



UNDER SECRETARY OF DEFENSE
4000 DEFENSE PENTAGON
WASHINGTON, DC 20301-4000

PERSONNEL AND
READINESS

MAY 29 2014

The Honorable Carl Levin
Chairman
Committee on Armed Services
United States Senate
Washington, DC 20510

Dear Mr. Chairman:

The enclosed report responds to section 737 of the National Defense Authorization Act for Fiscal Year 2013 (Public Law 112-239) that requires the Secretary of Defense to report on the number and characteristics of members of the Armed Forces serving on Active Duty who were diagnosed with breast cancer from 2000 to 2010. The report includes a description of treatments received, the availability of breast cancer specialists, a comparison of rates with comparable civilian populations, military service-related risk factors, current and proposed research agendas, a review of effectiveness of outreach programs, and the Department's recommendations for changes in policy or law to improve the prevention, detection, and treatment of breast cancer.

The Department welcomes the opportunity to address this important topic, and a disease that affects the health of many active component members of the Armed Forces. We have devoted considerable effort to development of this report and include data from both military and civilian cancer registries for a comprehensive assessment and accurate comparative perspective. A similar letter is being sent to the Chairpersons of the other congressional defense committees.

Thank you for your interest in the health and well-being of our Service members, veterans, and their families.

Sincerely,


Jessica L. Wright
Acting

cc:
The Honorable James M. Inhofe
Ranking Member



UNDER SECRETARY OF DEFENSE
4000 DEFENSE PENTAGON
WASHINGTON, DC 20301-4000

PERSONNEL AND
READINESS

MAY 29 2014

The Honorable Howard P. "Buck" McKeon
Chairman
Committee on Armed Services
U.S. House of Representatives
Washington, DC 20515

Dear Mr. Chairman:

The enclosed report responds to section 737 of the National Defense Authorization Act for Fiscal Year 2013 (Public Law 112-239) that requires the Secretary of Defense to report on the number and characteristics of members of the Armed Forces serving on Active Duty who were diagnosed with breast cancer from 2000 to 2010. The report includes a description of treatments received, the availability of breast cancer specialists, a comparison of rates with comparable civilian populations, military service-related risk factors, current and proposed research agendas, a review of effectiveness of outreach programs, and the Department's recommendations for changes in policy or law to improve the prevention, detection, and treatment of breast cancer.

The Department welcomes the opportunity to address this important topic, and a disease that affects the health of many active component members of the Armed Forces. We have devoted considerable effort to development of this report and include data from both military and civilian cancer registries for a comprehensive assessment and accurate comparative perspective. A similar letter is being sent to the Chairpersons of the other congressional defense committees.

Thank you for your interest in the health and well-being of our Service members, veterans, and their families.

Sincerely,


Jessica L. Wright
Acting

cc:
The Honorable Adam Smith
Ranking Member



PERSONNEL AND
READINESS

UNDER SECRETARY OF DEFENSE
4000 DEFENSE PENTAGON
WASHINGTON, DC 20301-4000

MAY 29 2014

The Honorable Barbara A. Mikulski
Chairwoman
Committee on Appropriations
United States Senate
Washington, DC 20510

Dear Madam Chairwoman:

The enclosed report responds to section 737 of the National Defense Authorization Act for Fiscal Year 2013 (Public Law 112-239) that requires the Secretary of Defense to report on the number and characteristics of members of the Armed Forces serving on Active Duty who were diagnosed with breast cancer from 2000 to 2010. The report includes a description of treatments received, the availability of breast cancer specialists, a comparison of rates with comparable civilian populations, military service-related risk factors, current and proposed research agendas, a review of effectiveness of outreach programs, and the Department's recommendations for changes in policy or law to improve the prevention, detection, and treatment of breast cancer.

The Department welcomes the opportunity to address this important topic, and a disease that affects the health of many active component members of the Armed Forces. We have devoted considerable effort to development of this report and include data from both military and civilian cancer registries for a comprehensive assessment and accurate comparative perspective. A similar letter is being sent to the Chairpersons of the other congressional defense committees.

Thank you for your interest in the health and well-being of our Service members, veterans, and their families.

Sincerely,


Jessica L. Wright
Acting

cc:
The Honorable Richard C. Shelby
Vice Chairman



UNDER SECRETARY OF DEFENSE
4000 DEFENSE PENTAGON
WASHINGTON, DC 20301-4000

PERSONNEL AND
READINESS

MAY 29 2014

The Honorable Harold Rogers
Chairman
Committee on Appropriations
U.S. House of Representatives
Washington, DC 20515

Dear Mr. Chairman:

The enclosed report responds to section 737 of the National Defense Authorization Act for Fiscal Year 2013 (Public Law 112-239) that requires the Secretary of Defense to report on the number and characteristics of members of the Armed Forces serving on Active Duty who were diagnosed with breast cancer from 2000 to 2010. The report includes a description of treatments received, the availability of breast cancer specialists, a comparison of rates with comparable civilian populations, military service-related risk factors, current and proposed research agendas, a review of effectiveness of outreach programs, and the Department's recommendations for changes in policy or law to improve the prevention, detection, and treatment of breast cancer.

The Department welcomes the opportunity to address this important topic, and a disease that affects the health of many active component members of the Armed Forces. We have devoted considerable effort to development of this report and include data from both military and civilian cancer registries for a comprehensive assessment and accurate comparative perspective. A similar letter is being sent to the Chairpersons of the other congressional defense committees.

Thank you for your interest in the health and well-being of our Service members, veterans, and their families.

Sincerely,


Jessica L. Wright
Acting

cc:
The Honorable Nita M. Lowey
Ranking Member



UNDER SECRETARY OF DEFENSE
4000 DEFENSE PENTAGON
WASHINGTON, DC 20301-4000

PERSONNEL AND
READINESS

MAY 29 2014

The Honorable Joseph R. Biden, Jr.
President of the Senate
United States Senate
Washington, DC 20510


Dear Mr. President:

The enclosed report responds to section 737 of the National Defense Authorization Act for Fiscal Year 2013 (Public Law 112-239) that requires the Secretary of Defense to report on the number and characteristics of members of the Armed Forces serving on Active Duty who were diagnosed with breast cancer from 2000 to 2010. The report includes a description of treatments received, the availability of breast cancer specialists, a comparison of rates with comparable civilian populations, military service-related risk factors, current and proposed research agendas, a review of effectiveness of outreach programs, and the Department's recommendations for changes in policy or law to improve the prevention, detection, and treatment of breast cancer.

The Department welcomes the opportunity to address this important topic, and a disease that affects the health of many active component members of the Armed Forces. We have devoted considerable effort to development of this report and include data from both military and civilian cancer registries for a comprehensive assessment and accurate comparative perspective. A similar letter is being sent to the Speaker of the House and the Chairpersons of the congressional defense committees.

Thank you for your interest in the health and well-being of our Service members, veterans, and their families.

Sincerely,


Jessica L. Wright
Acting



**UNDER SECRETARY OF DEFENSE
4000 DEFENSE PENTAGON
WASHINGTON, DC 20301-4000**

**PERSONNEL AND
READINESS**

MAY 29 2014

The Honorable John A. Boehner
Speaker of the House
U.S. House of Representatives
Washington, DC 20515

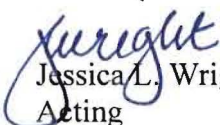
Dear Mr. Speaker:

The enclosed report responds to section 737 of the National Defense Authorization Act for Fiscal Year 2013 (Public Law 112-239) that requires the Secretary of Defense to report on the number and characteristics of members of the Armed Forces serving on Active Duty who were diagnosed with breast cancer from 2000 to 2010. The report includes a description of treatments received, the availability of breast cancer specialists, a comparison of rates with comparable civilian populations, military service-related risk factors, current and proposed research agendas, a review of effectiveness of outreach programs, and the Department's recommendations for changes in policy or law to improve the prevention, detection, and treatment of breast cancer.

The Department welcomes the opportunity to address this important topic, and a disease that affects the health of many active component members of the Armed Forces. We have devoted considerable effort to development of this report and include data from both military and civilian cancer registries for a comprehensive assessment and accurate comparative perspective. A similar letter is being sent to the President of the Senate and the Chairpersons of the congressional defense committees.

Thank you for your interest in the health and well-being of our Service members, veterans, and their families.

Sincerely,


Jessica L. Wright
Acting

REPORT TO CONGRESS

**NATIONAL DEFENSE AUTHORIZATION ACT FOR FISCAL
YEAR 2013 (HR 4310), SECTION 737
STUDY ON INCIDENCE OF BREAST CANCER AMONG MEMBERS
OF ARMED FORCES SERVING ON ACTIVE DUTY**



**SUBMITTED BY THE OFFICE OF THE ASSISTANT SECRETARY OF
DEFENSE (HEALTH AFFAIRS)**

JUNE 2014

CONTENTS

CONTENTS.....	2
PURPOSE	4
EXECUTIVE SUMMARY	5
Report Organization.....	5
Highlighted findings include:	5
Breast Cancer Incidence.....	5
Breast Cancer Prevention, Detection, and Treatment.....	6
Breast Cancer Risk Factors Associated with Active Duty Service.....	6
Policy and Research Implications.....	6
INTRODUCTION.....	7
Military Population Overview	7
U.S. Breast Cancer Overview	8
Department of Defense Cancer Epidemiology and Care Programs.....	9
Organization of the Report	12
PART 1. INCIDENCE OVER TIME AND BY DEMOGRAPHIC CHARACTERISTICS	12
Introduction	12
Task 1. A determination of the number of members of the Armed Forces who served on active duty at any time during the period from 2000 to 2010 who were diagnosed with breast cancer during such period.....	13
Task 2. A determination of demographic information regarding such members, including race, ethnicity, sex, age, and rank	13
Summary	16
References	16
PART 2. COMPARATIVE INCIDENCE OF THE ACTIVE COMPONENT AND CIVILIANS	17
Introduction	17
Task 5. A comparison of rates of members of the Armed Forces serving on active duty who have breast cancer to civilian populations with comparable demographic characteristics	17
Discussion.....	20
Limitations.....	21
Summary	21
References	22
PART 3. BREAST CANCER OUTREACH, TREATMENT SPECIALISTS, AND DOD TREATMENTS RECEIVED.....	22
Introduction	22
Task 8. An assessment of the effectiveness of outreach to members of the Armed Forces to identify risks of, prevent, detect, and treat breast cancer	23
Routine Clinical Screening – Facilitated by Electronic Reminder System	23
Breast Cancer Awareness Education	23
The TRICARE Benefit	23
Outreach Performance Standards	24
Summary	26
Task 4. The availability and training of breast cancer specialists within the Military Health System	26
Screening and detection	26
Diagnosis.....	26
Summary	27
Task 3. An analysis of breast cancer treatments received by such members and the source of such treatments	28
Methods.....	28

Results	28
Limitations.....	30
Summary	31
References	31
PART 4. RISK FACTORS ASSOCIATED WITH BREAST CANCER.....	32
Introduction	32
Task 6. Identification of potential factors associated with Military Service that could increase the risk of breast cancer for members of the Armed Forces serving on Active Duty	32
Framework and Concepts	32
Approach to the Literature	34
Personal Lifestyle, Risk Factors	35
<i>Distribution of Lifestyle Breast Cancer Risk Factors in Active Duty</i>	41
Environmental and Occupational Risk Factors	44
Known Military Occupational or Environmental Exposures	46
Known Toxic Exposures Related to Deployment	46
DoD Environmental and Occupational Risk Management	50
Summary	52
References	53
PART 5. POLICY CHANGES AND RESEARCH AGENDA.....	56
Introduction	56
Task 9. Recommendations for changes to policy or law that could improve the prevention, early detection, awareness, and treatment of breast cancer among members of the Armed Forces serving on Active Duty.....	57
Awareness and Outreach.....	57
Prevention, Detection and Treatment.....	57
Task 7. A description of a research agenda to further the understanding of the Department of Defense of the incidence of breast cancer among such members.....	59
Research Context Established in This Report.....	59
Current Research Programs	60
A Vision for Future Research that Could Be Supported by Military Databases.....	61
Summary	67
References	67
APPENDIX A.....	68
Methods and Data for Incidence Rate Comparison.....	68
References	68
APPENDIX B.....	70
Methods and Data for Treatment Modalities.....	70
References	73
GLOSSARY OF ACRONYMS	74
ACKNOWLEDGMENTS.....	75
From Defense Health Agency:	75
From the Schneider Institutes for Health Policy, Institute for Behavioral Health, Heller School for Social Policy and Management, Brandeis University:.....	75
From the Armed Forces Health Surveillance Center:	75
From the Navy and Marine Corps Public Health Center:.....	75
Murtha Cancer Center/Walter Reed National Military Medical Center (MCC/WRNMMC):	76
Joint Pathology Center.....	76

PURPOSE

The Department of Defense (DoD) submits this report in accordance with the National Defense Authorization Act for Fiscal Year 2013 (HR 4310), section 737, which directs the Secretary of Defense to report on the following items:

Task 1. A determination of the number of members of the Armed Forces who served on active duty at any time during the period from 2000 to 2010 who were diagnosed with breast cancer during such period.

Task 2. A determination of demographic information regarding such members, including race, ethnicity, sex, age, and rank.

Task 3. An analysis of breast cancer treatments received by such members and the source of such treatment.

Task 4. The availability and training of breast cancer specialists within the Military Health System.

Task 5. A comparison of the rates of members of the Armed Forces serving on active duty who have breast cancer to civilian populations with comparable demographic characteristics.

Task 6. Identification of potential factors associated with military service that could increase the risk of breast cancer for members of the Armed Forces serving on active duty.

Task 7. A description of a research agenda to further the understanding of the Department of Defense of the incidence of breast cancer among such members.

Task 8. An assessment of the effectiveness of outreach to members of the Armed Forces to identify risks of, prevent, detect, and treat breast cancer.

Task 9. Recommendations for changes to policy or law that could improve the prevention, early detection, awareness, and treatment of breast cancer among members of the Armed Forces serving on active duty.

EXECUTIVE SUMMARY

The Department of Defense (DoD), Defense Health Agency submits this report in accordance with the National Defense Authorization Act for Fiscal Year 2013, section 737, that calls on the Secretary of Defense to conduct a study on the incidence of breast cancer among members of the Armed Forces.

We have used our most comprehensive sources of military health data and applied rigorous, widely accepted statistical methods to respond to this request. The results here are encouraging for our efforts to promote force readiness, population health, and effective preventive and treatment strategies. Specifically, while breast cancer incidence among active service members is a rare event, female breast cancer incidence rates among this population has not changed significantly across the study period, 2000 through 2010. Moreover, age-adjusted incidence rates are significantly lower over that time period when compared with national incidence rates reported by the National Cancer Institute (NCI). Additionally, nearly three quarters of all breast cancer patients are first diagnosed at stages 0, I or II, which suggests that the Department's outreach efforts to promote awareness and use of screening services have been effective for detecting tumors at the earliest and most treatable stages. We are proud to report that once detected, service members have access to robust treatment options that reflect evidenced-based clinical practices and cutting-edge technologies offered in nationally-accredited cancer programs within the Military Health System. Since TRICARE has a process to assimilate emerging cancers technologies, medications, and practice into the benefit, the need for changes to law or policy are not apparent for the Department to sustain a high level of commitment to quality cancer care.

Report Organization

This report is organized into five parts, in which specific tasks requested by Sec. 737 are separately addressed and cross-referenced. The five major parts are:

- Part 1. Incidence over time and by demographic characteristics (Tasks 1, 2)
- Part 2. Comparative incidence of tumors in the active component and civilians (Task 5)
- Part 3. Breast cancer outreach, treatment specialists, and DoD treatments (Tasks 8, 4, 3)
- Part 4. Risk factors associated with breast cancer (Task 6)
- Part 5. Policy changes and research agenda (Tasks 9, 7)

Highlighted findings include:

Breast Cancer Incidence

- Through an examination of administrative data from 2000-2010, 906 incident cases of female breast cancer and 36 incident cases of male breast cancer were identified. Among females, 22.2% (201) were carcinoma in situ (localized), while 77.8% (705) were for invasive breast cancer diagnoses. These numbers represent an incidence rate of 39.9 per 100,000 person-years for female breast cancer and 0.3 per 100,000 person-years for males.
- After statistical adjustment for age group, Black, non-Hispanic female active duty members have a significantly higher probability of invasive cancer (odds ratio = 1.30, $p < .01$) compared with white and Hispanic members, a finding similar to prior research on female active duty members.
- Using cases extracted from the Automated Central Tumor Registry (ACTUR) and comparing them to National Cancer Institute's (NCI) Surveillance, Epidemiology, and End Results (SEER) database we found significantly lower age-adjusted malignant breast cancer rates among AD females (93.68 per 100,000 population (95%CI 91.63, 95.76)), relative to the SEER female population (107.76 per 100,000 population (95%CI 107.35, 108.18)).

Breast Cancer Prevention, Detection, and Treatment

- The clinical expertise within the MHS includes both primary care providers and breast cancer specialists who are appropriately trained to provide services throughout the spectrum of breast care. In cases where specialty services are not locally available, the patient is referred to one of many providers within the robust TRICARE network of military and civilian facilities. This network includes thirteen military treatment facilities around the country that are accredited by the American College of Surgeons Commission of Cancer, as well as the center of excellence at the Center of Excellence for Breast Care/Walter Reed National Military Medical Center (WRNNMC) which is also accredited by National Accreditation Program for Breast Centers.
- Outreach efforts for breast cancer awareness, risk-assessment, prevention, detection, and treatment is accomplished in the clinical setting by incorporating U.S. Preventive Services Task Force (USPSTF) evidence-based recommendations a link to the National Cancer Institute's Breast Cancer Risk Calculator into the workflow used by providers to conduct and document individual patient exams. On the population level, outreach is accomplished through newsletters and webinars to promote use of the robust cancer prevention services covered under the TRICARE benefit.
- The availability of qualified health care professionals and the effectiveness of outreach are also apparent in the treatments rendered to our breast cancer patients. Approximately 72% of women diagnosed over 2000-2010 were either Stage 0, I or II, indicating that the screening practices of clinical breast examinations and mammography are detecting tumors early while they can still be treated with the hopes of cure or an extended life expectancy. Efforts are ongoing to leverage technology to expand access to specialized services that may not be widely available. An excellent example of this is the telegenetics program at the MCC/WRNNMC that enables service members to access genetics specialists located at the MCC, from any military treatment facility.

Breast Cancer Risk Factors Associated with Active Duty Service

- A thorough review of the literature confirmed that the factors that contributed the greatest risk for breast cancer are largely non-modifiable characteristics, most importantly aging, as well as genetic contributions, and other biological differences, all relatively immutable. There is strong evidence, however, that some behavioral and lifestyle choices may increase breast cancer risk, including use of hormonal contraceptives and alcohol consumption. Breast-feeding appears to be a protective factor.
- A wealth of information is available that links exposures to particular chemicals or sources of radiation to increased cancer risk in general, but little evidence is available linking toxic exposures to increased breast cancer risk. Study of breast cancer incidence associated with military occupational assignments, deployments, or other Service-related experiences is greatly constrained by the latency between exposure and onset of cancer, as well as, the Department's inability to conduct surveillance on most service members, after they leave service.

Policy and Research Implications

These findings reflect the Military Health System's (MHS) commitment to implement policies and laws that are most likely to improve the quality and effectiveness of breast care to include prevention, early detection, and awareness of risks for breast cancer among all MHS eligible beneficiaries. The foundation of this commitment is the design and delivery of a comprehensive breast care benefit that continuously assesses each component of the breast care experience and that draws on evidenced-based clinical practices, cutting-edge cancer diagnostics, treatment technologies, and evidence from high-priority clinical cancer trials. Consistent with an overarching theme of MHS transformation, we emphasize that

keen oversight and attention is being directed to discover improved strategies that optimize patient health and resources available to that end. Our internal efforts and considerations are ongoing and have not required changes to law or policy for implementation. Within the current policy, legislative framework, and future directions for research, the military health benefit will continue to support a comprehensive consideration of promising technologies and treatments for breast cancer preventive care and treatments.

INTRODUCTION

This introduction provides background to set context for interpreting the study's findings. It contains a brief summary of relevant demographic characteristics of the active duty members of the armed forces, the relative disease burden of cancer in the military, and an overview of breast cancer trends in the U.S. general population.

The final section briefly overviews the Department of Defense (DoD) programs that share responsibility for the overall breast cancer program for active duty members. Combined, they conduct surveillance and monitoring programs, offer outreach, detection, and treatment services, and recommend changes to policy or benefits that govern DoD health programs.

Military Population Overview

Breast cancer primarily occurs among females, with less than 1 percent of cases among males. International studies have reported a male breast cancer rate of in England, Scotland, Canada and Australia ranging from 0.4 to 0.8 per 100,000 population¹. While the majority of armed forces members are male, females are 14.5 percent of enlisted and 15.9 percent of officer active duty component members in 2011². From 2000 to 2011, the total number of female officers grew from 31,356 to 37,889 and the number of female enlisted slightly declined from 169,084 to 166,815 in the active component. Active duty females represent a more diverse racial/ethnic background than the U.S. population overall as well as active duty males; 52 percent of active component females are white, 30 percent black, 9 percent Hispanic, 4 percent Asian/Pacific Islander, and 2 percent American Indian.³ This heterogeneity of backgrounds, combined with a uniform health delivery system, provide a useful platform for study of health care delivery on breast cancer and other topics⁴.

Characteristics of the military population and the Military Health System provide both advantages and disadvantages for longitudinal studies of cancer incidence and treatment. The disease and healthcare burden of cancer for a substantial minority of female members who retire in the military are captured for 20 years and longer in DoD surveillance programs. This capacity to study long-term trends in the U.S. in a well-characterized population with relatively uniform access to health care is unique.

On the other hand, nearly all active component members are very young; the median age of females is 25, and only 9.4 percent of females is age 40 or older⁵. This youthful age distribution means the vast majority of female members are in age groups where detection (incidence) of breast cancer is rare, and annual screening mammography is not recommended for women of average risk⁶. When studying incidence of cancer, the small number of cases and low rate complicates any investigation of time trends or differences among subgroups⁷.

Further, while some U.S. armed forces members do retire from military service (e.g., some officers and senior enlisted members), the majority of service members do not. Because the DoD has no access to medical records of members after discharge, the cancers that emerge after their discharge are not included in DoD reporting systems. Currently, no mechanism exists for DoD to monitor diagnoses

rendered under care received from the Department of Veterans Affairs or other health insurance for members who are no longer TRICARE eligible.

Annual reports of the Armed Forces Health Surveillance Center (AFHSC) establish important context about the disease burden associated with all cancers in the military. There is no apparent long-term trend in crude incident cancer rates⁸. Cancer deaths while on active duty are rare since military members with chronic disease that interferes with duties are medically-retired and no longer captured in active component records. Deaths attributable to any form of cancer contribute minimally to all deaths among female and male active component members, on average 8 percent of all deaths and 11 percent of non-combat deaths⁹. During the 2000-2012 surveillance period, there were 1,185 cancer deaths among female and male active duty members (inclusive of reserve component members who were activated) of which the most common were lung/bronchus, brain/central nervous system, and colon/rectum cancer; breast cancer deaths never exceeded 5 cases in one year^{10,11}. Unlike many acute and chronic conditions common among the relatively young and healthy armed forces population, the etiology of cancer is complex and not attributable to a single exposure or to one risk factor alone¹². Further, changes in population exposure to carcinogens (i.e., radiation), or changes in behavior practices that may affect cancer risk (i.e., smoking), may have long clinical latency, thus, not be apparent in immediate trends and could appear after active duty members have separated or retired from the military.

Regarding other established measures of disease burden, in terms of the annual number of days with medical encounters among female and male active duty members, cancer diagnoses rank 16th among major categories and conditions used in global burden of disease studies¹³. Among all 31,802 hospitalizations of active component females in 2012, there were 827 females hospitalized with a neoplasm diagnosis, with 48 females hospitalized specifically with a breast cancer diagnosis¹³.

U.S. Breast Cancer Overview

Breast cancer is predominantly a disease among females, and life-changing health event associated with significant morbidity and mortality. An estimated 2.8 million women in 2010 had been diagnosed with cancer of the breast, including those in remission, and include those newly diagnosed and undergoing active treatment. The five-year relative^a survival rate for 2003-2009 is high, but higher for white women (90.4 percent) than black women (78.7 percent). The majority of cases (61 percent) were identified at a stage when cancer is localized to the breast and 5-year relative survival is nearly universal. About one-third of cases (32 percent) were identified at a stage when breast tissue and regional lymph nodes were involved, and survival is slightly diminished (84 percent). The remaining cases (7 percent) were attributable to distant or unstaged cases, for which survival rates are substantially lower¹⁴.

The median age at diagnosis for breast cancer was 61 years of age in the U.S. during the period 2006-2010. Under 2 percent of breast cancers were diagnosed in women younger than 35; only one-in-ten diagnoses were in women between the ages of 35 and 44. Incidence rates have fluctuated and mortality rates have declined over time, when examining U.S. trends starting in 1975¹⁴. Nonetheless, historic patterns of age at diagnosis may not describe the optimal pattern. Given breast cancer is more likely to be curable when it is detected early, early detection is imperative to reduce mortality, extend years of productive life, contain the cost of cancer treatment, and contribute to improved quality of life after diagnosis for women with breast cancer¹⁵.

^a Relative survival is a measure of net survival which measures survival of cancer patients to a comparable set of people that do not have the cancer.

Definition of terms and concepts is important to understanding information presented about breast cancer. Breast cancer is either noninvasive, confined to the site of origin (referred to as *in situ*), or invasive (spreading). Different reports may include or exclude *in situ* cases, which may comprise 20 to 30 percent of all cases. When speaking of risk factors for breast cancer, it is understood that establishing that a characteristic is associated with increased risk for cancer (e.g., estrogen exposure, density of breast tissue) is not sufficient evidence that the factor causes breast cancer. Thus, understanding the distribution of risk factors in a population may help target detection interventions to higher risk subgroups. However, changing a risk factor that is associated with breast cancer, but not causative, is not likely to prevent the occurrence of cancer.

The term incidence is used by epidemiologists to mean *new cases*, and it ignores the recurrence of disease among existing cases. This report describes incidence in two ways, both a new person with breast cancer (Tasks 1 and 2), and a new malignant breast tumor (Task 5), including those in females with a prior malignant tumor.

A well-organized and sustainable cancer detection program must target the right age and population groups with the correct actions. Mammography screening is the indicated screening method with a preponderance of evidence that it is effective in reducing mortality through early detection of breast cancer¹⁵. Routine clinical breast examination is the primary strategy useful for detection in women of average risk under age 40 years, for whom mammography is not indicated. While breast self-examination alone does not have evidence supporting its effectiveness in detecting early breast cancer, it is still used as one strategy to raise awareness among women who may be above average in risk for breast cancer⁶.

Caution is required when translating evidence and healthcare protocols useful in the general population to the military population⁶. Both clinical and epidemiologic expertise specific to the military provide important insights into future research directions and policy initiatives which may yield the most benefit. For example, given that the vast majority of active component females are too young to benefit from mammography (i.e., under age 40), detection interventions must be carefully targeted; widespread (i.e., untargeted) screening in populations with low prevalence will result in undue anxiety among women (and burden to the health system) from medical evaluation of additional cases of benign tumors (i.e., false positives), and must be balanced with the number of malignant tumors that are detected at a time when prognosis is likely to improve.

Department of Defense Cancer Epidemiology and Care Programs

Important activities contributing to the understanding and treatment of breast cancer occurrence (and all cancers) in the armed forces are widely dispersed among several different agencies and offices within the DoD enterprise, and include many functions, such as: disease surveillance and occupational risk surveillance, reducing harm (increased radiation, over treatment) associated with false positive screens in a young population, cancer prevention and treatment services, and healthcare performance and analytic studies. To complete this report to Congress, the Defense Health Agency (DHA) consulted with and received contributions from several major DoD organizations, each with specific missions and responsibilities, to include:

- Armed Forces Health Surveillance Center (AFHSC)
- Joint Pathology Center (JPC)
- John P. Murtha Cancer Center (MCC) at the Walter Reed National Military Medical Center (WRNMMC)
- Department of Navy Cancer Surveillance and Registry Program (DON/CSRP)
- Navy and Marine Corps Public Health Center's (NMCPHC) Health Analysis team

- Office of the Chief Medical Officer (OCMO)

The DHA was able to provide a comprehensive and coherent snapshot of DoD breast cancer activities because it hosted non-routine, frequent, periodic teleconference meetings of experts from these organizations to gather, assess, and discuss the evidence contained in this report. The group stimulated a synergy of ideas, as the multidisciplinary team of these distinct organizations met to identify information sources, generate new analysis, and articulate standard operations not currently written. This approach of frequent meetings and discussion permitted a powerful synthesis of information and is particularly reflected in the observations for policy initiatives and future research agenda. Despite the report's comprehensive DHA perspective, certain specialized programs were deemed beyond the scope of the Congressional request, specifically programs that were: 1) undertaken by individual services (e.g., Air Force), 2) occupational medicine not directed towards breast cancer prevention; and 3) experimental protocols being investigated through the Congressionally-directed Medical Research Program. These programs and activities could be the subject of future investigation.

The overall mission of each contributing organization and its specific role regarding breast cancer surveillance, prevention, or treatment are briefly summarized here:

The *AFHSC* provides timely, relevant, actionable, and comprehensive health surveillance information in order to promote, maintain, and enhance the health of military and military-associated populations. Regarding cancer surveillance, the Epidemiology and Analysis Division performs surveillance and analysis of health related information, and leverages the Defense Medical Surveillance System (DMSS) which contains up-to-date and historical data on diseases and medical events.

The *JPC* is a fully accredited laboratory through the Accreditation Committee of the College of American Pathologists (CAP) that provides diagnostic subspecialty pathology consultation, education and research services to federal agencies and operates the National Pathology Tissue Repository in support of the mission of the Department of Defense and other federal agencies. It also provides contract and funding oversight, but relies on the subject matter experts from the three Medical Services for functional oversight of the DoD Automated Central Tumor Registry (ACTUR)^b, a cancer surveillance/registry program and analytic software that permits analysis of breast cancer cases (and other cancer cases) confirmed by pathology and their treatments within the DoD and other treatments when reported by the patient. ACTUR is hosted by the Defense Manpower Data Center (DMDC) and interfaces with the Defense Enrollment Eligibility Reporting System (DEERS). DEERS in turn provides ACTUR with personal information on all active duty personnel, retirees, and beneficiaries. Cancer registrars at individual MTFs are trained on registry procedures and certified through the National Cancer Registrars Association. Cancer registries within cancer programs accredited by the American College of Surgeons Commission on Cancer (ACS-CoC) provide non-identified information to the National Cancer Data Base (NCDB) of ACS-CoC a nationwide oncology outcomes database. Local MTF cancer registries provide valuable information for the cancer team on useful monitoring for prevention, early diagnosis, pretreatment evaluation, staging, treatment follow-up, rehabilitation, and surveillance for recurrence and multiple primary cancers.^c

The *MCC* at Walter Reed is a tri-service military healthcare facility operating the DoD Cancer Center of Excellence. It is staffed by military and civilian oncologists and other cancer-trained clinicians and researchers. Through *MCC*, active component and other military-related patients have access to cutting-

^b For more information on the JPC see: <http://www.jpc.capmed.mil/index.asp>

^c For example of activities of local cancer registrars see: <http://www.med.navy.mil/directives/ExternalDirectives/6320.92.pdf>

edge cancer diagnostic and treatment technologies. It further contains a strong core of translational research to optimize access to evidenced-based clinical practices and clinical cancer trials for military patients. Within MCC is the DoD Center of Excellence for Breast Care (CBCP)^d. The program utilizes a multidisciplinary approach to breast disease, integrating prevention, screening, diagnosis, and treatment with advances in risk reduction, tissue banking, research, and informatics. The services provided or supported include:

- Detection and follow-up screening at the newly designed Breast Imaging Center
- Pre and post-operative breast care
- Physical therapy including pre-operative assessment, post-operative therapy and lymphedema management
- Educational resources
- Case management
- Social work services such as individual or family counseling/psychotherapy and various support groups
- Genetic counseling
- Breast cancer research

The *DON/CRSP* provides Navy Medicine with wide oversight of the quality of data entered into (ACTUR) and monitors the success in meeting DON standards for cancer patient follow-up.^e The NMCPHC's *Health Analysis* department is a multi-disciplinary advanced analytic team with specialists in the following: scientific methodology, peer review publication, advanced biostatistics, advanced epidemiology, data management, advanced SAS programming, physician advisors, population health specialists and staff to support research and clinical investigation and the manager of the *DON/CRSP* is part of this Health Analysis team.

The *OCMO* provides leadership and/or oversight for a range of quality assessment /quality improvement, patient safety, and population-based health management programs across the MHS, affecting both the direct care and purchased care components of TRICARE. The *OCMO* provides medical consultative guidance for the TRICARE benefit appeals, development, validation and reimbursement process. Among its six divisions are three that are directly pertinent to breast cancer and its treatment: Clinical Quality; Health Care Benefits & Risk Management; and Health Promotion & Disease Prevention.

The Clinical Quality Division develops and implements clinical policy for MHS peacetime health care delivery and reports on MHS clinical quality processes, including a Health Plan Employer Data and Information Set (HEDIS) performance measure for routine mammograms. The Health Care Benefits Division oversees the clinical aspects of benefit development and maintenance of benefit currency. The Health Promotion and Disease Branch focus on modifying and preventing a person's disease and injury risk by effectively changing behaviors to optimize health and enhance fitness, among other things.

Among its many functions, *DHA* prepares periodic reports to Congress. The *DHA* supports performance-based decision-making and execution initiatives through scientific studies and operational support. The broad categories of activities include being a proponent for corporate data systems, responsible for corporate survey programs of Military Health System beneficiaries and providers, and health system

^d For more information on the MCC see <http://www.wrnmmc.capmed.mil/cancercenter/SitePages/Home.aspx>

^e For more information on the *DON/CRSP* see: <http://www.med.navy.mil/sites/nmcphc/health-analysis/special-programs/Pages/default.aspx>

evaluation studies and analyses. The DHA maintains two periodic health risk behavior surveys (one each of active duty and reserve component), which contain some data useful for characterizing personal behaviors that might increase or decrease personal risk of cancer (e.g., smoking, alcohol consumption, measures to combat obesity). DHA analyses routinely utilize health professional allocation data, institutional and ambulatory medical records, and with permission deployment records and post deployment health surveillance records, all potentially useful for conducting studies useful to understanding cancer incidence and treatments.

In summary, surveillance, policy, and execution of programs regarding breast cancer and its treatment are not contained within a single entity or organization but dispersed among several major entities within the DoD enterprise. Each of these organizations have specialized expertise that contributes an important slice of information necessary to construct a comprehensive understanding of breast cancer detection and treatment among active component service members.

Organization of the Report

The remainder of this report is organized conceptually, and, within parts, specific tasks requested by Sec. 737 are separately addressed and cross-referenced. The five major parts are:

- Part 1. Incidence over time and by demographic characteristics (Tasks 1, 2)
- Part 2. Comparative incidence of tumors in the active component and civilians (Task 5)
- Part 3. Breast cancer outreach, treatment specialists, and DoD treatments (Tasks 8, 4, 3)
- Part 4. Risk factors associated with breast cancer (Task 6)
- Part 5. Policy changes and research agenda (Tasks 9, 7)

PART 1. INCIDENCE OVER TIME AND BY DEMOGRAPHIC CHARACTERISTICS

Introduction

In this part, the incidence of breast cancer in active duty members of the Armed Forces is presented along with the demographics regarding these members. The statistics cover the period January 1, 2000 through December 31, 2010 and include all service members on active duty or activated^f, at any time during that period. Using data from records routinely maintained by the Defense Medical Surveillance System (DMSS), the AFHSC used the following ICD-9-CM diagnoses codes to identify for each member the first medical encounter with the following diagnoses: carcinoma in situ (233.0) and malignant neoplasm of the female breast (174.0-174.9) and for male cases (175.0-175.9). To be counted as a case, three unique records with the diagnosis within 90 days were required to eliminate counting persons undergoing screening and assessment only. Cases are unique persons. Prevalent breast cancer cases were removed from the analyses and not counted as an incident case in future years. Also, incidence cases do not include cases of breast cancer that emerge after a service member has left active duty or has left the military.

Rates are expressed per 100,000 person-years to take into account the number of active duty members, the months each member was on active duty and the months before a breast cancer diagnosis. An

^f The AFHSC methodology defined the Reserve and National Guard members who were activated and serving on active service as included in the numerator if diagnosed with breast cancer for the first time while on active duty. All activated National Guard and Reserve personnel contributed to the denominator (person years) based on each service member's date of activation and until the date of "release from active duty" (REFRAD).

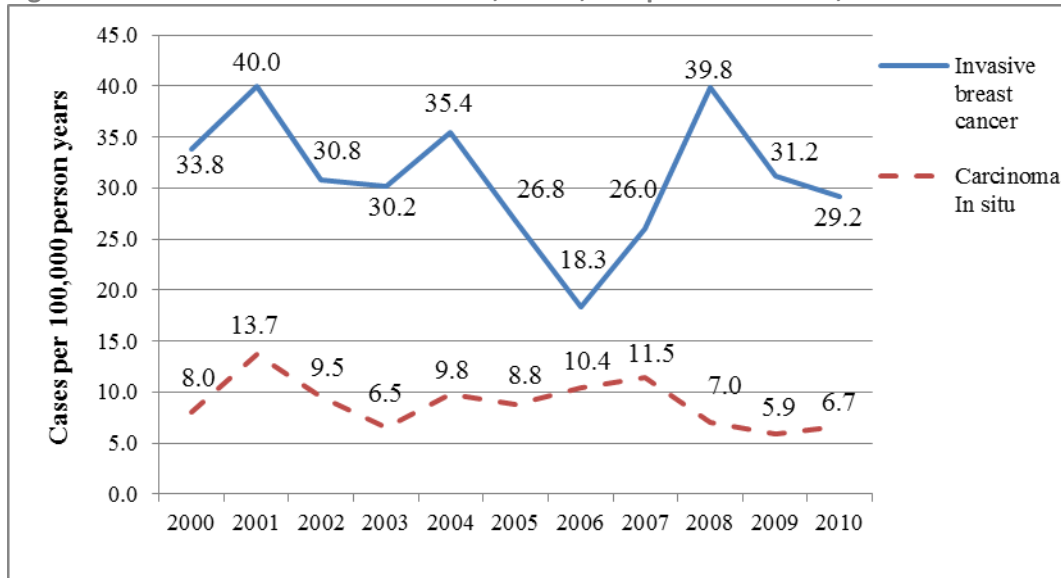
individual on active duty from January 2005 - December 2008 would contribute 48 months of person-time to the denominator, one person-year in each of four years. An individual on active duty with an incident diagnosis of breast cancer in June 2005, would only contribute six months of person-time to the denominator.

Statements below concerning the statistical significance of a characteristic in affecting the incidence of breast cancer are based on logistic regressions.

Task 1. A determination of the number of members of the Armed Forces who served on active duty at any time during the period from 2000 to 2010 who were diagnosed with breast cancer during such period.

During the period from 2000-2010, 906 incident cases of female breast cancer and 36 incident cases of male breast cancer were diagnosed among members of the Armed Forces who served on active duty. Among females, 22.2% (201) were carcinoma in situ (localized) for an average of 18 new cases per year, while 77.8% (705) were for invasive breast cancer diagnoses, an average of 64 new cases per year. These numbers represent an incidence rate of 39.9 per 100,000 person-years for female breast cancer, which breaks down to 8.9 per 100,000 person-years for carcinoma in situ and 31.1 per 100,000 person-years for invasive breast cancer. Among men, the incidence rate was 0.3 per 100,000 person-years.

Figure 1. Incidence rate of breast cancer, active, component females, U.S. armed forces, 2000-2010



Note: Rates for men are not shown because small numbers make the annual rates unstable.

Source: Data prepared by Armed Forces Health Surveillance Center (AFHSC), Defense Medical Surveillance System (DMSS) data as of 04-SEP

The crude incidence rate per 100,000 person-years for invasive breast cancer diagnoses does not show significant trends over time and fluctuates, annually ranging from 18.3 (low in 2006) to 40.0 (high in 2001); the incidence rate for carcinoma in situ also ranged from 5.9 (low in 2009) to 13.7 (high in 2001). It is key to note, that small number of cases contributing to these annual rates are too few to support rigorous analysis of patterns in cancer incidence over the study period.

Task 2. A determination of demographic information regarding such members, including race, ethnicity, sex, age, and rank

The incidence of breast cancer is largely determined by the age distribution of a population. In the Armed Forces, age distributions vary by race/ethnicity group, service, and rank. For example, the

median age of women in the armed services is 25. To understand which military group bears the morbidity burden of breast cancer, it is appropriate to examine the absolute number of cases. However, to understand the relative risk for breast cancer, it is appropriate to hold constant the differences in age distribution.

Table 2.1 shows incidence rates among female members per 100,000 person-years for carcinoma in situ and invasive cancer by age group during the 2000-2010 timeframe. Reflecting the biology of breast cancer, incidence rates differed significantly by age group with older active duty females having higher incidence rates of both carcinoma in situ and invasive breast cancer. While females over age 40 account for only 7.9 percent of the active duty person-years, they account for 66.7 percent of incident cases of carcinoma in situ and 53.0 percent of incident cases of invasive cancer. Because breast cancer incidence increases so significantly with age, it is essential to adjust for age in analyzing the possible impact of any other characteristic. Other apparent differences in incidence rates (for example, by military pay grade) may well disappear once age is taken into account.

Table 2.1. Incident cases of breast cancer, rate by age group per 100,000 person-years, and distribution by age group of cases, active duty females, U.S. Armed Forces, January 2000-December 2010

Age Group* (years)	Carcinoma In Situ			Invasive Cancer		
	Number of Cases	Percentage of Total Cases**	Rate per 100,000	Number of Cases	Percentage of Total Cases**	Rate per 100,000
All Age Groups	201	100.0	8.9	705	100.0	31.1
<20	0	0.0	0	0	0.0	0
20-24	2	1.0	0.2	23	3.3	2.8
25-29	8	4.0	1.6	42	6.0	8.5
30-34	17	8.5	5.8	101	14.3	34.4
35-39	40	19.9	17.6	165	23.4	72.6
40-44	74	36.8	63.1	188	26.7	160.2
45-49	38	18.9	88	125	17.7	289.6
50-54	20	10.0	156.6	43	6.1	336.8

*Data not reported for age 55 and over because of small number of cases, small base population and unstable rates.

**Distribution may not add to 100 percent because of rounding.

Source: Data prepared by Armed Forces Health Surveillance Center (AFHSC), Defense Medical Surveillance System (DMSS) data as of 04-SEP-2013.

Table 2.2 shows the burden of incident cases of breast cancer among active duty females. For both carcinoma in situ and invasive cancer, the majority of cases are among services members in the Army or Air Force. White, non-Hispanic female service members account for almost half of all incident cases. Reflecting the age distribution, the large majority of cases is found among senior enlisted service members or officers. In terms of military occupation, most cases occur among female service members working in administration/supply, followed by health care. Breast cancer cases among combat support occupations were relatively infrequent. The distribution of incident cases reflects both the numbers of female service members serving in each group shown below as well as the different age distributions across groups.

Table 2.2 Incident cases of breast cancer and distribution by service, race/ethnicity, military pay grade, and military occupation, active duty females, U.S. Armed Forces, January 2000-December 2010

Characteristic	Carcinoma In Situ		Invasive Cancer	
	Number of Cases	Percentage of Total Cases	Number of Cases	Percentage of Total Cases
<i>Race/Ethnicity</i>				
White, non-Hispanic	97	48.3	354	50.2
Black, non-Hispanic	72	35.8	237	33.6
Hispanic	8	4.0	43	6.1
Other	24	11.9	71	10.1
<i>Service</i>				
Army	71	35.3	259	36.7
Navy	37	18.4	161	22.8
Air Force	85	42.3	251	35.6
Marine Corps	4	2.0	19	2.7
Coast Guard	4	2.0	15	2.1
<i>Military pay grade</i>				
Junior enlisted (E1-E4)	6	3.0	49	6.9
Senior enlisted (E5-E9)	108	53.7	389	55.2
Junior officers (O1-O3, W1-W3)	20	9.9	82	11.6
Senior officers (O4-O10, W4-W5)	67	33.3	185	26.2
<i>Military occupation</i>				
Combat support	6	3.0	39	5.5
Health Care	51	25.4	202	28.6
Admin/Supply	98	48.8	299	42.4
Other	46	22.9	165	23.3

Source: Data prepared by Armed Forces Health Surveillance Center (AFHSC), Defense Medical Surveillance System (DMSS) data as of 04-SEP-2013.

To explore differences among groups of female active duty members in the incidence rates of invasive cancer, Table 2.3 presents the age group-specific rates of invasive breast cancer by race/ethnicity, service and military occupation.

After statistical adjustment for age group⁶, Black, non-Hispanic female members have a significantly higher probability of invasive cancer (odds ratio = 1.30, $p < .01$) compared with white and Hispanic members, a finding similar to prior research on female active duty members⁴. However, this difference was completely due to the higher incidence rates of invasive breast cancer among female members younger than 40 years old. Among female members 40 years or older, there was no significant difference in invasive breast cancer incidence rate by race/ethnicity. Significant differences were not

⁶ Regression analysis was conducted on the data contained in a spreadsheet on breast cancer cases and female active duty person-years. The spreadsheet was organized by age group and a second characteristic (occupation, service, or race/ethnicity). The spreadsheet provided a breast cancer case count (i.e., numerator) and the female person-years (i.e., denominator) for each age group-characteristic cell. The logistic regression model estimates the odds ratio for a "positive case" defined as incidence of cancer for someone with the characteristic (race/ethnicity, service, military occupation) compared to someone without. When the cancer incident rate is extremely low, logistic models provide biased results and underestimate the odds ratio for the characteristic. Thus, any significant finding is unlikely to be a false finding. However, as the logistic models are biased downward, it is possible a characteristic without a significant odds ratio may be a false negative. In this analysis, no other characteristic than black race appeared close to significant, which is some indication that false negative findings are not an issue.

found by service nor by military occupation either across all age groups or when restricting the analysis to members 40 years or older, where the incidence of invasive breast cancer is much higher.

Table 2.3 Incident cases and crude rate per 100,000 person-years of invasive breast cancer by age, active duty females, U.S. Armed Forces, January 2000-December 2010, by race/ethnicity, service, and military occupation

Characteristic	20 - 24 years*		25 - 29 years		30 - 34 years		35 - 39 years		40 - 44 years		45 - 49 years		50 - 54 years	
	Number of Cases	Rate per 100,000	Number of Cases	Rate per 100,000	Number of Cases	Rate per 100,000	Number of Cases	Rate per 100,000	Number of Cases	Rate per 100,000	Number of Cases	Rate per 100,000	Number of Cases	Rate per 100,000
<i>Race/Ethnicity</i>														
White non- Hispanic	9	2.2	13	5.4	42	30.4	77	70.2	97	159.5	76	304.1	30	364.5
Black, non-Hispanic	8	3.8	19	13.6	42	43.2	59	71.8	64	160.3	34	282.9	7	256.8
Hispanic	4	3.8	5	9.7	8	31.2	7	47.1	10	152.6	5	233.5	1	173.8
Other	2	2.1	5	8.1	9	27.4	22	107.7	17	169.2	10	249.0	5	404.4
<i>Service</i>														
Army	9	3.3	14	8.1	36	32.6	67	79.0	66	148.8	44	264.8	13	250.9
Navy	3	1.4	13	11.3	17	25.9	31	61.1	40	153.8	38	350.9	16	465.1
Air Force	10	3.9	12	7.0	42	41.2	62	76.8	69	165.1	39	277.1	13	347.7
Marine Corps	1	1.7	2	9.8	3	31.8	4	64.1	6	253.3	1	150.4	1	624.1
Coast Guard	0		1		3		1		7		3		0	
<i>Military Occupation</i>														
Combat	2	3.3	6	17.5	7	43.1	7	72.3	10	224.7	7	500.8	0	0.0
Health Care	7	5.7	6	6.0	23	32.5	37	68.2	49	146.9	51	296.9	19	287.4
Admin/Supply	8	2.5	22	11.2	48	37.7	83	77.7	85	165.7	35	233.2	14	421.2
Other	6	1.8	8	4.9	23	29.0	38	67.3	44	155.7	32	334.0	10	389.9

*No breast cancer cases were identified among Active Duty females under 20 years of age. Data not reported for age 55 and over because of small number of cases, small base population and unstable rates.

Source: Data prepared by Armed Forces Health Surveillance Center (AFHSC), Defense Medical Surveillance System (DMSS) data as of 04-SEP-2013.

Summary

The analysis of AFHSC data found 36 male breast cancer cases for a crude rate of 0.3 per 100,000 person-years. This crude rate is lower than the U.S. age-adjusted male breast cancer rate of 1.4 per 100,000 persons for the period 2006-2010¹⁶.

The incidence rate of breast cancer among active duty female members found significantly higher incidence among older age female active duty members, consistent with U.S. civilian data and reflecting the established knowledge that the strongest predictor of breast cancer risk is age⁶. Black, non-Hispanic active duty females younger than age 40 have statistically higher rates of invasive breast cancer than young white, non-Hispanic females, similar to epidemiologic findings in U.S. civilians^{6, 16}. In the general population, across all age groups, white women have higher incidence rates for female breast cancer African American women,¹² but this pattern is reversed among women under age 44.

While there are differences in crude breast cancer incidence rates and across services, military occupation, and military pay grade, these are not statistically different from what would be expected after adjusting for the different age distributions within these groups.

References

1. White, J., et al., *Male breast carcinoma: increased awareness needed*. Breast Cancer Res, 2011. **13**(5): p. 219.
2. *2011 Demographics: Profile of the Military Community, 2012*, Office of the Deputy Under Secretary of Defense (Military Community and Family Policy).
3. U.S. General Accountability Office, *Military personnel: reporting additional servicemember demographics could enhance congressional oversight*, 2005: Washington DC.

4. Enewold, L., et al., *Racial variation in breast cancer treatment among Department of Defense beneficiaries*. *Cancer*, 2012. **118**(3): p. 812-20.
5. Defense Manpower Data Center, *m01fy05.pdf TABLE 2-17A Female active component personnel strength in thousands and percent distribution*, 2005, Department of Defense.
6. Stojadinovic, A., et al., *Consensus recommendations for advancing breast cancer: risk identification and screening in ethnically diverse younger women*. *J Cancer*, 2011. **2**: p. 210-27.
7. Zhu, K., et al., *Cancer incidence in the U.S. military population: comparison with rates from the SEER program*. *Cancer Epidemiol Biomarkers Prev*, 2009. **18**(6): p. 1740-5.
8. *Incident diagnoses of cancers and cancer-related deaths, active component, U.S. Armed Forces, 2000-2011*. *MSMR*, 2012. **19**(6): p. 18-22.
9. *Deaths while on active duty in the U.S. Armed Forces, 1990-2011*. *MSMR*, 2012. **19**(5): p. 2-5.
10. Storeng, R., et al., *Infertility treatment and the risk of cancer*. *Tidsskr Nor Laegeforen*, 2012. **132**(22): p. 2494-9.
11. *Personal communication with COL William Corr, AFHSC, based on work done for MSMR 19(6):18-22, 2012, 2014*.
12. Andaya, A.A., et al., *Socioeconomic disparities and breast cancer hormone receptor status*. *Cancer Causes Control*, 2012. **23**(6): p. 951-8.
13. Macon, M.B. and S.E. Fenton, *Endocrine disruptors and the breast: early life effects and later life disease*. *J Mammary Gland Biol Neoplasia*, 2013. **18**(1): p. 43-61.
14. Howlader, N., et al., *SEER Cancer Statistics Review, 1975-2010*, 2013, National Cancer Institute: Bethesda, MD.
15. Enewold, L., et al., *Surveillance mammography among female Department of Defense beneficiaries: a study by race and ethnicity*. *Cancer*, 2013. **119**(19): p. 3531-8.
16. U.S. Cancer Statistics Working Group. *United States Cancer Statistics: 1999–2010 Incidence and Mortality Web-based Report*. 2013 [cited 2014 February 19, 2014]; Available from: www.cdc.gov/uscs.

PART 2. COMPARATIVE INCIDENCE OF THE ACTIVE COMPONENT AND CIVILIANS

Introduction

In this Part, a comparison of rates of female members of the Armed Forces serving on active duty who have breast cancer to civilian populations of the same age group is presented. DON CSRP identified breast cancer cases from the Automated Central Tumor Registry (ACTUR) for female active duty members ages 20-59 using methods to support comparison to U.S. civilian data from the National Cancer Institute's (NCI) Surveillance, Epidemiology, and End Results (SEER) database.

Task 5. A comparison of rates of members of the Armed Forces serving on active duty who have breast cancer to civilian populations with comparable demographic characteristics

The population of interest includes AD female breast cancer cases diagnosed between January 1, 2000 and December 31, 2010 documented within ACTUR, for women 20-59 years of age, an approach taken previously by Zhu, Devesa, Wu et al¹. Incident cancer cases were consolidated according to SEER and North American Association of Central Cancer Registries (NAACCR) rules^{2,3,4}. Only malignant tumor codes were used, following state and federal surveillance reports methods^{5,6,7}. SEER's multiple primary rules were applied within the same record⁸.

Age-specific and age-adjusted rates were calculated and compared to the SEER population with SEERStat⁹ software (SEER-18¹⁰) used to generate the incident rates. The age-specific incident rate is the number of malignant tumor cases in the study period divided by the sum of the annual population counts as of 30 September for each 5-year age-group.

The age-adjusted rates for AD and civilian populations, weights the age distribution of the two populations to the U.S. Census 2000 distribution¹¹. The AD population data were calculated from DEERS records and include all women who were in active service including National Guard and Reservists activated as of 30 September of each year. The reader is referred to Appendix A for additional technical information.

It is important to note that breast cancer case definitions and rate calculations among active duty women presented here used methodology comparable to that used by SEER. The case finding approach and calculations differ from the methods used in Part 1 of this report and the rates reported in Part 1 and in this section cannot be directly compared.

A total of 719 incident breast cancer cases in AD females for ages 20-59 years were identified in years 2000-2010 (Table 1). Army had the highest percentage of incident cases (42%) followed by Air Force (32%), respectively. Over half of the incident cases were white females (55%), and most cases (58%) were age 40 years or older. A total of 368 (51%) cases were first diagnosed in the six-year period from 2000 through 2005; the remaining 351 (49%) cases were first diagnosed in the five-year period from 2006 through 2010.

Table 1: Overall number of incidence malignant breast cancer, by Military Service, race, age group and year of diagnosis, Active Duty females, 20-59 Years, 2000-2010

Characteristic	Number of Cases	Percentage of Total Cases
<i>Total</i>	719	100.0
<i>Service</i>		
Army	299	41.6
Navy	144	20.0
Air Force	233	32.4
Marine Corps	19	2.6
Coast Guard	6	0.8
Other	18	2.5
<i>Race</i>		
White	395	54.9
Black	264	36.7
Other/Missing/Unknown	60	8.3
<i>Age Group*</i>		
20-24 years	19	2.6
25-29 years	27	3.8
30-34 years	91	12.7
35-39 years	167	23.2
40-44years	176	24.5
45-49 year	138	19.2
50-54 years	67	9.3
55-59 years	34	4.7
<i>Year of Diagnosis</i>		
2000 - 2005	368	51.2
2006 - 2010	351	48.8

*No breast cancer cases were identified among Active Duty females under 20 years of age.

Source: Automated Central Tumor Registry Data (ACTUR), and Standard Inpatient Data Repository (SIDR).

Tables 2 and 3 present the age-specific rates and overall age-adjusted rates of breast cancer for the AD females and the SEER-18 population, respectively. The age-adjusted rate during 2000-2010 for AD females was 93.68 per 100,000 population (95%CI 91.63, 95.76)), while the age-adjusted rate for civilian females was 107.76 per 100,000 population (95%CI 107.35, 108.18); thus, AD women had a statistically significant lower incidence of breast cancer. As expected, the breast cancer age-specific rates increase dramatically among age groups in both populations.

Table 2: Age-Specific and Age-Adjusted Incidence Rates, AD Females, All Races, Ages 20-59 Years, 2000-2010

Age Group	Number of Cases	AD Females	Age-Specific Rate (per 100,000)	US Census 2000 Population Weights (P25 - 1130)*
20-24 years	19	938,082	2.03	0.12
25-29 years	27	599,079	4.51	0.12
30-34 years	91	371,336	24.51	0.13
35-39 years	167	303,916	54.95	0.15
40-44years	176	194,181	90.64	0.15
45-49 year	138	91,137	151.42	0.13
50-54 years	67	36,380	184.17	0.11
55-59 years	34	11,102	306.25	0.09
Final Age-Adjusted Female Active Duty Rate (per 100,000)				
20-59 years	719	2,545,213	93.68 (95% CI 91.63, 95.76)	

NMCPHC Health Analysis
Source: ACTUR and DMDC data, DEC 2013
Numerators include malignant incident cancer cases.
*Rates are per 100,000 and adjusted using the U.S. 2000 Standard Population (P25-1130) ⁶.
Note: 95% Confidence Intervals for Adjusted Rates were calculated using the method of Fay and Feuer (1997).

Table 3: Age-Specific and Age-Adjusted Incidence Rates, SEER-18 Female Population, All Races, Ages 20-59 Years, 2000-2010

Age Group	Number of Cases	Population Counts	Age-Specific Rate (per 100,000)	US Census 2000 Population Weights (P25 - 1130)*
20-24 years	449	31,066,160	1.45	0.12
25-29 years	2570	31,088,736	8.27	0.12
30-34 years	8286	31,572,688	26.24	0.13
35-39 years	19970	33,411,213	59.77	0.15
40-44years	41627	34,549,546	120.48	0.15
45-49 year	63645	33,916,407	187.65	0.13
50-54 years	71,292	30,912,198	230.63	0.11
55-59 years	74,368	25,980,833	286.24	0.09
Final Age-Adjusted Female SEER-18 Rate (per 100,000)				
20-59 years	282,207	252,497,781	107.76 (95% CI 107.35, 108.18)	

NMCPHC Health Analysis
Source: Surveillance, Epidemiology, and End Results (SEER) Program (www.seer.cancer.gov)
SEER*Stat Database: Incidence – SEER 18 released April 2013, based on the November 2012 submission.
Numerators include malignant incident cancer cases.
*Rates are per 100,000 and adjusted using the U.S. 2000 Standard Population (P25-1130) ⁶.

Discussion

While the breast cancer cases reported in Part 1 of this Report are defined differently from the cases based on ACTUR data, the findings from the two analyses are consistent. Using administrative data in Part 1, we reported 705 cases of invasive breast cancer among AD women aged 20 – 54, compared with

the 719 malignant tumor cases, in women aged 20 – 59 here using ACTUR data. In both analyses, the incidence rate increased with increasing age group. The following differences in methodology are noted:

- Breast cancer cases are defined in ACTUR as diagnosed and primary cancer treatment received in a military treatment facility (MTF). Breast cancer cases with diagnosis and primary treatment rendered primarily in a civilian setting will not be documented in ACTUR.
- Since each ACTUR case is an incident tumor, replicating SEER methodology, AD females may be counted more than once, if they had multiple primary tumors. In Part 1 the analysis counted unique women as breast cancer cases. SEER multiple primary rules were applied⁸.
- ACTUR cases are identified and classified using pathology findings and malignant tumor behavior codes following state and federal surveillance reports methods^{5,6,7}. Part 1 cases were identified using a diagnosis on a claim record which is not based on pathology findings.

A previous study of cases diagnosed between 1990 and 2004 found that AD females had significantly higher incidence rates relative to civilians. The difference in findings has several possible explanations. In addition to the difference in time periods examined, the two studies are affected by a change in the composition of the AD female population, and possibly a difference in methodology. During the period between 2000 and 2010, Reservists and National Guard women on active duty comprised 10.5 to 19.0 percent of the total AD female population. This phenomenon was largely related to the conflicts in Iraq and Afghanistan. Reserve and National Guard women comprised 27 percent of women deployed during this period. ACTUR data does not capture data needed to distinguish cases for Active component women from Reserve/Guard component women, so we cannot determine the number of each that contributed to our total case count.

Limitations

There are some limitations associated with the data sources. Under-reporting of breast cancer cases within ACTUR that may have affected these findings. While DoD policy requires reporting of each cancer case from a MTF into ACTUR across the three Medical Services, some MTFs, especially small ones, may not have the staffing to fully comply with this requirement. If breast cancer cases were diagnosed and treated primarily at military facilities that are not resourced adequately to meet reporting requirements, it would result in missing cases. In addition, civilian facilities that render cancer treatment to DoD beneficiaries under the TRICARE benefit are not required to report data to ACTUR. Thus, if active duty women with breast cancer are identified and treated primarily in civilian settings, they may be excluded in this analysis. Activated Reserve and Guard component women may be more likely to receive their treatment in civilian facilities. Because it is not possible to separate cases in ACTUR by component, it is unclear how many cases each component contributes to the total number of cases, and, therefore, how many cases might be missing. The similarity in the number of malignant tumors reported here and number of invasive breast cancer cases reported in Part 1 which includes activated Reserve and Guard women, suggests however, that underreporting in ACTUR likely had a minimal effect on this analysis.

Summary

This analysis of female breast cancer tumor incidence in active duty members and civilians from 2000 – 2010, using SEER case definitions and consolidation rules, found significantly lower age-adjusted breast cancer rates among AD females relative to the SEER female population. The rates among the military population, however, may be underestimated, if the active duty breast cancer patients received most of their cancer treatment in civilian facilities. The number of cases of breast cancer among the AD population was consistent with those reported in Part 1, which used administrative data to identify cases and a different definition.

References

1. Zhu K, Devesa S, Wu H, Zahm S, Jatoi I, Anderson W, Peoples G, Maxwell L, Granger E, Potter J, McGlynn K. Cancer Incidence in the U.S. Military Population: Comparison with Rates from the SEER Program. *Cancer Epidemiology Biomarkers Prev*, 2009 June; 18(6):1740-1745. Doi:10.1158/1055-9965.EPI-09-0041.
2. National Program of Cancer Registries-Modeling Electronic Reporting Project (NPCR-MERP), Centers for Disease Control and Prevention, Department of Health and Human Services. Accessed December 20, 2013 from http://www.cdc.gov/cancer/npcr/informatics/aerrod2/pdf/merp_glossary_1100708.pdf
3. SEER Cancer Registration & Surveillance Modules, Case Consolidation. Accessed December 20, 2013 from <http://training.seer.cancer.gov/operations/standards/scope/consolidation.html>
4. North American Association of Central Cancer Registries (NAACCR) Standards for Cancer Registries Volume III. Standards for Completeness, Quality, Analysis, Management, Security, and Confidentiality of Data. Accessed December 20, 2013 <http://www.naacr.org/LinkClick.aspx?fileticket=hfVzJKUCRM8%3d&tabid=134&mid=474> .
5. Prostate Cancer Monograph. Health Analysis, Navy & Marine Corps Public Health Center, August 2012. NAACCR Annual Conference 2013 poster abstract location (P-01): <http://naacr.org/EducationandTraining/2013ACPosters.aspx>.
6. Cancer Statistics, Trends, and Multiple Primary Cancer Analyses from the SEER Program. Hayat M, Howlader N, Reichman M, and Edwards B. Accessed January 2, 2014 from this site <http://theoncologist.alphamedpress.org/content/12/1/20.full>
7. Howlader N, Noone AM, Krapcho M, Garshell J, Neyman N, Altekruse SF, Kosary CL, Yu M, Ruhl J, Tatalovich Z, Cho H, Mariotto A, Lewis DR, Chen HS, Feuer EJ, Cronin KA (eds). SEER Cancer Statistics Review, 1975-2010, National Cancer Institute. Bethesda, MD, based on November 2012 SEER data submission, posted to the SEER website April 2013. Accessed January 8, 2014 from http://seer.cancer.gov/csr/1975_2010/
8. SEER Cancer Registration & Surveillance Modules, Multiple Primaries & Histology Coding Rules, Accessed December 20, 2013 from <http://training.seer.cancer.gov/rules/changes/>.
9. Gordis L. *Epidemiology*, Fourth Edition. Saunders Elsevier, 2009.
10. Surveillance, Epidemiology, and End Results (SEER) Program (www.seer.cancer.gov) SEER*Stat Database: Incidence – SEER 18 Regs Research Data + Hurricane Katrina Impacted Louisiana Cases, Nov 2012 Sub (2000-2010) <Katrina/Rita Population Adjustment> - Linked To County Attributes – Total U.S., 1969-2011 Counties, National Cancer Institute, DCCPS, Surveillance Research Program, Surveillance Systems Branch, released April 2013, based on the November 2012 submission
11. Current Population Reports. Population Projections of the United States by Age, Sex, Race, and Hispanic Origin: 1995 to 2050. United States Census P25-1130. U.S. Department of Commerce, Economics and Statistics Administration, Bureau of the Census. Issued February 1996. Accessed <http://www.census.gov/prod/1/pop/p25-1130/p251130.pdf> on December 28, 2013.

PART 3. BREAST CANCER OUTREACH, TREATMENT SPECIALISTS, AND DOD TREATMENTS RECEIVED

Introduction

In this Part, we describe the methods used within the MHS to enhance awareness of breast cancer, assess breast cancer risk, and promote adherence to evidence-based practices for prevention, early detection, and treatment of breast cancer among all MHS beneficiaries, including AD service members.

Patients' access to clinicians who are trained to provide breast care, as well as facilities that have obtained the highly regarded ACS CoC is discussed. Finally a detailed summary of treatments rendered to breast cancer patients diagnosed between 2000 and 2010 is examined by pathologic stage and year of diagnosis.

Task 8. An assessment of the effectiveness of outreach to members of the Armed Forces to identify risks of, prevent, detect, and treat breast cancer

Outreach to AD service members occurs primarily at the point of care, including individual risk-assessment, and through annual community-wide marketing efforts aimed at increasing breast cancer awareness through education on breast health and informing beneficiaries of the care available at the MTF and their coverage for breast care provided by their TRICARE benefit.

Routine Clinical Screening – Facilitated by Electronic Reminder System

Outreach for breast cancer in the clinical setting occurs during routine appointments for screening related to women's health, by self-referral if a beneficiary identifies a suspicious lesion or simply has concerns, or simultaneously as part of another preventive services examination. The clinic visit provides the first and best opportunity for a provider and patient to address breast health, a discussion which is facilitated by embedded reminders within the electronic interface used by providers to document clinical care. This provider reminder tab is based on the U.S. Preventive Services Task Force (USPSTF) evidence-based recommendations regarding preventive measures, including screening tests, counseling, immunizations, and preventive medications¹. The breast care reminder is embedded both in the standard patient encounter note and within the workflow for a more focused well-woman examination. Additionally, when attempting to assess breast cancer risk, the interface provides a link to the National Cancer Institute's Breast Cancer Risk Calculator <http://www.cancer.gov/bcrisktool/> allowing the provider to assess the patient's individual risk of breast cancer, communicate about risk, and to refer the patient for the appropriate follow up².

Breast Cancer Awareness Education

Each year during the month of October, TRICARE promotes breast cancer awareness through outreach efforts celebrating breast cancer awareness month. Articles on breast cancer are published annually in newsletters, on the DHA and Managed Care Support Contractors websites. Additionally, webinars on the Preventive Services offered under the TRICARE benefit are broadcasted live and archived, offering beneficiaries the opportunity to learn more about their TRICARE benefit through viewing or listening to the webinar as well as having the opportunity to ask questions if participating during the live broadcast. Each individual Service also reaches out to AD service members through celebrating breast cancer awareness month and through local efforts such as health fairs and newsletters.

The TRICARE Benefit

The TRICARE benefit is the clear illustration of the Department's commitment to ensuring access to quality preventive care and cancer treatment. Consistent with USPSTF recommendations, the current TRICARE benefit the following services are provided or covered:

1. Clinical breast exams for women under age 40 may be performed during a covered periodic preventive health exam. After age 40, clinical breast exams should be performed annually.
2. Annual screening mammograms for women beginning at age 40. For women who have a 15% higher risk, TRICARE covers mammograms annually beginning at age 30.
 - Annual screening breast magnetic resonance imaging (this is in addition to the annual screening mammogram) beginning at age 30, for women who have a 20% or greater

- lifetime risk of breast cancer, according to risk assessment tools based on family history, or who have any of the following risk factors: °
- Women with a known BRCA1 or BRCA2 gene mutation
 - Women with a first degree relative (parent, child, sibling) with a BRCA1 or BRCA2 mutation, and have not had genetic testing themselves
 - History of radiation therapy to the chest between the ages of 10 and 30
 - History of LiFraumeni, Cowden, or hereditary diffuse gastric cancer syndrome, or first-degree relative with a history of one of these syndromes
3. Additionally, TRICARE may cover Breast magnetic resonance imaging (MRI) for the following indications:
- Occult breast cancer with a negative physical exam and negative mammography
 - Presurgical planning for locally advanced breast cancer, before and after completion of neoadjuvant chemotherapy
 - Evaluation of suspected cancer recurrence
 - Detection of muscle or chest wall invasion in patients with posteriorly located tumor
 - Guidance for procedures such as vacuum assisted biopsy or preoperative wire localization of lesions
4. Genetic Testing and Counseling
- Testing is covered when medically proven and appropriate, and when the results of the test will influence the medical management of the patient. Routine genetic testing is not covered
 - Counseling services that are not medically necessary for the treatment of a diagnosed medical condition.

Outreach Performance Standards

Within the Active component, 94.5% of enlisted and 74.5% of officers are under the age of 41, and mammography screening is not recommended for these women defined as average risk^{3,4}. Indeed, routine screening of lower age women may introduce more risks (anxiety, unnecessary biopsies, and radiation exposure) than appropriate given the small number of breast cancers that would be identified in this population. The MHS utilizes The Healthcare Effectiveness Data and Information Set (HEDIS®), a set of process measures widely used by health plans to measure performance across a range of health care and service activities, in its overall assessment of the quality of care provided throughout the MHS. The HEDIS® mammography measure is used by TRICARE to assess the effectiveness of outreach efforts for breast cancer screening in those AD service women for whom it is appropriate. Of note from 2010 through 2013, mammography screening for AD members, meeting age criteria (40-69 years of age), exceeded the 90th percentile of the average national HEDIS score, the benchmark for comparing organization performance against that of commercial health plans, Medicare and Medicaid.

Effectiveness of outreach may also be assessed by examining self-report data contained in the Military Health System (MHS), Health Care Survey of DoD Beneficiaries (HCSDB), which includes a measure for utilization of mammography within the past 12-24 months. The HCSDB is a congressionally mandated annual survey designed to measure users' satisfaction with and access to health care in the MHS. The survey is revised and sent to a new sample of approximately 200,000 users every year. Beginning in January, 2001, surveys are mailed out every quarter. Many questions are taken from the Consumer Assessment of Healthcare Providers and Systems (CAHPS) Health Plan Survey version 4.0, which is often used to assess civilian users' experiences with health care. Other questions are devised to meet the special needs of the MHS.

The benchmarks for the HCSDB are taken from Healthy People national objectives (2010 and 2020) the goals of which are set by the federal government for the percentage of Americans receiving preventive care. Regarding the utilization of mammography for breast cancer screening, within the MHS, the percentage of beneficiaries overall and in particular AD service members, who report having received a mammogram within the past 12-24 months and who met age criterion exceeded the national benchmarks set by Health People on an annual basis from 2002-2012; being above the 81% and 70% goal for those years (Health Care Surveys of DoD Beneficiaries 2002-2010).

Despite the robust benefit, the Department recognizes that access to genetics testing and counseling is limited for many beneficiaries, due to either location or circumstance. The MCC has begun to investigate the possibility of increasing genetics testing and counseling outreach to the MTFs through the use of telegenetics. The MCC telegenetics project will focus on individuals with an inherited susceptibility to cancer and will be designed to assess diagnostic accuracy, impact of service delivery on patient outcomes as well as confidence and satisfaction of telegenetic encounters(s) by healthcare providers, patients and their families.

Genetic tests have the potential to move beyond specialty genetic services into the mainstream health care arena at an unprecedented rate due to the development of evidence-based practice guidelines, commercially available genetic tests, insurance coverage, and legislative protection against genetic discrimination. The ultimate aim of these discoveries is to optimize the public's health. This benefit is hinged on health care professionals having an adequate understanding of the clinical implications of genetic and genomic technologies and information. Most immediately, the need is to increase the ability of health care professionals to use genetic information to identify those who may be at risk to develop disease and would benefit from genetic testing, as well as to provide tailored interventions to detect cancer early and/or reduce disease risk.

Identification of individuals at high risk for cancer requires a detailed family history assessment which is performed in all healthcare setting by all types of healthcare providers^{5,6}. Cancer family histories are used in two primary ways: identifying at-risk individuals who have evidence of a cancer syndrome in themselves or their family and may be a candidate for a genetic test; and/or to establish individual cancer risk predictions over time which can inform cancer risk management⁷. More than 55 hereditary cancer syndromes have been identified,⁸ and the most common syndromes are those associated with breast, ovarian, and gastrointestinal cancers. Evidence based guidelines, such as those for individuals who carry a hereditary breast or colorectal cancer susceptibility mutation, provide recommendations for more intensive cancer screening and risk reduction interventions that can significantly reduce morbidity and mortality in this population^{9,10,11}. The identification of patients with hereditary cancer syndromes or other familial predisposition to cancer, is integral to the delivery of appropriate, evidence based potentially life-saving, risk reducing and cost-saving care. However, despite the evidence of benefit, studies have shown that health care providers need access to experts to assist in the identification of individuals who need risk assessment, genetic counseling and/or testing as well as access to these services¹².

Family history remains a critically useful and underutilized tool for health risk assessment and identification of those who would be candidates for genetic testing or changes in medical management^{6,13}. Yet even when family history is collected, interpretation may require consultation with a genetic healthcare specialist before referring a patient for consideration of genetic testing. Current access to qualified genetic healthcare providers within the world-wide Military health system is

extremely limited. Once referrals are generated, traditional in-person consultations often require more than one visit, extended time away from work with travel to the facility in which the provider is stationed, and/or referral into the community via Tricare. Each of these creates both economic and workforce hardships. While the number and proximity of genetic specialists both inside and outside the Military Health System is extremely limited, the telegenetics program offers the hope of making these services more accessible for beneficiaries who need them¹⁴.

Summary

Outreach efforts for breast cancer in the MHS promote dialog between patients and their providers about breast cancer awareness, risk, prevention, detection, and treatment. This is accomplished in the clinical setting by incorporating USPSTF evidence-based recommendations a link to the National Cancer Institute's Breast Cancer Risk Calculator into the workflow used by providers to conduct and document individual patient exams. On the population level, outreach is accomplished through webinars and newsletters on the DHA and Managed Care Support Contractors websites, which promote use of the robust cancer prevention services covered under the TRICARE benefit. The effectiveness of these outreach efforts is apparent by the qualitative and quantitative evidence that the number of AD woman who received mammography, when indicated, exceeds national benchmark. Efforts are ongoing to leverage technology to expand access to specialized services that may not be widely available. An excellent example of this is the telegenetics program at the MCC/WRNNMC that enables service members to access genetics specialists located at the MCC, from any MTF.

Task 4. The availability and training of breast cancer specialists within the Military Health System

Comprehensive breast care within the MHS is a collaborative multidisciplinary effort enlisting a range of healthcare professionals. The professionals include primary care providers and breast cancer specialists, at various levels of care, who are accessible to active component members locally or regionally through MTFs, through TRICARE's civilian provider network, or through the DoD tertiary care system including the CBCP located in the MCC/WRNNMC.

Screening and detection

Breast cancer screening and detection, the first level of care, may begin with a patient's self-referral for a suspicious lesion, or with a provider identifying risk factors for breast cancer as part of a patient's medical and family history, and/or following a clinical breast examination (CBE). Risk factor identification and CBE are performed predominantly by primary care providers (family practitioners, internists, physician assistants, and nurse practitioners), obstetricians and gynecologists and general surgeons. Specific training to perform CBEs is included as part of their general professional training. Within the MHS, some radiation technicians also receive this training and are certified to perform CBEs in conjunction with administering mammography. Another member of the breast care team, whose capability is readily available either on site or remotely, is the radiologist, who reviews both screening and diagnostic mammograms as well as breast MRIs, thereby supporting efforts to detect lesions that may or may not require further evaluation. Of note TRICARE follows guidelines set by USPTF regarding screening mammography including specific criteria for both when MRI is indicated instead of mammography (i.e., high risk individuals) and recommendations for the use of genetic testing.

Diagnosis

When a diagnostic evaluation is required, and when treatment for breast cancer is initiated, the next level of care available to the active component patient is primary treatment by a general surgeon. When recommended, other breast cancer specialists, including medical and radiation oncologists, also are

available within the MHS, each collaborating to develop an individualized treatment plan. Following surgical treatment, plastic surgeons are also available within the MHS to provide cosmetic, reconstructive and plastic surgery as part of comprehensive care for the patient with breast cancer. These specialists obtain their training and are certified through an established Board certification process or fellowship within their respective specialties. If a required specialty care is not available at a local MTF, patients can be referred to breast cancer specialists in the civilian network of TRICARE authorized providers, to larger military medical centers, including the WRNNMC, which represents the third level of care.

When local or regional medical or surgical capabilities are exceeded or otherwise desired, patients also can self-refer or be referred by their healthcare provider to the CBCP/WRNNMC which utilizes a multidisciplinary approach to breast disease, integrating prevention, screening, diagnosis, and treatment with advances in risk reduction, tissue banking, research, and informatics. Here detection and follow-up screening occur within a newly designed Breast Imaging Center. Treatment includes pre and post-operative breast care, physical therapy (including pre-operative assessment, post-operative therapy and lymphedema management), education through a variety of resources, case management, social work services (such as individual or family counseling/psychotherapy and various support groups), and genetic counseling. Genetic counseling is also available, either in-person or remotely through telecommunication consultation, at the CBCP/WRNNMC.

Of note, thirteen DoD healthcare facilities have obtained the highly regarded ACS-CoC (i.e., 2 Air Force, 8 Army and 3 Navy). This certification process documents that a healthcare facility supports the full complement of breast care competencies and is committed to ongoing monitoring and quality improvement. Only a very few MTFs are accredited registry programs with the CoC. These programs require specialized administrative, as well as clinical capabilities, in which the cancer registrars play a critical role. Registry staff are active participants in tumor boards and coordinate the local cancer committees. In accordance with ACS standards, the local cancer committee is responsible for identifying avenues for providing high quality, state-of-the-art personalized cancer care; improving the quality of care and support for health education initiatives (prevention, screening and early detection). Under the DON registry umbrella, there are three accredited cancer registries: WRNNMC, Navy Medical Center Portsmouth, Navy Medical Center San Diego. Because of their accreditation, these facilities are required to track compliance with CoC quality performance metrics; formerly 3 standards but increased to 6 standards February 2014. The three facilities track their own compliance with feedback provided by the CoC; compliance is compared within respective states, regions and by type of facility. All three of these facilities have teaching program accreditation defined by an extensive range of residency programs and an annual caseload of more than 500 analytic cases a year. WRNNMC is the only Breast Center in the DoD that is accredited separately by the more rigorous National Accreditation Program for Breast Centers, also administered by the ACS.

Summary

The clinical expertise within the MHS includes both primary care providers and breast cancer specialists who are appropriately trained to provide services throughout the spectrum of breast care. In cases where specialty services are not locally available, the patient is referred to one of many providers within the robust TRICARE network of military and civilian facilities. This network includes thirteen MTFs around the country that are accredited by the ACS-CoC, as well as the CBCP/WRNNMC which is also accredited by National Accreditation Program for Breast Centers. Efforts are ongoing to continually improve the service member's access to genetic testing and other special services through telemedicine that enhance prevention and early detection of breast cancer.

Task 3. An analysis of breast cancer treatments received by such members and the source of such treatments

In this task, an analysis of breast cancer treatments received by female members of the Armed Forces serving on active duty is presented. The population of interest for treatment assessment included AD female in-situ and invasive breast cancer cases diagnosed between 2000 and 2010, documented within ACTUR for women 18-59 years of age.

Methods

Because data from the central registry was unavailable for this analysis, ACTUR records from each reporting facility were examined to identify the best source of treatment for each patient. Approximately 70% of ACTUR data represent single source records while 30% are multiple records representative of patients diagnosed and treated in more than one facility for treatment of a single episode of cancer. Care was taken to select the record that was most representative of the entirety of treatment received at multiple facilities; higher class of case for multiple records for the same patient were given preference. Conforming to nationally recognized cancer data standards, only analytic cases were included in this analysis¹⁵. Patients diagnosed with recurrent disease were excluded. Histology was limited to carcinoma. Non-carcinomas of the breast have different AJCC staging schemas and treatment options.

Stage at time of diagnosis is a critical element in the determination of treatment for breast cancer. In this analysis, documented treatment is stratified by pathologic stage. Due to the expansiveness of the data, surgical codes are concatenated into more manageable groupings. Data was stratified using the American Joint Committee on Cancer (AJCC) pathologic stage group system, the major language for cancer reporting and statistical analysis. Stage group is a derivative of three elements, tumor (T), node (N) and metastasis (M). Data (years 2000-2002) are consistent with the 5th edition of the manual;¹⁵ 2003-2009 data conforms to the breast schema delineated in the 6th edition of the AJCC Staging Manual¹⁶ Patients diagnosed in 2010 (exclusively) reflect pathologic stage groups defined in the 7th Edition of the AJCC Staging Manual¹⁷. Pathologic stage reflects the edition of the AJCC Staging Manual in use at time of diagnosis; 5th Edition (2000-2002), Sixth Edition (2003-2009) and Seventh Edition (2010).

The Facility Oncology Registry Data Standards for 2013 (FORDS) is the source for treatment codes and definitions¹⁸. Additional technical detail is provided in Appendix B.

Results

Table 1 provides frequency counts of treatment (surgery, radiation and systemic) among both in situ and invasive breast cancer cases, by pathologic stage grouped by year of diagnosis. Overall, 360 (97%) and 374 (91%) of cases in 2000 – 2005 and 2006 – 2010, respectively, received a documented surgical intervention. Among the 37 cases with no documented surgical intervention, 32 had no documented staging information. For Stage 0, 71% and 64% of women in 2000 – 2005 and 2006 – 2010, respectively received lumpectomies as opposed to mastectomies. As staging progresses from Stage I through Stage IV, lumpectomy was provided with decreasing frequency and mastectomy was provided with increasing frequency. Radical mastectomy occurred with less than 2% frequency across the whole study period.

Adjuvant therapy comprises the range of radiation, chemotherapy, or hormonal therapies and is generally considered part of the primary treatment in breast cancer along with the surgical intervention. Most of the women in all stage classifications received at least one form of adjuvant therapy following surgery and many received multiple therapies. Radiation therapy, predominantly beam therapy, was given to approximately 50% of women in both year groups. Brachytherapy was given to only 2 patients

across the whole study period. Chemotherapy was administered to 76% and 60%, and hormone therapy was administered to 40% and 50% of women, in 2000 – 2005 and 2006 – 2010, respectively.

Neoadjuvant therapy is treatment given as a first step to shrink a tumor before the main treatment (usually some form of surgery) is rendered. This treatment is usually applied to advanced forms of cancer. Few women over the study period received neoadjuvant therapy, likely due to the high number of cases that are being diagnosed at earlier stages. Note: Data items reflective of neo-adjuvant therapy (1) radiation/surgical sequence and (2) systemic/surgery sequence were added as required data items in 2004 and 2006 respectively.

Specific differences between the 5th, 6th and 7th Editions of the AJCC Staging Manual (site breast) become apparent upon inspection of Table 1. Involved supraclavicular nodes are classified as (M1) distant metastasis in the AJCC 5th Edition but reclassified to regional nodal involvement (N3) in the 6th Edition. Patients with involved supraclavicular nodes diagnosed between 2003 and 2009 would not be assigned to Stage IV reflecting a change from Edition 5 to Edition 6. There are 8 cases designated as IV cases (diagnosed between 2000 and 2002). Review indicates that assignment to pathologic stage IV was based on metastasis to distant organs such as brain or lung not nodal involvement. Therefore stage IV cases for 2000-2002 in Table 1, would not be down-staged utilizing 6th Edition criteria. The 7th Edition of the AJCC Staging Manual was published in 2010. Cases diagnosed in 2010 reflect changes to the 7th Edition (site breast) TNM and pathologic stage groupings. The table includes 85 cases diagnosed in year 2010. Twenty-nine of these cases were staged as IA (26 cases) or IB (3 cases) reflecting a sub-stratification of Stage I into (IA and IB) respectively. The stratification of Stage I reflects a need to distinguish small tumors T1 with no nodal involvement with small tumors (IA) (with exclusively micrometastases in lymph nodes (N1mi)(IB).

Table 3.1: Treatment Modalities Stratified by Pathologic Stage, Years 2000-2005 and 2006-2010, AD Females (Ages 18-59) Diagnosed with Carcinoma of the Breast (in situ and invasive)

Diagnosis Years	Number of Cases	Number (% by stage) of Surgical Patients						Number (% by stage) of Radiation Patients		Number (% by stage) of Systemic Patients		Number (% by stage) of neoadjuvant therapy Patients (Pre-Surgical)	
		No Surgery of Primary Site	Local Tumor Destruction	(BCS) Lumpectomy	Mastectomy*	Radical Mastectomy	Unknown if Surgery Performed/Not Documented	Beam	Brachytherapy	Chemotherapy	Hormone Therapy	Systemic Therapy**	Radiation Therapy***
2000 - 2005													
All stages	370	5 (1.4)	0	169 (45.7)	185 (50.0)	6 (1.6)	5 (1.4)	194 (52.4)	0	281 (75.9)	148 (40.0)	5 (1.4)	0
Stage 0	7	0	0	5 (71.4)	1 (14.3)	1 (14.3)	0	3 (42.9)	0	1 (14.3)	1 (14.3)	0	0
Stage I	126	0	0	73(57.9)	52 (41.3)	1 (0.8)	0	63 (50.0)	0	73 (57.9)	52 (41.3)	0	0
Stage IA	0	0	0	0	0	0	0	0	0	0	0	0	0
Stage IB	0	0	0	0	0	0	0	0	0	0	0	0	0
Stage II	4	0	0	2 (50.0)	2 (50.0)	0	0	2 (50.0)	0	3 (75.0)	2 (50.0)	0	0
Stage IIA	101	0	0	56 (55.4)	44 (43.6)	1 (1.0)	0	50 (49.5)	0	87 (86.1)	36 (35.6)	4 (4.0)	0
Stage IIB	45	0	0	15 (33.3)	29 (64.4)	1 (2.2)	0	31 (68.9)	0	44 (97.8)	20 (44.4)	0	0
Stage III	1	0	0	0	1 (100)	0	0	1 (100)	0	1 (100)	0	0	0
Stage IIIA	28	0	0	4 (14.3)	23 (82.1)	1 (3.6)	0	20 (71.4)	0	26 (92.9)	18 (64.3)	1 (3.6)	0
Stage IIIB	9	0	0	3 (33.3)	6 (66.7)	0	0	7 (77.8)	0	9 (100)	3 (33.3)	0	0
Stage IIIC	8	0	0	0	8 (100)	0	0	6 (75.0)	0	8 (100)	4 (50.0)	0	0
Stage IV	12	0	0	2 (37.5)	10 (83.3)	0	0	5 (41.7)	0	11 (91.7)	3 (25.0)	0	0
Unknown/Not Stated	29	5 (3.4)	0	9 (31.0)	9 (31.0)	1 (3.4)	5 (17.2)	6 (20.7)	0	18 (62.1)	9 (31.0)	0	0
2006 - 2010													
All stages	410	5 (1.2)	1 (0.2)	159 (38.8)	205 (50.0)	9 (2.2)	31 (7.6)	202 (49.3)	1 (0.2)	245 (59.8)	206 (50.2)	36 (8.8)	5 (1.2)
Stage 0	69	0	0	44 (63.8)	24 (34.8)	1 (1.4)	0	34 (49.3)	0	2 (2.9)	35 (50.7)	2 (2.9)	0
Stage I	87	0	0	43 (49.4)	41 (47.1)	2 (2.3)	1 (1.1)	41 (47.1)	0	52 (59.8)	41 (47.1)	0	0
Stage IA	26	0	0	11 (42.3)	14 (53.8)	0	1 (3.8)	9 (34.6)	1 (3.8)	12 (46.1)	17 (65.4)	2 (7.7)	1 (3.8)
Stage IB	3	0	0	2 (66.7)	1 (33.3)	0	0	2 (66.7)	0	2 (66.7)	2 (66.7)	0	0
Stage II	1	0	0	0	1 (100)	0	0	0	0	1 (100)	1 (100)	0	0
Stage IIA	71	0	0	26 (36.6)	43 (60.6)	2 (2.8)	0	30 (42.3)	0	61 (85.9)	39 (54.9)	9 (12.7)	0
Stage IIB	29	0	0	8 (27.6)	20 (70.0)	1 (3.4)	0	18 (62.1)	0	27 (93.1)	13 (44.8)	2 (6.9)	1
Stage III	1	0	0	0	1 (100)	0	0	1 (100)	0	1 (100)	1 (100)	1 (100)	0
Stage IIIA	41	1 (2.4)	1 (2.4)	6 (14.6)	31 (75.6)	1 (2.4)	1 (2.4)	29 (70.7)	0	37 (90.2)	26 (63.4)	5 (12.2)	0
Stage IIIB	3	0	0	0	1 (33.3)	1 (33.3)	1 (33.3)	2 (66.7)	0	2 (66.7)	1 (33.3)	2 (66.7)	0
Stage IIIC	7	0	0	2 (28.6)	5 (71.4)	0	0	6 (85.7)	0	7 (100)	4 (57.1)	2 (28.6)	0
Stage IV	7	4 (57.1)	0	0	3 (42.9)	0	0	4 (57.1)	0	5 (71.4)	4 (57.1)	2 (28.6)	0
Unknown/Not Stated	65	0	0	17 (26.2)	20 (30.8)	1 (1.5)	27 (41.5)	26 (40.0)	0	30 (46.2)	22 (33.8)	9 (13.8)	3 (4.6)

NMCPHC Health Analysis

Source: ACTUR data, Dec 2013

*Mastectomy includes: Subcutaneous mastectomy; total simply mastectomy with or without contralateral (uninvolved) breast, with or without reconstruction; bilateral mastectomy for inflammatory carcinoma, and modified radical mastectomy with or without removal of contralateral (uninvolved) breast with or without reconstruction.

** Systemic/Surgery (systemic treatment prior to surgery) data element added 2004

*** Radiation/Surgery Sequence (radiation therapy prior to surgery or before and after surgery or intraoperative) data element added in 2006

Limitations

Accurate, comprehensive cancer data for purposes of clinical research and Congressional inquiries is dependent on support for a strong cancer reporting system. Essential components include: a robust central cancer registry, a viable, up-to-date standards compliant data collection application and trained, certified cancer registrars. Under-reporting is a concern within ACTUR. DoD policy requires reporting of each cancer case from a MTF in ACTUR and is required per Army, Navy, and Air Force directives. Some MTFs, especially small ones, are not adequately resourced to meet reporting standards, primarily due to unfilled registrar positions. The absence of trained registrars impairs the collection of vital cancer data, resulting in incomplete or missing case reports.

The ACTUR system, itself, also limits the number of treatments that may be entered, and does not require the user to enter the date when treatment was rendered, which impairs the analysis of the timing and sequencing of treatments among those that receive multiple treatments. Furthermore, some

treatments may only be reported in text fields that cannot be electronically queried. This requires the registrar to manually extract information from each record to compile aggregate treatment information.

In addition, civilian facilities that render cancer treatment to DoD beneficiaries under the TRICARE benefit are not required to report data to ACTUR and cases identified and treated in civilian settings are not included in this analysis. For these reasons, the treatments described here may not be complete picture of all treatments rendered.

Summary

Treatment modalities by year of diagnosis and pathologic stage illustrate several positive trends in the diagnosis and treatment of breast cancer. Approximately 72% of women diagnosed over 2000-2010 were either Stage 0, I or II, indicating that the screening practices of clinical breast examinations and mammography are detecting tumors early while they can still be treated with the hopes of cure or an extended life expectancy. Additional evidence supporting the notion of effective early detection measures include the frequent application of breast conserving surgery and the infrequent use of neo-adjuvant therapy, typically offered prior to surgery for more advanced cancers. While these treatment findings are believed to be reasonable complete, the compilation of these data, required manual review and extraction of data from facility-level registry and administrative records that could not be electronically queried.

References

1. U.S. Preventive Services Task Force. U.S. Preventive Services Task Force Home Page. <http://www.uspreventiveservicestaskforce.org/index.html>. Accessed February 25, 2014.
2. National Cancer Institute. Breast Cancer Risk Assessment Tool. 2013; <http://www.cancer.gov/bcrisktool/Default.aspx>. Accessed February 25, 2014.
3. Institute of Medicine. Breast cancer and the environment: A life course approach. DC: National Academy of Sciences; 2012.
4. Enewold L, McGlynn KA, Shriver CD, Zhu K. Mammography screening by race/ethnicity among U.S. servicewomen, 2009-2010. *Mil Med*. Dec 2012;177(12):1513-1518.
5. Murff HJ, Byrne D, Syngal S. Cancer risk assessment: quality and impact of the family history interview. *Am J Prev Med*. Oct 2004;27(3):239-245.
6. Qureshi N, Wilson B, Santaguida P, et al. Collection and use of cancer family history in primary care. *Evid Rep Technol Assess (Full Rep)*. Oct 2007(159):1-84.
7. Calzone K, Wattendorf D, Dunn BK. The application of genetics and genomics to cancer prevention. *Semin Oncol*. Aug 2010;37(4):407-418.
8. Lindor NM, McMaster ML, Lindor CJ, Greene MH. Concise handbook of familial cancer susceptibility syndromes - second edition. *J Natl Cancer Inst Monogr*. 2008(38):1-93.
9. National Comprehensive Cancer Network. Breast Cancer: National Comprehensive Cancer Network; 2013.
10. National Comprehensive Cancer Network. Colorectal Cancer Screening. NCCN Clinical Practice Guidelines in Oncology: National Comprehensive Cancer Network; 2013.
11. Domchek SM, Gaudet MM, Stopfer JE, et al. Breast cancer risks in individuals testing negative for a known family mutation in BRCA1 or BRCA2. *Breast Cancer Res Treat*. Jan 2010;119(2):409-414.
12. Brandt R, Ali Z, Sabel A, McHugh T, Gilman P. Cancer genetics evaluation: barriers to and improvements for referral. *Genet Test*. Mar 2008;12(1):9-12.
13. Valdez R, Yoon PW, Qureshi N, Green RF, Khoury MJ. Family history in public health practice: a genomic tool for disease prevention and health promotion. *Annu Rev Public Health*. 2010;31:69-87 61 p following 87.

14. Burke W, Culver J, Pinsky L, et al. Genetic assessment of breast cancer risk in primary care practice. *Am J Med Genet A*. Mar 2009;149A(3):349-356.
15. *AJCC Cancer Staging Manual, Fifth Edition*, American Joint Committee on Cancer, Lippincott-Raven, Philadelphia, 1997.
16. *AJCC Cancer Staging Manual, Sixth Edition*, American Joint Committee on Cancer, Springer, New York, 2002.
17. *AJCC Cancer Staging Manual, Seventh Edition*, American Joint Committee on Cancer, Springer, New York, 2010.
18. *Facility Oncology Registry Data Standards (FORDS) Manual (2013) and earlier editions*. Commission on Cancer of the American College of Surgeons, Chicago, 2013.

PART 4. RISK FACTORS ASSOCIATED WITH BREAST CANCER

Introduction

Parts I and II presented new analyses of military data sources on the incidence of breast cancer among females and males in the Armed Forces. This part addresses potential risk factors that may contribute to breast cancer risk among service members when activated, also reviews lifestyle and personal factors independent of military status. The focus is on risk factors for female breast cancer because very little is known about male breast cancer which is extremely rare.

Task 6. Identification of potential factors associated with Military Service that could increase the risk of breast cancer for members of the Armed Forces serving on Active Duty

This section presents a summary of research, expert panel findings, and occupational studies about risk factors for breast cancer most directly relevant to the active duty population. The focus of risk factor literature is on females, as male breast cancer is extremely rare,^{1,2} there are few direct epidemiological studies, and any attempt to understand separate risk factors in males may require international studies in order to accrue enough cases¹⁻⁵. It opens with a framework and introduction of key concepts regarding risk. After this introduction, the section is organized into three broad topics.

- Lifestyle risk
- Environmental and occupational risk factors
- DoD environmental and occupational risk management programs

Framework and Concepts

A vast array of scientific research is contributing to a more sophisticated understanding of the complexity of multiple factors associated with risks of breast cancer. An Institute of Medicine framework⁶ that focused on post-menopausal breast cancer incidence, organized individual risk factors in three broad domains:

- societal/cultural (e.g., country of birth, race/ethnicity, physical activity),
- physical/chemical (e.g., latitude, radiation/medical imaging, endocrine disrupters), and
- biological (e.g., breast density, age at menarche, ancestry).

The 6th edition of the Breast Cancer Fund⁷ review was focused on the connection between the environment and breast cancer risk. It focused on four environmental domains and their interaction with other risk factors known to influence breast cancer risk.

- estrogens and progestins,
- radiation,

- other industrial non-endocrine disrupting chemical (non-EDC) compounds, and
- xenoestrogens and other endocrine disrupting chemicals (EDCs).

Several overarching themes emerge from any risk factor framework that are important considerations when interpreting studies of breast cancer incidence and trying to draw conclusions about trends over time (i.e., 2000 vs. 2010) or differential rates among population groups (i.e., active duty military vs. civilians). These overarching themes, some evident in Figure 6-1, include:

- a complex model of causation for cancer,
- recognition that the personal life-cycle is comprised of windows of variation in vulnerability to particular risk factors,
- the notion that latency between exposure to environmental toxins and development of cancer is unknown, and
- recognition that association of risk factors with breast cancer does not establish causation.

Each theme is briefly summarized next:

Complex Model of Causation. One model of causation for breast cancer, displayed in Figure 6-1, demonstrates its complexity, with many unknown relationships among genetic, lifestyle, and environmental factors. There may be both direct effects of some factors on mammary tissue, but also interactive effects on cellular and extracellular processes in mammary tissues⁷⁻⁹. There are interactions between various environmental chemicals and radiation, as well as interactions of environmental exposures with genetic, reproductive history, and other lifestyle factors^{6,10}.

Personal life-cycle. Contributing to this complexity, is the role of life-cycle; particular factors may exert stronger effects during different stages of the life-cycle (e.g., childhood, reproductive events, menopausal stage, and age).

Long latency. Regarding environmental exposures, the latency period between exposure and development of malignant tumors is unknown, and again multifactorial¹¹. Research on minimal latency periods is scarce. An authoritative summary created for the World Trade Center (9/11 event) Health Program provides important insights; it demonstrates that latency periods differ among types of cancer (e.g., mesothelioma, solid tumors, thyroid) and by type of solid tumor (e.g., breast cancer vs. other). Latency also varies by type of carcinogenic agent and the latency window may be very wide. Based on the WTC Health Program literature review, one best estimate of a minimum latency period for all solid tumors is 4 years, but could be as high as 20 years.

In sum, complex causation, life-cycle influences, latency between exposure and tumor formation, are all critical to consider when interpreting trends in breast cancer incidence among active duty females or comparative differences in incidence between active duty and civilians. This means it is rarely feasible to determine the causal role of any specific factor to breast cancer in active duty females. Further, caution is required when translating evidence based on studies of the general population to the military population. Expertise specific to the military life-cycle, occupational requirements, and exposures during deployments, provides important insights in interpreting the risk factor literature.

Finally, given the above themes, it is important to recognize that epidemiologic studies that are based on DoD data only, that is, are based on observations of the active duty period only, are severely limited in detecting cancers with longer latency periods. To truly understand the effect of specific exposure events would require follow-up over many years, longer than the period that most service members remain active duty. Specifically, the vast majority of active duty females are very young and the majority

of enlisted members (not officers) separate after relatively short contracts of military service (from as little as two years to four years). Other approaches are needed to supplement active duty data. The VA, for example, has established the Gulf War Registry, for Veterans who have served in the Gulf during the 1990-1991 Gulf War, and extending through Operation Iraqi Freedom and Operation New Dawn.^h These themes also imply that cases of breast cancer among the youngest women may not be associated with any military factors but predominantly influenced by pre-military factors.

Approach to the Literature

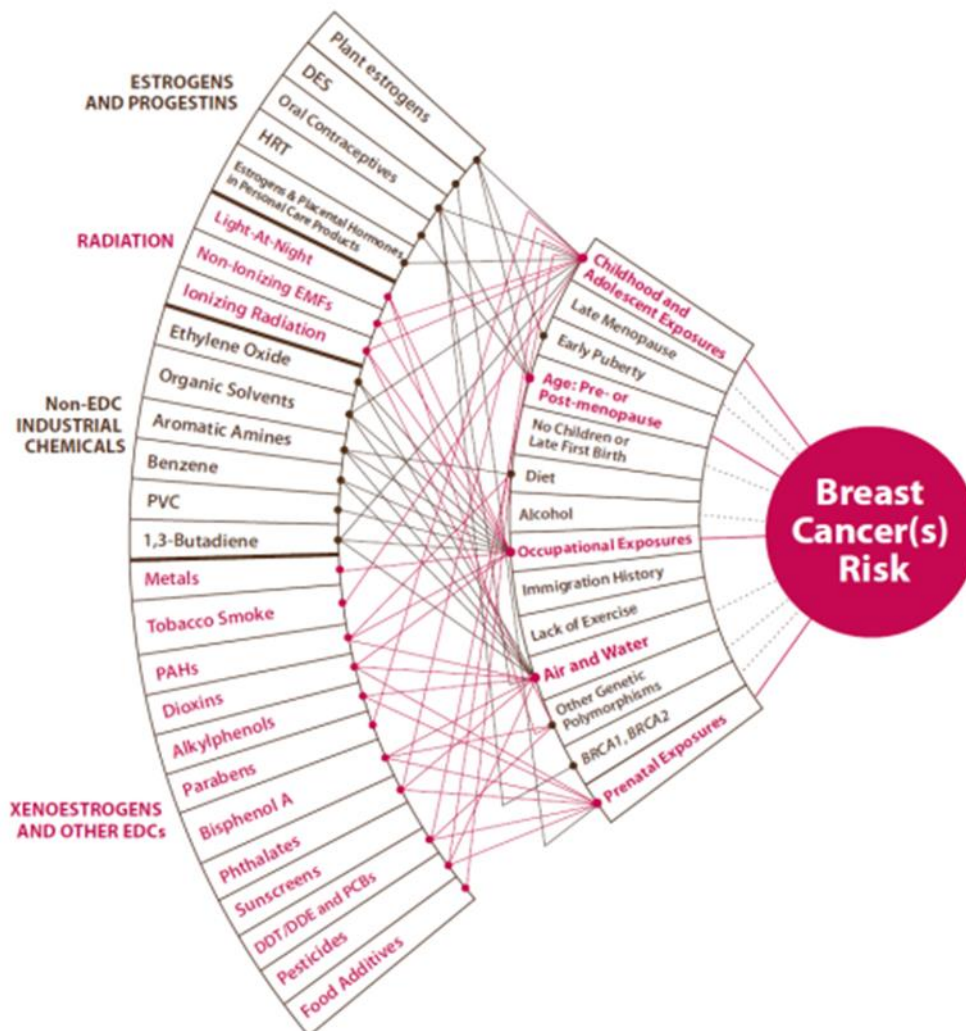
A systematic literature review was conducted to summarize and evaluate breast cancer risk factors. The review had three main objectives: (a) to identify well-established, high to medium risk factors for female breast cancer; (b) to find prevalence and exposure rates to risk factors for active duty women, and if possible, in comparison to civilian women; and (c) to identify studies of active duty women (or all military) specific to environmental and occupational exposure to risk factors and learn about DoD risk management and surveillance programs.

This review relies heavily on seminal reports of expert groups or other authoritative organizations, rather than a new assessment of the cancer literature. We identified and reviewed the most frequently referenced summary reports, and looked for consistency of the evidence across reports. We found additional peer-reviewed journal articles (e.g., meta-analyses and systematic reviews) to complement these expert reviews on some factors where evidence has recently changed and to identify cancer studies and occupational exposure studies of active duty populations. The literature review was conducted using PubMed, Defense Technical Information Center (DTIC), JSTOR, and Google Scholar databases. We also conducted extensive review of DoD and VA websites to retrieve public reports on military exposure events and retrieve descriptions of military occupational risk management programs. Below, personal or lifestyle risk factors are reviewed first, organized as modifiable or non-modifiable, followed by a review of evidence on environmental and occupational risk factors.

^h For more information see <http://www.publichealth.va.gov/exposures/gulfwar/benefits/registry-exam.asp>

Figure 6-1 Complexity of Breast Cancer Causation

Reprinted with permission from the State of the Evidence: The Connection between Breast Cancer and the Environment.⁷



Personal Lifestyle, Risk Factors

This review of personal risk factors emphasizes those that are modifiable because these are most amenable to being influenced by institutional prevention strategies and policies, and, understanding of these factors is most useful to women who wish to adopt lifestyles that minimize their own risk. Modifiable risk factors are defined as those related to personal lifestyle choice, or institutional policy choice, that influence the amount of, timing of, or who is exposed.

This review of personal risk factors also is focused on risk factors with strong evidence of elevating breast cancer risk, defining strength of evidence broadly, and assessing strength of evidence based on the two seminal reports, the New Zealand Health Technology Assessment (NZHTA) and the 6th edition, and The World Cancer Research Fund/American Institute for Cancer Research report.

The New Zealand Health Technology Assessment (NZHTA) report, Risk factors for breast cancer in women: a systematic review of the literature¹², was based on a systematic literature review using the

National Health and Medical Research Council criteria to assess the strength of the evidence. The NZHTA reported relative risk (RR) when assessing the magnitude of specific risk factors. Relative risks compare the risk of exposure to a disease for a population exposed to a specific risk factor compared to those without the same exposure⁸. Relative risks provide information about the strength of a relationship between an exposure, or risk factor, and a disease, in this case breast cancer. If there is no relationship between an exposure and a disease, the RR is 1.0. If an exposure increases the risk of a disease, the RR increases above 1.0. Thus, a higher RR indicates an elevated risk of developing a disease in association with a specific risk factor¹³.

The World Cancer Research Fund/American Institute for Cancer Research (WCRF/AICR), Breast cancer 2010 report: food, nutrition, physical activity, and the prevention of breast cancer¹⁰, an update of two prior reports, relied on an expert consensus panel, informed by systematic literature reviews, to consider the level of evidence and to draw conclusions about what they determined to be convincing or probable causes of breast cancer. The WCRF/AICR defined convincing evidence as the equivalent of “established” or “beyond reasonable doubt,” and where feasible distinguished conclusions specific to premenopausal versus postmenopausal women.

Modifiable, Well-Established Evidence

This section focuses on modifiable risk factors for breast cancer relevant for the active duty population in which there has been well-established evidence.

Summarized here and in Table 6-1 are specific individual risk factors with well-established evidence that has been documented by these two groups. The magnitude of risk categories used on Table 6-1 corresponds to the following estimated RR ratio ranges: strong (RR > 4.0), moderate (RR 2.0-4.0), and small (RR < 2.0).

While the relative risk for some factors may be relatively small, it is important to consider they may be cumulative and sometimes are expressed for small incremental behavioral changes. Thus, these modifiable factors may contribute, as a group, to observable differences in breast cancer incidence rates over time, or between breast cancer levels in the active duty military versus the general public.

The NZHTA concluded that hormonal contraceptives are a risk factor for breast cancer, and that recency of use was of importance. Specifically, current users of hormonal contraceptives had the highest risk, and the relative risk decreased as the number of years since stopping the contraceptives increased. The NZHTA noted that the panel considered other exposures, including oestrogen dose, type of oral contraceptives, use of non-hormonal contraceptives, and timing of use of contraceptives by age group; however, there were not enough eligible studies to formulate conclusions.

The NZHTA also concluded that current or long term use of hormone replacement therapy (HRT) is likely associated with a low level of increased risk of breast cancer, with relative risks up to 1.5.

Alcohol consumption was assessed by both the NZHTA and WCRF/AICR as increasing the risk of breast cancer. The NZHTA reported that as alcohol intake increased, there was a moderate increase in risk of breast cancer, with relative risks ranging from 1.5-2.0. By examining three systematic reviews, the panel concluded that the approximate increased risk was 10 percent for 10 grams of alcohol per day, 25 percent for 25 grams of alcohol per day, and 55 percent for 50 grams of alcohol per day. Thus, it concluded that there was convincing evidence that alcoholic drinks are a cause of premenopausal breast

cancer and that a dose-response relationship is apparent. The report noted that the expert panel did not identify a safe level, or safe threshold, for alcohol intake.

The WCRF/AICR concluded that there is convincing evidence that *lactation*, or breastfeeding, is protective for premenopausal breast cancer and that there is evidence of a dose-response relationship. The report explains that lactation is associated with an increase in the differentiation of breast cells, as well as lower exposure to endogenous sex hormones while breast feeding (during amenorrhea). Further, during lactation there is great exfoliation of breast tissue, and large epithelial cell death at the end of lactation, which may both contribute to a decreased risk in breast cancer due to elimination of cells with potential DNA damage.

The NZHTA concluded that *nulliparity*, defined as having never given birth to a viable infant, was a risk factor for breast cancer. Studies showed an increasing level of protection against breast cancer, as the number of births increased. The report noted that the lack of statistical control for the influence of breastfeeding may have biased some study estimates.

The Collaborative Group on Hormonal Factors in Breast Cancer¹⁴ conducted meta-analyses and found that the societal trends of industrial countries associated with small family size and short duration of breast-feeding, contributed substantially to the higher, and increasing, rates of breast cancer in industrial versus developing countries. While this group understood that women today would not be returning to the pattern of childbearing, it pointed out that shortened duration of breast-feeding was a major contributor to increased risk. The analyses found that the relative risk of breast cancer was reduced by 4.3 percent (95th percentile confidence interval [CI] 2.9-5.8) for each year that woman breastfeeds, in addition to a reduction of 7.0 percent (95 CI 5.0-9.0) for each birth¹⁴.

Finally, the WCRF/AICR concluded that *greater body fatness* is protective of breast cancer in premenopausal women, the age group of the majority of active duty women; however adult weight gain increases breast cancer risk among postmenopausal women. There is a substantial amount of evidence to support a dose-response relationship, yet there is no single well established mechanism to explain this. The expert panel explained that body fatness impacts hormone levels and oestrogens, which in turn support carcinogenesis and reduce programmed cell death, and stimulate inflammation in the body, which may contribute to initiation of cancers. On balance, throughout one's life, the decreased risk of premenopausal breast cancer associated with body fatness would be outweighed by the increased risk of postmenopausal breast cancer associated with body fatness because breast cancer is primarily diagnosed among post-menopausal women.

Modifiable, Less Established Evidence – Further Research Needed

Other frequently cited literature was reviewed to identify modifiable risk factors where the evidence is less established. Findings reported from these reports did not meet our criteria of “well established” evidence or evidence appeared inconsistent.

Cigarette smoking: Three of four frequently cited reports concluded that active cigarette smoking increases the risk of breast cancer⁶⁻⁸. Several studies also suggested that the duration of smoking and initiation of smoking at a younger age increased incidence of breast cancer¹⁵.

Physical activity: Evidence suggests that regular physical activity will reduce the risk for postmenopausal breast cancer⁸⁻¹⁰. However, evidence for physical activity as a protective factor for premenopausal breast cancer is limited^{10,16}.

Night Shift Work: Wang et al. completed a meta-analysis on 10 studies and found a modest increased in the relative risk associated with being ever exposed to night shift work and breast cancer (adjusted RR was 1.19 CI 1.05–1.35)¹⁷. They further found a dose–response relationship, that every 5-year increase of exposure to night shift work would correspondingly enhance the risk of breast cancer of the female by 3 percent and that an increase in 500-night shifts would result in a 13 percent increase in breast cancer risk. The findings of this meta-analysis confirm other meta-analyses^{18,19}, although the newer study reports a smaller magnitude of risk. However, further work is needed to understand the mechanism of action. At least one recent study stills find the balance of evidence is still weak.^{20,21} The IARC has classified night-shift work as possibly carcinogenic to humans, and the leading hypotheses suggest that exposure to artificial light at night leads to circadian system alteration and melatonin output reduction, which in turns gives rise to the levels of reproductive hormones such as estrogen^{19,22,23}.

Modifiable, None or Only Limited Evidence

Other personal lifestyle risk factors have been mentioned in prior research literature but the evidence appears limited or is otherwise inconclusive:^{7-10,24}

- Stress
- Chronic anxiety and depression
- Diet (including fat, soy, dairy, meat, and fruits and vegetables, dietary fiber, vitamin D)

The following modifiable risk factors had no evidence in the literature that they contribute to increased risk of breast cancer:^{7-10,24}

- Abortion
- Breast implants
- Wearing a bra or type of bra
- Hair dyes
- Antiperspirants or deodorants

Table 6-1. Modifiable risk factors for breast cancer, well-established in the scientific literature

Modifiable Risk Factors	Source	
	New Zealand Health Technology Assessment Report (NZHTA)	World Cancer Research Fund/American Institute for Cancer Research (WCRF/AICR)
Hormonal Contraceptives		
Current users	RR 1.24	--
1-4 years after stopping	RR 1.16	--
5-9 years after stopping	RR 1.07	--
10+ years after stopping	RR 1.01	--
Hormone Replacement Therapy	RR 1.0-1.5	--
Alcohol Consumption	RR 1.5-2.0	Convincing risk factor
Body Fat	--	Probable protective factor
Nulliparity	RR 1.0-1.5	--
Lactation	--	Probable protective factor

Notes: RR = relative risk

Non-Modifiable Risk Factors for Breast Cancer

The factors that appear to confer the greatest risk for breast cancer are largely non-modifiable characteristics, most importantly aging, as well as genetic contributions, and other biological differences, all relatively immutable. These characteristics are displayed in Table 6-2 and briefly listed below.

Breast cancer medical experts use information on these risk factors when counseling an individual woman concerned about her own risk. Medical providers may use a cumulative risk score to identify high risk women for aggressive preventive screening. Further, cancer experts know that some of these characteristics are associated with more aggressive forms of cancer, or with estrogen receptor-positive vs estrogen receptor-negative breast cancer.

There are six groups of personal characteristics that most literature agrees contribute to the highest increase in risk, that is, more than 4 times average risk, when present:

- the aging process (with each additional year comes increased risk),
- presence of certain genes (e.g., BRCA1 or BRCA2),
- having had a breast cancer tumor confers risk of a new tumor,
- atypical hyperplasia (that is, accumulation of abnormal cells in a breast duct or lobule),
- lobular carcinoma in situ (i.e., a noncancerous tumor), and
- increased density of breast tissue.

Moderate increased risk of breast cancer, that is an elevated risk of 2 to 4 times the average female, is associated with

- elevated levels of two hormones (endogenous postmenopausal estrogen and endogenous androgen), and
- having first degree relatives who have breast cancer.

Other biological factors that slightly increase the risk for breast cancer include:

- a history of benign breast disease,
- younger age at menarche,
- greater birth weight, and
- late menopause.

Table 6-2. Non-modifiable risk factors for breast cancer organized by estimates of relative risk, well-established in scientific literature

Personal Characteristic	Literature Sources
<i>High increased risk: 4 times or greater relative risk</i>	
Age, each year	NBOCC
50 and older vs. under age 50	ACS
65+ vs. <65 years, increases across all ages until age 80	
Personal gene mutations (BRCA1, BRCA2, ATM or TP53 gene)	NBOCC, ACS
Personal history of breast cancer (various indicators)	ACS
First breast cancer under age 40	NCBOCC
Breast cancer in opposite breast	NCBOCC
Ductal carcinoma in situ in same breast	
Atypical hyperplasia	ACS; NBOCC = 2.0-3.99*
Ductal	ACS
Lobular	
Lobular carcinoma in situ	NBOCC, ACS
Mammographically dense breast	ACS, NBOCC; NZHTA=greater than 2.0*
<i>Moderate increased risk: 2 to 4 times relative risk</i>	
High endogenous estrogen levels, postmenopausal	NBOCC, ACS
High androgen levels (i.e. testosterone)	ACS; NBOCC = 1.25-1.99*
First-degree relatives with breast cancer	
Two or more	NBOCC; ACS = greater than 4.0*
One	ACS; IOM=1.36-2.6*; NBOCC=1.25-1.99*
<i>Low increased risk: under 2 times relative risk</i>	
Personal history of benign breast disease	
Proliferate benign breast disease without atypia	NBOCC
Benign breast disease	IOM,
Personal history of endometrium, ovary, or colon cancer	NBOCC, ACS
Ashkenazi Jewish heritage	ACS
Early menarche	IOM, ACS, NBOCC
under 12 years old	IOM
Between 12-13 years old	IOM
under 15 years old	
Late menopause	IOM
45 or more years old	NBOCC, ACS
more than 55 years old	
Anthropometry / Height	IOM
At age 25, taller than 160cm	ACS, NBOCC
taller than 175 cm	
Notes: IOM = Institute of Medicine; ACS = American Cancer Society; NZHTA= New Zealand Health Technology Assessment Report; NBOCC - Australian National Breast and Ovarian Cancer Centre	
* Reported estimate in this source differs from overall category and is separately stated	

Distribution of Lifestyle Breast Cancer Risk Factors in Active Duty Females

Table 6-3 shows the prevalence of selected personal risk factors for breast cancer among the active duty female population, for which published data could be found. Where possible, this section presents comparative statistics for the active duty population and civilian women. While certain factors can be studied using routine DoD population surveys or analysis of DMSS data, for some factors only limited information on population or personal behaviors were found.

The DoD Survey of Health Related Behaviors among Active Duty Military Personnel (HRB Survey) is an anonymous, worldwide population-based assessment of active duty service members that is an important resource for capturing overall epidemiological trends of some of these measures. There are several items on the HRB survey that provide information about modifiable risk factors for breast cancer, including alcohol consumption, smoking, and items assessing body mass index and obesity.ⁱ

Alcohol Use: Almost 18 percent of active duty women either abstained from using alcohol or were former drinkers. Approximately one-quarter of active duty females reported binge drinking (4+ drinks on one occasion) at least once in the past month, compared to 19% of the general public. However, these estimates are not age-adjusted²⁵.

Smoking: Active duty women had nearly equivalent prevalence of current smoking compared to civilians (17.8% versus 18.6%); again these estimates are not age adjusted²⁵.

Body Mass Index: The 2011 HRB survey relied on the Centers for Disease Control and Prevention's definition of body mass index (BMI), based on height and weight, and found that among active duty women, over one-fourth of those aged 20 and older were considered overweight (BMI greater than or equal to 25 but less than 30), with estimates increasing with age, such that 40% of those aged 46-65 were considered overweight. Few active duty women were considered obese (BMI greater than or equal to 30), with the highest prevalence (10.4%) among those aged 36-45. The HRB survey found that among active duty women, over one-fourth of those ages 20 and older were considered overweight, with estimates increasing with age, such that 40% of those aged 46-65 were considered overweight. Few active duty women were considered obese, with the highest prevalence (10.4%) among those aged 36-45²⁶.

Oral Contraceptive Use: Using data from the Military Health System in 2004-2005, one study found that the age-adjusted prevalence of oral contraceptives among active duty females was 34.4%, which was statistically higher than in the general public (29.4%). Prevalence estimates in the military varied by race/ethnicity with black (29.8%) and Hispanic (32.2%) women having lower rates than Non-Hispanic whites (38.0%)²⁷.

Breastfeeding: One study of mothers giving birth at one National Navy Medical Center found that among the active duty members, 23% breastfed to 12 months postpartum, compared to 20% of civilian females in the U.S.²⁸.

Birth and Fertility Rates: The age-specific birth rates among active component women during the period 2001-2010 is presented in Table 6-3 and comparison to civilian women is presented in Table 6-4. The

ⁱ Information on the HRB Survey can be found at <http://tricare.mil/tma/dhcape/surveys/coresurveys/surveyhealthrelatedbehaviors/SHRB.aspx>

majority of births (51.8%) in the military were to very young women, ages 18-24 years; the mean maternal age at delivery increased from 24.9 years to 26.0 years over the period²⁹. Table 6-4 also presents the age-specific birth rates for civilian women in 2010³⁰. Caution must be taken in comparing active component and civilian rates; the active component is an average rate over 10 years while the civilian rate is for one year, and birth rates have been declining in the U.S. over this decade. Further, births to active component women before or after being in the military are not counted, so the actual rate is undoubtedly higher. The birth rate among very young active component women is higher than civilian counterparts, possibly conferring some protection against breast cancer. The birth rate in other age groups is lower in military women, which may be indicative of a lower total fertility rate.

Table 6-3. Prevalence of selected breast cancer risk factors, female active duty service members

Risk Factors	Source/Sample	Prevalence
Alcohol Use ^a	2011 HRB Survey Main Report: Surveyed active duty members from August 2011 – January 2012	11.8% abstainers
		6.1% former drinkers
		68.3% infrequent/light drinkers
		5.4% moderate
		8.3% heavy drinkers
Cigarette Smoking ^a	2011 HRB Survey Main Report: Surveyed active duty members from August 2011 – January 2012	67.6% abstainers
		14.6% former smokers
		5.8% infrequent smokers
		10.4% light/moderate smokers
		1.5% heavy smokers
Oral Contraceptive Use ^b	Military Health System Management Analysis and Reporting Tool (M2): Surveyed active duty members from October 2004 – September 2005	Age 18-19 – 33.2%
		Age 20-24 – 39.7%
		Age 25-29 – 39.7%
		Age 30-34 – 34.4%
		Age 35-39 – 36.2%
		Non-Hispanic White – 38.0%*
		Non-Hispanic Black – 29.8%*
Hispanic – 32.2%*		
Birth Rate ^c	Active duty members, 18-49 years old, hospitalization data, 2001-2010. (Age-specific birth rate per 1,000 person years)	Age 18-19 – 37.4
		Age 20-24 – 100.3
		Age 25-29 – 92.4
		Age 30-34 – 76.3
		Age 35-39 – 41.4
Breastfeeding ^d	51 active duty mothers of 253 surveyed mothers giving birth at National Naval Medical Center	23% of active duty mothers breastfed to 12 months postpartum
Overweight/Obesity BMI Measures ^a	2011 HRB Survey Main Report: 185,247 active duty members were surveyed.	Overweight, all ages – 34.4%
		Age 18-19 – 13.1%
		Age 20-25 – 29.7%
		Age 26-35 – 34.7%
		Age 36-45 – 45.1%
		Age 46-65 – 40.0%
		Obese, all ages – 6.4%
		Age 18-19 – N/A
		Age 20-25 – 4.0%
		Age 26-35 – 7.2%
		Age 36-45 – 10.4%
Age 46-65 – 8.0%		

[a Barlas, Frances M., Higgins, William Bryan, Pflieger, Jacqueline C., & Diecker, Kelly. \(2013\). 2011 Department of Defense Health Related Behaviors Survey of Active Duty Military Personnel. Fairfax, Virginia: ICF International](#)

[b Enewold, L. et al. Oral contraceptive use among women in the military and the general U.S. population. Journal of women's health 19, 839-845, doi:10.1089/jwh.2009.1706 \(2010\)](#)

[c U.S. Armed Forces Health Surveillance Center. Vol. 18, 16-17 \(2011\)](#)

[d Mao, C. Y., Narang, S. & Lopreiato, J. Breastfeeding practices in military families: A 12-month prospective population-based study in the national capital region. Military Medicine 117, 229-234 \(2012\)](#)

Table 6-4. Births per 1,000 person-years for active component females and 2005 and 2010 birth rate, civilian women

Age group	Active component ^a	Civilian women ^b
	Period 2001-2010	2010
20-24 years	100.3	90
25-29 years	92.4	108.3
30-34 years	76.3	96.5
35-39 years	41.4	45.9

a U.S. Armed Forces Health Surveillance Center. Vol. 18, 16-17 (2011)

b Table 6-4, footnote b. Martin JA, Hamilton BE, Ventura SJ. Births: Final Data for 2010. Vol 61. Hyattsville, MD: National Center for Health Statistics; 2012.

Environmental and Occupational Risk Factors

This section on environmental and occupational risk factors summarizes literature from many diverse sources. It begins with a review of chemicals identified in the Breast Cancer Fund report as linked to increased breast cancer risk. It then discusses publicly available reports of toxic exposures in U.S Armed Forces populations, and findings from studies of specific chemical exposures associated with selected job titles of active duty women.

Chemicals Classified as Breast Cancer Risk by Expert Organizations

Many chemicals have never been studied in ways that could indicate whether they might be relevant to breast cancer^{6,31}. For some chemicals or pollutants with unknown status, laboratory research may have established that the chemical causes mammary gland tumors in animals⁶. The assessment process in humans is hindered by many factors and methodological problems: inadequate exposure assessment, lack of access to populations with known high exposure, lack of preclinical markers that are useful given disease latency may be long.

Two expert organizations periodically review the body of evidence on hundreds of chemicals being used by households, by commercial organizations and in industrial settings as well as general air, water, and soil pollutants. They classify each chemical based on findings from research studies and the strength of the evidence.

- The IARC, the International Agency for Research on Cancer, a program of the World Health Organization, prepares monographs that provide government authorities with expert, independent, scientific opinion on environmental carcinogenesis.^j

^j See the following website for additional information on IARC principles and methods. <http://monographs.iarc.fr/ENG/Preamble/CurrentPreamble.pdf>

- The NTP is the National Toxicology Program of the U.S. National Institute of Environmental Health Sciences. One function carried out by the NTP is to inform the public about agents and chemicals that are known or reasonably anticipated to cause cancer in humans, which it communicates to the U.S. Health and Human Services Secretary in The Report on Carcinogens, a congressionally mandated, science-based, public health document.³² The report identifies agents, substances, mixtures, and exposure circumstances that are *known or reasonably anticipated* to cause cancer in humans.

Table 6-5. Environmental Chemicals Linked to Breast Cancer Classified by IARC and NTP Ratings

Chemical	Sources	Endocrine-disrupting
Classified as Known/Probable Link		
1,3-butadiene (industrial)	NTP, IARC	
Aromatic amines (persistent organochlorines)	IARC, (NTP=R.A.)	√
Benzene (industrial)	IARC, NTP	
DDT/ DDE (persistent organochlorines)	NTP, (IARC=Possible)	√
Dioxins	IARC, NTP	√
Ethylene oxide	IARC, NTP	
Metals	IARC, NTP	√
PCBs (persistent organochlorines)	IARC, (NTP=R.A.)	√
Polycyclic aromatic hydrocarbons (PAHs)	IARC, (NTP=R.A.)	√
Tobacco smoke (active and passive exposures)	IARC, NTP	√
Vinyl chloride (industrial)	IARC, NTP	
Classified as Possible/Reasonably Anticipated (R.A.)		
Heptachlor (pesticide/herbicide)	IARC	√
Unknown Link		
Alkylphenols	-	√
Bisphenol A (BPA)	-	√
Dieldrin and aldrin (pesticide/herbicide)	-	√
Parabens	-	√
Phthalates	-	√
Phytoestrogens	-	√
Polybrominated diphenyl ether (PBDE) fire retardants	-	√
Recombinant bovine somatotropin (rBST)	-	√
Sunscreen (UV filters)	-	√
Triazine herbicides: Atrazine	-	√
Zeranol (Ralgro)	-	√

[Source: Adapted from STATE OF THE EVIDENCE: THE CONNECTION BETWEEN BREAST CANCER AND THE ENVIRONMENT, 6th Edition2](#)

Table 6-5 presents the classifications attributed to the IARC and NTP, adapted from the 6th Edition of the Breast Cancer Fund research report, of the more common chemicals that females may be exposed to in U.S. households, industrial work sites as well as military activities^{7,33}. Chemicals that are hormonally active, in particular that mimic estrogen, a naturally-occurring hormone that is linked to breast cancer

risk, are particularly concerning. Other chemicals are suspected to affect the ability of the mammary glands to repair damage from carcinogenesis³¹.

Even among known carcinogens, many factors determine how much influence chemical exposure will have on a population of females, such as length of exposure, concentration, life-stage timing, and genetic susceptibility or vulnerability. However in general, the influence of these environmental toxins appears smaller than personal risk factors associated with genetic make-up or personal lifestyle.

Known Military Occupational or Environmental Exposures

The material in this section was derived primarily from literature and educational materials available to medical professionals and service members on DoD and VA websites. This information is presented in three sections: 1) exposures related to deployment activities, 2) other reported exposure events, and 3) studies on occupational exposures.

A final subsection describes extant surveillance programs of the military that maintain occupational and deployment information useful to operational commanders, medical professionals, or to specific service members who have a specific health concern.

Known Toxic Exposures Related to Deployment

The results of a small number of DoD environmental exposure assessments involving a large number of troops are documented on DoD or VA websites. This subsection contains a brief summary of public information, and any statement contained in those statements of risk specific to female service members or to cancer risk. Other DoD assessments are publicly available from websites of the U.S. Army Public Health Command or the VA.

Deployment-related exposures are relevant to the health of the majority of female active duty members, as one-half (50.6%) of female active duty members in 2011 have served on at least one deployment to Iraq and Afghanistan, with more than 21 percent deploying on two or more occasions (Table 6-6).

Table 6-6. Profile of deployment status of active component females, U.S. Armed Forces as of September 30, 2011

Number of deployments (OIF/OEF/OND)	% of females
Any deployment	50.6%
One deployment	29.3%
Two deployments	13.8%
Three or more deployments	7.4%

Source: Table adapted from the Armed Forces Health Surveillance Center, Medical Surveillance Monthly Report, Vol 18, no. 12, 201129

Qarmat Ali Water Treatment Facility (Iraq): The U.S. Army Public Health Command reported that during the spring and summer of 2003, about 830 Service members (number of males and females unknown) guarded a water treatment facility in the Basrah oil fields, and may have been exposed for a short period to hexavalent chromium³⁵. In September 2003, the water treatment plant site grounds were cleaned and covered with asphalt and no further exposure occurred, and, in October 2003 the U.S. Army conducted an environmental exposure assessment and medical evaluations of Soldiers. Long-term adverse health effects, such as cancer, are not expected from relatively brief, short-term exposure. Additionally, the VA has set up a free, special medical surveillance program to monitor the health of

Veterans who were at Qarmat Ali,^k and is proactively contacting individuals who were identified as ever being at the site and offering screening examinations.

Iraq and Afghanistan Burn Pits: Burn pits have operated widely at military sites in Iraq and Afghanistan. A 2011 report of the Institute of Medicine³⁶, focused on pulmonary function, and found inadequate or insufficient evidence of a relation between exposure to combustion products and cancer. It recommended improved methods be used to monitor air samples and assess the long-term health impacts on troops exposed to toxins from burn pits.

Other Reported Exposure Events

Depleted Uranium: Depleted uranium (DU) has the same chemical toxicity as natural uranium, but 40 percent less radioactivity. The National Toxicology Program (NTP), International Agency for Research on Cancer (IARC), and the EPA have not classified natural uranium or depleted uranium with respect to carcinogenicity. Nevertheless, to address risks associated with DU, the DoD has formal policies and practices in place to monitor potential DU exposure, a medical follow-up program, and training programs for personnel who could be exposed to DU³⁷. The U.S. military began using DU on a large scale during the 1990-1991 Gulf War in tank armor and some bullets made to penetrate enemy armored vehicles. Some active component members who served in OEF/OIF/OND have retained toxic embedded fragments in their bodies after combat blast injuries and are monitored for clinical care, and participate in a registry, at the Toxic Embedded Fragment Surveillance Center at the Baltimore VA Medical Center^{38,39}.

Waste Incinerator in Atsugi, Japan: From 1985 to 2001, personnel at the Naval Air Facility in Atsugi, Japan may have been exposed to environmental contaminants from off-base waste incinerators. The U.S. Navy found a potential for increased health risks and worked with the Japanese government to close the SIC in May 2001. Given the potential for long-term health effects, such as a possible increase in the lifetime risk for cancer, the Navy has informed those sailors and their families who lived at Atsugi during this period about the possible long-term health effects⁴⁰.

Japan's Nuclear Reactor Event: Three Fukushima Daiichi reactors in Japan released radiation into the environment on March 11, 2011, following an earthquake and tsunami. The DoD has determined that, based on air samples taken at the time of the incident, the estimated radiation doses calculated for all members of U.S Armed Forces groups are well below levels associated with adverse medical conditions. The additional risk of cancer from this exposure is considered extremely small. Specific information comes from a registry that the DoD established soon after the event, the Operation Tomodachi Registry (OTR)⁴¹ which includes nearly 75,000 DoD-affiliated individuals (active component and civilians) who were on or near the mainland of Japan from March 12, 2011 to May 11, 2011. The DoD has shared shore-based and/or fleet-based radiation dose estimates reports^l on a public website.

Occupational Exposure Studies Involving Military Women

While the scientific literature review found occasional small studies of toxic exposures in military populations, most studies on occupational exposure were not specific to military members. This section reviews research that reports on the type of exposure experienced by military women. Military women, being more likely than civilians to be in non-traditional jobs that may involve exposure to environmental

^k For additional information visit the VA website <http://www.publichealth.va.gov/exposures/qarmat-ali/index.asp>

^l See the dosage estimates for specific locations at <https://registry.csd.disa.mil/registryWeb/Registry/OperationTomodachi/DisplayEstimatedAreaDoses.do>

chemicals, have been the focus or included in a substantial proportion of the limited research conducted on occupational exposure to carcinogens among population of women.

The broad occupational titles, and the percent of positions that are filled by women, is contained in Table 6-7. The occupational data presented in the table is not a distribution, but rather the percent of all service members in the occupation that is female. Occupations such as electrical/mechanical equipment or infantry or gun crew specialties which may be classified as having higher exposure to toxic substances, have the lowest proportion of women in this enlisted positions, with 8.5 percent and 2.8 percent, respectively. Ideally, more detailed description on job titles of active duty females could be reported as it would be more useful when characterizing potential risk associated with occupation.

Table 6-7. Occupational profile of active component females, U.S. Armed Forces as of September 30, 2011

Occupational Category	% of Females within Category
Enlisted Occupations	
Health care specialists	30.5%
Functional support and administration	30.1%
Service and supply handlers	16.4%
Communications and intelligence specialists	14.3%
Other occupations enlisted	13.0%
Electronic equipment repairers	10.1%
Electrical/mechanical equipment repairers	8.5%
Infantry, gun crews, and seamanship specialists	2.8%
Officer Occupations	
Health care	39.2%
Administrators	26.6%
Supply, procurement and allied	19.1%
Other occupations	15.2%
Engineering and maintenance	10.9%
Tactical operations	5.2%

Source: Table adapted from the Armed Forces Health Surveillance Center, Medical Surveillance Monthly Report, Vol 18, no. 12, 2011 29

Volatile Organic Compounds in Army Women. Perhaps the most relevant study of breast cancer risk from occupational exposure is a study conducted by Christopher Rennix of the Navy Environmental Health Center and colleagues⁴² of breast cancer incidence in more than 270,000 enlisted active duty Army women who served between 1980 and 1996. It applied an innovative methodologically, to link job title histories, to workplace chemical evaluations of Army industrial hygienists. The hygienists subjectively evaluated each job title for exposure potential (high, medium, low, and none) of each of 21 volatile organic compounds (VOCs). VOCs include a range of organic solvents which are readily stored in breast tissue and have a known or suspected role in breast cancer, including chlorinated hydrocarbons, benzene, kerosene, and paint solvents. Although the data are now dated in terms of its perspective on current occupational assignments of women, this study is notable for several reasons. The authors comment on several occupation titles performed by Army women disproportionately when compared to civilian women (e.g., petroleum supply specialist). They studied how long Army women remained in the same job title (4.5 years), to assess duration of exposure. Through review of industrial hygiene records,

they classified 150 of 300 enlisted military occupation titles as having moderate to high exposure potential to VOCs, including some described as administrative in the job description. Finally, this study accounted for age, race, year of diagnosis, and person-time as confounders in its analysis of breast cancer incidence. Rennix et al.⁴² found there was a 48 percent increased risk (incidence rate ratio 1.48, 95% confidence interval 1.03-2.12) of breast cancer among enlisted Army women holding job titles rated by industrial hygienists as having a moderate to high potential for exposure to at least one VOC studied while on active duty between 1980-1996. It also examined the incidence for the top 21 job titles occupied by women and did not find significantly elevated risks among any of the job titles. The most serious limitation of this study, and of all active duty studies without longitudinal follow-up data, is the lack of information on breast cancer tumors that developed in the cohort after discharge from the military.

Compounds in Jet Fuel in Female Airmen. While not directly addressing the risk of breast cancer, in one study, 170 female Airmen and female civilians at 10 Air Force bases consented to a study of the potential effects of fuel and solvent exposure on menstrual cycle function by maintaining daily diaries and collecting daily urine samples⁴³. The authors established a link between two measures of the internal exposure dose of compounds in fuel, and measures of certain hormones prior to ovulation. Another notable study examined inhalation exposure among active component Airmen to jet propulsion fuel-8 (JP-8), the primary jet fuel used by the U.S. military⁴⁴. It collected personal air samples which were analyzed for benzene, ethylbenzene, toluene, xylenes, total hydrocarbons (THC), and naphthalene, and interviewed 73 Airmen, including 12 females, about their personal exposure to jet fuel. The job titles among Airmen included in the study were: Fuel systems, Fuel distribution/maintenance, Aircraft inspection/maintenance, and Administrative/clerical/healthcare. This study found that Airmen's self-report of personal exposure to jet fuel was a better surrogate for actual inhalation exposure than job title alone⁴⁴.

Radiation Exposure. Not unlike certain civilian occupations, certain military occupations include routine, and usually safe, exposure to radiation. Service members in these occupations receive special training and are monitored to ensure radiation exposure remains at safe levels. The broad occupations who are monitored for radiation exposure include those who:

- Serve on nuclear submarines and other nuclear ships or in shipyards
- Are involved in nuclear weapons handling and maintenance, including clean-ups after accidents
- Serve as X-ray or dental technicians

Blake and Komp of the U.S. Army discuss findings from the total exposure cohort with monitoring records (1945- 2012), over 2.27 million unique military-affiliated individuals. Presenting 2006 data, the collective effective dose was low in all branches: annually, 0.6-person Sv in the Air Force, 1.0 person-Sv in the Army and 1.3 person-Sv in the Navy and Marine Corps. The personnel working in Naval Reactors had a higher collective dose (20.0 person-Sv), similar to the nuclear industry as a whole⁴⁵.

Millennium Cohort Study. There are over 77,000 participants in the Millennium Cohort Study, a longitudinal interview study which includes oversamples of those who had been previously deployed, Reserve and National Guard members, and women. One study investigated the concordance between self-report and electronic occupations among female cohort active duty members, and described the proportion of women reporting they had ever been exposed to chemical or biological warfare, and the proportion that reported exposure within the last 3 years to potentially toxic environmental chemicals (i.e., depleted uranium, pesticides in sprays or uniform treatments and pesticides applied in the environment or around living facilities⁴⁶). Among 10,539 female respondents, self-report exposures

varied by occupational group. More than one-fifth of healthcare specialists and functional support specialists reported exposure to chemical or biological warfare in their lifetime. More than one-quarter of female electrical/mechanical specialists reported exposure to depleted uranium, and one-quarter of healthcare specialists and functional support specialists reported exposure to pesticides. While the classification of both occupation and chemical exposure in this study may be too gross to support the study of future breast cancer incidence in the cohort, the study demonstrates the feasibility and potential value of obtaining self-report measures for longitudinal studies of future health problems.

DoD Environmental and Occupational Risk Management

Some literature documents that the DoD, in some areas, such as radiation surveillance, has been a leader in establishing exposure guidelines and risk management procedures, and documents the significant improvements made by the DoD in documenting and assessing deployment environmental hazards and threats since 1991. Preventive medicine, environmental surveillance, and forward laboratory teams now deploy with troops to establish health protection deployment strategies^{47,48,49}. The DoD reports that its approach to medical surveillance of environmental exposures during deployments has seven steps: (1) exposure assessment, (2) identification of the target population, (3) surveillance for current exposures, (4) surveillance for long-term effects, (5) record keeping for environmental data, (6) analysis of surveillance data, and (7) communication of results⁵⁰.

For example, from 2001 to 2009 alone, deployed personnel collected over 24,500 air, water, soil, and bulk samples during deployment operations. These efforts have led to the creation of an environmental health surveillance database that has been used to investigate public health issues. However, gaps exist, especially in the assessment of individual exposures during deployment⁵¹.

Other than the specific event assessment already reported and the radiation data reviewed in the previous section⁴⁵, we did not find publicly available compiled data on the number of active component males and females with possible exposure to carcinogens from these surveillance programs.

The need for increased surveillance capacity was one lesson learned from the 1991 Gulf War. Hyam, Riddle, Trump et al.⁴³ reviewed the health findings of the 1991 Gulf War and changes to DoD health surveillance programs that have emerged, in part, in response to these lessons learned. Among the 697,000 U.S. troops deployed to the Gulf theater of operations in 1991, was included a higher proportion of women (7 percent) than previous combat operations. Although the deployed environment was harsh, there were very few wartime combat injuries, an unexpectedly low number of combat deaths (n=147), and the overall health of the returning troops was good. Nevertheless, within the U.S. and other countries with deployed forces, months after return there were emerging reports of varied illnesses and somatic symptoms that were characterized as unexplained^{47,52}. A study of Persian Gulf veterans matched data from central cancer registries in the District of Columbia and New Jersey with the records veterans who deployed to the Persian Gulf and non-Gulf veterans. Using a proportional incidence ratio, testicular cancer was found to be the only significantly increased malignancy among deployed Persian Gulf War veterans. The increase in malignancy became apparent 2 to 3 years after the war and peaked 4 to 5 years afterward⁵³.

Another investigation concluded that, up to 5 years since the end of the Persian Gulf War, no unique health problems were identified among women veterans, and during deployment their health needs were similar to that of men, with the exception of gynecological problems⁵⁴.

Discussion is ongoing regarding the current DoD approach to linking individual service members and environmental exposure data in order to assess health risks in a timely way. This discussion has focused on gaps, challenges in linking data for research purposes, and the areas where solutions are readily apparent and not apparent⁵⁵. In 2010, the AFHSC and the Uniformed Services University (USU) cosponsored an educational symposium and workshop on the assessment of potentially hazardous environmental exposures among military populations. Although not specific to breast cancer risk, the participants reached a consensus that environmental surveillance, and all the actions that must follow, must be improved and must start with early comprehensive planning⁵⁶. The consensus paper documents the type of data that should be used to define and characterize risks for an area, prior to occupying that area. It described the need for competent, trained personnel in adequate numbers to be sent to theaters of operation, and necessary sampling plans and communication with military leaders. Importantly, it advised a more comprehensive approach involving DoD partnerships with other agencies in the Federal government, such as the VA, to plan and execute environmental exposure scientific research⁵⁶.

Environmental Medicine Programs

Within the U.S. Army Public Health Command (USAPHC) are portfolios related to: maintaining and improving environmental health on installations and in deployment locations; providing laboratory sciences worldwide, providing commanders with informational products and the consultative services of occupational and environmental medicine, execution of DoD Instructions regarding the conduct of occupational medical examinations.

Hazards of military concern during deployment include even low levels of chemical warfare agents and toxic industrial chemicals in air, soil, and water. And, the health effects considered include delayed or chronic outcomes. The U.S. Army Center for Health Promotion and Preventive Medicine (now the USAPHC) establishes the military-specific exposure guidelines for deployed military personnel and uses a risk assessment process compatible with existing military operational risk management doctrine⁴⁹. HPPM also establishes the requirements for pre- and post-deployment evaluations and risk management decisions⁴⁸. USAPHC supports an environmental medicine program useful to deployment known as the Periodic Occupational and Environmental Monitoring Summaries (POEMS). POEMS are official DoD summaries of environmental exposures and health impacts at deployment base camps.

The USAPHC also has an environmental medicine program specific to occupational health, the Defense Occupational and Environmental Health Readiness System (DOEHRS). DOEHRS-IH is an information system allows the DoD Military Health System to manage occupational and environmental health risk data and actively track biological, chemical, physical health hazards and engineered nano object process to Service members worldwide⁵⁷. Relevant to this study, the DOEHRS-IH facilitates the following:

- Captures comprehensive, operational and work task potential exposures-based medical surveillance recommendations
- Tracks DoD lifetime personnel exposure data
- Captures workplace practices, use & recommendations of protection equipment, and occupational & environmental surveillance data in support of military operations worldwide (garrison, depot, shore-based, pre & post deployment)
- Captures environmental surveillance data for deployed and garrison locations
- Captures and maintains environmental exposure registries
- Provides an enterprise approach to identifying and documenting global and local occupational and environmental health hazards

- Captures information to monitor compliance with occupational health and safety federal law and directives
- Provides a foundation for the individual longitudinal exposure record.

An example of a well-established occupational risk monitoring program exists for *surveillance of radiation exposure*. Because of its unique employment of ionizing and non-ionizing radiation sources, the U.S. military has often been at the forefront in developing radiation safety technology and safety guidelines⁴⁵. Additionally, the DoD annually monitors 70,000 individuals for occupational ionizing radiation exposure. Blake and Komp⁴⁵ also describe a program to provide forward deployed dosimetry support when required by military operations, such as during Japan's nuclear power station disaster, and other unique programs specific to environmental exposures.

Environmental Health Surveillance Registries

The DoD may establish an environmental health surveillance registry when: 1) occupational and environmental health exposures could cause illness, or 2) when the exposure is not expected to cause illness, but individuals need access to exposure data. In either case, these registries will contain the names of all the individuals who were known or believed to have been exposed along with estimates of their exposure. An example of such a registry is the Operation Tomodachi Registry described previously. The DoD is developing other complex tools that identify chemicals in deployment environments with the potential to reduce human performance capacity, and that represent a complex database management system, integrating global satellite surveillance input to provide real-time decision-making support for deployed military personnel⁵⁸. The application of these real-time tools is unclear, however, for the monitoring of toxins that may have distal, rather than immediate, effects on health outcomes such as cancer incidence. The DoD Serum Repository (DoDSR) is an example of a central archive potentially useful for cancer and other public health research projects.^m Over 55 million sera are available for medical surveillance purposes and approximately 2.3 specimens are added each year.

Deployment Surveillance

The DoD's post deployment surveillance program requires that a health assessment be completed within 30 days after return from deployment, and a second health assessment to be completed 3-6 months post deployment⁵⁹. The post-deployment health assessment (PDHA) and post-deployment health reassessment (PDHRA) are completed by service members and have a clinician assessment component in which service members can have problems identified and receive referrals for treatment or follow-up care.

The PDHA also includes self-report items assessing if service members are worried about their health because of specific exposures, including, but not limited to: chlorine gas, depleted uranium, fog oils, industrial pollution, ionizing radiation, JP8 or other fuels, paints, pesticides, radar/microwaves, smoke from burning trash or feces, smoke from oil fire, solvents, tent heater smoke, vehicle or truck exhaust fumes, DEET insect repellent applied to skin, pesticide-treated uniforms, or nerve agent antidote injectors.

Summary

This Task section began with a description of the complex model of causation of risk factors associated with breast factor, and the special challenges associated with incidence of breast cancer in a population

^m For more information on the DoDSR go to <http://www.afhsc.mil/dodsr>.

of young women^{6,8-10,12}. The introduction included a caution that studies based only on observations of breast cancer in active duty females were limited because most females are observed for only a short window of time and the latency period after exposure, while unknown, is typically many years.

This review of risk factors has provided information on both modifiable and non-modifiable personal characteristics associated with breast cancer incidence, and summarized current understanding of the possible role of occupational and deployment-related exposures.

This information may be useful in several ways:

- Knowledge of these risk factors provides for better interpretation of comparative studies of breast cancer, such as, trends over time within active duty females, comparisons across occupational groups, and comparisons of active duty to the general population.
- DoD can review its health education and prevention messages and incorporate this risk factor information into advice and counseling for active component females, particularly those with a personal cancer history or at higher than average risk of breast cancer (e.g., family history of, prior breast tumor). For example, women should be counseled that alcohol consumption increases breast cancer risk, and women with above average risk may be advised to limit alcohol consumption.
- DoD can review whether its personnel procedures hinder or promote the choice of active duty women to breastfeed (and duration of breastfeeding). This may involve additional DoD research to understand the factors influencing the decision by active component women to initiate and continue breastfeeding.
- Research to identify the mechanism of action behind certain risk factors may permit the discovery of ways to mimic the therapeutic effect of factors that are impractical to change (e.g. biological changes associated with number of live births).
- There are knowledge gaps identified in this literature review where additional research might support improved knowledge of, and action to reduce, breast cancer risk factors among active duty women. These gaps include:
 - Lack of surveillance data on active duty women on some well-established risk factors: breastfeeding history and behaviors and factors influencing choices, number of women in occupations requiring night shift work and average number of night shifts worked, family history of breast cancer.
 - Lack of up-to-date, detailed chemical exposure data on occupations held by active duty women. DoD could support the replication of the Rennix et al. study.
 - Lack of longitudinal studies of cohorts of active duty women suspected to have experienced chemical or carcinogen exposure while on combat deployment. A 2010 educational conference co-sponsored by AFHSC and Uniformed Service University discussed the challenges that need to be addressed to study and take action on the environmental hazards exposures among military personnel.

References

1. Chavez-Macgregor M, Clarke CA, Lichtensztajn D, Hortobagyi GN, Giordano SH. Male breast cancer according to tumor subtype and race: a population-based study. *Cancer*. May 1 2013;119(9):1611-1617.
2. White J, Kearins O, Dodwell D, Horgan K, Hanby AM, Speirs V. Male breast carcinoma: increased awareness needed. *Breast Cancer Res*. 2011;13(5):219.
3. Ruddy KJ, Winer EP. Male breast cancer: risk factors, biology, diagnosis, treatment, and survivorship. *Ann Oncol*. Jun 2013;24(6):1434-1443.
4. Zygogianni AG, Kyrgias G, Gennatas C, et al. Male breast carcinoma: epidemiology, risk factors and current therapeutic approaches. *Asian Pac J Cancer Prev*. 2012;13(1):15-19.

5. Teo JY, Tan PH, Yong WS. Male breast cancer in Singapore: 15 years of experience at a single tertiary institution. *Ann Acad Med Singapore*. Jun 2012;41(6):247-251.
6. Institute of Medicine. Breast cancer and the environment: A life course approach. In: Medicine Tlo, ed 2012.
7. Breast Cancer Fund. State of the evidence: The connection between breast cancer and the environment. 6th ed. San Francisco: The Breast Cancer Fund; 2010.
8. American Cancer Society. Breast Cancer Facts & Figures 2013-2014. In: Society AC, ed. Atlanta, GA: American Cancer Society; 2013.
9. Australian National Breast and Ovarian Cancer Centre. Breast cancer risk factors: a review of the evidence. Surry Hills, New South Wales: National Breast and Ovarian Cancer Centre; 2009.
10. World Cancer Research Fund; American Institute for Cancer Research. Food, nutrition, physical activity and the prevention of cancer: a global perspective. Washington DC 2010.
11. Howard J. *White Paper on Minimum Latency & Types or Categories of Cancer*: World Trade Center Health Program; 2013.
12. Weir R, Day P, Ali W. *Risk factors for breast cancer in women: A systematic review of the literature*: Christchurch School of Medicine and Health Services; 2007.
13. Aschengrau A, Seage III GR. *Essentials of Epidemiology in Public Health*. Sudbury, MA: Jones and Bartlett Publishers, Inc.; 2003.
14. Collaborative Group on Hormonal Factors in Breast Cancer. Breast cancer and breastfeeding: collaborative reanalysis of individual data from 47 epidemiological studies in 30 countries, including 50302 women with breast cancer and 96973 women without the disease. *Lancet*. 2002;360(9328):187-195.
15. Collishaw NE, Boyd NF, Cantor KP, et al. Canadian Expert Panel on Tobacco Smoke and Breast Cancer Risk. In: Unit COTR, ed. Toronto: Canada: Ontario Tobacco Research Unit; 2009.
16. Monninkhof EM, Elias SG, Vlems FA, et al. Physical activity and breast cancer: a systematic review. *Epidemiology*. Jan 2007;18(1):137-157.
17. Wang F, Yeung KL, Chan WC, et al. A meta-analysis on dose-response relationship between night shift work and the risk of breast cancer. *Ann Oncol*. Nov 2013;24(11):2724-2732.
18. Jia Y, Lu Y, Wu K, et al. Does night work increase the risk of breast cancer? A systematic review and meta-analysis of epidemiological studies. *Cancer Epidemiol*. 2013.
19. Megdal SP, Kroenke CH, Laden F, Pukkala E, Schernhammer ES. Night work and breast cancer risk: a systematic review and meta-analysis. *Eur J Cancer*. Sep 2005;41(13):2023-2032.
20. Ijaz S, Verbeek J, Seidler A, et al. Night-shift work and breast cancer--a systematic review and meta-analysis. *Scand J Work Environ Health*. Sep 1 2013;39(5):431-447.
21. Kamdar BB, Tergas AI, Mateen FJ, Bhayani NH, Oh J. Night-shift work and risk of breast cancer: a systematic review and meta-analysis. *Breast Cancer Res Treat*. Feb 2013;138(1):291-301.
22. Davis S, Mirick DK, Stevens RG. Night shift work, light at night, and risk of breast cancer. *Journal of the National Cancer Institute*. Oct 17 2001;93(20):1557-1562.
23. Leonardi GC, Rapisarda V, Marconi A, et al. Correlation of the risk of breast cancer and disruption of the circadian rhythm (Review). *Oncol Rep*. Aug 2012;28(2):418-428.
24. International Agency for Research on Cancer. World Cancer Report 2008. In: International Agency for Research on Cancer, ed. Lyon, France: World Health Organization; 2008.
25. Barlas FM, Higgins WB, Pflieger JC, Diecker K. *2011 Department of Defense Health Related Behaviors Survey of Active Duty Military Personnel*. Fairfax, Virginia: ICF International; 2013.
26. Barlas FM, Higgins WB, Pflieger JC, Diecker K. *2011 Department of Defense Health Related Behaviors Survey of Active Duty Military Personnel*. Fairfax: ICF International; 2013.

27. Enewold L, Brinton LA, McGlynn KA, Zahm SH, Potter JF, Zhu K. Oral contraceptive use among women in the military and the general U.S. population. *Journal of women's health*. May 2010;19(5):839-845.
28. Mao CY, Narang S, Lopreiato J. Breastfeeding practices in military families: A 12-month prospective population-based study in the national capital region. *Military Medicine*. 2012;117:229-234.
29. U.S. Armed Forces Health Surveillance Center. Births, active component 2001-2010, MSMR. Vol 182011:16-17.
30. Martin JA, Hamilton BE, Ventura SJ. Births: Final Data for 2010. Vol 61. Hyattsville, MD: National Center for Health Statistics; 2012.
31. Brody JG, Moysich KB, Humblet O, Attfield KR, Beehler GP, Rudel RA. Environmental pollutants and breast cancer: epidemiologic studies. *Cancer*. Jun 15 2007;109(12 Suppl):2667-2711.
32. National Toxicology Program (NTP). Report on Carcinogens. 12 ed: U.S. Department of Health and Human Services, National Toxicology Program,; 2011.
33. Gray J, Evans N, Taylor B, Rizzo J, Walker M. State of the evidence: the connection between breast cancer and the environment. *International journal of occupational and environmental health*. Jan-Mar 2009;15(1):43-78.
34. U.S. Armed Forces Health Surveillance Center. Numbers and Characteristics of Women in the Active Component, U.S. Armed Forces, 2011. Vol 182011:18-19.
35. U.S. Army Public Health Command. Health Assessment of 2003 Qarmat Ali Water Treatment Plant Sodium Dichromate Incident. Edgewood, MD U.S. Army Public Health Command,; 2010.
36. Institute of Medicine. *Long-Term Health Consequences of Exposure to Burn Pits in Iraq and Afghanistan*: The National Academies Press; 2011.
37. Force Health Protection & Readiness Policy & Programs. Policies: DoD Policies on Possible Depleted Uranium Exposure. 2014; http://fhp.osd.mil/du/dod_policy.jsp. Accessed February 8, 2014.
38. U.S. Department of Veterans Affairs. Toxic Embedded Fragment Surveillance Center. *Public Health, Military Exposures* 2014; http://www.publichealth.va.gov/exposures/toxic_fragments/surv_center.asp#. Accessed February 8, 2014.
39. U.S. Department of Veterans Affairs. Depleted Uranium. *Public Health, Military Exposures* 2013; http://www.publichealth.va.gov/exposures/depleted_uranium/index.asp#. Accessed February 8, 2014.
40. U.S. Department of Veterans Affairs. Waste Incinerator in Atsugi, Japan. *Public Health, Military Exposures* 2013; <http://www.publichealth.va.gov/exposures/sand-dust-particulates/atsugi.asp>. Accessed February 10, 2014.
41. U.S. Department of Defense EHSR. Operation Tomodachi Registry. <https://registry.csd.disa.mil/registryWeb/Registry/OperationTomodachi/DisplayAbout.do>. Accessed February 10, 2014.
42. Rennix CP, Quinn MM, Amoroso PJ, Eisen EA, Wegman DH. Risk of breast cancer among enlisted Army women occupationally exposed to volatile organic compounds. *Am J Ind Med*. Sep 2005;48(3):157-167.
43. Reutman SR, LeMasters GK, Knecht EA, et al. Evidence of reproductive endocrine effects in women with occupational fuel and solvent exposures. *Environ Health Perspect*. Aug 2002;110(8):805-811.
44. Merchant-Borna K, Rodrigues EG, Smith KW, Proctor SP, McClean MD. Characterization of inhalation exposure to jet fuel among U.S. Air Force personnel. *Ann Occup Hyg*. Jul 2012;56(6):736-745.

45. Blake PK, Komp GR. Radiation exposure of U.S. military individuals. *Health Phys.* Feb 2014;106(2):272-278.
46. Smith TC, Jacobson IG, Smith B, Hooper TI, Ryan MA. The occupational role of women in military service: validation of occupation and prevalence of exposures in the Millennium Cohort Study. *Int J Environ Health Res.* Aug 2007;17(4):271-284.
47. Hyams KC, Riddle J, Trump DH, Wallace MR. Protecting the health of United States military forces in Afghanistan: applying lessons learned since the Gulf War. *Clin Infect Dis.* Jun 15 2002;34(Suppl 5):S208-214.
48. Hauschild VD. Chemical exposure guidelines for deployed military personnel. *Drug Chem Toxicol.* Feb 2000;23(1):139-153.
49. Hauschild VD, Lee AP. Assessing chemical exposures during military deployments. *Mil Med.* Feb 2004;169(2):142-146.
50. Brix K, O'Donnell FL. Panel 1: medical surveillance prior to, during, and following potential environmental exposures. *Mil Med.* Jul 2011;176(7 Suppl):91-96.
51. Martin NJ, Richards EE, Kirkpatrick JS. Exposure science in U.S. military operations: a review. *Mil Med.* Jul 2011;176(7 Suppl):77-83.
52. Unexplained illnesses among Desert Storm veterans. A search for causes, treatment, and cooperation. Persian Gulf Veterans Coordinating Board. *Arch Intern Med.* Feb 13 1995;155(3):262-268.
53. Levine PH, Young HA, Simmens SJ, et al. Is testicular cancer related to Gulf War deployment? Evidence from a pilot population-based study of Gulf War era veterans and cancer registries. *Mil Med.* Feb 2005;170(2):149-153.
54. Murphy F, Browne D, Mather S, Scheele H, Hyams KC. Women in the Persian Gulf War: health care implications for active duty troops and veterans. *Mil Med.* Oct 1997;162(10):656-660.
55. Riddle M, Lyles M. Panel 4: linking service members and exposure data to support determination of risk-proceedings of an educational symposium on assessing potentially hazardous environmental exposures among military populations. *Mil Med.* Jul 2011;176(7 Suppl):105-109.
56. DeFraites RF, Richards EE. Assessing potentially hazardous environmental exposures among military populations: 2010 symposium and workshop summary and conclusions. *Mil Med.* Jul 2011;176(7 Suppl):17-21.
57. U.S. Department of Defense Military Health System. Defense Occupational and Environmental Health Readiness System – Industrial Hygiene [DOEHRS-IH]. 2013; http://www.health.mil/Libraries/2011_MHS_Conference_Breakout_G/New_Fact_Sheet_-_DOEHRS_IH_V3.pdf.
58. Rossi J, 3rd, Ritchie GD, Nordholm AF, et al. Application of neurobehavioral toxicology methods to the military deployment toxicology assessment program. *Drug Chem Toxicol.* Feb 2000;23(1):113-138.
59. U.S. Department of Defense Deployment Health Clinical Center. DD Form 2796 Primer: Post-Deployment Health Assessment (PDHA) 2012.

PART 5. POLICY CHANGES AND RESEARCH AGENDA

Introduction

This part addresses broad areas of recommended changes that could improve the early detection and treatment of breast cancer and outlines a research agenda that address Departmental needs for information. For these tasks, the approach was to briefly review the current, relevant DoD

infrastructure and protocols, describe the current achievements and accomplishments, and then to summarize goals being pursued and desired changes that would contribute to improvements related to each task.

Task 9. Recommendations for changes to policy or law that could improve the prevention, early detection, awareness, and treatment of breast cancer among members of the Armed Forces serving on Active Duty

A review of the epidemiological analyses in this report has found that many active duty females with breast cancer tumors are diagnosed with breast cancer at early stages, which typically carries a better prognosis. Additionally, age-adjusted breast cancer rates were noted to be significantly lower among AD females as compared to the civilian (SEER) female population.

These findings are encouraging and consistent with MHS commitment to implement policies and laws that improve the continuum of breast care to include prevention, early detection, awareness and treatment of breast cancer among AD service members. The foundation of this commitment is the provision and marketing of a comprehensive breast care benefit that continuously assesses each component of the breast care continuum to facilitate the delivery of evidenced-based clinical practices, cutting-edge cancer diagnostic and treatment technologies and high-priority clinical cancer trials. Consistent with an overarching theme of the MHS transformation, an emphasis is being applied on the integration, evaluation and optimization of clinical care in general and the breast care continuum specifically. These internal efforts and considerations, summarized below by component, are ongoing and have not required changes to law or policy for implementation. Within the current policy and legislative framework, the TRICARE benefit supports the systematic consideration of promising screening, diagnostic tests and treatments for breast cancer.

Awareness and Outreach

The DHA Benefits, Education and Support Division (BE&S) routinely evaluates the frequency, intensity and placement of marketing efforts for effective health messaging regarding breast cancer awareness and preventive benefits for breast care. In tandem with the representatives from the individual Services, this outreach is intended to increase breast cancer awareness among all eligible beneficiaries and in particular AD service members. Currently, breast cancer awareness activities peak during breast cancer awareness month each October. Outreach activities are ongoing with consideration of alternative schedules and for health messaging as well as the continued delivery of content via diverse vehicles such as traditional and social media, educational web videos, podcasts, and external outreach. Additionally these activities are flexible enough to provide outreach to ethnically diverse AD women.

Prevention, Detection and Treatment

The early detection and treatment of breast cancer in AD service members has significant personal, professional and readiness implications in that breast cancer detected in earlier stages is generally associated with improved clinical outcomes and an increased potential for the AD members to return to service. As described previously, this group is disproportionately young, with most female members in age groups where detection of breast cancer is rare, and where in women of average risk, annual screening mammography is not recommended¹. Therefore, efforts to identify members that are at above average risk for breast cancer and who fall in age groups where there is an absence of effective guidance from recommendation-setting organizations is of critical importance to the MHS. Activities under way that support this goal have not required changes to policy or law and include the iterative enhancement of breast cancer risk assessments tools with the efforts to integrate decision support tools for providers evaluating AD service members at the point of care. The integration and analysis of clinical and demographic information and medical history in the context of risk factors for breast cancer may

improve individual risk stratification through development of more robust screening algorithms¹. These efforts would provide another opportunity to facilitate and collect accurate, comprehensive cancer data for purposes of clinical research, supporting a stronger cancer reporting system. The continuum of breast care is supported by the availability of accurate, comprehensive cancer data facilitated by a strong cancer reporting system. Essential components include: a robust central cancer registry, a viable, up-to-date standards compliant data collection application and trained, certified cancer registrars. Iterative improvement of the robustness of a cancer reporting system would not require changes to policy or law, but is shared here as a goal that can be coordinated by subject matter experts and other stakeholders, some of whom have contributed to this report.

In recent years, promising developments in screening and diagnostic technology have enabled healthcare providers to identify some individuals with above average risk for breast cancer, and in individuals diagnosed with breast cancer, to tailor treatment based on the specific characteristic of the patients' tumor. BE&S maintains a process that ensures the TRICARE benefit supports the consideration of significant developments in the screening, diagnosis and treatment of breast cancer. By federal law, TRICARE can only provide coverage for treatments that are proven to be both safe and effective with the intent to protect patients from potentially harmful therapies. We recognize that the field of medicine is constantly evolving and improving, and what was experimental in the past, may be the standard of care today. In order to ensure that our beneficiaries receive services that meet the standard of care, the Code of Federal Regulations (32 CFR 199.4(g)(15)) requires that there be reliable evidence showing that any medical treatment or procedure has been the subject of well controlled studies of clinically meaningful endpoints that demonstrate safety and efficacy compared with the standard means of treatment or diagnoses.

32 CFR 199.2 and Chapter 1, Section 2.1 of the TRICARE Policy Manual provide the TRICARE hierarchy of reliable evidence used to determine whether a drug, device, medical treatment or procedure has moved from the status of unproven to the position of nationally accepted medical practice as follows:

1. Well controlled studies of clinically meaningful endpoints, published in refereed medical literature
2. Published formal technology assessments
3. Published reports of national professional medical associations
4. Published national medical policy organization positions
5. Published reports of national expert opinion organizations.

Specifically excluded from the hierarchy of reliable evidence are reports, articles, or statements by providers or groups of providers containing only abstracts, anecdotal evidence, or personal professional opinions. Also excluded is the fact that a provider or number of providers have elected to adopt a drug, device, or medical treatment or procedure(s) as their personal treatment or procedure of choice or standard of practice. Within the current framework, the TRICARE benefit supports the systematic consideration of promising screening, diagnostic tests and treatments for breast cancer.

The Military Health System, although encouraged by the findings in this report, remains deeply committed to evaluating opportunities to further improve the effectiveness of prevention, early detection, awareness and treatment of breast cancer among AD service members.

Task 7. A description of a research agenda to further the understanding of the Department of Defense of the incidence of breast cancer among such members

This section describes a research agenda that is designed to more fully understand breast cancer incidence in the DoD. The first part presents the findings established in this report and identifies research agenda items that flow from these findings. Next, we describe the entities and functions of the current cancer registry and surveillance program and identify areas for improvement in this program. A final section outlines a vision for expanded research aimed at optimizing the allocation of DoD health-oriented resources for the prevention, outreach, diagnosis and treatment of breast cancer within the Armed Forces.

Research Context Established in This Report

DoD data from the DMSS and ACTUR were independently analyzed to describe trends over time during the period 2000-2010, and to compare incident rates among age groups, race/ethnicity groups, rank and occupational groups. ACTUR data were analyzed to compare incident rates in active duty females to civilian rates after standardizing the age-distribution of the populations. ACTUR data were analyzed to describe detailed information about types of surgical and adjuvant treatment by stage of diagnosis.

The findings presented from these analyses found that compared to civilian females, active component females had lower overall rates, and age-specific rates of breast cancers. The majority of cancers are detected at stages 0, 1, and 2. The analyses found that male breast cancer cases were extremely rare, with only 36 cases detected in DMSS between 2000 and 2010.

These findings also suggest possible areas for future research to increase understanding of the incidence of breast cancer. Using AFHSC data, analysis found that the difference in rates between African American and white active component females appeared to be accounted for by cases among females under age 40.

The analyses conducted here must be viewed with some caution because most women separate from (i.e., leave) the military after a relatively short period of service rather than retire from military service. Hence, any breast cancer tumors in these women that were detected after separation are not contained in military medical records. Future research could be conducted that looks at breast cancer among military retirees in DoD data, and that links cohorts of women leaving the military to medical records in the VA system or the Medicare system; however any cases among women not enrolled or insured in these two systems would still go undetected.

The analyses demonstrate the application of valuable data contained in DMSS on cancer diagnoses and in the DoD tumor registry (ACTUR) on the stage of diagnosis, pathological findings associated with cancer diagnoses, and clinical details on the treatments received. The analyses derived of ACTUR data require certain hand tabulations and consolidation of records. Future research would benefit from modernized improvements to the ACTUR registry system, which in turn would facilitate replication of these findings and extension of future research. These improvements would increase confidence that the ACTUR system is capturing all cancer cases, as is required.

Further, a literature review on risk factors for breast cancer identified several personal lifestyle factors, and occupational exposures that may be associated with differential breast cancer rates, but are difficult to study with existing data sources. For example, increased parity and increased months of breastfeeding are protective for breast cancer but there are no routine data available to examine whether changes in these practices are contributing to the change in rates over time or the differential rates among races. This suggests that DoD should give consideration to modifying the health behavior

survey or another routine survey to include additional health behaviors important to understanding cancer incidence.

Finally, the DoD maintains many other sources of data not analyzed here that would contribute to a more complete understanding of: population health factors associated with breast cancer (occupational title, months of deployment); and, utilization and costs of preventive practices (periodicity of mammograms and clinical breast exams, follow-up care after breast cancer surgery, costs of mammograms, costs of breast cancer surgeries in civilian settings).

Current Research Programs

Overall, the current DoD breast cancer research agendas have established comprehensive translational research platforms consisting of an internationally known breast tissue repository; clinical trials; bioinformatics, genomics, military epidemiology, and population sciences cores; and translational clinical and academic capabilities. These entities support present efforts and enhance the DoD's ability to make future discoveries leading to the identification of advanced technologies and emerging trends in breast cancer incidence, prevention, diagnosis, treatments, and cures for active duty, retirees and beneficiaries.

As reviewed in this report, there are existing surveillance and monitoring programs that contribute to information on breast cancer incidence within AFHSC, the JPC, the DON/CSRP, and the NMCPHC's Health Analysis team.

Cancer epidemiologists and other researchers within the DoD pursue some of epidemiological research questions through investigator-initiated research grants, and other competitive research award mechanisms within the DoD, the National Institutes of Health, and other funding sources. The Services sponsor some research such as the Health Outcomes Research Center of Excellence (HORCE) located at the NMCPHC. Other informative research is conducted by researchers within the Department of Veterans Affairs (VA) with VA funding.

Within the DoD, the *AFHSC* is the MHS entity that provides the primary source of timely, relevant, actionable, and comprehensive health surveillance information across all services. Such comprehensive surveillance information is utilized by the services to promote, maintain, and enhance the health and readiness of military and military-associated populations. Regarding cancer surveillance, the AFHSC Epidemiology and Analysis Division (EAD) has performed periodic comprehensive surveillance and analysis of cancer incidence rates, including breast cancer, for annual periods, and most recently, has provided annual updates. The EAD leverages the DMSS which contains comprehensive, up-to-date and historical data on diagnoses and procedures within all direct care facilities and purchased care, civilian facilities. Hence, the information is as complete as possible and not restricted to certain qualified reporting facilities. DMSS data also has certain limitations for study of incidence. In the DMSS, incident cases are based on diagnosis codes, and the diagnosis is not based on pathologic data, thus information on tumor pathology such as stage and grade are not available. Thus, the DMSS is limited in its ability to fully and accurately monitor the frequency and trends in types of tumors.

The AFHSC publishes its cancer surveillance analysis in the [Medical Surveillance Monthly Report (MSMR)], a monthly journal read by military medical professionals and indexed on PubMed, hence its study abstracts are available worldwide to cancer research communities². This surveillance of annual trends in breast cancer and other cancers is expected to continue given the importance of this disease to overall morbidity and mortality among the armed forces.

The MCC's Epidemiology program has conducted and continues to conduct studies on incidence, screening mammography and tumor stage as evidenced by its publications^{3, 4, 5, 6}. The Health Outcomes

Research Center of Excellence (HORCE) located at the Navy and Marine Corps Public Health Center forms research collaborations between MHS staff and non-federal experts. HORCE also has the capability to link DoD cancer registry data with the MHS Data Repository (MDR) via IRB approved protocols. One of its research studies is the "Breast Cancer Outcomes Study" composed of many sub-studies.

The DoD Center of CBCP located in the MCC/WRNMMC has a prominent research program to fight against breast disorders and cancer that is focused on decreasing the morbidity and mortality of breast cancer among women. The CBCP has a five pronged-interlocking approach based on its five pillars: (1) Breast Cancer Risk Reduction, (2) Biorepository, (3) Focused Research (Including: Genomics, Proteomics, and Immunology Research), (4) Biomedical Informatics, and (5) Clinical Care.

One of the CBCP's research groups, Translational Breast Cancer Research Group, has undertaken a number of projects including the identification of chromosomal regions critical to the development, progression and metastasis of primary breast tumors, identification of novel genetic factors contributing to clinical phenotypes in large families with BRCA1 and BRCA2 mutations and the development of biological models to differentiate aggressive from indolent DCIS. The DCIS effort seeks to identify genes involved in determining the underlying behavior of DCIS lesions and will move the diagnosis and classification of DCIS beyond current pathology standards and will allow women with pre-invasive breast disease to receive the appropriate, customized treatments. In addition to work on early breast disease, the group has focused on identification of genetic causes associated with the more aggressive type of breast cancer seen in African American women through the study of genetic admixture, gene expression and proteomic approaches. Other research projects include identification of gene expression signatures associated with breast metastasis, deciphering the genetic pathways of development of high- and low-grade breast carcinomas, identification of polymorphic DNA changes associated with increased risk of developing breast cancer and assessment of the role of imprinting in the development of breast cancer. Together, these efforts will improve our understanding of the biological processes associated with breast pathogenesis as well as leading to improved diagnostics and the development of novel molecular therapeutics to improve the outcome and quality-of-life for patients with breast cancer.

A Vision for Future Research that Could Be Supported by Military Databases

The vision for future research that will contribute to improvements in the understanding of breast cancer incidence in military populations is described in this section, organized under five goals and suggests future directions.

1. To Maintain and Improve the DoD Cancer Registry and Surveillance Program

Demand for oncology data for purposes of research and disease surveillance is high. Active duty military, retirees and beneficiaries comprise a unique cohort for study. A complete and accurate cancer registry is essential for assessing if the incidence rates of cancer in the military differ from those in the general population. National cancer registry programs operated are operated by the National Cancer Institute (SEER, used in these analyses) and the Centers for Disease Control and Prevention. The DoD cancer registry follows the guidelines established by the NAACCR for quality assurance.

In terms of this report's research on cancer incidence, the DON Cancer Surveillance and Registry Program contributed substantially to the analysis presented in this report. It was created in January 2009 under DON instructionsⁿ. Both the Army and Air Force have equivalent registry 'instructions' and have also established a cancer oversight position at the Services level.

ⁿ Specifically, BUMED Instruction 6320.92

The functional entities with responsibilities for the coordinated DoD Cancer Registry and Surveillance program include registrar programs at MTFs, which are funded and supported by Service registry Instructions and oversight programs, and the operation of a consolidated repository is the responsibility of the JPC.

Military facility-based registries. Cancer registries are an essential part of an integrated MTF based cancer program and for research on cancer incidence. The goal of these cancer registries is to provide complete, accurate and timely data on patients seen at the facility; thus, providing the backbone for monitoring the incidence of cancers, detecting changes in occurrence or types, and defining the treatments received within the ever-evolving cancer care program. Funding for the approximate 100 cancer registries at the DoD MTF-level worldwide is provided by each Service. In turn, each Service maintains a separate instruction governing the organization of its functional MTF-based registries and a subject matter expert that oversees the program.

ACTUR data repository and consolidated records. All registry data funnels into the ACTUR data repository through the ACTUR software application. It is the function of the JPC CCR to consolidate the ACTUR records across all Services, because patients can be treated not only within a Service network but also across Service lines. For example, patients seen at Langley AFB often are provided systemic treatment at Navy Medical Center Portsmouth.

At an operational level, the JPC supports the DoD ACTUR which is used for the coordinated system of detection, diagnosis, treatment planning and follow-up for those patients with cancer. JPC's involvement in the DoD Cancer Registry and Surveillance Program is focused on the following: (1) funding of maintenance of the ACTUR data collection application via a contractual agreement with DMDC; (2) funding and oversight of a CCR contract intended to validate data and consolidate multiple patients' records from ACTUR, and (3) oversight of the release of ACTUR/CCR data for purposes of clinical and epidemiologic research. While the CCR was intended to be used for the present analyses, it was not available and DON analysts relied on ACTUR records.

Areas Requiring Improvements to Enhance Research Based on Registry Data

Accurate comparisons of the military and general populations are challenging because of gaps in data format and content between the national cancer registry and the DoD cancer registry data. It is important that the Services ensure sufficient and well trained registry staff for without competent data entry there may be missing or incomplete cancer surveillance records, or data submission may be delayed and not timely for analyses. Accredited registry programs must meet certain quality assurance standards related to data collection and other functions and so it is vitally important that we have the staff support required to develop the data used for research to compare the cancer incidence in the military to national figures.

The Department can also support the Services in this function by providing DoD-wide training. Training budgets have been decreased DoD-wide due to recent budget pressures and so alternative training approaches such as video conferences may be important stop-gap measures to prevent further slippage of registry capabilities.

Finally, in order to develop future robust and meaningful research initiatives regarding cancer incidence and changes in occurrence, it is important that DoD cancer registries throughout the MHS have updated software tools that effectively collects, analyzes and disseminates cancer data. The DoD Cancer Registry Coordination Committee with representatives from all Services has addressed this issue and recently voted to take steps to examine new approaches and technologies to overcome these deficiencies.

2. Enhance capacity for integrating clinical and administrative data to support research

Cancer is a major health problem for the general population as well as the DoD healthcare beneficiaries. However, cancer distribution and related factors in the military are not well known. Understanding epidemiological characteristics of cancer and related factors is a precondition for cancer prevention and control. Thus, it is important to conduct epidemiological surveillance and studies of cancer in military population.

Linkage of Cancer Registry to MDR. Cancer registries contain relatively high-quality data on cancer diagnosis and pathology following the national guidelines. However, cancer registries generally do not routinely collect detailed information on cancer treatment, co-morbidities, and follow-up care and thus have limitations for clinical research. They also do not obtain information on individuals without cancer and as a result, comparisons with a reference population cannot be made to identify cancer-related factors. On the other hand, medical claims data include individuals with and without cancer, and the information on cancer is accompanied by data on other medical conditions and treatment. Linkage of data from the two sources diminishes the potential limitations of using registry or medical claims data alone and extends their usage for cancer research. Thus, the National Cancer Institute and the Centers for Medicare and Medicaid Services collaborated with each other and linked the SEER (cancer registries) and Medicare (medical claims) data in the general population.

The MHS generates and maintains extensive databases such as the MDR which contains beneficiary eligibility, administrative and medical care claims data, as well as recent additions of laboratory, pathology results and limited clinical data as well. Many specialized system, e.g., DEERS, feed the MDR on a routine basis. There may be great benefit by providing a solid foundation to ensure cancer registry data follows a routine process of extraction and housed within the MDR where scientists are able to conduct scientific studies on historic DoD beneficiary's data using approved study protocols.

MilCanEpi. The MCC's Military Epidemiology and Population Sciences Program aims to conduct descriptive studies of cancer and identify factors that may be related to cancer occurrence, prevention and control among DoD beneficiaries, using various available DoD healthcare resources. Particularly, to facilitate cancer research among DoD beneficiaries, the MCC, with support and collaboration from the National Cancer Institute, has developed a system called "MilCanEpi," a data system that links the DoD medical care and DoD cancer registry databases. A state-of-the-art computer interface linking the two databases has been developed. This system has set up a good foundation for research on breast cancer and other tumors. Currently, the system contains only cancer patients. A random sample of control population, which can be used as a reference, is importantly needed.

The "MilCanEpi" can be improved so that it can serve not only research but also surveillance of cancer in the military with more complete and accurate information. Currently, the data linkage for the system is conducted once every several years based on the current procedures and so the system does not contain most recent available data. A data system that includes relatively recent data can help identify recent temporal trends in breast cancer incidence in the military and timely investigations of emerging issues on breast cancer research, prevention and control in the population.

Additionally, the NCI defines "cancer health disparities" as "differences in the incidence, prevalence, mortality, and burden of cancer and related adverse health conditions that exist among specific population groups in the United States." The social and cultural construct of the military decreases the number of variables that influence the outcomes of many disparity studies and enhance to objectivity of biologically-driven research into race and human disease. This research will pursue this critical avenue of research via its unique military population base and its advanced translational research resources.

3. To merge and link databases with biospecimens for special studies

Tissue Repository. Although there have been remarkable improvements in breast cancer diagnosis and management, most of the complex molecular mechanisms associated with the onset, progression and/or severity of breast cancer are still not well understood. In order to increase this understanding, the MCC is acquiring and banking breast tissue, lymph nodes, serum/plasma and other blood derivatives from informed and consented research volunteers. The MCC and its component translational research laboratory performs molecular profiling, tumor biology, biochemical, and histological analysis of breast tissue and/or blood and blood components from breast cancer patients to provide insights into the molecular mechanisms that may be relevant in the development of breast cancer and breast diseases. The MCC Tissue Repository presently houses one of the largest collections of breast tissue: over 50,000 well documented specimens from over 5,000 patients. The collection has been used in many studies including recent national collaboration with The Cancer Genome Atlas Network on the Breast cancer genome⁷.

To achieve this aim, a large supply and a wide variety of good quality tissue samples are needed. Unfortunately, good quality donor breast tissue is extremely scarce and when available is often not backed by a comprehensive medical history and/or is not a good representation of the target population or study area. The non-availability of a steady and consistent supply of good quality tissue limits the systematic analysis of tissues and negatively impacts the generation of biologically useful information in research laboratories and by extension negatively impacts new findings that benefit clinical practice. The objective of this project is therefore the acquisition and banking of breast tissue, lymph nodes, serum/plasma and other blood derivatives from informed and consenting donors. The end results will be an extensive biorepository as a major resource for breast disease research, the ability to leverage the breast tissue biorepository to maximize the utilization of the tissue for the overall benefit of breast cancer patients, and research and participation in national/international projects that can benefit from resources of the biorepository. All of this is to benefit the DoD active duty, reserves and beneficiaries.

WRNMMC's MCC Clinical Breast Care Project (CBCP) system. As science advances, biological biomarkers become more and more important for cancer research. Presently, genetic and non-genetic biomarkers are widely used for not only cancer etiologic but also cancer-control research. The combination of biological, etiologic, clinical, and behavioral information can generate significant and comprehensive research results that can be translated into cancer prevention, care, and control. It represents the direction of further breast cancer research.

The CBCP of the MCC at the WRNMMC is a DoD breast cancer research program that recruits breast cancer patients and high-risk individuals from WRNMMC and some satellite MTFs. The CBCP has a large tissue and blood repository from patients, which stores biological specimens with the highest quality. The repository contains clinicopathologic data of the patients with an excellent data management system. However, the current system is not linked to the DoD cancer registry and DoD medical claims data. More complete information over time from other MTFs is manually extracted when needed for a research project. While this does not apply to all individuals in the CBCP system, the manual extraction costs a large labor while the information exists in the DoD medical claims and cancer registry data.

The development of a mechanism with which the DoD cancer registry and medical claims data can be extracted and linked to the CBCP data may provide better resources for cancer control research by generating more complete and temporally serial data and promote development of the CBCP system into one of the most valuable resources in the country and to the benefit of breast cancer patients throughout the world.

4. To support future multidisciplinary collaborations

An important opportunity may exist for additional cancer detection and prevention-oriented research conducted by a multidisciplinary research team of epidemiologists, pathologists, cancer clinicians, and specialists in occupational and environmental medicine. The DoD maintains many repositories of tissue samples, blood samples, self-report assessment surveys, and environmental surveillance tests, all which could be used in future; research to study the incidence of disease in military populations. Given the overall low incidence of breast cancer, it would be prudent to consider when research is appropriate solely on breast tumors and when a broader focus on carcinogens and other cancers as well as breast is appropriate. These repositories can be used now, and in the future, to explore timely, more efficient, and ultimately more valid research on topics related to environmental exposure and health. Two particular topic areas are highlighted.

First, there is considerable interest in the toxicology and health fields in the use and application of *biomarkers* that will identify chemical exposures in human from occupational and environmental situations⁸. Major research goals in this area relate to developing and validating biomarkers of specific types of exposures. Advances in this area would be applicable beyond breast cancer, to other cancers, and to other diseases. Some of this work may help to identify individual susceptibility to cancer and non-cancer disease. Ultimately, with better prediction of the risk of disease in individuals and groups, the DoD could apply such knowledge to reduce the risk of cancer.

Second, there are various DoD repositories of toxic exposure events, associated either with a geographic site or occupational exposures, and a newer repository specific to deployment locations. The deployment program, implemented after the 1991 Gulf War, involves standard data gathering by trained teams, before and while troops are based in new locations. Together, these repositories provide objective measures of the level of select toxins and hazardous agents (carcinogens) in air, water, and soil samples, gathered real-time, linkable by location and time. Other data (i.e., post-deployment health assessments) are based on self-report of exposure to certain agents while deployed. The presence of these prospective data collection programs will support more rapid research with toxic exposure data collected in real time, if linked to service members who were known to reside in specific areas, perform specific occupational tasks with exposure, or be deployed to areas with recorded hazardous levels of toxin. While it is impossible to expect a complete census of toxic exposures, some of these programs replace prior retrospective data gathering activities fraught with incompleteness. Historically, research to retrospectively identify if certain groups were exposed to toxins was more cumbersome, more costly, and less valid, as it was based on surveys involving recall of military members⁹. Some repository data, for a specific purpose, has been associated or translated into a person registry. This person registry can be linked to future DoD health data or form the basis of future follow-up studies to determine the long-term health effects of specific toxic exposure events or periods.

To support research of this nature, the DoD will explore timely, cost-efficient ways to merge data from disparate repositories, held by various enterprise entities, into research databases. The topic of the individual research project would dictate the type of data and organization of the data; hence, while it might not be possible or cost-effective to construct a universal database for all research topics, an advisory group of cancer researchers and scientists could specify the most relevant information to include in a database that promotes study of cancer incidence. This database might be developed in stages. In phase 1, cancer researchers could review a summary of exposure reports, to identify events (or rank events) based on exposure duration, magnitude, or population characteristics (e.g., reproductive age females), that merit additional tracking and surveillance. Second, attention would be paid to developing efficient procedures for merging environmental medicine reports from specific geographic areas and specific date windows, to military units or groups. Then, in the third phase,

criteria would be developed for the population groups to be included in research studies and appropriate ways to identify which specific individuals in the unit or group should be included. In some cases, it may be determined that a registry of these individuals be created that can be used for longitudinal tracking studies or to re-contact potentially affected individuals.

5. To translate research findings into practice for military medicine

As indicated throughout this report, the Military Health System has unique resources that can be used to address military relevant research questions and translate them to approaches to prevent cancer and create new Clinical Practice Guidelines (CPGs). This Report contains descriptions of a variety of computerized databases containing clinical, occupational, and other information. It also highlights several centers that collect a large number of unique military pre and post diagnostic serum samples and pathology specimens that can be utilized for various research topics such as the identification of biomarkers for early detection of cancer. These provide critical resources for research important for scientific advances in the prevention, diagnosis, treatment and care of breast cancer.

For example, embedded in the MCC is the CBCP which is using these data and highly characterized/annotated specimens to provide research support for the most basic research studies to advanced development. They utilize a multidisciplinary bed-to-bench-to-bedside approach as the standard for treating and studying breast diseases and breast cancer. This multidisciplinary model integrates advances in risk reduction, prevention, screening, diagnosis, treatment and continuing care with cutting edge research incorporating advanced methods from biomedical informatics, tissue banking, high throughput biology and translational research. These efforts focus on decreasing the morbidity and mortality of breast cancer among American women.

The overall purpose of this research is to provide a balanced environment between the two competing and yet complementary research paradigms of hypothesis-driven research and hypothesis-generating research, in a translational research organization that unites clinical capabilities (patients, nurses, clinicians) with research capabilities (genomics, proteomics, immunohistochemistry and whole genome DNA sequencing) to analyze molecular and developmental pathways that are central to the diagnosis and treatment of breast disease. The critical foundations to this approach are provided by the tissue biorepository and biomedical informatics platforms

There are three broad areas where the MCC CBCP stands poised to make major contributions to breast cancer research and its translation into clinical practice. These areas include the identification of molecular profiles of disease with high clinical relevance, the enhancement of understanding of breast tumor biology, and, deepening understanding of the genetic risk of breast disease.

Clinically Relevant Molecular Profiling. This is cross-cutting theme with clinical, risk assessment and basic research components. The primary focus of this theme is to evaluate the utility of existing molecular profiles that have relevance to risk assessment, diagnosis, prognosis and therapy in a clinical setting and to discover new profiles that can be evaluated in the clinic. Projects within this theme have well defined translational goals. The development of comprehensive and highly informative molecular profiles will be a foundation for the development and delivery of personalized/individualized medicine. A variety of research modalities will be used to identify these profiles including immunohistochemistry, gene and protein expression analysis and genetic profiling including Next Generation DNA Sequencing. These efforts will drive new initiatives such as involving the development and testing of clinically relevant immunohistochemical profiles for disease stratification and therapeutic guidance and using complete genomics sequencing of tumor and matched normal DNA to develop clinically relevant profiles that could aid in disease diagnosis, prognosis and therapy selection.

Tumor Biology. A unique combination of resources and expertise put the CBCP in a strong position to further our understanding of the basic biology of breast disease including breast cancer. Many of the projects address basic problems associated with tumor heterogeneity. The tumor microenvironment and stromal interactions, metastasis and recurrence, as well as the role of cancer stem cells and tumor evolution affecting the efficacy of treatment are emphasized. It is firmly believed that a robust understanding of breast tumor biology is a key to the successful translation of the research to clinical applications.

It is believed that by harnessing the myriad assets integrated in the DoD MHS described in this report that the high-value repository of biospecimens, the strong biomedical informatics infrastructure and the research base with strong internal and external collaborations puts DoD in an excellent position to make contributions to the understanding of breast disease that will have impact on the quality of life for military and civilian breast cancer patients and their families.

Genetic Risk. The rapid developments of high throughput genotyping and genomic sequencing of individuals has reminded the research community of the power of family studies in the assessment of genetic risk. Evaluating family risk and translating that into individual risk is the primary goal of this theme. There is both clear clinical relevance and a strong basic research component to this theme. Understanding the underlying biology of observed racial disparities in disease prevalence, presentation and outcome will also be a major part of this effort.

Summary

In sum, the DoD Breast cancer program will continue to pursue studies and strive to maintain capabilities that support diverse research purposes aimed at discovering risk factors, surveillance of trends, improving quality of care, discovery, and contributing to worldwide knowledge on breast cancer.

References

1. Stojadinovic A, Summers TA, Eberhardt J, et al. Consensus recommendations for advancing breast cancer: risk identification and screening in ethnically diverse younger women. *J Cancer*. 2011;2:210-227.
2. *Incident diagnoses of cancers and cancer-related deaths, active component, U.S. Armed Forces, 2000-2011*. MSMR, 2012. **19**(6): p. 18-22.
3. Enewold, L., et al., *Surveillance mammography among female Department of Defense beneficiaries: a study by race and ethnicity*. *Cancer*, 2013. **119**(19): p. 3531-8.
4. Enewold, L., et al., *Racial variation in breast cancer treatment among Department of Defense beneficiaries*. *Cancer*, 2012. **118**(3): p. 812-20.
5. Enewold, L., et al., *Racial variation in tumor stage at diagnosis among Department of Defense beneficiaries*. *Cancer*, 2012. **118**(5): p. 1397-403.
6. Zhu, K., et al., *Cancer incidence in the U.S. military population: comparison with rates from the SEER program*. *Cancer Epidemiol Biomarkers Prev*, 2009. **18**(6): p. 1740-5.
7. *Comprehensive molecular characterization of human colon and rectal cancer*. *Nature*, 2012. **487**(7407): p. 330-7.
8. Watson, W.P. and A. Mutti, *Role of biomarkers in monitoring exposures to chemicals: present position, future prospects*. *Biomarkers*, 2004. **9**(3): p. 211-42.
9. McCauley, L.A., et al., *Illness experience of Gulf War veterans possibly exposed to chemical warfare agents*. *Am J Prev Med*, 2002. **23**(3): p. 200-6.

APPENDIX A.

Methods and Data for Incidence Rate Comparison

NMCPHC Health Analysis Department staff were engaged to provide data and analysis for Task 5 after it was determined that data in the DoDCCR was unavailable.

SEER utilizes age-specific¹ methodology and direct standardization¹ to calculate age-adjusted and race stratified age-adjusted rates². Health Analysis utilized a similar approach from the previous report³. Cancer surveillance is carried out at the state level yearly to compare rates to SEER populations,⁴ and enables direct comparisons to the U.S. population using the U.S. Census Standard 2000 population⁵ weights.

The population of interest includes AD female breast cancer cases diagnosed in 2000 to 2010 documented within ACTUR, for women 20-59 years of age, an approach taken previously by Zhu, Devesa, Wu et al⁶. Incident cancer cases were consolidated according to SEER and North American Association of Central Cancer Registries (NAACCR) rules^{7,8,9}. Only malignant behavior codes were used following state and federal surveillance reports methods^{4,10,11}. SEER multiple primary rules were applied within the same record¹².

AD females aged 20-59 years during the years 2000 to 2010 comprised the population-at-risk. AXIOM Resource Management tabulated the population data set using DEERS data and provided to Health Analysis. The population included all women from the Active and Reserve components who were on active service as of 30 September of each observation year.

SEERStat¹ generates malignant incident cancer cases and population-at-risk denominators for each strata of age and race combination. For this analysis, we utilized SEER-18¹³ queried on females aged 20-59 years diagnosed in years 2000 to 2010. This dataset includes diagnosis years 2000 to 2010, comprises 27.8% of the U.S. population, and includes the following registries: Atlanta, Connecticut, Detroit, Hawaii, Iowa, New Mexico, San Francisco-Oakland, Seattle-Puget Sound, Utah, Los Angeles and San Jose-Monterey, Rural Georgia, Alaska Native tumor registry, Greater California, Kentucky, Louisiana, New Jersey, plus Greater Georgia.

Race was coded as White, African-American, or Other/Unknown for these analyses. For ACTUR and DMDC data, "Other/Unknown" race included other, missing, and unknown codes. For SEER-18 data, "Other/Unknown" race included American Indian/Alaska Native, Asian or Pacific Islander, or unknown. For U.S. Census 2000 data, "Other/Unknown" includes American Indian, Eskimo, and Aleutian as well as Asian and Pacific Islanders.

Age-specific, age-adjusted rates were calculated by diagnosis year categories 2000 - 2005, 2006 - 2010, and overall 2000 - 2010. Race stratified age-adjusted rates were computed only for the overall diagnoses years 2000 – 2010. Age-specific, age-adjusted rates, and race stratified age-adjusted rates were computed for age groups 20-29 years, 30-39 years, 40-49 years, and 50-59 years. These groupings can be calculated by SEERStat and are typically done at the state level⁴.

Health Analysis generated 95% confidence intervals to compare rates to the SEER-18 rates^{14,15,16}.

References

1. Gordis L. *Epidemiology*, Fourth Edition. Saunders Elsevier, 2009.
2. National Cancer Institute (NCI) Surveillance, Epidemiology, and End Results (SEER) SEERStat software statistical program age-adjusted calculations, accessed January 2014 located here <http://seer.cancer.gov/seerstat/tutorials/aarates/definition.html>.

3. Prostate Cancer Monograph. Health Analysis, Navy & Marine Corps Public Health Center, August 2012. NAACCR Annual Conference 2013 poster abstract location (P-01): <http://naaccr.org/EducationandTraining/2013ACPosters.aspx>.
4. Cancer Incidence and Mortality in New Jersey, 2006-2010. Cancer Epidemiology Services, Public Health Services Branch, New Jersey Department of Health, August 2013. Accessed December 20, 2013 from <http://www.nj.gov/health/ces/documents/report06-10.pdf> .
5. Current Population Reports. Population Projections of the United States by Age, Sex, Race, and Hispanic Origin: 1995 to 2050. United States Census P25-1130. U.S. Department of Commerce, Economics and Statistics Administration, Bureau of the Census. Issued February 1996. Accessed <http://www.census.gov/prod/1/pop/p25-1130/p251130.pdf> on December 28, 2013.
6. Zhu K, Devesa S, Wu H, Zahm S, Jatoi I, Anderson W, Peoples G, Maxwell L, Granger E, Potter J, McGlynn K. Cancer Incidence in the U.S. Military Population: Comparison with Rates from the SEER Program. *Cancer Epidemiology Biomarkers Prev*, 2009 June; 18(6):1740-1745. Doi:10.1158/1055-9965.EPI-09-0041.
7. National Program of Cancer Registries-Modeling Electronic Reporting Project (NPCR-MERP), Centers for Disease Control and Prevention, Department of Health and Human Services. Accessed December 20, 2013 from http://www.cdc.gov/cancer/npcr/informatics/aerro2/pdf/merp_glossary_1100708.pdf .
8. SEER Cancer Registration & Surveillance Modules, Case Consolidation. Accessed December 20, 2013 from <http://training.seer.cancer.gov/operations/standards/scope/consolidation.html>.
9. North American Association of Central Cancer Registries (NAACCR) Standards for Cancer Registries Volume III. Standards for Completeness, Quality, Analysis, Management, Security, and Confidentiality of Data. Accessed December 20, 2013 <http://www.naaccr.org/LinkClick.aspx?fileticket=hfVzJKUcRM8%3d&tabid=134&mid=474>
10. Cancer Statistics, Trends, and Multiple Primary Cancer Analyses from the SEER Program. Hayat M, Howlader N, Reichman M, and Edwards B. Accessed January 2, 2014 from this site <http://theoncologist.alphamedpress.org/content/12/1/20.full> .
11. Howlader N, Noone AM, Krapcho M, Garshell J, Neyman N, Altekruse SF, Kosary CL, Yu M, Ruhl J, Tatalovich Z, Cho H, Mariotto A, Lewis DR, Chen HS, Feuer EJ, Cronin KA (eds). SEER Cancer Statistics Review, 1975-2010, National Cancer Institute. Bethesda, MD, based on November 2012 SEER data submission, posted to the SEER website April 2013. Accessed January 8, 2014 from http://seer.cancer.gov/csr/1975_2010/ .
12. SEER Cancer Registration & Surveillance Modules, Multiple Primaries & Histology Coding Rules, Accessed December 20, 2013 from <http://training.seer.cancer.gov/rules/changes/>.
13. Surveillance, Epidemiology, and End Results (SEER) Program (www.seer.cancer.gov) SEER*Stat Database: Incidence – SEER 18 Regs Research Data + Hurricane Katrina Impacted Louisiana Cases, Nov 2012 Sub (2000-2010) <Katrina/Rita Population Adjustment> - Linked To County Attributes – Total U.S., 1969-2011 Counties, National Cancer Institute, DCCPS, Surveillance Research Program, Surveillance Systems Branch, released April 2013, based on the November 2012 submission
14. Johnson NL, Kotz S. *Distribution in Statistics: Discrete Distributions*. John Wiley, New York, 1969.
15. Fay MP, Feuer EJ. Confidence Intervals for directly standardized rates: a method based on the gamma distribution. *Statistics in Medicine* 1997 Apr 15;16(7):791-801.
16. Breslow NE and Day NE. *Statistical Methods in Cancer Research. Volume II-The Design and Analysis of Cohort Studies*. New York: Oxford University Press. 1987.

APPENDIX B.

Methods and Data for Treatment Modalities

The NMCPHC Health Analysis Department staff provided data and analysis for Task #3. The population of interest for treatment assessment included AD female in-situ and invasive breast cancer cases diagnosed from 2000 to 2010, documented within ACTUR for women 18-69 years of age.

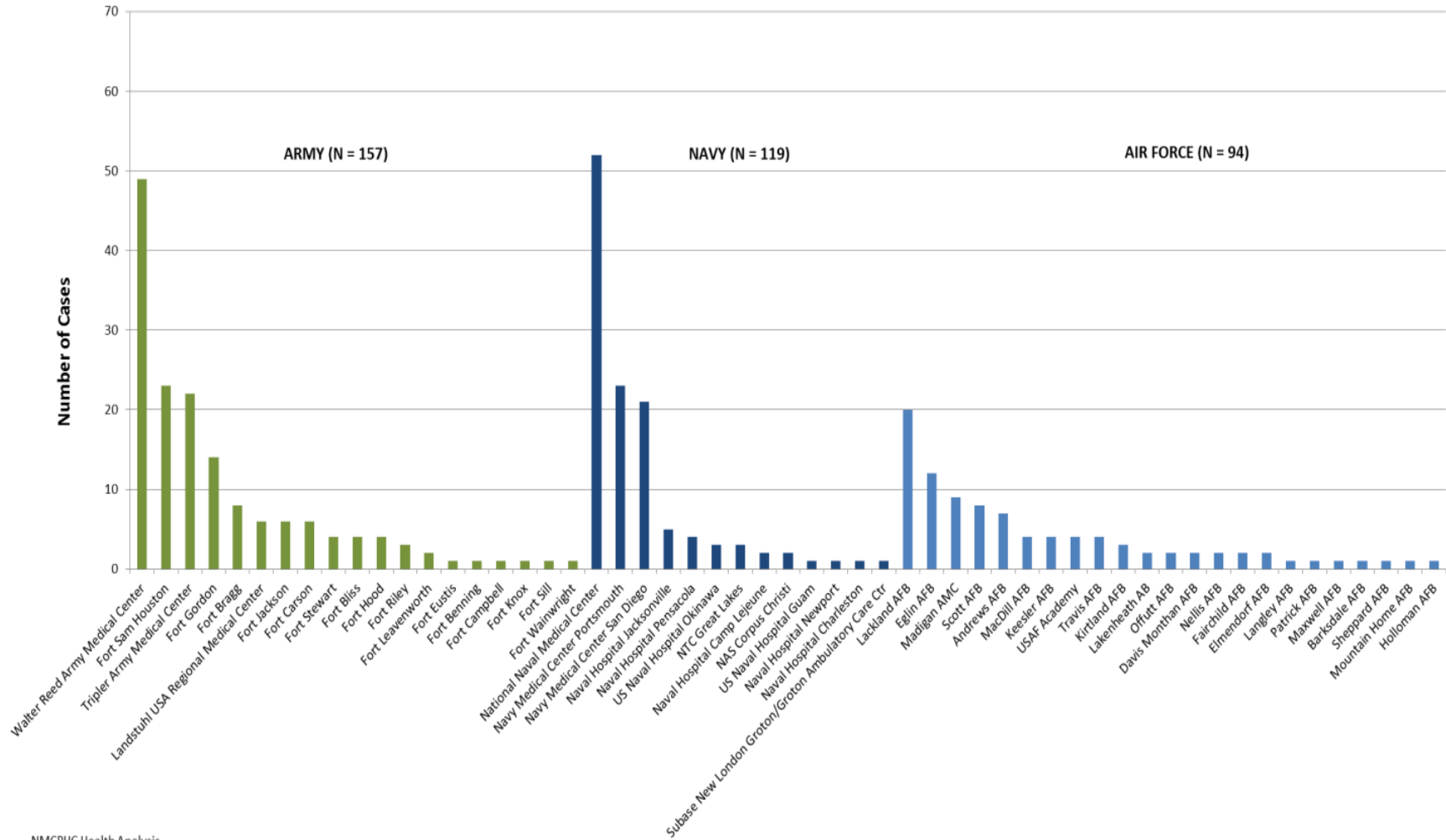
Stage at time of diagnosis is a critical element in the determination of treatment for breast cancer. Data was stratified using the AJCC pathologic stage group system, the major language for cancer reporting and statistical analysis. Stage group is a derivative of three elements, tumor (T), node (N) and metastasis (M). Data (years 2000-2002) are consistent with the 5th edition of the manual;¹ 2003-2009 data conforms to the breast schema delineated in the 6th edition of the AJCC Staging Manual² Patients diagnosed in 2010 (exclusively) reflect pathologic stage groups defined in the 7th Edition of the AJCC Staging Manual³. The stage at time of diagnosis according to the appropriate staging manual, 5th Edition (2000-2002), Sixth Edition (2003-2009) and Seventh Edition (2010) was reported. Pathologic stage has not be altered (down staged or upstaged) to reflect changes in various editions.

The Facility Oncology Registry Data Standards for 2013 (FORDS) is the source for treatment codes and definitions⁴. Due to the expansiveness of the data, surgical codes are concatenated into more manageable groupings but can be expanded if necessary. Treatment was aggregated by pathologic stage grouped by treatment type (surgery, radiation and systemic) and year of diagnosis.

The appropriate source for robust, integrated cancer data is the DoDCCR. The DoDCCR is charged with maintaining a DoD-wide cancer incidence reporting system, monitoring data accuracy, reliability and completeness through systematic quality assurance procedures and consolidation of data from multiple reporting sources into a single record. Because data from the DoDCCR was unavailable for this report, the NMCPHC Health Analysis staff was enlisted to (1) extract data from the ACTUR database; (2) and review multi-record entities for best source selection. Per DoDCCR staff, approximately 70% of ACTUR data are single source records, 30% are multiple records representative of patients diagnosed/treated in more than one MTF; hence, more than one record is available. Health Analysis staff utilized proven methodology to select the record that was most representative of the entirety of treatment received at multiple facilities; higher class of case for multiple records for the same patient were given preference. Class of case reflects the facility's role in managing cancer. A lower class of case code (00) indicates that the patient was diagnosed at the reporting facility but patient was referred elsewhere for treatment. Class of case codes in the (10) series indicates that the patient was not only diagnosed at that facility, but all or partial treatment was provided by the reporting facility. Class of case (20) series indicates that the patient was diagnosed elsewhere other than the reporting facility. All or partial treatment post diagnosis was done at this facility. A complete registry record must document all treatment received regardless of where treatment was done (MHS/civilian). Conforming to nationally recognized cancer data standards, only analytic cases were included in this analysis⁴. Patients diagnosed with recurrent disease were excluded. Histology was limited to carcinoma. Non-carcinomas of the breast have different AJCC staging schemas and treatment options.

Figures 1 and 2 are contributions by reporting facility, broken down by individual facility and service and diagnosis years. These figures are based on raw data.

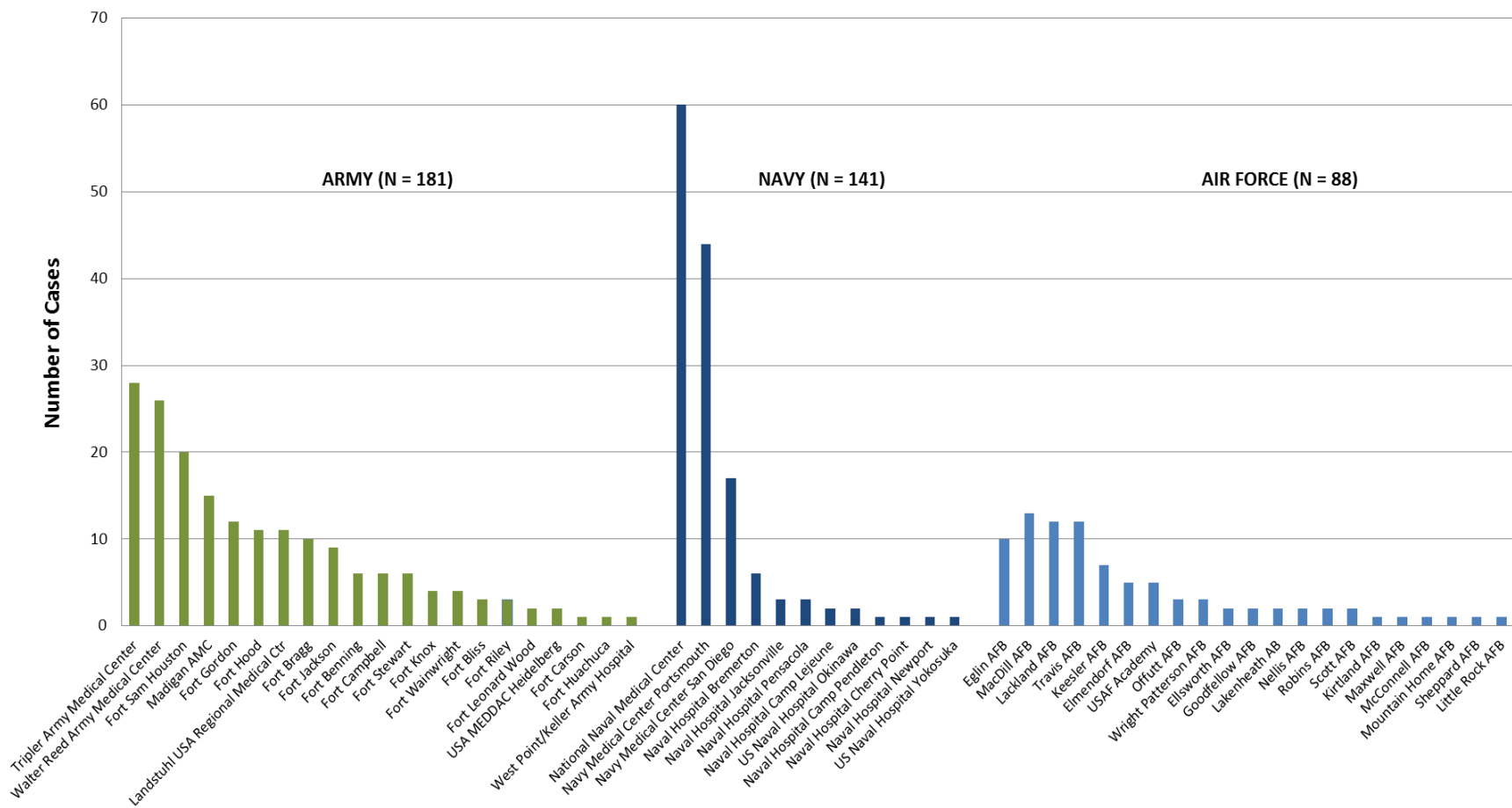
**Figure 1: Cases Reported by Service and Facility,
Active Duty Females Diagnosed with Breast Cancer 2000-2005, (N = 370)**



NMCPHC Health Analysis
Source: ACTUR data, DEC 2013

Notes: The population of interest for treatment assessment included AD female in situ and invasive breast cancer cases diagnosed in 2000 to 2010 documented within ACTUR for women 18-69 years of age. Data were stratified using the American Joint Committee on Cancer (AJCC) pathologic stage group system, the major language for cancer reporting and statistical analysis. Stage group is a derivative of three elements, tumor (T), node (N), and metastasis (M). Treatment was aggregated by pathologic stage grouped by treatment type (surgery, radiation and systemic) and year of diagnosis, using FORDS standards. Health Analysis staff utilized proven methodology to select the most representative record in cases of multiple records. Patients diagnosed with recurrent disease were excluded. Histology was limited to carcinoma.

**Figure 2: Cases Reported by Service and Facility,
Active Duty Females Diagnosed with Breast Cancer 2006-2010, (N = 410)**



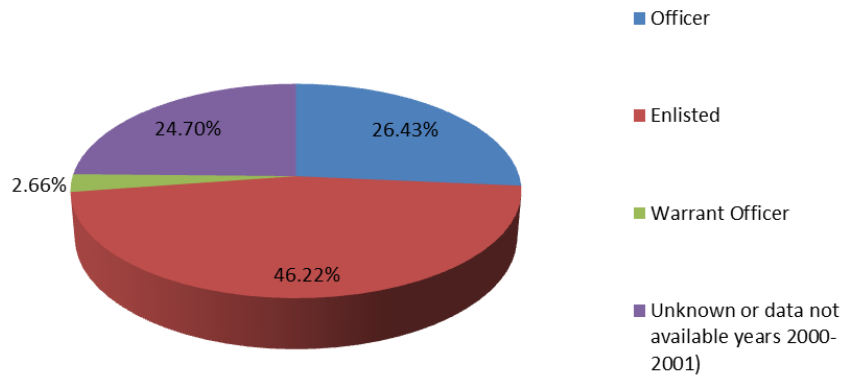
NMCPHC Health Analysis

Source: ACTUR data, DEC 2013

Notes: The population of interest for treatment assessment included AD female in situ and invasive breast cancer cases diagnosed in 2000 to 2010 documented within ACTUR for women 18-69 years of age. Data were stratified using the American Joint Committee on Cancer (AJCC) pathologic stage group system, the major language for cancer reporting and statistical analysis. Stage group is a derivative of three elements, tumor (T), node (N), and metastasis (M). Treatment was aggregated by pathologic stage grouped by treatment type (surgery, radiation and systemic) and year of diagnosis, using FORDS standards. Health Analysis staff utilized proven methodology to select the most representative record in cases of multiple records. Patients diagnosed with recurrent disease were excluded. Histology was limited to carcinoma.

Figure 3 is a stratification of military rank aggregated for years 2002-2010. Data for years 2000-2001 were unavailable for extraction. The difference between n=753 and n=780 are attributed to cases diagnosed from 2000-2001 that were not extractable. There were 780 breast cancer cases included in this analysis.

Figure 3: AD Females (18-69) diagnosed with Breast Cancer, Rank at time of Diagnosis, Year of diagnosis 2002-2010* N=780



NMCPHC Health Analysis
 Source: Military Health System Data Repository (MDR), Defense Enrollment Eligibility Reporting System (DEERS), Feb 2014
 *Data for years 2000-2001 is unavailable for extraction.

References

1. AJCC Cancer Staging Manual, Fifth Edition, American Joint Committee on Cancer, Lippincott-Raven, Philadelphia, 1997.
2. AJCC Cancer Staging Manual, Sixth Edition, American Joint Committee on Cancer, Springer, New York, 2002.
3. AJCC Cancer Staging Manual, Seventh Edition, American Joint Committee on Cancer, Springer, New York, 2010.
4. Facility Oncology Registry Data Standards (FORDS) Manual (2013) and earlier editions. Commission on Cancer of the American College of Surgeons, Chicago, 2013.

Additional reference material:

National Comprehensive Cancer Network (NCCN)[®] Clinical Practice Guidelines in Oncology, NCCN Treatment for Treatment of Cancer by Site Breast,
http://www.nccn.org/professionals/physician_gls/f_guidelines.asp.

American College of Surgeons Cancer Programs Commission on Cancer Quality of Care Measures (2007)
<http://www.facs.org/cancer/qualitymeasures.html>.

International Classification of Disease for Oncology, third edition. April Fritz, Constance Percy, et al., editors. World Health Organization, Geneva, 2000.

GLOSSARY OF ACRONYMS

ACS-CoC	American College of Surgeons Commission of Cancer
ACTUR	Automated Central Tumor Registry
AD	Active duty
AFB	Air Force Base
AFHSC	Armed Forces Health Surveillance Center
AJCC	American Joint Committee on Cancer
BE&S	Benefits, Education and Support Division
CAHPS	Consumer Assessment of Healthcare Providers and Systems
CAP	College of American Pathologists
CBCP	Center of Excellence for Breast Care
CBE	Clinical breast examination
CoC	Commission on Cancer
CPGs	Clinical Practice Guidelines
DEERS	Defense Enrollment Eligibility Reporting System
DHA	Defense Health Agency
DMDC	Defense Manpower Data Center
DMSS	Defense Medical Surveillance System
DoD	Department of Defense
DoDCCR	DoD Comprehensive Cancer Registry
DoDSR DoD	Serum Repository
DOEHRS	Defense Occupational and Environmental Health Readiness System
DON/CSRP	Department of Navy Cancer Surveillance and Registry Program
DTIC	Defense Technical Information Center
DU	Depleted uranium
EAD	Epidemiology and Analysis Division
EDCs	Endocrine disrupting chemicals
EPA	Environment Protection Agency
FORDS	Facility Oncology Registry Data Standards
HCSDB	Health Care Survey of DoD Beneficiaries
HEDIS	Health Plan Employer Data and Information Set
HORCE	Health Outcomes Research Center of Excellence
HRB Survey	Survey of Health Related Behaviors among Active Duty Military Personnel
IARC	International Agency for Research on Cancer
JPC	Joint Pathology Center
MCC	John P. Murtha Cancer Center
MDR	MHS Data Repository
MHS	Military Health System
MRI	Magnetic resonance imaging
MSMR	Medical Surveillance Monthly Report
MTF	Military Treatment Facility
NAACCR	North American Association of Central Cancer Registries
NCDB	National Cancer Data Base
NCI	National Cancer Institute
NMCPHC	Navy and Marine Corps Public Health Center's
Non-EDC	Non-Endocrine Disrupting Chemical
NTP	National Toxicology Program

NZHTA	New Zealand Health Technology Assessment
OCMO	Office of the Chief Medical Officer
OEF/OIF/OND	Operations Enduring Freedom/Operation Iraqi Freedom/Operation New Dawn
PDHA	Post-Deployment Health Assessment
PDHRA	Post-Deployment Health Reassessment
POEMS	Periodic Occupational and Environmental Monitoring Summaries
REFRAD	Release From Active Duty
RR	Relative Risk
SEER	National Cancer Institute's (NCI) Surveillance, Epidemiology, and End Results
SIC	Shinkampo Incinerator Complex
USAPHC	U.S. Army Public Health Command
USPSTF	U.S. Preventive Services Task Force
USU	Uniformed Services University
VA	Veteran's Affairs
VOCs	Volatile Organic Compounds
WCRF/AICR	World Cancer Research Fund/American Institute for Cancer Research
WRNMMC	Walter Reed National Military Medical Center

ACKNOWLEDGMENTS

From Defense Health Agency:

Thomas V. Williams, PhD, Director, Methods, Measures and Analysis

Andrew D. Plummer MD, MPH, CDR, USPHS, Clinical Support Division Chief, Evaluation and Analysis Branch

Richard K. Gromadzki, D.Sc, Vice President Systems and Quantitative Analysis. (Contractor, Axiom Resource Management, Inc.)

Andrea Linton, MS, Research Associate (Contractor, Axiom Resource Management, Inc.)

Rae Bremer, BA, Administrative Assistant (Contractor, Axiom Resource Management, Inc.)

From the Schneider Institutes for Health Policy, Institute for Behavioral Health, Heller School for Social Policy and Management, Brandeis University:

Mary Jo Larson, PhD, Senior Scientist

Deborah Garnick, ScD, Professor

Rachel Sayko Adams, PhD, Senior Research Associate

Ruslan V. Nikitin, MS, Research Associate

Grant A. Ritter, PhD, Senior Scientist

From the Armed Forces Health Surveillance Center:

William P. Corr. Colonel, Medical Corps, United States Army, Assistant Director, Epidemiology & Analysis Division

Leslie Clark PhD, MS, Senior Managing Epidemiologist (Contractor, General Dynamics Information Technology)

From the Navy and Marine Corps Public Health Center:

Paul D. Rockswold, MD, MPH, FAAFP, CAPT, MC, USN (UMO/DMO), Head, Health Analysis

Elizabeth Butts, MPH, Department of Navy Cancer Registry and Surveillance Program Manager.

Tara Raleigh Blando MPH, Epidemiologist/ Senior Consultant (Contractor: Booz Allen Hamilton)

**Murtha Cancer Center/Walter Reed National Military Medical Center
(MCC/WRNMMC):**

COL Craig D. Shriver, MD, FACS, MC, Murtha Cancer Center Director

Kangmin Zhu, MD, PhD, Associate Director for Military Epidemiology and Population Sciences
(Contractor: Henry Jackson Foundation)

James F. Bates, PhD, Chief Administrative Officer (Contractor: Henry Jackson Foundation)

William P. Mahr, LTC (U.S.A. Retired), M.S., CIP, Deputy Chief Administrative Officer (Contractor: Henry Jackson Foundation)

Jo Kruse, Certified Tumor Registrar, Manager, Murtha Cancer Center Cancer Registry

Joint Pathology Center

Francisco J. Rentas, PhD, SBB, Director, Research, Education, Tissue Repository Operations

Lisa P. Holmes, MA, Program Manager, DoD Central Cancer Registry