

APPENDIX D. REVIEW FOR PROTECTION OF HUMAN RESEARCH VOLUNTEERS FROM RESEARCH RISKS

INSTITUTIONAL REVIEW BOARD RECOMMENDATION

MODIFICATION REVIEW

Date of Review: 25 June 2009 Protocol Number: NHRC.2000.0007
Research Protocol Title: Prospective Studies of U.S. Military Forces: The Millennium Cohort Study
Principal Investigator: Tyler C. Smith, M.S., Ph.D.
Work Unit and Number: Deployment Health Research, 60002
Approximate Dates of the Research: 01 Oct 2000 to 30 Sept 2022
No. of Previous Reviews: 18

The principal investigator submitted a modification to this minimal risk study. The objective of this research is to examine any trends in the health of U.S. military veterans over time. Toward that end, the health of a cohort of regular Active Duty, National Guard, and Reserve military personnel will be followed for 18 years via surveys. Participants are allowed to complete the questionnaire by paper-and-pencil or online at www.millenniumcohort.org.

The modification seeks to allow spouses of participating active duty members to be surveyed in order to obtain insights into the impacts of family dynamics on the health of service members and their immediate family. Service member participants in Panel 4 of the Millennium Cohort will be asked for authorization to contact their spouse to seek participation and to being a secondary subject in the survey administered to their spouse (some questions asked will be about the service member). The service member will be provided a web link to allow viewing of the survey that would be administered to his/her spouse if both parties consent. Questions will also be asked about minor children in the household but the survey questions will not seek to identify any individual child. Survey administration of spouses will be conducted online and through secure servers. Consenting spouses will have their survey responses linked to DoD medical and personnel records. Signed consent for online survey procedures was waived in accordance with 32 CFR 219.117(c)(2) in that the research is minimal risk and involves no procedures for which written consent is normally required outside the research context. Subjects will type their name online and check a box signifying consent. None of the new outside collaborators for "Family Millennium Cohort" (Drs. Schlenger, Marmar, and Fairbank) will receive any identifiable data.

The 'Family Millennium Cohort' survey must receive OMB approval, and that approval documentation must be provided to the NHRC IRB before any enrollment. Similarly, screen shots of the website must be provided to the IRB for review before enrollment, and the IRB must be provided access to website for a practice run-through before any enrollment. The Panel 4 survey for service members has not been reviewed yet, and thus must also receive IRB approval before it is administered. That survey of service members will need DoD approval.

The Board agreed that based on the investigators' presentation of the research and the requested modifications being made, the 32 CFR § 219.111 criteria for the approval of research have been met. With a vote of 8 for, 0 against, Chair abstaining, and 0 members disqualified from the review, the Board recommended to approve this modification after the requested changes were addressed. Those changes were made and approval is recommended.

The next scheduled review is on or before 12 May 2010.

Christopher G. Blood, JD, MA
Chair, NHRC IRB


Signature & Date

DETERMINATION OF APPROVING AUTHORITY

(gsh) (1.) I concur with the recommendation of the IRB, and I approve this modification.

Next review is required no later than: 12 May 2010.

2. I concur with the recommendations of the IRB, but I require additional modifications or restrictions prior to providing continuing approval (Attach modifications or restrictions required).

Next review is required no later than:

3. I disagree with the recommendations of the IRB and recommend (Attach statement regarding recommendations and reasons).

Signature

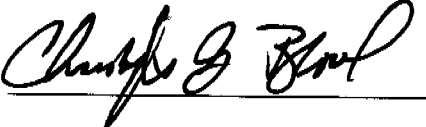

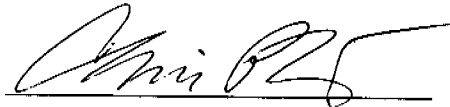
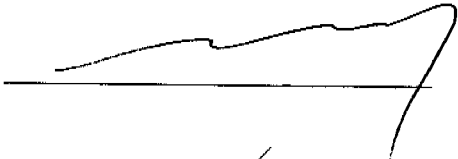

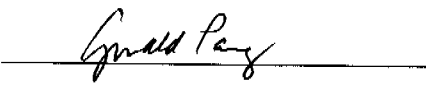
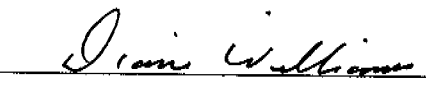
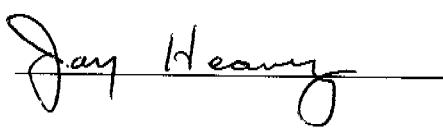

Date (DD/MM/YY)

CAPT K. R. THOMPSON, MSC, USN
Commanding Officer

Gregory C. Utz 19 Aug 2009.
Acting

GREGORY C. UTZ, MD
INF. DIS. & INT. MED. STAFF
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INSTITUTIONAL REVIEW BOARD MEMBERS

<u>Name and Affiliation</u>	<u>Signature</u>	<u>Date</u>
Christopher Blood, J.D., M.A. Naval Health Research Center IRB Chairperson		<u>25 June 09</u>
Mr. Walter Leverette Naval Medical Center San Diego Chaplain Representative		<u>25 JUN 09</u>
Christopher Kneib, J.D., LL.M. Space and Warfare Systems Center, San Diego Legal Representative		<u>25 Jun 09</u>
CDR Dennis Faix, MC, USN Naval Health Research Center Medical Representative		<u>25 JUN 09</u>
HMCS Aurelio Velazquez, Jr. The Naval School of Health Sciences, San Diego Military Representative		<u>25 June 09</u>
Gerald Pang, M.S. Naval Health Research Center Dept 161 Representative		<u>25 JUN 09</u>
Diane Williams, Ph.D. Naval Health Research Center Dept 161 Representative		<u>25 Jun 09</u>
Jay Heaney, M.A. Naval Health Research Center Dept 162 Representative		<u>25 Jun 09</u>
Valerie Stander, PhD Naval Health Research Center Dept 163 Representative		<u>25 JUN 09</u>

06 August 2009

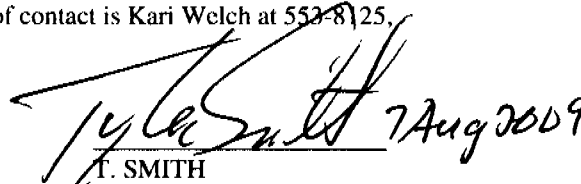
From: Tyler Smith, MS, PhD, Principal Investigator
To: Chair, Institutional Review Board, Naval Health Research Center, San Diego, CA

Subj: MODIFICATION TO PROTOCOL # NHRC.2000-0007, "PROSPECTIVE STUDIES OF U.S. MILITARY FORCES: THE MILLENNIUM COHORT STUDY"

Ref: (a) NAVHLTHRSCHCENINST 3900.2E

Encl: (1) Entire protocol with proposed changes highlighted.

1. Enclosure (1) is submitted to fulfill the reference (a) requirement for the Principal Investigator to document all significant changes being made to an approved protocol.
2. I certify that all study personnel have been informed of and accept the proposed changes.
3. Point of contact for further information is Tyler Smith, MS, PhD, Principal Investigator. I may be contacted at 553-7593, tyler.c.smith@med.navy.mil. My alternative point of contact is Kari Welch at 553-8125, kari.welch@med.navy.mil.


T. SMITH
PI Signature and Date



MODIFICATION OF IRB PROTOCOL

1. **PROTOCOL NUMBER:** NHRC.2000-0007
2. **PROTOCOL TITLE:** Prospective Studies of U.S. Military Forces: The Millennium Cohort Study
3. **WORK UNIT TITLE AND NUMBER:** Deployment Health Research, 60002
4. **PRINCIPAL INVESTIGATOR(S):** Tyler C. Smith, MS, PhD
5. **RISK LEVEL:** Minimal risk
6. **CURRENT STUDY STATUS:** Ongoing
7. **CHANGES SINCE LAST REVIEW:** I respectfully request the following modifications to the protocol:

Collaborating Institution(s): Abt Associates, Inc., Cambridge, MS; University of California, San Francisco, San Francisco, CA; Duke University Medical Center, Durham, NC

Millennium Cohort Family Collaborator(s):

William Schlenger, PhD, Abt Associates, Inc, Cambridge, MS

Charles Marmar, MD, University of California, San Francisco, San Francisco, CA

John Fairbank, PhD, Duke University Medical Center, Durham, NC

- The collaborators listed above will provide expertise on family behavioral and mental health epidemiologic issues. They will assist in the study and survey instrument design, and collaborate and/or serve as their intuition's liaison on research projects for the Millennium Family Cohort Study. All data exchanged which will include self-reported survey data as well as supportive military medical/personnel records, will be deidentified and will follow JRRR/BAA/MOU guidance as directed by NHRC IRB.
 - Each collaborator is operating under a valid assurance to protect human subjects involved in research.
 - CVs for each collaborator are attached.
 - The Naval Health Research Center's IRB will provide primary review over the Millennium Family Cohort Study necessary approvals.

Background

- In recent decades, mental health and related outcomes for US military service members following deployment have been documented for multiple conflicts. Much less attention has been paid, however, to deployment-related outcomes for spouses and other family members of those deployed. Family member functioning can be degraded by separation and associated worries, and service member functioning can be degraded when concern over events at home reduces their ability to concentrate or to be attentive and vigilant. Additionally, war zone stress exposure has been shown to have substantial impact on service members after they return home, which can produce additional stressors for both the service member and their families when they are re-united.
- Family relationships play an important role in the functioning and well-being of US military service members. It has been suggested that family relationships can be an important source of support that bolsters force readiness, or alternatively, a stressor that depletes service members' resources and reduces readiness. Few epidemiologic studies have examined the impact of war zone deployment on family members and family functioning. The Millennium Cohort Study is strategically positioned to complete this research. This research will also facilitate identification of specific interventions, such as deployment-related stress, family member resilience, family support dynamics, service member and family well-being, and force readiness.

Objectives

- The primary Millennium Cohort Family Study objective is to compare the adjusted probabilities of new onset diseases and conditions among military spouses and children.

- The secondary Millennium Cohort Family Study objective is to assess the importance of family support and other factors on positive and negative health outcomes.

Hypothesis

- Stressors associated with deployment (e.g. geographical separation, increased risk of being wounded or killed) are associated with adverse mental health and related outcomes for spouses and children of deployed service members.
- Strong family support is associated with positive mental health and related outcomes for spouses and children of deployed service members.

Procedures

- Based on recommendations from sponsors and advisory committees, and the success of the Millennium Cohort, a fourth enrollment panel will be added to the next survey cycle beginning in 2010. The Millennium Cohort was originally designed to follow three panels of participants that enrolled in 2001, 2004, and 2007 through 2022. The team plans to invite approximately 250,000 individuals of active-duty, Reserve, or National Guard status, with 2-5 years military service experience, oversampling for women, Reserve/National Guard, and those with a deployment-related injury. Out of the 250,000, an estimated 62,500 new participants will enroll. This group will be consented to complete 7 follow-up surveys over 21 years, with one survey to complete every 3 years. The invited group will be a stratified random sample from the Defense Manpower Data Center. The current total number enrolled is 151,597, so this new enrollment will bring the total number enrolled to approximately 214,000 individuals.
- In addition to Panel 4, a Family Cohort component will be added to the next survey cycle beginning in 2010. In order to assess the interrelated health effects of military service and deployment on service members, spouses, and co-resident children, the Millennium Cohort Study team and collaborators will survey the spouses of newly enrolled Panel 4 participants that consent to this assessment. The team estimates that about 10,000 spouses will enroll in the study, about half of whose service member will have been deployed to the conflicts in Iraq and Afghanistan at least once.
- Surrogate data on children health will be obtained from the spouse. The data collected on these children will be generalized. No child will be individually identified for the purposes of this study. Because families and family relationships change over time and to maintain methodological consistency with the Millennium Cohort Study, spouses will be asked to complete 7 follow-up surveys over 21 years, with one survey to complete every 3 years. Participants of the Family Cohort Study will only have the option of completing a web survey.
 - In October of 2009, 250,000 service members will be randomly selected from military rosters. These individuals will be invited to participate in the Millennium Cohort's fourth enrollment cycle once OMB and RCS approvals are in place. These participants will be referred to as Panel 4 participants/members. Out of these Panel 4 members, the married service members will view the following: the Millennium Cohort Family Study survey instrument, and the Panel 4 Millennium Cohort Family Study informed consent document and permission form. From this group of consenters, the first 100 spouses to consent to the study and complete their surveys will be included in a pilot sample. This group of 100 individuals will be treated the same as the large group of Millennium Cohort Family Study participants, however, the internal team of analysts will review their survey to ensure participants are understanding the survey questions. Based on survey research, missing data along with data completion rates will indicate how the survey is interpreted. Also, an open-ended question will be added to the end of the first 100 surveys, "Is there anything you didn't understand or would change in this survey?" This will provide us with information on how the questions were interpreted and understood. We will not be requesting further feedback from these participants
 - Millennium Cohort Study contact methods will be employed, including the modified Dillman survey methodology. Complex algorithms will be developed for email, mail and response tracking.
 - A separate website will be built for this sub-study, but will link directly to the Millennium Cohort Study website, www.millenniumcohort.org. The URL will be www.familycohort.org
 - Like the Millennium Cohort Study, nominal incentives will be offered to participants that complete the survey online, participants will be offered the choice of a \$10 gift card to the following; military exchange (AAFES/NEX gift card), Starbucks, or Amazon.com. AAFES/NEX and Starbucks gift cards will be mailed to participants within 6 weeks of survey completion, and Amazon.com electronic gift cards will be emailed

within one week of survey completion. None of the gift cards are exchangeable for cash.

Data Analysis

The adjusted probabilities of new-onset diseases and conditions among military spouses will be conducted by examining self-reported data, and by validating these data with objective electronic medical data when possible. Spouse-reported data on children will be analyzed but not linked with objective data. Multivariable logistic regression modeling will be used for each outcome, and multivariable Cox proportional hazard modeling when possible. Similar to previous analyses conducted within the Millennium Cohort Study, covariate adjustment will include age, gender, occupation, marital status, race ethnicity, deployment status, branch of service, income, and length of service. SAS statistical analysis program software (SAS Institute, Inc., Cary, NC) will be used for the Millennium Cohort Family Study analyses.

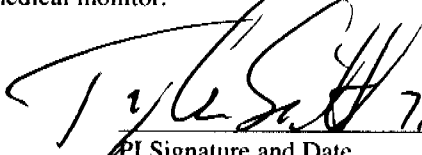
Risks

The data collection procedures are not expected to involve any risk or discomfort for spouses or children. The only risks are those associated with the inappropriate disclosure of data provided. However, this research group has collected similar information from several studies over many years without any cases of inappropriate disclosure.

Data

- We will link to Department of Defense personnel and medical records obtained from the following sources: DMDC (Data Manpower Data Center) and TMA (Tricare Management Activity). For mortality data only, we will link to AFIP (Armed Forces Institute of Pathology), NDI (National Death Index), and VA (US Dept of Veterans Affairs). In addition, if the spouse is an active duty member and retires or separates from military service and utilizes Department of Veterans Affairs for medical services, we will link to VA medical and personnel data as well as the DoD Joint Theater Trauma Registry and the Navy/Marine Corps Trauma Registry. These data will complement subjective measures with objective measures of exposures and health outcomes. These databases are accessed electronically through secure computers located at the Naval Health Research Center. Unique identifiers are used to link each participant with their electronic data. No data regarding a child and his/her health will be linked from any source for the purposes of this study.
- The term "Family" will be defined as: An individual(s) living in household for majority of the time who has an impact on the household environment. Co-residency is not a requirement for the spouse.
- The term "Sponsor" will be defined as the military service member who is a member of the Millennium Cohort Study and has named the invited participant as his/her spouse. The term "your sponsor" will be referred to as "your spouse" throughout the survey. Continued participation of a spouse regardless of relationship status is important since the aim of the study is to look at the long-term health effects. Therefore, co-residency of the spouse is not necessary since some spouses are non-co-residents (i.e. military to military married who are in different services, and spouses that live with parents or other family members while military member is deployed or stationed overseas); however, co-residency of children will be a requirement. Following participants in the study long after they are divorced, separated, or no longer co-residing is still relevant, since such data will be used to assess the long-term health of family members. The relevancy of collected data on the sponsor may be diminished if contact with the ex-spouse becomes limited.
 - Attached is the Panel 4 Millennium Family Cohort consent form. This web-based consent form is to be digitally signed by the Panel 4 Millennium Cohort member prior to his/her spouse being invited to participate in the Millennium Family Cohort Study. Prior to providing permission for the spouse to participate, there will be a link to the Millennium Family Cohort Study survey for review, and the Panel 4 participant will be able to print the consent form for his/her records. Once electronic consent has been obtained, the spouse of the Panel 4 member will be contacted and invited to participate in the Millennium Family Cohort Study.
 - Confirmation of electronic consent will be recorded by each participant (both the Panel 4 member and spouse) typing out their full name and checking the "voluntary consent" box. All information collected through the Internet survey is done by Microsoft Sequel Server and is backed up daily by NHRC database systems.
 - Note, we request a waiver of signed informed consent for both spousal informed consent and Panel 4 participant consent to be a secondary subject, as consenting will occur online.

- The Millennium Family Cohort Survey instrument and consent form are attached. The survey instrument uses a number of validated scales to assesses the following (sources listed on pg. 33 of Family Survey):
 - Demographic information
 - Relationship status
 - Child information
 - General health (including sleep)
 - Spouse, family, child, and service member stress
 - Impact of deployment
 - Impact of military service
 - Family cohesion, expressiveness and conflict
 - Child behavioral, developmental and health problems
 - Services received
 - Alcohol and tobacco use
 - Military specific questions for spouses serving in the military
- CAPT Margaret Ryan's (Naval Hospital Camp Pendleton) status has changed from co-investigator to solely acting as the Millennium Cohort Study's medical monitor.


T. L. Smith 7 Aug 2009
PT Signature and Date