1 to E-4 included, as they were not represented in this study. Role and/or position may have influenced reporting style, as conformity to military culture tends to increase with time in service [191]. Although there was good representation of each branch of service, it would be worthwhile knowing if lower ranking enlisted members responded in similar ways regarding the impact of fatigue and PCOS. This conformity to military culture, which influences behaviors, is a factor to consider in future studies.

The final limitation was the lack of biomarkers to document the pro-inflammatory state of military women with PCOS. Chronic conditions such as SLE, RA, and MS have

a pro-inflammatory component that increases the experience of fatigue [46]. PCOS, which is also a pro-inflammatory condition, may have this same risk. Documentation and comparison of biomarkers, such as IL-6, CRP and TNF-alpha, in women with and without PCOS would provide a broader picture of the potential presence of inflammation and hence a potential biologic explanation for increased fatigue in women with PCOS versus those without.

RECOMMENDATIONS

Fatigue severity and dimensions are increased in military women with PCOS as compared to military women without PCOS. Many questions remain unanswered, and further research is needed to clarify the implications of PCOS on fatigue. Gaps include (a) quantifying the impact of fatigue on performance, (b) evaluating fatigue in various occupational settings (c) understanding sex-differences in fatigue presentation, and physical and psychological impact, (d) understanding the role of PCOS in fatigue, (e) influence of military culture on reporting, coping and presentation of fatigue, (f) education regarding fatigue symptomology, and (g) effective management options for fatigue. For these reasons future investigations should include (a) intervention studies evaluating fatigue and performance, (b) treatment options to overcome fatigue, such as physical fitness programs, nutritional therapy as well as complementary and alternative methods, (c) investigation of sex differences with manifestations and experiences of fatigue, (d) larger samples with all ranks considered, and (e) qualitative studies to understand the role of military culture, and PCOS on fatigue.

To date only three qualitative studies focused on a woman's experience of PCOS have been published [86, 87, 106]. No study has analyzed the symptom experience

beyond the aesthetic and reproductive implications of this condition. Additionally no studies have analyzed the impact of this condition in a military setting. During the semi-structured interviews, concerns of PCOS beyond reproduction, and fatigue emerged. Women discussed frustrations of living with and managing PCOS in a military setting. Further qualitative studies are essential for exploring the meaning of the symptom experiences of not only fatigue in PCOS, but also the meaning of the symptom experiences of PCOS in the military.

CONCLUSION

The purpose of this study was: (a) to describe the occurrence, dimensions and severity of fatigue in a sample of military women with and without PCOS, (b) to examine differences between a sample of military women with and without PCOS, (c) to identify predictors of fatigue among military women with and without PCOS, and (d) to explore how women with and without PCOS describe the various dimensions of fatigue.

Fatigue is a symptom that every individual has experienced at one time or other in their life. Acute fatigue is normal and healthy, chronic fatigue is not. The results of this study confirm that chronic fatigue (a) is present in military women, independent of perinatal status, (b) impacts functioning and quality of life, (c) is related to decreased physical, social and professional activity, and (d) is associated with lower motivation levels. These data support investigations of fatigue in chronic conditions, where similar results of the negative impact of fatigue on functioning, quality of life and decreased physical and mental performance have been found [192, 193]. As seen in the current study, with decreased functioning and performance reported; fatigue has the potential to change the level of readiness in military women. With the knowledge that fatigue can impact

mission readiness; there is a need for awareness, education, and intervention studies to mitigate the negative influences of this symptom. Additional attention and research should also focus on techniques reported by both women with and without PCOS to adapt and accommodate for fatigue, as there are no studies that have looked at this aspect. These techniques employed may offer a target for intervention studies. The presence of PCOS and fatigue provides an opportunity for nurses and APNs to develop plans for assessment and management to consider the health and wellness needs of these women.

Figure 1. Inter-relationship of fatigue and PCOS

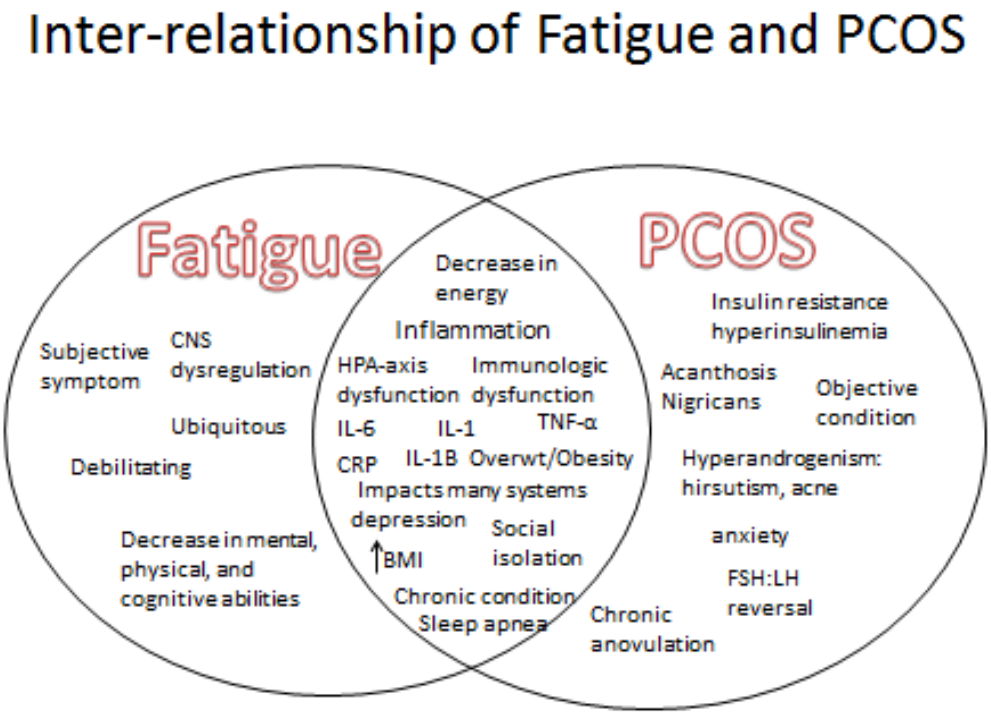


Figure 2. Process of Literature Review for Fatigue and Military Women

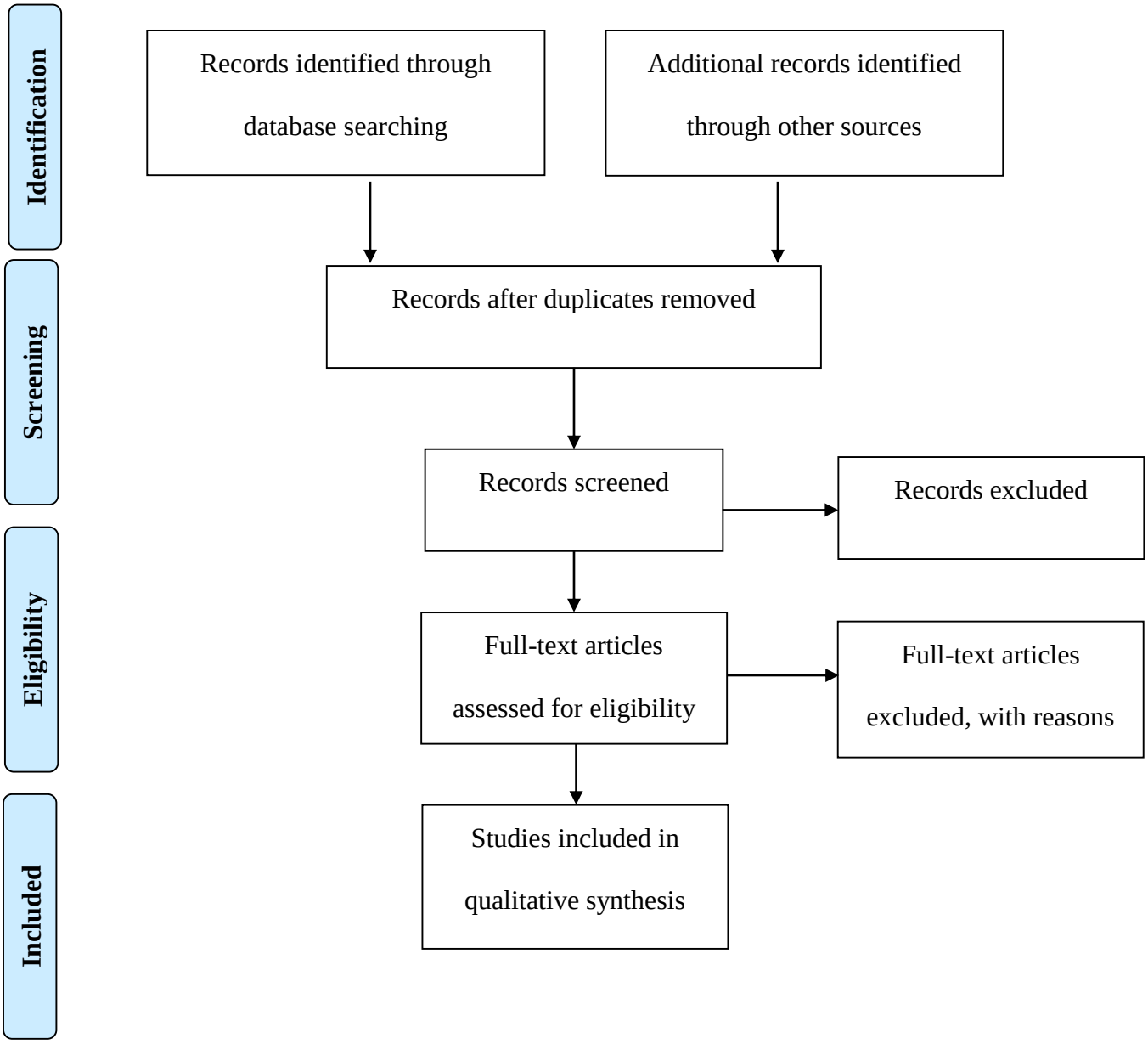


Figure 3. Conceptual Model: Theory of Unpleasant Symptoms-Fatigue

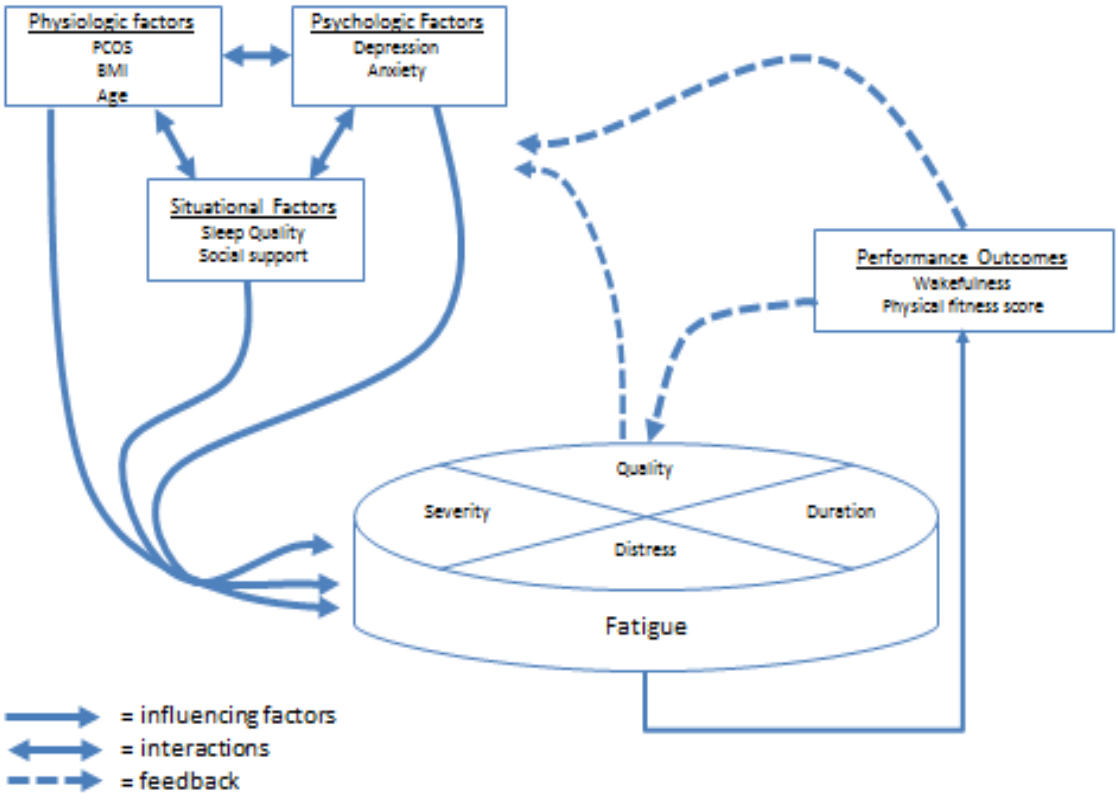
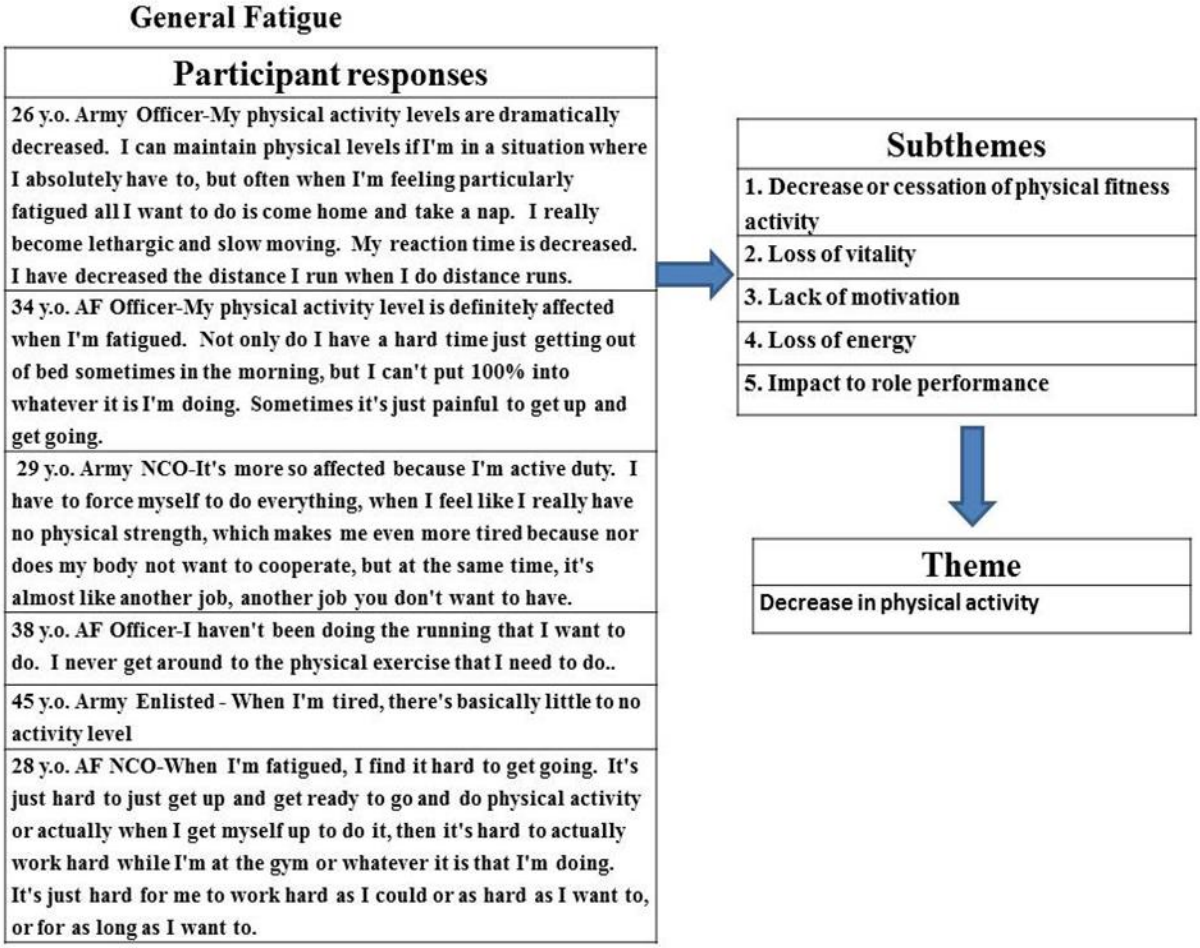


Figure 4. Process of qualitative analysis



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APPENDIX A:

IF PARTICIPATING IN THIS STUDY CAUSES YOU ANY DISTRESS AND YOU FEEL LIKE YOU NEED TO SPEAK WITH A PROFESSIONAL; BELOW ARE RESOURCES AVAILABLE TO ALL ACTIVE DUTY MEMBERS. PLEASE CONSIDER USING THEM.

Behavioral Health Resources

Adult Behavioral Health (Outpatient):
301-295-0792/0500.

Department of Pastoral Care Chaplains: Chaplains are available 24hrs/7 days a week 301-295-1510
Monday - Friday (0730—1600).
After Hours and weekends: 301-295-4611 select options 4 and ask to have the Duty Chaplain paged.

Military One Source: 1-800-342-9647
Militaryonesource.mil click on confidential help tab.

Your local MTF primary care provider

Dawnkimberly Hopkins
militarywomenparticipating@gmail.com
Tel: 757-839-7587

APPENDIX B:

You have been asked to take part in this study because you are an active duty military member between 19 and 45 years and receive health services in the military health system. Your participation is voluntary. Refusal to participate will not result in any punishment or loss of benefits to which you are otherwise permitted. Please read the study information below before deciding if you want to take part.

PURPOSE OF THE STUDY

The purpose of the study is to learn about fatigue in active duty women with and without polycystic ovary syndrome (PCOS). PCOS is a condition that affects a woman's ability to have children. It also is a condition that causes health conditions like diabetes and high blood pressure

Very few (five) studies have looked at fatigue in active duty military women. No studies to date have looked at fatigue in active duty military women with PCOS.

PROCEDURES TO BE FOLLOWED

If you agree to be in this study, you will be asked to:

Complete a demographic sheet, six (6) short surveys and possibly undergo a personal interview by the primary investigator, Kim Hopkins.

The personal interview will follow up on a small sample of women so they can talk about their experience of fatigue. If you are selected, the follow-up interview will be scheduled when it is best for you, but you do not have to complete the interview if you do not want to. Follow-up participants will be contacted within 14 days after completing surveys. During the interview you would be asked seven (7) questions. Interviews usually take about 30 minutes, but the actual time will be determined by the woman being interviewed. Interviews will be recorded to ensure accuracy of information received.

I am willing to participate in a personal interview if selected:

- ○ Yes
- ○ No

HOW YOUR IDENTITY WILL BE MAINTAINED

By acknowledging this consent document, you give your permission for information gained from your participation in this study to be placed in medical literature, discussed for educational purposes, and used generally to further medical science. However, you will not be personally identified in any ways

as all information will be presented as a group and nameless data. Your name will not appear in any published paper or presentation related to this study.

Do you agree to the above terms?

- ○ Yes
- ○ No

By selecting Yes, you consent that you are willing to answer the questions in the six surveys.

Next

APPENDIX C:

PROMIS Item Bank v1.0 – Fatigue – Short Form 8a

Fatigue – Short Form 8a

Please respond to each question or statement by marking one box per row.

During the past 7 days…

	Not at all	A little bit	Somewhat	Quite a bit	Very much
I feel fatigued……	□	□	□	□	□
	1	2	3	4	5
I have trouble starting things because I am tired……	□	□	□	□	□
	1	2	3	4	5

In the past 7 days…

How run-down did you feel on average?					
	□	□	□	□	□
	1	2	3	4	5
How fatigued were you on average?					
	□	□	□	□	□
	1	2	3	4	5
How much were you bothered by your fatigue on average?					
	□	□	□	□	□
	1	2	3	4	5

To what degree did your fatigue interfere

with your physical functioning?

□	□	□	□	□
1	2	3	4	5

In the past 7 days…

	Never	**Rarely**	**Sometimes**	**Often**	**Always**
How often did you have to push yourself to get things done because of your fatigue?	□	□	□	□	□
	1	2	3	4	5
How often did you have trouble Finishing things because of your Fatigue?	□	□	□	□	□
	1	2	3	4	5

APPENDIX D

MFI® MULTIDIMENSIONAL FATIGUE INVENTORY - 20

Instructions:

By means of the following statements we would like to get an idea of how you have been feeling **lately.**

There is for example the statement:

"I FEEL RELAXED"

If you think that this is entirely true, that indeed you have been feeling relaxed lately, please, place an **X** in the extreme left box, like this

yes, that is true ○1 ○2 ○3 ○4 ✕5 **no, this is not true**

The more you **disagree** with the statement, the more you can place an **X** in the direction of the "no, this is not true". Please do not miss out a statement, and place only one **X**, in a box for each statement.

1	I feel fit.	Yes, that is true	○1	○2	○3	○4	○5	No, that is not true
2	Physically, I feel only able to do a little	Yes, that is true	○1	○2	○3	○4	○5	No, that is not true

3	I feel very active	Yes, that is true	○1	○2	○3	○4	○5	No, that is not true
4	I feel like doing all sorts of nice things	Yes, that is true	○1	○2	○3	○4	○5	No, that is not true
5	I feel tired	Yes, that is true	○1	○2	○3	○4	○5	No, that is not true
6	I think I do a lot in a day.	Yes, that is true	○1	○2	○3	○4	○5	No, that is not true
7	When I am doing something, I can keep my thoughts on it	Yes, that is true	○1	○2	○3	○4	○5	No, that is not true
8	Physically I can take lot	Yes, that is true	○1	○2	○3	○4	○5	No, that is not true
9	I dread having to do things	Yes, that is true	○1	○2	○3	○4	○5	No, that is not true

10	I think I do very little in a day	Yes, that is true	○1	○2	○3	○4	○5	No, that is not true
11	I can concentrate well	Yes, that is true	○1	○2	○3	○4	○5	No, that is not true
12	I am rested	Yes, that is true	○1	○2	○3	○4	○5	No, that is not true
13	It takes a lot of effort to concentrate on things	Yes, that is true	○1	○2	○3	○4	○5	No, that is not true
14	Physically I feel I am in a bad condition	Yes, that is true	○1□	○2□	○3	○4	○5	No, that is not true
15	I have a lot of plans	Yes, that is true	○1	○2	○3	○4	○5	No, that is not true
16	I tire easily	Yes, that is true	○1	○2	○3	○4	○5	No, that is not true

17	I get little done	Yes, that is true	○1	○2	○3	○4	○5	No, that is not true
18	I don't feel like doing anything	Yes, that is true	○1	○2	○3	○4	○5	No, that is not true
19	My thoughts easily wander	Yes, that is true	○1	○2	○3	○4	○5	No, that is not true
20	Physically I feel I am in an excellent condition	Yes, that is true	○1	○2	○3	○4	○5	No, that is not true

APPENDIX E

Self – Evaluation Questionnaire

Developed by Charles Spieberger in collaboration with R.L. Gorsuch, R. Lushene, P.R. Vagg, and G.A. Jacobs

STAI Form Y-2

Directions: A number of statements which people have used to describe themselves are given below. Read each statement and then select the appropriate circle to the right of the statement to indicate how you generally feel, that is, at the moment. There is no right or wrong answers. Do not spend too much time on any one statement but give the answer which seems to describe how you generally feel.

	Almost Never	Sometimes	Often	Almost Always
21. I feel Pleasant	○	○	○	○
22. I feel nervous and restless	○	○	○	○
23. I feel satisfied with myself	○	○	○	○
24. I wish I could be as happy as others seem to be	○	○	○	○
25. I feel like a failure	○	○	○	○
26. I feel rested	○	○	○	○
27. I am “calm, cool, and collected”	○	○	○	○

28. I feel that difficulties are piling up so that I cannot overcome them	○	○	○	○
29. I worry too much over something that doesn't matter	○	○	○	○
30. I am happy	○	○	○	○
31. I have disturbing thoughts	○	○	○	○
32. I lack self-confidence	○	○	○	○
33. I feel secure	○	○	○	○
34. I make decisions easily	○	○	○	○
35. I feel inadequate	○	○	○	○
36. I am content	○	○	○	○
37. Some unimportant thoughts run through my mind and bother me	○	○	○	○
38. I take disappointments so keenly that I can't put them out of my mind	○	○	○	○
39. I am a steady person	○	○	○	○
40. I get in a state of tension or turmoil as I think over my recent concerns and interests	○	○	○	○

Y-2

APPENDIX F

Centers for Epidemiologic Studies Depression Scale (CES-D)

Below is a list of some of the ways you may have felt or behaved. Please indicate how often you've felt this way during the **past week**. Respond to all items.

Place an X in the appropriate column. **During the past week…**	**Rarely or none of the time (less than 1 day)**	**Some or a little of the time (1–2 days)**	**Occasionally or a moderate amount of time (3-4 days)**	**All of the time (5-7 days)**
1. I was bothered by things that usually don't bother me.				
2. I did not feel like eating; My appetite was poor.				
3. I felt that I could not shake off the blues even with help from my family.				
4. I felt that I was just as good as other people.				

5. I had trouble keeping my mind on what I was doing.				
6. I felt depressed.				
7. I felt that everything I did was an effort.				
8. I felt hopeful about the future.				
9. I thought my life had been a failure.				
10. I felt fearful.				
11. My sleep was restless				
12. I was happy.				
13. I talked less than usual.				
14. I felt lonely.				
15. People were unfriendly.				
16. I enjoyed life.				
17. I had crying spells.				
18. I felt sad.				

19. I felt that people disliked me				
20. I could not “get going.”				

Source: Radloff, L.S. (1977). The CES-D scale: A self-report depression scale for research in the general population. Applied Psychological Measurement, 1:385-401.

APPENDIX G

PITTSBURGH SLEEP QUALITY INDEX

INSTRUCTIONS:

The following questions relate to your usual sleep habits during the past month only.

Your answers should indicate the most accurate reply for the majority of days and nights in the past month.

Please answer all questions.

1. During the past month, what time have you usually gone to bed at night?

BED TIME_____

2. During the past month, how long (in minutes) has it usually taken you to fall asleep each night?

NUMBER OF MINUTES_____

3. During the past month, what time have you usually gotten up in the morning?

GETTING UP TIME_____

4. During the past month, how many hours of actual sleep did you get at night? (This may be different than the number of hours you spent in bed.)

HOURS OF SLEEP PER NIGHT_____

For each of the remaining questions, check the one best response. Please answer <u>all</u> questions.

5. During the past month, how often have you had trouble sleeping because you…

a) Cannot go to sleep within 30 minutes

Not during the past month_____	Less than once a week_____	Once or twice a week_____	Three or more times a week_____

b) Wake up in the middle of the night or early morning

Not during the past month_____	Less than once a week_____	Once or twice a week_____	Three or more times a week_____

c) Have to get up to use the bathroom

Not during the past month_____	Less than once a week_____	Once or twice a week_____	Three or more times a week_____

d) Cannot breathe comfortably

Not during the past month_____	Less than once a week_____	Once or twice a week_____	Three or more times a week_____

e) Cough or snore loudly

Not during the past month_____	Less than once a week_____	Once or twice a week_____	Three or more times a week_____

f) Feel too cold

Not during the past month_____	Less than once a week_____	Once or twice a week_____	Three or more times a week_____

g) Feel too hot

Not during the past month_____	Less than once a week_____	Once or twice a week_____	Three or more times a week_____

h) Had bad dreams

Not during the past month_____	Less than once a week_____	Once or twice a week_____	Three or more times a week_____

i) Have pain

Not during the past month_____	Less than once a week_____	Once or twice a week_____	Three or more times a week_____

j) Other reasons (s), please describe_____

_____

How often during the past month have you had trouble sleeping because of this?

6. During the past month, how would you rate your sleep quality overall?

Very good _____

Fairly good _____

Fairly bad _____

Very bad _____

7. During the past month, how often have you taken medicine to help you sleep (prescribed or "over the counter")?

Not during the past month_____	Less than once a week_____	Once or twice a week_____	Three or more times a week_____

8. During the past month, how often have you had trouble staying awake while driving, eating meals, or engaging in social activity?

Not during the past month_____	Less than once a week_____	Once or twice a week_____	Three or more times a week_____

9. During the past month, how much of a problem has it been for you to keep up enough enthusiasm to get things done?

No problem at all _____

Only a very slight problem _____

Somewhat of a problem _____

A very big problem _____

APPENDIX H

Epworth Sleepiness Scale

How likely are you to doze off or fall asleep in the following situation, in contrast to feeling just tired?

This refers to your usual way of life in recent times.

Even if you haven't done some of these things recently try to work out how they would have affected you.

Use the following scale to choose the **most appropriate number** for each situation.

0 = would ***never*** doze

1 = ***slight chance*** of dozing

2 = ***moderate chance*** of dozing

3 = ***high chance*** of dozing.

It is important that you answer each question as best as you can.

Situation	**Chance of Dozing (0-3)**
Sitting and reading	
Watching TV	
Sitting, inactive in a public place (e.g. a theater or a meeting)	
As a passenger in a car for an hour without a break	

Lying down to rest in the afternoon when circumstances permit	
Sitting and talking to someone	
Sitting quietly after a lunch without alcohol	
In a car, while stopped for a few minutes in the traffic	

APPENDIX I

Demographic Sheet

1. What is your age?
2. What is your weight (in pounds)?
3. What is your height (in feet and inches)?
4. Medical History

Below is a list of common medical conditions. Have you EVER been diagnosed with any of the conditions listed below? Choose yes or no.

a. Diabetes? Yes/No

b. High blood pressure or hypertension? Yes/No

c. High cholesterol? Yes/No

d. Heart disease? Yes/No

e. Thyroid problems? Yes/No

f. Infertility? Yes/No

g. Endometriosis? Yes/No

h. Migraines? Yes/No

i. Depression? Yes/No

j. Anxiety? Yes/No

k. Anemia? Yes/No

k. Other:

5. What Service are you in?

○ Army ○ Navy ○ USAF ○USMC ○ Other_____

6. What is your pay grade?

○ E1-E4 ○ WO1-CW5 ○ O1-O3

○ E5-E9 ○ O4-O6 ○ O7-O10

7. What is your duty title:

8. What was your last physical fitness score:_____

9. Were you on a profile during your last physical fitness test? Yes/No If Yes, what was the reason for your profile?

10. What is your highest level of education?

○ Did not graduate from high school

○ High School Diploma/GED

○ Some college but not a 4-year degree

○ Associates Degree

○ 4-year college degree (BA, BS or equivalent)

○ Post-Bachelor's Degree

11. What is your current relationship status?

○Single ○Married ○In a relationship, not legally married

○Divorced ○Separated ○Widowed

12. Who (or what) provides your strongest source of support to cope with illnesses, adversities and/or other issues (choose all that apply)?

a. No support
b. Partner/spouse
c. Family member
d. Friend
e. Health professional
f. Religious affiliation
g. Other_____

Describe how this person (or these people) is (are) supporting you? (for example: What type of support are they providing?)

13. What is your Race? (Mark one or more to indicate what you consider yourself to be.)

○ African American or Black

○American Indian/Alaska Native

○ Asian

○ Native Hawaiian or Other Pacific Islander

○ White

○ More than one race

○ Latina

○ Other

14. What is your Ethnicity?

○Hispanic or Latina

○Not Hispanic or Latina

15. How old were you with your first menstrual cycle?
16. What was the date of last menstrual period (lmp) (first day of bleeding or spotting)
17. What is your usual cycle length (interval between first day of one menstrual period to the start day of the next menstrual period)?
18. What is the number of days of bleeding in an average menses?
19. Do you experience heavy or intermenstrual bleeding?
20. Do you experience painful bleeding during your menses?
21. How many pregnancies have you had regardless of outcome of the pregnancy?
22. Of your pregnancy(ies), how many resulted in delivery?
23. How many children do you currently have living with you?
24. How old were you when you were diagnosed with PCOS?
25. What medications are you taking and for what condition?
26. What nutritional supplements are you taking and why?

APPENDIX J

Semi-Structured Questions: No PCOS Template

General fatigue:

1. In your own words describe what the word “fatigue” means to you.

Physical fatigue:

2. In as much detail as possible can you describe how your physical activity level is affected when you are fatigued?

Mental fatigue:

3. In as much detail as possible can you describe how your emotions, and/or mood are affected when you are fatigued?

4. In as much detail as possible can you describe how your concentration is affected when you are fatigued?

Reduced activity:

5. In as much detail as possible can you describe any personal or professional activities that you stop doing or decrease doing when you are fatigued?

Reduced motivation:

6. In as much detail as possible can you describe how your motivation is affected when you are fatigued?

Additional questions

7. How long would you say you have been affected by fatigue

8. Is there anything else that you would like to tell me about your experience of fatigue?

APPENDIX K

Semi-Structured Questions: PCOS Template

General fatigue:

1. In your own words describe what the word “fatigue” means to you.

Physical fatigue:

2. In as much detail as possible can you describe how your physical activity level is affected when you are fatigued?

Mental fatigue:

3. In as much detail as possible can you describe how your emotions, and/or mood are affected when you are fatigued?

4. In as much detail as possible can you describe how your concentration is affected when you are fatigued?

Reduced activity:

5. In as much detail as possible can you describe any personal or professional activities that you stop doing or decrease doing when you are fatigued?

Reduced motivation:

6. In as much detail as possible can you describe how your motivation is affected when you are fatigued?

Additional questions

7. How long would you say you have been affected by fatigue

8. In as much detail as possible can you describe how have your relationships with friends and family changed since being diagnosed with PCOS?

9. Is there anything else that you would like to tell me about your experience of fatigue or PCOS?