SUPPORTING STATEMENT – PART B

Health Status Evaluation of an Infantry Battalion Following Deployment in Support of Operation Iraqi Freedom (2004-2005), 0702-AABB

1. Description of the Activity

The purpose of this initiative is to evaluate the post-deployment health status among Soldiers and Veterans that deployed to Iraq with the 1-24th Infantry Battalion and 1st Stryker Brigade Combat Team, 25th Infantry Division (1-24 IN) in 2004-2005. The investigation is being conducted at the request of the Chief of Staff of the Army, Gen. Milley, who tasked APHC with investigating the health status of former members of the above identified group. This tasking was itself motivated by members of the 1-24 IN who have voiced concern regarding the high numbers of Soldiers among their ranks who have been diagnosed with lymphoma, leukemia, bile duct cancer, prostate cancer, Crohn's Disease, sleep apnea, asthma, depression, liver disorders, among others conditions and symptoms. In an attempt to evaluate the broad spectrum of health concerns raised by members of the 1-24 IN, the survey will include a large number of health conditions, including cancer, mental health conditions, and conditions affecting the circulatory system, the respiratory system, the gastro-intestinal tract, the genitourinary system, the kidneys, the liver, and sensory organs.

2. Procedures for the Collection of Information

Describe any of the following if they are used in the collection of information:

a. **Statistical methodologies for stratification and sample selection;**
b. **Estimation procedures;**

c. **Degree of accuracy needed for the purpose discussed in the justification;**

d. **Unusual problems requiring specialized sampling procedures; and**

e. **Use of periodic or cyclical data collections to reduce respondent burden.**

In order to characterize the health status of the 1-24 IN, the Army Public Health Center (APHC) will invite former members of the 1-24 IN and their parent unit, the 1st Stryker Brigade Combat Team (1 SBCT), to participate in a post-deployment health survey. All (non-deceased) personnel that deployed with the 1 SBCT are eligible to participate in the survey, including both current military members and Veterans. APHC has obtained a roster of the 1 SBCT from Headquarters, Department of the Army G-1 (n=4,213), and will use both military records and LexisNexis to obtain contact information for potential participants. Participants will have the option to complete a paper-based version or an electronic version of the survey. The survey instrument was designed to mirror a health

survey utilized by the Millennium Cohort Study (MCS), an ongoing longitudinal cohort study of military personnel and Veterans headquartered at the Naval Health Research Center (NHRC).

APHC will provide de-identified survey response data to collaborators at NHRC, who will then conduct an analysis comparing 1 SBCT participants' survey responses to corresponding responses of a selected subset of Millennium Cohort Study participants. The reference group consisting of Millennium Cohort Study participants will be selected by the NHRC investigators to be comparable to 1 SBCT participants with respect to baseline demographics (e.g., gender, age, current or former Soldiers, deployment history). NHRC will also compare the responses of 1 SBCT personnel to MCS participants who did not deploy in support of Operation Iraqi Freedom, Operation Enduring Freedom, or Operation New Dawn. Comparisons with MCS participants will be conducted only for health conditions reported by at least 10 1 SBCT survey respondents.

Under a reasonable assumption about the proportion of eligible Soldiers and Veterans who agree to participate and complete the survey (800 respondents, or roughly 20% of ~4,000 former 1 SBCT personnel) we expect to have adequate statistical power (>80%) to evaluate a doubling in prevalence of health conditions among 1 SBCT respondents, relative to an equal number of MCS participants (further assuming a prevalence among MCS participants of at least 3%, alpha=0.05, and a two-sided test of the null hypothesis, and a conventional test of two independent proportions (Pearson's Chi-squared test)).

We do not expect to have sufficient statistical power to compare survey responses among the subset of former 1-24 IN personnel (approximately 800 Soldiers and Veterans in total) to MCS personnel. We would require 100% participation in the survey to achieve comparable statistical power as estimated for the evaluation of all former 1 SBCT personnel (described above). Assuming only 20% of former 1-24 IN personnel participate in the survey, achieving statistical power greater than 80% would require that the prevalence of health conditions observed among 1-24 IN respondents be 2.8x the prevalence among MCS participants (further assuming a prevalence among 800 MCS participants of at least 3%, alpha=0.05, and a two-sided test of the null hypothesis). The investigators are aware that inadequate statistical power is a limitation of this work; Incidence of cancer, for example, is sufficiently rare that it requires large numbers of individuals – orders of magnitude larger than the size of the 1-24 IN – in order to evaluate even moderately large associations with sufficient statistical power.

3. Maximization of Response Rates, Non-response, and Reliability

Discuss methods used to maximize response rates and to deal with instances of non-response. Describe any techniques used to ensure the accuracy and reliability of responses is adequate for intended purposes. Additionally, if the collection is based on sampling, ensure that the data can be generalized to the universe under study. If not, provide special justification.

Personnel identified as having deployed with the 1 SBCT will be invited to complete a health survey. Individuals who agree to participate in the survey and sign an informed consent document will have the option of completing the survey online using a secure APHC survey website, or using a hardcopy survey which will be returned to APHC via certified mail in an envelope with postage provided to the participant by APHC. The post-deployment health survey was designed by APHC to closely mirror relevant portions of the MCS health survey, an instrument which has been previously evaluated for validity, consistency and stability.(Smith, Smith et al. 2007) An invitation to complete the survey will be sent via email, U.S. mail, and telephonically if no response is received after email or mail-based invitation attempts. Responses to paper-based surveys and surveys delivered telephonically will be entered into the online survey application by APHC staff. After a quality control check by a second data entry staff, the paper-based surveys will be destroyed using a government-approved cross-cut paper shredder.

Based on evidence from previous survey efforts in DOD and VA populations (Kang, Natelson et al. 2003) as well as the epidemiologic literature in general (Cobb, Singer et al. 2014), we anticipate that that achieving a high proportion of survey response will be a challenge. To maximize response rates, we have taken the following steps in the design and execution of the survey.

First, our power calculations are based on the assumption of a 20% response proportion. Second, we have endeavored to keep the survey instrument as short as possible, and still provide necessary data on health status that is comparable to those obtained from the comparison population (MCS participants); Survey questions were designed to be simple and straightforward. Additionally, the survey will include only a minimal number of questions regarding demographic and military characteristics (data on demographic and military variables are available from DMDC and VA OPH records).

Third, APHC will take the following additional steps in the execution of the survey: An APHC investigator will attempt to contact all individuals who do not complete and return the survey, beginning 14 days after the initial invitation to participate was mailed. The first follow-up contact will be via an email sent to all individuals who have not returned a completed survey. This email will include a telephone number to call if the potential respondent has questions about participation in the survey. The email will also include an invitation to call if the individual would prefer to complete the survey telephonically. In the absence of an email or phone response indicating an intention to complete the survey, this initial reminder email will be followed one day later by a telephone call. If an APHC investigator is able to make contact with a potential respondent via telephone, the investigator will offer to allow the individual to complete the questionnaire over the phone. In the event that the investigator is not able to contact the individual, a second email will be sent to the individual that includes 1) the fact that the call was attempted, 2) a contact number to use if the individual would like to complete the survey telephonically, and 3) a specified time that the investigator will call again. This time will be no more than two days from the time the email is sent, and

will be a different time of day from the previous call. These steps will be repeated eight times over the course of one month (twice per week), before the individual is deemed a potential “non-responder”. A letter will then be mailed to potential non-responders, indicating that we had attempted to contact the individual by letter, phone and email, and once again inviting them to complete the survey. All of the paperwork initially sent to the individual will be included in this letter. The letter will also include an invitation for the individual to call APHC to complete the survey telephonically.

Finally, we will evaluate the potential for non-response bias by comparing distributions and frequencies of parameters (e.g., demographic and military characteristics) that are known for both responders and non-responders. Similarly, we will evaluate differences between survey responses between participants who completed the paper-based survey, the on-line survey, and the survey delivered telephonically.(Sax, Gilmartin et al. 2003)

References

Cobb E. M., Singer D. C. and Davis M. M. (2014). "Public interest in medical research participation: differences by volunteer status and study type." Clin Transl Sci 7(2): 145-149.

Kang H. K., Natelson B. H., Mahan C. M., Lee K. Y. and Murphy F. M. (2003). "Post-traumatic stress disorder and chronic fatigue syndrome-like illness among Gulf War veterans: a population-based survey of 30,000 veterans." Am J Epidemiol 157(2): 141-148.

Sax L. J., Gilmartin S. K. and Bryant A. N. (2003). "Assessing Response Rates and Nonresponse Bias in Web and Paper Surveys." Research in Higher Education 44(4): 409-432.

Smith TC, Smith B, Jacobson IG, Corbeil TE, Ryan MAK, for the Millennium Cohort Study Team. (2007). “Reliability of standard health assessment instruments in a large, population-based cohort study.” Annals of Epidemiology 17(7):525-532.

4. Tests of Procedures

Describe any tests of procedures or methods to be undertaken. Testing of potential respondents (9 or fewer) is encouraged as a means of refining proposed collections to reduce respondent burden, as well as to improve the collection instrument utility. These tests check for internal consistency and the effectiveness of previous similar collection activities.

The investigators are relying on an established survey instrument designed for, and used with success in, the Millennium Cohort Study. Started in 2001, the MCS is the largest

prospective health study in the military, with more than 200,000 participants having been enrolled. Evaluation of non-response in the Millennium Cohort Study has been documented. (Corry et al. 2017)

The statistical analyses to be implemented are conventional. Univariate and stratified analysis (Chi-square tests or the Fisher's Exact Test, as appropriate) and multivariate negative binomial regression or Poisson regression models will be constructed, as appropriate. Relative risks adjusted for age, race/ethnicity, and total number of deployments for each health outcome will be estimated, along with corresponding 95% confidence intervals. For incident rate models, person-time will be censored at the earliest occurring date among the following censoring conditions: the first medical encounter with the specific diagnosis code, separation from service for those that do not become VA beneficiaries, and death for those that are deceased. Because in-theater medical records are not available in either of the health record databases, person-time will also be interval censored during subsequent deployments. Covariates that will be evaluated for inclusion in multivariate models include age at diagnosis (derived from date of birth and date of diagnosis), time in service (derived from date of accession and date of deployment for those that deployed, and the date of the deployment of the 1 SBCT for personnel that did not deploy in support of OIF or OEF), current beneficiary status (DoD, VA, or other), gender, race/ethnicity, and rank. To evaluate the bias inherent in selecting individuals known to have the outcome conditions under study as the "exposed" group, we will conduct parallel analyses including, and excluding 1-24 IN personnel.

Reference

Corry N.H., Williams C.S., Battaglia M, McMaster H.S. and Stander V.A. (2017). "Assessing and adjusting for non-response in the Millennium Cohort Family Study." BMC Med Res Methodol. 17(1):16.

5. Statistical Consultation and Information Analysis

a. Provide names and telephone number of individual(s) consulted on statistical aspects of the design.

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b. Provide name and organization of person(s) who will actually collect and analyze the collected information.

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