



*The Millennium Cohort Study:
Answering Long-term Health Concerns
of U.S. Military Service Members by
Integrating Longitudinal Survey Data
With Military Health Systems Records*

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Part II. Pre-deployment. The Millennium Cohort Study:
Answering Long-term Health Concerns of US Military
Service by Integrating Longitudinal Survey Data
with Military Health System Records

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Summary

Military service involves unique occupational experiences and intense stressors that may have profound impact on long-term health. Most studies of military-related exposures are limited by retrospective and cross-sectional design, convenience sampling, and/or short follow-up. The Millennium Cohort Study is the largest population-based prospective health study in US military history, designed to evaluate the long-term health impact of military service. The Cohort currently consists of four panels enrolled separately in 2001, 2004, 2007, and 2011, totaling approximately 200,000 participants from all service branches, and includes both active-duty and Reserve and National Guard personnel. Participants are surveyed at three-year intervals for up to 21 years while in service and post service. At least one follow-up has been completed by over 70% of the Cohort, and >50% of the current participants have deployed in support of the wars in Iraq and Afghanistan. The Millennium Cohort Study is setting a new standard for prospective evaluation of the long-term health consequences of military occupational exposures, among both active military personnel and the growing number of veterans who have separated or retired from military service and entered the civilian population. The rigorous design and strength of these data provide invaluable information on the associations between military service experiences, such as deployment, and a variety of mental and physical health outcomes. Results of this study have both military and national public health significance and will be useful in designing policy and preventive strategies in the years to come.

Background of the Millennium Cohort Study

The impetus for the initiation of the Millennium Cohort Study was in large part a result of the events that followed the 1991 Gulf War, a conflict which deployed nearly 700,000 US service members to Kuwait after the invasion by Iraqi Forces (Committee on Measuring the Health of Gulf War Veterans, 1999). Shortly after the conflict, thousands of service members reported a variety of symptoms and illnesses. Questions arose as to whether these health issues were a result of the military deployments; however, no epidemiologic study was in place to address these concerns. Over a billion dollars were subsequently spent on post-symptom assessments, but such efforts were limited by the lack of baseline data to assess temporal associations and were subject to a variety of biases, including recall bias (Committee on Measuring the Health of Gulf War Veterans, 1999). In short, most studies of military-related exposures were limited by retrospective or cross-sectional design, convenience sampling, and/or short follow-up (Department of Veterans Affairs 1999; Gray 1998; Kang 1995).

In the late 1990s, the US Department of Defense (DoD) identified the need for a coordinated epidemiological research study to determine if military experiences, including deployment, affect long-term health outcomes. The Institute of Medicine (IOM) specifically advocated for a large, prospective study for evaluating exposures and their potential effects on a broad range of health outcomes, which was endorsed by Congress (Gray 2002; Secretary of Defense 1998). Section 743 of the Strom Thurmond National Defense Authorization Act (1999) declared: "The Secretary of Defense is hereby authorized to establish a center devoted to a longitudinal study to evaluate data on the health conditions of members of the Armed Forces upon their return from deployment on military operations for purposes of ensuring the rapid

identification of any trends in diseases, illnesses, or injuries among such members as a result of such operations” (Strom Thurmond National Defense Authorization Act for Fiscal Year 1999, 1999). For that reason, the DoD Center for Deployment Health Research was established at the Naval Health Research Center (NHRC) in San Diego, California.

In response to the recommendation for a large, longitudinal study of US members, the Millennium Cohort Study was conceived in 1999. The study received institutional (NHRC) and DoD approval and began in July of 2001. Fortuitously, the research was initiated before the current operations (pre-9/11); hence, it established baseline pre-deployment health and behavioral data for a large cohort of US military service members.

The Millennium Cohort Study was designed in collaboration with all military services and the Department of Veterans Affairs to meet the research needs of the DoD and Veteran Service Organizations (VSOs). The Cohort consists of military members from all service branches and includes active-duty, Reserve, and National Guard personnel. Compared to the prior Gulf War registries, this study has the advantage of collecting prospective individual-level data regarding both pre- and post-deployment health data to robustly assess changes over time.

The primary study objective of the ongoing Millennium Cohort is to evaluate the impact of military service, including deployments and other occupational exposures, on long-term health. Important health outcomes include both subjective measures of symptoms and functional health, as well as objective clinical diagnoses obtained from medical records. Information is collected pre-deployment and post-deployment to allow for the assessment of the impact of military deployments and other experiences. The longitudinal study design will collect data among participants over a 21-year period (20 years of military service, plus one year). Over the

last decade (since 2001), the Millennium Cohort Study has become the largest population-based prospective health study in US military history, providing significant contributions to the understanding of the long-term health impacts of military service.

Study Population

The Cohort currently consists of four panels enrolled separately in 2001, 2004, 2007, and 2011, totaling approximately 200,000 participants from all service branches. Participants are surveyed at three-year intervals (termed 'waves') for up to 21 years while in service and post service. Participation in the study is by invitation to ensure that a random sample of the military population is enrolled; this strategy was utilized to overcome the limitation of Gulf War registry data, which may have been confounded by self-selection biases. Information on the dates and final enrollment numbers for each of the enrollment panels is shown in Table 1. In addition to re-surveying participants every three years, a new panel has also been enrolled every three years since 2001.

Oversampling of specific groups within the military for participation in each panel was performed in order to have adequate sample sizes to access health outcomes in specific groups of interest (Table 1). For example, some panels have oversampled Reserves/National Guard and women, given the higher numbers of these groups deployed in the current operations compared to previous conflicts.

To illustrate how the panels for the Millennium Cohort Study were constructed, 256,400 (11%) of the 2.2 million uniformed personnel (October 2000) in Panel 1 were invited to join the

study (data from Defense Manpower Data Center [DMDC]). This group represented a cross-sectional sample of the entire military service population. Of those invited, 214,388 were successfully contacted to participate, and 77,047 (36% of the contacted group) joined the study (Table 1). The numbers invited and response rates are shown in Tables 1 and 2. For Panel 1, oversampling was performed to achieve an enrollment of 30% who had been deployed to southwest Asia, Bosnia, and/or Kosovo after August of 1997. This group, therefore, provides data on the potential impact of prior deployment on future military and health outcomes. Additionally, Panel 1 was oversampled for Reserve, National Guard, and female service personnel (Table 1).

Oversampling was also performed for subsequent panels, as shown in Table 1. For example, Panel 4 was oversampled for married service members to assist with the enrollment of the concurrent Millennium Cohort Family Study, which was initiated in 2011. Since military families may be significantly affected by a service member's deployments and health outcomes, this concurrent study will survey spouses of active duty members to better understand the needs of family members.

Characteristics of the demographic and military composition of Panels 1-3 at enrollment are shown in Table 3. Response rates at the first and subsequent survey cycles for the first three panels are shown in Table 2. The overall baseline response rate was 31%, and at least one follow-up survey has been completed by >70% of the Cohort. As of this writing, 57% of the current participants (Panels 1-3) have deployed at least once in support of the wars in Iraq and Afghanistan, and 28% have deployed multiple times. These data exemplify that the Millennium Cohort Study has adequate numbers to compare deployed vs. non-deployed service members and

their outcomes. Moreover, currently, 33% of the Cohort have left military service and continue to be followed over time, which allows for the evaluation of the potential long-term effects of service after separation or retirement (Table 3).

To summarize, since the end of the 2007-2008 survey cycle, the Cohort had >150,000 participants, making it the largest prospective study in US military history. This research offers unprecedented information on the potential effects of military experience, including deployment and combat, on a variety of mental and physical health outcomes. With the 21+ year follow-up planned, this study will also assess longer-term outcomes, including those which develop after military service. With the initiation of the Millennium Cohort Family Study, data on both the service member and spouse will now be available to better inform DoD policies. Further information about the Millennium Cohort Study and Family Study can be found at <http://www.MillenniumCohort.org> and <http://www.FamilyCohort.org>.

Study Methodology

Survey Instrument

A questionnaire was developed by focus groups and tested in a pilot study (n=1000) to provide data which are not available in other DoD datasets. Specifically, the Millennium Cohort survey includes self-reported, individual-level data. It consists of 100 items, many with multiple components (total of >450 questions), and completion takes approximately 30-45 minutes.

The questionnaire collects information on the service member's physical, behavioral, and mental health and utilizes a variety of standardized questionnaires (shown in Table 4). Additionally, the survey captures data on military experiences (including deployments, combat, and occupation exposures) and other metrics (e.g., sleep, diet, alcohol and tobacco use, complementary and alternate therapies, and physical activity). Specific questions assessing combat, occupational, and chemical/biological/radiological warfare exposures are shown in Table 5. Follow-up surveys (administered every three years) allow for capture of the changing nature of the members' experiences and health; for example, symptoms can be followed over time and characterized as new-onset, persistent, relapsed, or resolved. The survey is modifiable and has been revised during each survey cycle to expand information on new militarily relevant issues - e.g., questions on exposure to burn pits, sustaining head trauma, and resiliency factors have recently been incorporated.

Participants respond to an invitation to complete a survey via a secure website or a traditional paper survey. The Internet is of particular benefit to a highly mobile population, especially those who deploy or frequently relocate. Today, nearly 90% of our participants complete their surveys via the website. Advantages to the use of the Internet include more rapid use of the data, increased data reliability, and reduction in survey costs, such as postal mailings and electronic entry of the written records via Teleform, which are otherwise incurred.

Survey Methods

Standard methods for conducting the survey are utilized and have been modeled after the work of Dillman (Dillman 1978). Data on military rosters and initial contact addresses are obtained from DMDC. Information about the study is sent to participants via initial postcards, followed by emails. These messages inform service members about the study and request their voluntary participation. In order to gather a broad spectrum of military experiences, the study team encourages all military personnel who receive an invitation to complete the survey so that their unique experiences are included.

All forms of communication include the survey web link and a computer-generated study identification number. To ensure that the invited participant is the person entering the site, a 'digital signature,' comprised of both the subject identification number along with the last four digits of the member's Social Security number, is used; all transmissions of data occur over a secure and encrypted connection. Besides the web-based survey, participants receive a printed copy of the survey with a postage-paid return envelope. Repeat mailings are sent over the course of the survey cycle (typically 12-18 months to ensure those who may be deployed are able to respond during the cycle) until a completed survey is returned, the service member explicitly declines to participate, or the survey cycle concludes.

Each participant provides his or her preferred postal and email address and phone number. Updates on changes to the participants' contact information are requested on a regular basis, and returned mail (using "Return Service Requested") is logged into a system that tracks incorrect addresses using a mail item barcode. Service members may ask to have their names from the mail lists and/or to be withdrawn from the study at any time.

Retention is paramount in this 21-year longitudinal study, as it examines both short- and long-term outcomes. A variety of techniques is utilized to encourage continued participation, including a letter welcoming each participant to the Cohort, semiannual appreciatory postcards at Veterans and Memorial Day (Welch 2009), and newsletters that highlight the study's findings and its impact on DoD policies. Additionally, all correspondence contains the study's recognizable logo, which has been used since the study's initiation in 2001. Finally, upon completion of each survey, participants are offered a modest incentive such as a Millennium Cohort Study coin, hat, coaster, magnet, key chain, or phone or gift card.

Challenges to the success of surveying military members encompass not only the mobility of the population, but also concerns regarding the legitimacy of the research. The Millennium Cohort Study is DoD-sponsored research supported by all service branches and Veteran Affairs. The study has been approved by the Institutional Review Board (NHRC 2000.0007) and Office of Management and Budget (OMB Approval Number 0720-0029), and has a Report Control Symbol number (RCS Number DD-HA(AR)2106) for surveying both active duty members and separated personnel. Other approaches to confirm the study's validity are utilized, including messages on members' "Leave and Earning Statements" (LESSs), press releases to military newspapers, inclusion of the study site's DSN number and .mil address on communications to participants, and endorsement letters from service members. Further, the support of both military and Veterans Service Organizations (VSOs) has been critical. Overall, the success of these techniques is exemplified by the strong response since the study's inauguration over a decade ago.

Survey Responses

Non-response to the invitation to participate was assessed via phone interviews among Panel 1 (2001) nonresponders (n=3000); the main reason cited for not participating was stated as being 'out of the military. Additional comparisons of medical record data between responders and non-responders have been conducted and showed little bias (Wells 2008a). Finally, statistical assessments of non-response were performed after the 2004 survey cycle (Littman 2010). Continued assessments of the potential impact of non-response to the initial and follow-up surveys are planned.

Linkage with Other Medical and Military Data Sources

Participant survey data can be linked to a variety of other data sources to achieve a robust evaluation of the service members' health and military experiences. Potential sources of linkage are shown in Table 6. All data are confidentially maintained by using participant subject identification numbers and vigorous security measures; databases are protected behind firewalls restricted to local host access, and all user accounts require specific permissions for access.

Examples of available data linkages include both the Standard Ambulatory Data Record (SADR) and the Standard Inpatient Data Record (SIDR), which contain International Classification of Diseases, 9th Edition (ICD-9) codes from both outpatient and inpatient military medical records. Medical diagnoses from civilian facilities paid for using the TRICARE insurance system (Tricare Enrollment Data - Institutional [TEDi] and TRICARE Enrollment Data - Noninstitutional [TEDni] databases) are also utilized. Medication data are available from the Pharmacy Data Transaction System (PDTS), and immunization data are accessible from the

DMDC. Pre-service survey data among Marine Corps personnel who completed recruit training at the Marine Corps Recruit Depot in San Diego (via the Recruit Assessment Program) and all births among service members (DoD Birth and Infant Health Registry) can be linked for specific health outcomes; both of these large datasets are maintained at NHRC. Similarly, information can be obtained from the Career History Archival Medical and Personnel System (CHAMPS), a comprehensive database that provides an individually based, longitudinal record of career events and medical events from the date of enlistment until the date of separation or retirement. Additionally, data on deployments (DMDC) and environmental exposures are obtainable. Linkages with the Veterans Administration Systems are being explored, as an increasing number of participants have separated from the service. Overall, these data complement the survey's subjective measures with objective measures of exposures and health outcomes providing additional methods to capture data on the health of the Cohort.

Value of the Millennium Cohort Study

Nearly two million US troops have been deployed to Afghanistan and Iraq since October 2001, some of whom are returning with an array of mental and physical health complaints (Institute of Medicine 2010). As such, the Millennium Cohort Study is an essential component of the DoD's Force Health Protection strategy. This large study is setting a new standard for prospective evaluation of the potential short- and long-term health consequences of military occupational exposures, among both active military personnel and the growing number of veterans who have separated or retired from military service and entered the civilian population. Unlike data assembled from Gulf War veterans, the Millennium Cohort Study collects pre-

deployment information and follows service members over time to allow for the longitudinal assessment of military service experiences, such as deployment, and a variety of mental and physical health outcomes. This study will allow military leaders and researchers to understand the impact of military service and deployments more completely than ever before in US military history. Findings of this study can inform DoD policy, preventive and treatment programs, interventional studies, and military training requirements.

To address public and veteran concerns over the potential impact of military deployments to Iraq and Afghanistan on veterans' health, this longitudinal study allows for the collection of multiple exposures and potentially related outcomes. Further, owing to the prospective study design, the potential for participant recall bias (an issue with many of the Gulf War retrospective studies and registries) is markedly reduced. The survey can also be modified based on new threats to military personnel and newly discovered medical outcomes. Compared to the Framingham Heart Study (Gray 2002), this study may contribute knowledge which can be applied to the prevention or early management of diseases of public health importance among both military and civilian populations. Data from this study have already been used by Health Affairs to enhance preventive programs and by the IOM to define military health care needs (Institute of Medicine 2010).

Reserve and National Guard

As Reservists and National Guard members have been called to active duty service at an unprecedented rate over the past decade, understanding health outcomes among these groups is

critical. Debate exists over whether or not these groups have unique experiences that influence health outcomes (e.g., PTSD) post-deployment (Vasterling 2010). The Millennium Cohort Study is distinct in its collection of data among both active duty and Reserve/National Guard personnel. To date (Panels 1-3), a total of 54,608 Reserve/National Guardsmen are participants of the Millennium Cohort Study. The current enrollment cycles will enroll additional members from these vital groups.

To date, several of the Millennium Cohort Study papers have examined outcomes among Reserve/National Guard personnel. Of particular note is a study that showed increased alcohol outcomes (including binge drinking, heavy drinking, and alcohol-related problems) among Reserve/Guard personnel deployed with combat exposures. This finding is concerning in light of increased reliance on Reserve/Guard forces supporting the current operations. Possible explanations for increased risk in Reserve/Guard members after deployment include: inadequate training and preparation of civilian soldiers for the added stresses of combat exposures during deployment, increased stress transitioning between military and civilian occupational settings, lack of military unit cohesiveness, and less access to supportive services (Jacobson 2008). Such data are key in informing/influencing DoD policy and preventive strategies. Future research is planned with the Millennium Cohort Study to examine Reserve/National Guard members for a variety of additional health-related outcomes.

Foundational and Methodological Studies

The Millennium Cohort Study is the first large, longitudinal study of its kind in a US military setting. Initial publications regarding this study included several foundational papers to validate the reliability of the study's design and survey instrument. These studies examined internal reliability between survey responses, validity of responses by comparing survey data to both medical and military record data, potential response bias by comparing responders and non-responders, and differential responses by mail and Internet questionnaires. Overall, these foundational studies established that the Millennium Cohort Study Cohort was representative of US military service personnel and that the survey data were reliable.

The internal consistency of responses on the standardized instruments and concordance of responses in a test-retest setting were evaluated among 76,742 participants and enrollment of a subgroup of 470 participants who submitted an additional survey within six months of their original submission, respectively. The results of this study showed a high internal consistency for 14 of 16 health components, with lower internal consistency found among two alcohol components. Further, the subgroup analysis noted substantial test-retest stability for stationary variables. These results demonstrate the excellent internal consistency and stability of several standard health instruments utilized in the Cohort (Smith TC 2007a).

Additional studies assessed the accuracy of self-reported medical history and deployment data. In the first study, the accuracy of self-reported medical conditions was evaluated, since self-reported diagnoses may differ from medical record diagnoses, due to misunderstanding during clinician-patient communications and/or self-diagnosis of symptoms. Thirty-eight self-reported medical conditions were compared to the electronic medical record data. Using positive and negative agreement statistics for less-prevalent conditions, near-perfect negative agreement

and moderate positive agreement were found for the 38 diagnoses (Smith B 2008a). In a second study, self-reported and military deployment data were compared for >51,000 participants and agreed in 92% of cases. Agreement was substantial for deployment status, frequency, and number of deployments (kappa statistics = 0.81, 0.71, and 0.61, respectively) (Smith B 2007c). Reasons for instances of disagreement between self-report and the military records are unknown, but may be due to more recent deployment being reported by participants before military records are updated, deployment occurring at a different time or location, or that the member could not report his/her deployment (e.g., in the case of Special Forces). Overall, deployment timing and duration metrics, which are critical for military epidemiological studies, are valid in the Millennium Cohort Study.

Other studies have compared self-reported anthrax vaccination to electronic vaccine records for 67,018 participants (2001 and 2003) and found greater than substantial agreement (kappa=0.80): of all participants with electronic documentation of anthrax vaccination, 98% self-reported being vaccinated; of all participants with no electronic record of vaccination, 90% self-reported not receiving a vaccination (Smith B 2007a). Further agreement between self-reported smallpox vaccination and electronic vaccination records was examined among 54,066 participants. Substantial agreement (kappa =0.62) was found between self-report and electronic recording of smallpox vaccination: of all participants with an electronic record of smallpox vaccination, 90% self-reported being vaccinated; of all participants with no electronic record of vaccination, 82% self-reported not receiving a vaccination (LeardMann 2007). In addition, in both of these studies, discordant reporting of anthrax or smallpox vaccination was not associated with substantial differences in health among the participants. Finally, a study was conducted on the concordance between self-reported and electronic occupation codes for female participants

and demonstrated that self-reported occupation can be used with confidence (Smith TC 2007b). These foundational studies display the excellent reliability of survey responses and highlight the distinct advantage of the Millennium Cohort Study's ability of obtaining both medical and military data from multiple sources.

Analyses have also been conducted regarding the potential for response bias. One study determined if health, as measured by healthcare use preceding invitation, influenced responses to the invitation to participate in the Millennium Cohort Study. Inpatient and outpatient diagnoses were identified among more than 68,000 people during a one-year period prior to the invitation to enroll. Response rates were similar over a diverse range of inpatient and outpatient diagnostic categories and number of days assessing healthcare between responders and nonresponders (Wells 2008a). A second study examined possible nonresponse biases by evaluating data from the baseline and first follow-up survey among 76,775 eligible individuals. Similar to other studies (Cunradi 2005; Young 2006), characteristics associated with a greater probability of response included female gender, older age, higher education level, officer rank, active-duty status, and lack of chronic alcohol consumption, history of smoking, or major depressive disorder. There was no difference in response by history of PTSD, panic disorder, or mode of response (i.e., paper vs. the Internet). These findings suggest that the prospective data from this Cohort are not substantially biased by non-response at the first follow-up assessment (Littman 2010).

Finally an analysis of the use of the Internet vs. paper was conducted. Over 50% of the 77,047 Panel 1 participants chose the Internet, and as expected, Internet responders were slightly more likely to be male, to be younger, to have a college degree, and to work in information

technology. Question completion rates were 98.3%, on average, for both Internet and paper responders (Smith B 2007b). Since 2001, an increasing number of Millennium Cohort Study participants have responded via the Internet, with ~90% participating during the last survey cycle (2007) through this route.

Further methodology work will continue to ensure that the Cohort is representative of the US military population. Methods to encourage non-biased responses and retention in the Cohort are also in place and updated over time.

Health Outcomes: Findings to Date

Mental Health and Behavioral Findings

Given the high risk of mental health problems reported among service members returning from the current operations in Iraq and Afghanistan (Hoge 2004; Hoge 2006; Milliken 2007), several publications from the Millennium Cohort Study have focused on these outcomes and provided cutting-edge work in the areas of posttraumatic stress disorder (PTSD), depression, and alcohol and tobacco use among US service members. Because of the collection of pre-deployment data and follow-up longitudinal data, this study can assess the temporal association between exposures and outcomes and evaluate the natural history of symptoms and diseases over time.

In an early study, new-onset and persistent PTSD symptoms were evaluated using initial (July 2001 to June 2003) and follow-up data (June 2004 to February 2006). A positive screen for

PTSD was based on the checklist-civilian version using *Diagnostic and Statistical Manual of Mental Disorders*, Fourth Edition (DSM-IV) criteria (at least one intrusion symptom, three avoidance symptoms, and two hyperarousal symptoms at moderate or more extreme levels, and a total score ≥ 50). A positive screen for new-onset PTSD or self-report of a diagnosis from a health care provider were identified in 7.6-8.7% of deployers who reported combat exposures between baseline and follow-up, 1.4-2.1% of deployers who did not report combat exposures, and 2.3-3.0% of non-deployers. Among those with a positive screen for PTSD at baseline, deployment did not affect persistence of symptoms; however, among those with combat exposure, 43% continued to screen positive post-deployment. In summary, this work showed that combat deployers had a three-fold higher odds of PTSD symptoms, and that specific combat exposures, rather than deployment itself, significantly affect the onset of PTSD (Smith TC 2008a).

Additional work in the area of PTSD evaluated potential vulnerability or resiliency factors. One study found that a positive screen for new-onset PTSD or self-report of a diagnosis from a health care provider was >two-fold higher in both women and men who reported assault prior to a combat deployment (Smith TC 2008b). This study and others (Iversen 2008) demonstrate that prior assault confers an increased vulnerability for, rather than resilience against, PTSD symptoms among deployed military personnel who experience combat. A second study performed among combat deployers (n=5410) found that 7.3% had a positive screen for new-onset PTSD or newly reported diagnosis from a health care provider at follow-up. Individuals whose baseline mental or physical component summary scores were below the 15th percentile had a two-to three times risk PTSD compared with those in the 15th-85th percentile. These data suggest that service members with a history of assault or low mental/physical health

status before combat exposure may represent a more vulnerable group that could potentially benefit from interventions targeted to prevent PTSD (LeardMann 2009). In another study, participants who reported proportionately less physical activity were more likely to screen positive for PTSD. Specifically, those with ≥ 20 minutes of vigorous physical activity twice weekly had significantly decreased odds for new-onset (odds ratio [OR] 0.58, 95% confidence interval [CI] 0.49-0.70) and persistent (OR 0.59, 95% CI 0.42-0.83) PTSD symptoms. These data suggest that physical activity, especially vigorous activity, may be associated with decreased odds of screening positive for PTSD, and that a physical activity component may be valuable to PTSD treatment and prevention programs (LeardMann 2011).

Finally, a recent study using the Millennium Cohort Data assessed the relationship of predeployment psychiatric status and injury severity with postdeployment PTSD. The study involved participants who completed a baseline questionnaire (from July 2001 through June 2003) and at least one follow-up questionnaire (from June 2004 through February 2006 and from May 2007 through December 2008) and who were deployed in the intervening period. Of 22,630 eligible participants, 8.1% screened positive for PTSD at follow-up, and 0.8% sustained a deployment-related physical injury. The odds of screening positive for PTSD were 2.52 (95% CI, 2.01-3.16) times greater in those with ≥ 1 baseline mental health disorder and 1.16 (95% CI, 1.01-1.34) greater for every three-unit increase in the Injury Severity Score. Irrespective of injury severity, self-reported preinjury psychiatric status was significantly associated with PTSD at follow-up, suggesting that this group may benefit from interventions targeted to prevent or to ensure early identification and treatment of postdeployment PTSD (Sandweiss 2011).

Depression is also an important mental health outcome that may occur among service members. Using the Millennium Cohort data, new-onset depression was studied among service members recently deployed to the wars in Iraq and Afghanistan, and it was found that combat-deployed men and women were at increased risk for screening positive for new-onset depression compared with nondeployed men and women (men: OR 1.32, 95% CI, 1.13-1.54; women: OR 2.13, 95% CI, 1.70-2.65). However, deployers without combat exposures had a decreased odds for screening positive for new-onset depression compared with those who did not deploy (men: OR 0.66, 95% CI, 0.53- 0.83; women: OR 0.65, 95% CI 0.47-0.89), suggesting a “healthy warrior” effect that persons with underlying mental conditions may not be deployable. These data emphasize the importance of post-deployment mental health screening for US service members exposed to combat (Wells 2010).

Similar to PTSD and depression, high rates of alcohol misuse after combat deployment have been reported among personnel returning from war (Milliken 2007; Richards 1989). Data from the Millennium Cohort Study were utilized to determine whether deployment with combat exposures was associated with new-onset alcohol consumption, binge drinking, and alcohol-related problems. Participants who completed both a baseline (July 2001 to June 2003) and follow-up (June 2004 to February 2006) questionnaire were studied. After exclusion criteria were applied, the analyses included 48,481 participants (active duty, n=26,613; Reserve or National Guard, n=21,868). New-onset prevalence of heavy weekly drinking, binge drinking, and alcohol-related problems among Reserve or National Guard personnel who deployed with combat exposures was 8.8%, 25.6%, and 7.1%, respectively. Among active-duty personnel, new-onset rates were 6.0%, 26.6%, and 4.8%, respectively. Analyses revealed that Reserve and National Guard personnel who deployed and reported combat exposures were significantly more

likely to experience new-onset heavy weekly drinking (OR 1.63, 95% CI, 1.36-1.96), binge drinking (OR 1.46, 95% CI, 1.24-1.71), and alcohol-related problems (OR 1.63, 95% CI, 1.33-2.01) compared with nondeployed personnel. The youngest members of the cohort were at highest risk for all alcohol-related outcomes. These results suggest that targeted interventions regarding alcohol misuse should be implemented, especially among Reserve and National Guard personnel and younger service members who deploy with reported combat exposures (Jacobson 2008). These data were directly utilized by Health Affairs to enhance alcohol-related programs for Reserve and National Guard personnel.

Similarly, the impact of the stress of military deployments and combat may result in other maladaptive behaviors, including tobacco use. Using participants who submitted baseline data (July 2001-June 2003) and follow-up data (June 2004-January 2006), new-onset smoking was identified among baseline never-smokers and smoking recidivism among baseline past smokers. Smoking initiation was noted in 1.3% of nondeployers and 2.3% of deployers, and smoking recidivism in 28.7% of nondeployers and 39.4% of those who deployed. Additionally, deploying for >9 months and multiple deployments increased smoking recidivism. Since, military deployment was associated with both smoking initiation and recidivism, programs should be implemented during and after deployment to discourage tobacco use (Smith B 2008b). As cigarette use may be prohibited during some deployments (e.g., on the flight deck or in combat situations where the flame may reveal military position) and other forms of tobacco have known negative health effects, additional work examining smokeless tobacco use is currently underway.

Finally, the effect of military deployments and combat environments on disordered eating and weight changes has been studied in the Cohort, since maintaining an ideal weight is

important for overall health. Deployment was not significantly associated with new-onset disordered eating in women or men in the adjusted models. However, deployed women who reported combat exposures were 1.78 times (95% CI 1.02-3.11) more likely to report new-onset disordered eating and 2.35 times (95% CI 1.17-4.70) more likely to lose 10% or more of their body weight compared with non-combat deployers (Jacobson 2009a).

In summary, these data suggest that combat increases the odds for several mental health outcomes, and that certain military service members have increased odds of developing mental and behavioral conditions after combat deployments. Further work in the area of mental health will focus on specific populations (e.g., women and military augmentees), examine the effect of PTSD symptoms on weight changes and binge eating over time, describe the relationship between dwell time (i.e., time at home between deployments) and mental health outcomes, and assess the occurrence of maternal depression among women who deploy shortly after childbirth. Understanding vulnerable populations and how health outcomes are interrelated in service members can help inform the DoD and VA regarding focused preventive and early management programs.

Physical Health Findings

In addition to mental health issues, concerns regarding a variety of physical health outcomes have surfaced, including respiratory conditions among returning service members from Iraq and Afghanistan (King 2011). Data from Millennium Cohort Study participants who completed baseline (July 2001-June 2003) and follow-up (June 2004-February 2006)

questionnaires were studied for respiratory outcomes. Deployers had a higher rate of newly reported respiratory symptoms (persistent or recurring cough or shortness of breath) than nondeployers (14% vs. 10%), especially among ground troops (i.e., Army and Marine Corps). Regarding medical diagnoses, there were similar rates of chronic bronchitis or emphysema (1% vs. 1%) and asthma (1% vs. 1%) among deployers compared to nondeployers. These data suggest that ground-troop deployments may be associated with increased respiratory symptoms, and that specific exposures rather than deployment in general may be determinants of postdeployment respiratory illness (Smith B 2009). Further studies are planned including assessing the natural history of respiratory symptoms and determining if diagnoses of pulmonary diseases are changing over time.

Hypertension and diabetes mellitus are major causes of cardiovascular disease and impact survival. The role of military experiences on these conditions is largely unknown. For example, stressful situations (e.g., combat deployments) may heighten the risk for these conditions. Among Panel 1 participants, 6.9% reported newly diagnosed hypertension between the baseline and follow-up surveys. In the adjusted models, multiple combat exposures was associated with a higher odds of hypertension (OR 1.33, 95% CI 1.07-1.65) compared to non-combat deployers, possibly indicating a stress-induced hypertensive effect (Granado 2009). In a second study, the impact of military deployment, combat exposures, and mental health conditions were studied in relationship to newly reported diabetes mellitus. A total of 44,754 participants were studied (median age 36 years), and the incidence of new-onset diabetes was three cases per 1,000 person-years. After adjustments for covariates (e.g., age, sex, body mass index), screening positive for PTSD was significantly associated with newly reported diabetes (OR 2.07, 95% CI 1.31-3.29). Deployment with or without combat was not significantly associated with diabetes

(Boyko 2010). These data suggest that mental and physical health outcomes may be interrelated and that military members with combat experiences and PTSD may benefit from blood pressure and blood sugar measurements, respectively, to ensure the health of service members over time.

The issues of sleep quality and length have increasingly gained attention as the war has lingered into its second decade. Self-reported sleep patterns were studied among Millennium Cohort members who completed baseline (2001-2003) and follow-up (2004-2006) surveys. This study showed deployment significantly influenced sleep quality and quantity in this population, although the effect sizes were modest. Additionally, personnel reporting combat exposures or mental health symptoms were more likely to have trouble sleeping, suggesting that these subgroups may benefit from sleep assessments (Seelig 2010).

The Cohort has also been utilized to study headache disorders, a leading cause of missed days of work. The prevalence of migraines among men and women were 6.9% and 20.9%, respectively, and recurrent severe headaches, 9.4% and 22.3%, respectively. Combat deployers were found to have a higher odds of any new-onset headache disorder than non-deployers [OR 1.72 (95% CI 1.55-1.90) for men and 1.84 (95% CI 1.55-2.18) for women], while deployers without combat exposure did not. These data suggest that deployed personnel with reported combat exposure are more likely to have headache disorders and provide valuable information on healthcare needs among returning service members (Jankosky 2011).

In addition to medical outcomes, health care utilization has been studied. An early study in the Cohort showed that active duty service members had an increased risk of hospitalization after deployment compared to before deployment, but a lower risk when compared with nondeployers (Smith TC 2009). Recent studies have also examined the use of complementary

and alternative medicine (CAM) use among members of the US military. A cross-sectional study of participants who completed a survey from 2004 to 2006 found that 30% reported using at least one practitioner-assisted CAM therapy and 27% reported using at least one self-administered CAM therapy, whereas 59% did not report using any CAM therapy. Increasing health conditions and health-related symptoms were associated with CAM use (Jacobson 2009b). In a second study, the number and types of medical visits were compared between CAM and non-CAM users. Those who used CAM had a higher odds ratio for hospitalizations (OR 1.29, 95% CI 1.16-1.43) and more outpatient visits (7.0 days vs. 5.9 days, $p < 0.001$) compared to those not using CAM (White 2011). These data suggest that CAM use is common among military personnel and may be a marker for poorer underlying health.

Finally, Millennium Cohort data have been utilized to examine the impact of vaccinations given prior to deployment, including smallpox (beginning in 2001) and anthrax (beginning in the late 1990s). A study examined 40,472 individuals (8,793 of whom received the smallpox vaccine and 31,679 who did not) and found no significant adverse associations with self-reported health outcomes (Wells 2008b). Future studies in the Millennium Cohort will continue to provide policy makers and health care providers with critical information about the impact of military service on mental and physical health outcomes and healthcare utilization. For example, studies will evaluate a range of other health care issues, such as autoimmune diseases, heart disease, cancers, and mortality, which will be of particular interest as the Cohort ages. As new potential exposures (e.g., open air burn pit exposure) or health care concerns (e.g., traumatic brain injury, suicide, motor vehicle crashes) arise, the Millennium Cohort Study is in a valued position to provide critical information to both the DoD and VA. Finally, given the triennial

assessments of health over time, the survey data may detect changes in health over time, which may be the result of new military experiences or implemented preventive programs.

Future Areas of Research

In addition to the future work regarding mental and physical health outcomes, the Millennium Cohort can provide valuable data on a range of topics, including the impact of deployment and mental health symptoms on post-service employability and the health care needs of veterans, data which are critical for the development of VA programs. The newly initiated Millennium Cohort Family Study will also provide data on the dyad (both the service member and spouse) and children, and provide information regarding needed programs to support the military family. Moreover, as few longitudinal data exist on the outcomes of service members long after deployment experiences and service separation, this study will continue to provide important information for the next 21+ years. The study is also perfectly poised to collect invaluable data on the impact of future conflicts or exposures that may occur.

Conclusion

In summary, the Millennium Cohort Study has successfully enrolled over 150,000 US service members, with the goal of achieving >200,000 participants, including military spouses, during the current survey cycle. This is the first comprehensive study to prospectively evaluate the impact of military experiences, together with deployment and combat experiences, on mental and physical health outcomes of US service members. Through its collection of pre-deployment

data, longitudinal study design, and linkage with other medical and military data sources, never has such a wealth of data been available regarding long-term health of veterans. Findings from the Millennium Cohort Study have informed DoD policy to strengthen preventive and treatment programs. The success of this longitudinal study sets a new standard for data collection within both military and civilian populations. With a 21-year follow-up period, the Millennium Cohort Study will continue to provide long-term militarily relevant data on health outcomes and public health issues significant to both DoD and VA leaders and healthcare providers.

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Table 1: Composition of Each Panel in the Millennium Cohort Study

Panel	Dates Enrolled	Years of Service at Enrollment	Oversampled Groups	Roster Size (Date)	Number Contacted**	Total Enrolled (% of those contacted)
1	July 2001- June 2003	All durations (cross-section of military population)	Females, National Guard/Reserves, and prior deployers*	256,400 (Oct 2000)	214,388	77,047 (35.9%)
2	June 2004- February 2006	1-2 years	Females and Marine Corps	150,000 (Oct 2003)	123,001	31,110 (25.3%)
3	June 2007- December 2008	1-3 years	Females and Marine Corps	200,000 (Oct 2006)	154,270	43,439 (28.2%)
4	April 2011- ongoing	2-5 years	Females and Married	250,000 (Oct 2010)	***	***

*Deployment to southwest Asia, Bosnia, and/or Kosovo after August of 1997

**Invalid names/addresses and duplicates were excluded

*****Panel currently being enrolled**

Table 2: Data on Initial Response and Follow-up Rates in the Millennium Cohort Study

Panel/Wave	Initial and Follow-up Response Rates*
Panel 1	
Wave 1 (2001-2003)	77,047/214,388 (35.9% response rate)
Wave 2 (2004-2006)	55,021/77,047 (71.4% follow-up rate)
Wave 3 (2007-2008)	54,790/77,047 (71.1% follow-up rate)
Panel 2	
Wave 1 (2004-2006)	31,110/123,001 (25.3% response rate)
Wave 2 (2007-2008)	17,152/31,110 (55.1% follow-up rate)
Panel 3	
Wave 1 (2007-2008)	43,439/154,270 (28.2% response rate)

*Percentage based on number of members contacted

Table 3: Characteristics of Millennium Cohort Study Participants by Panel

	Panel 1	Panel 2	Panel 3
Characteristics at time of Enrollment	<i>n</i> = 77,019*	<i>n</i> = 31,110	<i>n</i> = 43,439
	(%)	(%)	(%)
Sex			
Male	73.2	61.6	64.3
Female	26.8	38.4	35.7
Birth year			
Pre-1960	21.6	0.7	0.2
1960–1969	37.9	5.4	1.7
1970–1979	34.6	31.9	15.7
1980–later	5.9	62.0	82.4
Race/ethnicity**			
White, non-Hispanic	69.6	71.4	72.2
Black, non-Hispanic	13.8	11.6	11.3
Asian/Pacific Islander	7.9	4.9	5.6
Hispanic	6.4	10.1	7.8
Other	2.3	2.0	3.1
Education†			
High school or less	74.4	84.6	84.8
Some college or more	25.6	15.4	15.2

Service branch			
Army	47.3	48.2	36.4
Air Force	29.0	26.6	29.7
Navy/Coast Guard	19.0	16.9	18.2
Marine Corps	5.1	8.3	15.7
Service component			
Active duty	57.0	59.9	79.3
Reserve/National Guard	43.0	40.0	20.7
Military pay grade			
Enlisted	77.0	88.3	88.5
Officer	23.0	11.7	11.5
Characteristics at Follow-up			
Deployed to current operations[†]			
Yes	47.2	64.5	67.4
No	52.8	35.5	32.6
Number of deployments[†]			
Two or more	23.7	31.9	31.9
One	23.5	32.6	35.5
None	52.8	35.5	32.6
% Separated from military service [†]	40.4	41.5	14.4
% Deceased [†]	0.9	0.4	0.2

*Some initial participants were withdrawn from the study population

** Number of missing values per Panel: P1 = 61, P2 = 42

† Number of missing values per Panel: P1 = 5, P2 = 2, P = 3

‡ Data reflected as of January 2011

Table 4: Standardized Instruments Embedded within the Survey

Construct	Inventory
Physical, mental, and functional health	Short-Form 36
Psychological assessment including symptoms of depression, anxiety, panic syndrome, binge-eating, bulimia nervosa, and alcohol abuse	Patient Health Questionnaire (PHQ)
Post-traumatic stress disorder	Posttraumatic Stress Disorder (PTSD) Checklist-Civilian Version
Alcohol problems	CAGE questionnaire
Specific war-time exposures – depleted uranium, chemical or biological warfare agents	Department of Veterans Affairs Gulf War Survey
Sleep	Insomnia Severity Index

Table 5: Self-reported Combat Experiences and Potential Occupational Exposures

Type of Questions	Specific Questions
Combat*	<ul style="list-style-type: none"> -Witnessing a person's death due to war, disaster, or tragic event -Witnessing instances of physical abuse (torture, beating, rape) -Dead and/or decomposing bodies -Maimed soldiers or civilians -Prisoners of war or refugees
Occupational Exposures	<ul style="list-style-type: none"> -Occupational hazards requiring protective equipment, such as respirators or hearing protection -Routine skin contact with pain and/or solvent and/or substances -Depleted uranium -Microwaves (excluding small microwave ovens) -Pesticides, including creams, sprays, or uniform treatments -Pesticides applied in the environment or around living facilities -Any exposure, physical or psychological, during a military deployment that had a significant impact on your health? Specify:

Table 6: Linkages of Millennium Cohort Study Data with Other Sources

Type of Data	Source
Medical record data from military medical facilities worldwide and civilian facilities covered by the DoD insurance system (TRICARE)	Standard Ambulatory Data Record (SADR) and the Standard Inpatient Data Record (SIDR) TRICARE Encounter Data (TED)
Immunization, deployment (location and dates) and contact data	Defense Manpower Data Center (DMDC)
Pharmaceutical data from military medical facilities and civilian pharmacies which medications are paid for by TRICARE	Pharmacy Data Transaction System (PDTS)
Service and medical data from time of enlistment to separation	Career History Archival Medical and Personnel System (CHAMPS)
Injury data from in theater	Joint Theater Trauma Registry (JTTR) and the Navy-Marine Corps Combat Trauma Registry Expeditionary Medical Encounter Database Total Army Injury and Health Outcomes Database (TAIHOD)
Baseline pre-service data on Marine Corps recruits	Recruit Assessment Program (RAP)
Data on pregnancies and birth outcomes (e.g., birth defects)	Birth and Infant Health Registry

Spouse health, behavioral and relationship data; some child outcomes	The Millennium Cohort Family Study
Environmental Exposures	US Army Public Health Command
Links occupational codes between the military services and civilian counterparts	Master Crosswalk File from the DoD Occupational Conversion Index Manual
Health symptoms and perception, as well as exposure data	Pre- and Post-Deployment Health Assessments (DD2795 and DD2796)
Medical status and resource utilization	Health Enrollment Assessment Review (HEAR)
Mortality data	Social Security Administration Death Master File, Department of Veterans Affairs (VA) files, Department of Defense Medical Mortality Registry, and National Death Index
Medical benefit eligibility and insurance, dates of service, military occupation and locations, centralized immunization data	Defense Enrollment Eligibility Reporting System (DEERS)
Medical encounters at the Veterans Administration Medical Centers	Veterans Administration*
Blood samples	DoD Serum Repository*

*Linkage not currently available

REPORT DOCUMENTATION PAGE

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13. SUPPLEMENTARY NOTES

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<p>Military service involves unique occupational experiences and intense stressors that may have profound impact on long-term health. Most studies of military-related exposures are limited by retrospective and cross-sectional design, convenience sampling, and/or short follow-up. The Millennium Cohort Study is the largest population-based prospective health study in US military history, designed to evaluate the long-term health impact of military service. The Cohort currently consists of four panels enrolled separately in 2001, 2004, 2007, and 2011, totaling approximately 200,000 participants from all service branches, and includes both active-duty and Reserve and National Guard personnel. Participants are surveyed at three-year intervals for up to 21 years while in service and post service. At least one follow-up has been completed by over 70% of the Cohort, and >50% of the current participants have deployed in support of the wars in Iraq and Afghanistan. The Millennium Cohort Study is setting a new standard for prospective evaluation of the long-term health consequences of military occupational exposures, among both active military personnel and the growing number of veterans who have separated or retired from military service and entered the civilian population. The rigorous design and strength of these data provide invaluable information on the associations between military service experiences, such as deployment, and a variety of mental and physical health outcomes. Results of this study have both military and national public health significance and will be useful in designing policy and preventive strategies in the years to come.</p>

15. SUBJECT TERMS Military, health outcomes, epidemiology, pre-deployment, deployment, combat, active duty, reserves
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