

Millennium Cohort: enrollment begins a 21-year contribution to understanding the impact of military service

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Abstract

Objective: In response to health concerns of military members about deployment and other service-related exposures, the Department of Defense (DoD) initiated the largest prospective study ever undertaken in the U.S. military.

Study Design and Setting: The Millennium Cohort uses a phased enrollment strategy to eventually include more than 100,000 U.S. service members who will be followed up through the year 2022, even after leaving military service. Subjects will be linked to DoD and Veterans Affairs databases and surveyed every 3 years to obtain objective and self-reported data on exposures and health outcomes.

Results: The first enrollment phase was completed in July 2003 and resulted in 77,047 consenting participants, well representative of both active-duty and Reserve/Guard forces. This report documents the baseline characteristics of these Cohort members, describes traditional, postal, and Web-based enrollment methods; and describes the unique challenges of enrolling, retaining, and following such a large Cohort.

Conclusion: The Millennium Cohort was successfully launched and is becoming especially relevant, given current deployment and exposure concerns. The Cohort is representative of the U.S. military and promises to provide new insight into the long-term effects of military occupations on health for years to come. © 2007 Elsevier Inc. All rights reserved.

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1. Introduction

Since the 1991 Gulf War, numerous studies and much effort has been expended to evaluate the health concerns of veterans. Several large epidemiologic studies have found no unexplained increase in morbidity among these veterans [1–6], and etiologies for increased symptom reporting remain elusive after more than a decade [7–12]. Some hypothesize that symptoms and symptom complexes among Gulf War veterans result from a more physically and psychologically demanding lifestyle in the military compared with the typical experiences of the civilian working

population [13,14]. Others suggest that the psychological and physical effects of deployment may have a greater impact on health [15–25]. Separation from family during prolonged deployments, irregular working hours, strenuous training, mastering technologically advanced weaponry, threats of exposure to unknown chemical or biological agents, witnessing extreme violence and death, and dynamics inherent to deployment missions may all contribute to increased symptom reporting or psychological distress during and after deployment [17–25]. Observations that U.S. Reserves/National Guard military personnel may be at greater risk for postdeployment illnesses have been of particular concern [1,6,8,12,26–28].

In response to the Department of Defense (DoD) recommendation for a coordinated effort to study, the potential effects of deployment-related exposures [29], and bolstered by the Institute of Medicine's recommendation for

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a systematic, longitudinal, population-based assessment of service members' health [30], the Millennium Cohort Study was launched in October 2000 [31]. Just as other Cohort studies have yielded important findings for the development of public health policy [32–35], the Millennium Cohort Study is poised to do the same. This prospective study incorporates temporal sequence for the study of potential causal pathways of deployment-related exposures and subsequent health outcomes. Ultimately it may improve the health of future service members by identifying both risk factors and preventive factors for chronic disease. In this paper, the authors present the successes and challenges of enrolling more than 77,000 service members in the first panel of the Millennium Cohort.

2. Materials and methods

2.1. Study population

The invited first panel of the Millennium Cohort included 256,400 randomly selected U.S. military personnel. To ensure adequate power for statistical inferences, several subgroups were oversampled, including those previously deployed, Reserve/Guard personnel, and female service members. The probability-based sample, representing approximately 11.3% of the 2.2 million men and women in service as of October 1, 2000, was provided by the Defense Manpower Data Center (DMDC) in California. DMDC data included sex, birth date, highest education level, marital status, race/ethnicity, recent deployment to southwest Asia, Bosnia, or Kosovo, pay grade, service component (active duty and Reserve/Guard), service branch (Army, Navy, Coast Guard, Air Force, and Marines), primary and duty occupations, unit identification code, date and reason for separation from service, Social Security number (SSN), name, and home and duty addresses.

2.2. Focus groups and pilot study

To improve the survey instrument, enhance tracking and database processing techniques, establish practical timelines, evaluate potential cost-savings initiatives, and test quality control measures for combining paper and electronic questionnaire submissions, three focus groups were conducted and the survey was pilot tested on approximately 1% of the initial sample. The resulting group of nonresponders afforded the opportunity to investigate reasons for nonresponse among 100 randomly chosen individuals by phone interview. These findings were then used to further refine the instrument and enrollments methods.

2.3. Enrollment invitations

Initial enrollment of the Millennium Cohort began with postcard mailings in July 2001, followed shortly by the terrorist attacks of September 11 and the anthrax attacks

through the U.S. Postal Service (USPS). To address these challenges, the research team used a modified Dillman method with extended enrollment cycles [36]. Both the initial and extended enrollment cycles included an introductory postcard, survey, and reminder postcard mailings outlined by Dillman, with repeat survey and reminder postcard mailings for nonresponders. To ensure adequate time for locating new addresses and processing returned mail, enrollment cycles were staggered, with each cycle lasting approximately 7 months. The final invitation to join the Cohort was mailed in December 2002.

Recognizing the possible limitations of enrollment through mail surveys alone due to increased deployment of service members, the team added an e-mail invitation cycle. E-mail invitations encouraged participation via the World Wide Web (Web) by providing a direct link to the online survey, but also encouraged completion of the paper surveys for those preferring that option. To further compensate the increase in military deployments and the highly mobile nature of our target population, the team added an extended enrollment cycle that mirrored the procedures used in the initial enrollment cycle.

2.4. Web enrollment

The growing ubiquity of e-mail and the web provided an alternate contact and recruitment modality. Although U.S. mail service to bases and camps overseas may be slow and sporadic, many deployed U.S. military personnel have Web and email access. The demonstrated shortcomings of standard mail, the clear benefit to data integrity, and substantial cost savings made Web enrollment especially advantageous. Due to the sensitive nature of these data, secure data transmission of survey responses via the Web was of paramount importance. Web site security licenses were sought and each participant's user identification and password were verified prior to granting access to the survey Web site. All transmissions between the participant's Web browser and the Web server software were based on the most secure technology available at the time, using well established and widely accepted Secure Sockets Layer technology with 128-bit encryption.

2.5. Cost-savings initiatives

The Web-based survey option was encouraged by the research team because of its potential to increase data quality and reduce costs. The Web site address was highlighted on mailed correspondence, and e-mail communication provided direct links to the survey log-in page. In addition, a free T-shirt or phone card was offered to those choosing the Web option. These cost-saving initiatives, or incentives, proved effective in increasing Web-based response steadily throughout the enrollment period, resulting in more than half of all participants completing their questionnaires online.

Most project costs were considered to have a shared association between Web-based and paper-based respondents. The study team conservatively estimated, however, that the costs associated with paper-respondents alone included questionnaire printing, return postage, scanning hardware and software, paper storage facilities, and personnel time for scanning, verifying, and filing the paper questionnaires. Costs that were considered associated with web respondents alone included web questionnaire design and coding, web security, server costs, and e-mail invitation costs. A conservative estimate of the differential cost indicated that Web response saved the project at least \$50 over paper-based response.

2.6. E-mail and postal addresses

Algorithms were developed for efficient mail tracking and for identifying accurate postal addresses. Initial addresses were obtained from DMDC, followed by inexpensive postcard mailings with return receipt to validate addresses. Address locator services were used for invalid addresses, including commercial locators and the Internal Revenue Service (IRS) through an agreement with the National Institute for Occupational Safety and Health. Assessment of the address-finding services was conducted by randomizing more than 375 service members with invalid addresses into two groups, one forwarded to a commercial locator and the other to the IRS. The IRS addresses were found to be correct more often than those from the commercial locator (62% vs. 28%) and at a substantial cost savings.

E-mail addresses held the added advantage in providing opportunities for increased contact with potential Cohort members as well as the substantial cost savings associated with the Web-based survey submission. Although ascertainment of e-mail addresses was challenging because DoD-wide electronic databases maintained by DMDC were new and evolving, e-mail addresses linked by SSN were obtained for Cohort members from the Army, Air Force, Navy, and Marines. In the future, because all military identification cards are converted to the microchip-containing Common Access Cards, DMDC will maintain a listing of current e-mail addresses, linked by SSN, for all service members.

2.7. Participant tracking after enrollment

Semiannual e-mails and postcards are used to track participants, sustain interest in continued study participation, and verify accuracy of contact information for this highly mobile population. The research team selected Memorial Day and Veterans Day to send postcards because these holidays may hold special significance for service members and are spaced approximately 6 months apart. Each holiday contact consists of a unique postcard and e-mail message thanking subjects for their contribution to military service and to the study, and directing them to the study Web site to update their contact information. In addition to this

cost-effective means of verifying the accuracy of contact information, the USPS “Return Service Requested” is used to obtain forwarding address information on undeliverable postcards.

2.8. Survey instrument

The Millennium Cohort questionnaire for first enrollment included more than 450 questions on diagnosed medical conditions, symptoms, psychosocial assessment, physical status, functional status, use of alcohol, tobacco, complementary and alternative medicine, occupations, military exposures, sleep patterns, and basic demographic and contact information [31]. Standardized instruments were incorporated whenever possible because of their established reliability and validity and to enable future comparisons with other populations. Such instruments included the Primary Care Evaluation of Mental Disorders (PRIME-MD) Patient Health Questionnaire (PHQ) [37–39], used to assess major depressive syndrome, panic syndrome, other anxiety syndrome, bulimia nervosa, alcohol abuse, and binge-eating disorders, (overall accuracy = 0.85, 85%); (sensitivity = 0.75, specificity = 0.90), as well as specific conditions such as major depressive disorder (sensitivity = 0.93, specificity = 0.89) [40], and panic disorder (sensitivity = 1.00, specificity = 0.63) [41]; the Medical Outcomes Study Short Form-36 for Veterans (SF-36V) [42,43] (eight components to assess physical functioning, role limitations caused by physical problems, bodily pain, general health, vitality, social functioning, role limitations caused by emotional problems, and mental health) found to have high internal consistency across all eight domains in a military population [44]; a Department of Veterans Affairs Gulf War survey of specific war-time exposures such as depleted uranium, and chemical or biological warfare agents [8,45]; the CAGE questionnaire for the detection of alcoholic problems [46]; and the Posttraumatic Stress Disorder (PTSD) Checklist—Civilian Version (PCL-C) [47–49] shown to be highly specific (specificity = 0.99) with slightly lower sensitivity (60%), a positive predictive value of 75%, and negative predictive value of 97% when using a cutoff of 50 [50]. Participants were identified as possibly having PTSD if they reported experiencing (at moderate or more extreme level) at least one intrusion symptom, three avoidance symptoms, and two hyperarousal symptoms [51], and had a total score of 50 or more on a scale of 17–85 [16,48,52,53]. Free text fields were included to allow participants to report conditions, problems, concerns, and exposures not listed elsewhere on the survey.

2.9. Data quality monitoring

To ensure the highest quality data, systematic validation and quality control processes were established for both paper and electronic submissions. The paper survey was created, scanned, and verified using mark-sense TELEform

Elite Software (Cardiff Software, Vista, CA, USA). For every 3,000-paper surveys that were scanned, 50 were randomly selected and compared with corresponding electronic records, with necessary adjustments made. In addition, all electronic records from scanned paper survey responses were searched for excessive missing values and then verified that the responses were truly missing. If, in fact, the responses were present (typically, very light pencil response was the cause), data were entered manually. The sensitivity of the scanning device was assessed throughout the process of scanning paper surveys, and thresholds were set for missing data that triggered further investigation.

The electronic version of the survey facilitated quality control by allowing direct data entry by responders. To ensure that all fields properly translated electronically, numerous mockup surveys were submitted both initially and throughout enrollment to check for correct data coding and transmission. Trends in missing data over the length of the survey that might indicate diminishing interest or survey fatigue were not detected (Fig. 1). Although no question was skipped by more than 15% of the responders, several questions tended to be associated with missing responses proportionally more often than other questions.

This prompted review of these questions for follow-up surveys.

2.10. The Cohort

Although the initial target population included 256,400 potential participants, 1,270 were excluded due to invalid SSNs, name, or address information; 2,560 were included in the pilot study [31]; and 38,182 could not be contacted after multiple address searches found no valid address (Fig. 1).

Among the 214,338 contacted members of the invited sample, enrollment in the Cohort was not completed for the following reasons: determined to be ineligible ($n = 8$), deceased (348), explicitly declined to participate ($n = 4,796$), survey completed by someone other than the invited service member ($n = 83$), consent form not returned ($n = 2,208$), and survey submitted after close of enrollment ($n = 11$). All others were considered to be nonresponders ($n = 129,887$). The 77,047 consenting participants in the first enrollment panel represent 36% response rate of those contacted and invited to enroll.

2.11. Analyses

Descriptive analyses of the initial Cohort included means and proportions of important demographic characteristics as well as selected survey questions of interest. Initial results were stratified by active-duty or Reserve/Guard status. Univariate statistics including chi-square and t tests of association were used to establish differences among the enrolled Cohort members, the invited sample, and the U.S. military in 2000. Data were warehoused and analyzed using SAS software (Version 9.1, SAS Institute, Inc., Cary, NC, USA) [54,55].

3. Results

Demographic data for the Cohort were complete for 76,715 of the 77,047 (99.6%) participants (Table 1). Univariate analyses of population demographics suggested that there were statistically significant differences between the Cohort, invited sample, and the composition of the 2000 U.S. military (Table 1). When compared with the 2000 U.S. military at large, Cohort members were slightly more likely to be female, older, better educated, married, officers, in the Air Force, and from health care occupations. The higher enrollment of women and those recently deployed reflects the intended oversampling.

Self-reported health behaviors and military exposures are shown in Table 2. The most frequently reported military-specific exposures included receiving at least one anthrax vaccination (32%) and witnessing a person's death due to war, disaster, or tragic event (26%) (Table 2). Five percent of the Cohort reported being exposed to chemical or biological warfare agents and 4% reported being

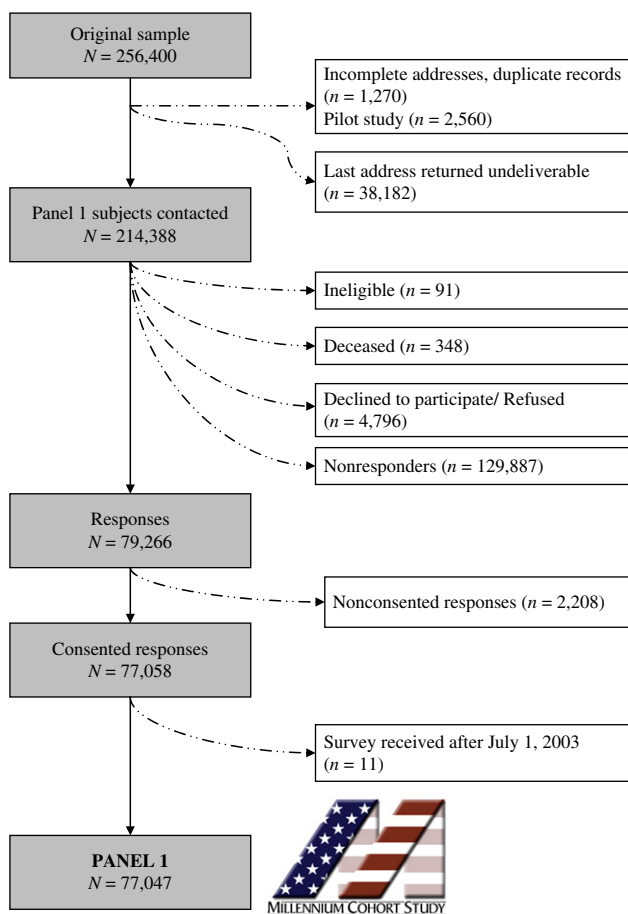


Fig. 1. Millennium Cohort Study flow of participants from sample to enrolled Cohort with Millennium Cohort Study logo.

Table 1
 Characteristics of Millennium Cohort Study responders (panel 1), compared to the invited sample and the U.S. military, as of October 2000

Variable	Cohort, <i>N</i> = 77,047; <i>N</i> (%)	Invited Cohort, ^a <i>N</i> = 256,400; (%)	U.S. military, ^b <i>N</i> = 2,273,793; (%)
Sex			
Male	56,415 (73.2)	76.0	84.7
Female	20,632 (26.8)	24.0	15.3
Unknown	0 (0.0)	<0.1	<0.1
Age, years			
17–24	14,559 (18.9)	30.8	32.5
25–34	27,083 (35.2)	35.4	33.9
35–44	25,400 (33.0)	25.1	25.0
>44	9,975 (13.0)	8.6	8.5
Unknown	30 (<0.1)	0.1	0.1
Education			
Less than high school diploma	4,722 (6.1)	7.6	8.0
High school diploma	32,957 (42.8)	50.4	53.0
Some college	19,655 (25.5)	23.6	20.3
Bachelor's degree	12,722 (16.5)	11.6	11.3
Master's/PhD degree	6,986 (9.1)	5.4	5.8
Unknown	5 (<0.1)	1.4	1.6
Marital status			
Single	23,183 (30.1)	40.5	41.7
Married	48,594 (63.1)	52.8	53.2
Divorced	5,270 (6.8)	5.7	5.0
Unknown	0 (0.0)	1.0	0.2
Race/ethnicity			
White non-Hispanic	53,459 (69.4)	64.7	67.3
Black non-Hispanic	10,576 (13.7)	19.0	18.7
Asian/Pacific Islander	6,068 (7.9)	6.1	3.3
Hispanic	4,921 (6.4)	7.5	7.9
Native American	677 (0.9)	0.9	1.0
Other	1,065 (1.4)	1.5	1.2
Unknown	281 (0.4)	0.4	0.8
Past deployment status			
Deployment experience	23,234 (30.2)	30.0	10.0
No deployment experience	53,813 (69.8)	70.0	90.0
Military pay grade			
Enlisted	59,318 (77.0)	84.6	84.3
Commissioned officer	16,346 (21.2)	14.3	14.5
Warrant officer	1,383 (1.8)	1.1	1.2
Service component			
Active duty	43,890 (57.0)	54.9	57.5
Reserve/Guard	33,157 (43.0)	45.1	42.5
Branch of service			
Army	36,481 (47.4)	44.0	45.5
Air Force	22,357 (29.0)	28.1	23.3
Navy	13,435 (17.4)	19.6	20.0
Marines	3,941 (5.1)	7.2	9.4
Coast Guard	833 (1.1)	1.2	1.9
Unknown	0 (0.0)	1.2	<0.1
Occupational category			
Combat specialists	15,425 (20.0)	20.9	21.9
Electrical repair	6,784 (8.8)	8.0	8.1
Communications/intelligence	5,428 (7.1)	6.7	7.0
Health care specialists	8,018 (10.4)	8.4	8.1
Other technical	1,972 (2.6)	2.4	2.7
Functional support specialists	15,413 (20.0)	17.9	17.6
Electrical/mechanic	11,387 (14.8)	16.2	15.1
Craft workers	2,390 (3.1)	3.5	3.7
Service support	6,686 (8.7)	8.9	9.4
Students, prisoners, other	3,523 (4.6)	5.8	3.7
Unknown	21 (<0.1)	1.3	2.8

^a Oversampled for women, recently deployed, and Reserve/Guard.

^b Based on 2000 U.S. military service rosters.

Table 2
Examples of unadjusted survey data—exposures and health behaviors among Millennium Cohort members upon enrollment

	Cohort, <i>N</i> = 77,047; <i>N</i> (%)	Active duty, <i>N</i> = 43,890; (%)	Reserve/Guard, <i>N</i> = 33,157; (%)
Self-reported military exposures			
Ever exposed to the following:			
Witnessed a person's death due to war, disaster, or tragic event	19,621 (25.5)	(25.1)	(26.0)
Chemical or biological warfare agents	4,175 (5.4)	(4.8)	(6.3)
Anthrax vaccine	24,701 (32.1)	(43.1)	(17.4)
Exposed within the past 3 years:			
Depleted uranium	2,826 (3.7)	(4.8)	(2.2)
Occupational hazards requiring protective equipment, such as respirators or hearing protection	41,430 (53.8)	(59.2)	(46.7)
Any exposure, physical or psychological, during a military deployment that had a significant impact on your health	5,181 (6.7)	(7.3)	(5.9)
Behavioral risk factors			
Alcohol			
Chronic drinkers ^a	5,801 (7.5)	(7.5)	(7.6)
Drank five or more drinks on ≥1 day(s) in past year	35,195 (45.7)	(48.2)	(42.3)
Smoking			
Never smoked >100 cigarettes in lifetime	42,557 (55.2)	(55.5)	(54.9)
Smoked >100 cigarettes in lifetime	31,460 (40.8)	(41.0)	(40.6)
Unknown	3,030 (3.9)	(3.5)	(4.5)
Pack-years (median, IQR) ^b	5.3 (12.3)	4.5 (10.0)	6.0 (13.5)
BMI (kg/m ²)			
Underweight (<18.5)	636 (0.8)	(0.8)	(0.9)
Normal (18.5–24.9)	27,758 (36.0)	(36.6)	(35.3)
Overweight (25.0–29.9)	39,194 (50.9)	(51.3)	(50.3)
Obese (≥30.0)	8,394 (10.9)	(10.0)	(12.0)
Unknown	1,065 (1.4)	(1.3)	(1.5)
Complementary and alternative medicine use			
Chiropractic care	8,424 (10.9)	(8.0)	(14.8)
Herbal therapy	7,312 (9.5)	(8.6)	(10.7)
Acupuncture	1,289 (1.7)	(1.7)	(1.7)

Abbreviation: IQR, interquartile range.

^a Chronic drinkers defined as >14 drinks in a typical week for men, and >7 drinks in a typical week for women.

^b Median pack-years and IQR calculated for participants smoking >100 cigarettes in their lifetime.

exposed to depleted uranium. Nearly three times the proportion of active-duty personnel had reported receiving the anthrax vaccine (43%) compared with Reserve/Guard personnel (17%).

Regarding modifiable risk behaviors, 46% of participants might be categorized as binge drinkers, whereas only 8% were categorized as chronic drinkers (Table 2). Active-duty and Reserve/Guard subjects appeared similar with regard to chronic use of alcohol; however, more active-duty members were classified as binge drinkers in the past year (48% and 42%, respectively). Approximately 40% of participants smoked at least 100 cigarettes in their lifetime (median pack-years = 5.3), whereas the majority of the Cohort (55%) had not smoked. Although active-duty and Reserve/Guard responders were similar with respect to having ever smoked 100 cigarettes in their lifetime, median pack-years were higher in Reserve/Guard than active-duty

members (6.0% and 4.5%, respectively). Reserve/Guard members were more likely to be obese as indicated by body mass index (BMI) and also more likely to have used complementary and alternative medicine therapies.

More than 60% of the Cohort reported that their general health was very good or excellent. There were 38 specific medical conditions and one free text option included on the questionnaire of which we report on one prevalent condition (hypertension, 10.2%), a condition of current high public health concern (diabetes mellitus, 1.3%), and a condition of much interest to veterans of past deployments (chronic fatigue syndrome, 1.3%) (Table 3). Major depressive disorder, as defined by the PRIME-MD PHQ, was reported by 3.3% of the Cohort. The PCL-C responses suggested that 2% of the Cohort has signs or symptoms of PTSD. The SF-36V assessment of functional status indicated relatively high means (range: 62.1–91.0), with the

Table 3
Examples of unadjusted survey data—physical and mental health among Millennium Cohort members upon enrollment

	Cohort, <i>N</i> = 77,047; <i>N</i> (%)	Active duty, <i>N</i> = 43,890; %	Reserve/Guard, <i>N</i> = 33,157; %
General health			
In general, would you say your health is...			
Poor	562 (0.8)	1.0	0.5
Fair	5,331 (7.1)	8.1	5.9
Good	23,373 (31.3)	33.1	28.9
Very good	30,437 (40.7)	39.3	42.6
Excellent	15,045 (20.1)	18.6	22.1
Specific medical conditions			
Hypertension	7,799 (10.2)	9.9	10.6
Chronic fatigue syndrome	1,015 (1.3)	1.3	1.4
Diabetes	1,008 (1.3)	1.2	1.5
PRIME-MD PHQ			
Major depressive disorder	1,002 (3.3)	3.6	2.9
Panic syndrome	890 (1.2)	1.2	1.2
Other anxiety syndrome	1,617 (2.1)	2.4	1.8
Eating disorders	2,457 (3.2)	3.5	2.9
PCL-C			
PTSD ^a	1,821 (2.4)	2.5	2.3
SF-36V^b			
	Mean	Mean	Mean
Physical functioning	91.0	90.6	91.6
Role physical	82.2	81.6	83.1
Bodily pain	75.4	73.8	77.5
General health	76.9	75.5	78.7
Vitality	62.1	60.7	64.1
Social functioning	87.1	86.4	88.2
Role emotional	83.7	83.7	83.7
Mental health	78.6	78.1	79.4

Abbreviation: PCL-C, Posttraumatic Stress Disorder Checklist-Civilian Version.

^a PTSD, posttraumatic stress disorder defined as moderate or above level of at least one intrusion symptom, three avoidance symptoms, and two hyperarousal symptoms, with a total score ≥ 50 on a scale of 17–85.

^b SF-36V, Medical Outcomes Study Short Form-36 for Veterans. Increasing score indicates better health and functioning status, with a maximum score of 100.

highest mean for physical functioning. SF-36V scores were somewhat higher, indicating better functional status, for Reserve/Guard than for active-duty responders (Fig. 2).

4. Discussion

The Millennium Cohort represents a major milestone in military and occupational epidemiologic research. The prospective study design responds to an important charge to assess objective health information by linking to DoD maintained inpatient, ambulatory, and pharmacy database, as well as subjective symptoms and level of functioning, among a large military population over several decades, during and beyond actual military service [30]. Health status is assessed through triennial questionnaires as well as by linking to large health care databases. Likewise, exposure experiences are evaluated through triennial questionnaires as well as linking to electronically maintained occupation, vaccine, deployment, and environmental exposure history data. With those data that currently overlap while in military service, preliminary investigation of concordance between

self-report and electronic occupation and vaccine data suggest substantial reliability in these data. A vital component of the study is the ability to compare Reserve/Guard forces with regular active-duty forces on both exposures and health outcomes. The Reserve/Guard represent the “citizen soldiers” and, as such, are an important comparison population for those choosing the military as a full-time occupation.

Despite extensive planning and pilot testing, the Millennium Cohort enrollment year was marked by numerous challenges. The study was launched shortly before the historic terrorist attacks of September 11 and the crippling effects of the anthrax scare on the U.S. postal system. Investigators mitigated these challenges by extending the invitation cycle, locating new addresses using the IRS, using e-mail as a contact mode, and encouraging enrollment via a secure Web site. These strategies, as well as use of semiannual Veterans Day and Memorial Day contact, will be leveraged to maintain participation and complete follow-up of the original Cohort every 3 years through 2022. These strategies will also be important in enrolling subsequent panels of the Cohort, in 2004 and one planned for 2007, to achieve a total enrollment of at least 140,000.

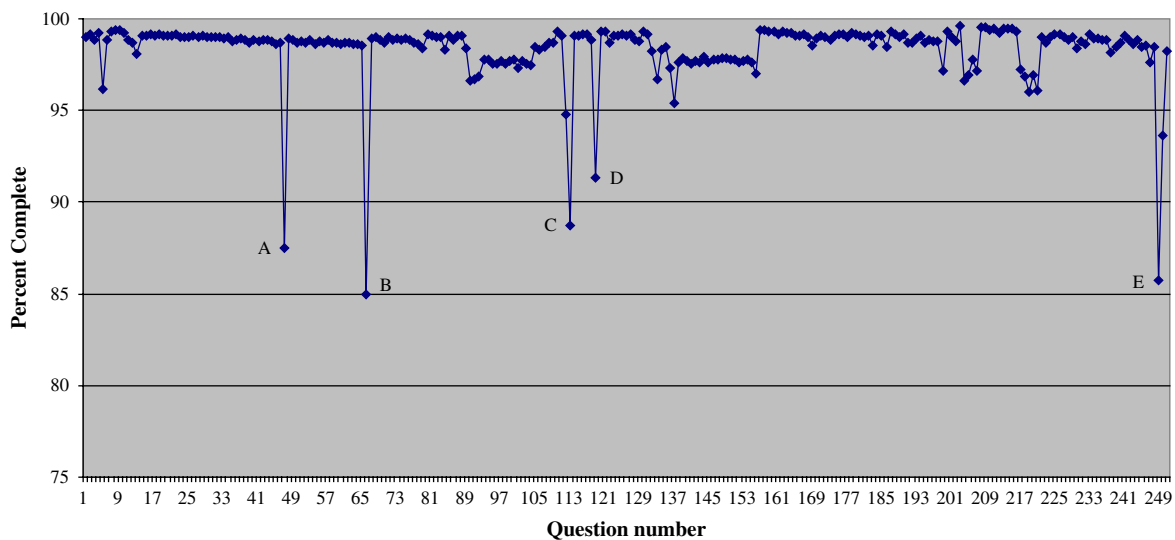


Fig. 2. Individual question completion percentages of Millennium Cohort questionnaire. Percentages incorporate skip patterns. A: 13% skipped “other” on the question “Has your doctor or other health professional ever told you that you have any of the following conditions?”; B: 15% skipped “other” on the question “During the last 12 months, have you had persistent or recurring problems with any of the following conditions?”; C: 11% of those indicating eating disorder skipped a frequency query on the problem; D: 9% of those who indicated problems skipped a query qualifying degree of challenge in “doing work, taking care of things at home, or getting along with other people?”; and E: 14% skipped a military occupational coding query.

Members of the Cohort were demographically older, more educated, married, and in the officer ranks, compared with individuals in the invited sample or the military population at large. The high operational tempo following the September 11 terrorist attacks in 2001 may be one explanation for underrepresentation of Marines and those aged 17–24 years, as large numbers of young service members participated in lengthy combat deployments; however, this trend of lower participation among younger invitees has been reported elsewhere [56]. Deployment aside, older and more educated individuals and those classified as health care specialists, may have more interest in health issues, perhaps increasing their propensity for enrollment. The sampling strategy to ensure adequate representation to assess rare outcomes in particular subgroups was largely successful, with women comprising nearly 27% of the Cohort, whereas those with prior deployment experience comprise 30% of the Cohort. The small proportional differences suggest that the Cohort is a reasonably representative sample of the military as a whole, and study findings should be generalizable to the target population. Subsequent panel enrollment will allow investigators to reflect the changing composition of the U.S. military.

Unlike the civilian workplace, there are inherent, unique, and sometimes unpredictable, hazards associated with military service [2,4,5,57]. More than half of the Cohort reported having used protective equipment because of potential occupational hazards (Table 2). Also, witnessing a tragic event, including death, can be an accompaniment of military service. About 25% of both the active-duty and Reserve/Guard components of the Cohort have personally experienced such events. Other potentially hazardous

exposures associated with military service include the target of lethal weapons, operating sophisticated weapons systems, and working under environmentally extreme conditions [58]. Finally, deployed military personnel are exposed to specific pharmaceuticals, multiple immunizations, and other products, which are rarely, if ever, administered to civilians [58–60]. The Millennium Cohort allows, for the first time, the opportunity to assess such exposures prospectively on a large sample.

The Millennium Cohort has the advantage of being systematically drawn from all branches and components of the armed forces, using repeated measures to monitor population trends over at least two decades. Individual self-reported behavioral data may be linked to specific and militarily relevant health outcomes, even among those who retire or otherwise leave military service. Robust comparisons between Reserve/Guard and active forces have heretofore not been possible because a standardized instrument has never been applied to study their similarities and differences in such a systematic and comprehensive fashion. Although explicit comparisons, adjusted for factors such as age and sex, are beyond the scope of this introductory paper, the preliminary data presented here suggest that military personnel will report health and behavioral habits even when these habits are relatively unhealthy. Early data suggest that there will be large subgroups of military personnel in different risk categories that may influence the occurrences of illnesses and injuries. For example, data from this baseline survey show that more than 50% of the Reserve/Guard and active component members of the Millennium Cohort are overweight but that only 10% are considered obese, with a slightly higher proportion of the

Reserve/Guard exceeding the BMI for obesity (Table 2). When compared with the Healthy People 2010 objectives, Millennium Cohort participants meet or surpass the objectives for alcohol moderation and weight control [61].

Given the relative youth of the Cohort and the physical fitness standards that must be met for military service, one might expect the general health among military service members to be considerably better than that of the U.S. average. In fact, over 90% of the Cohort rated their physical health as good or better, compared with 85% of U.S. residents included in the 2003 Behavioral Risk Factor Surveillance System (BRFSS) [61,62]. This was true for both Reserve/Guard and active-duty personnel. Of note, 51% of 2003 BRFSS participants were younger than 45 years of age compared to 87% of Cohort members. Similar high ratings of self-reported health have been reported for active-duty military personnel who participated in the 2000 BRFSS [63] as well as military personnel who returned from international deployments and were part of the Defense Medical Surveillance System, the central repository of U.S. military medical surveillance data [64]. However, active-duty military personnel were more likely to report greater number of days of activity limitation, pain, and not enough rest than their counterparts who were not in the military [63]. This appears to be consistent with relatively lower SF-36V scores for physical functioning, bodily pain, and general health in active duty when compared with Reserve/Guard responders (Table 3). Finally, the low rates of chronic conditions such as diabetes and hypertension were as expected, given the relative youth of the Cohort [65]. Self-reported prevalence of nonpregnancy-related diabetes and hypertension in the 2003 BRFSS (7% and 25%, respectively) was considerably higher than that seen in this Cohort [62]. A slightly higher prevalence of hypertension and diabetes was seen in Reserve/Guard vs. active-duty members, possibly explained by the somewhat higher prevalence of obesity (BMI \geq 30) in Reserve/Guard (Table 2).

In addition to describing baseline mental and physical health, this is the first population-based mental health survey of all components of the U.S. military (active duty, Guard and Reserve) that documents the substantial burden of symptomatic mental illness among all U.S. military members at rates similar to that of the general U.S. population. Worldwide, mental disorders accounted for nearly 11% of the disease burden in 1990 and are projected to affect 15% of the world population by 2020, causing a public health impact nearly as large as cardiovascular and respiratory diseases [66,67]. Thirteen percent of all military hospitalizations from 1990 to 1999 were reported as mental health disorders [68], and as many as 17% of serving members had symptoms of anxiety and 19% had symptoms of depression in 2001 [69]. Among Cohort members, meaningful levels of a number of common, potentially serious mental disorders were identified and found to be consistent with prevalence in other populations, such as major depressive disorder (3%), panic syndrome (1%), other anxiety

syndrome (2%), eating disorders (2%), and PTSD (2%). Future analyses will provide insight into risk factors that may be used to target groups at highest risk for intervention, as well as to discern the impact of deployment on mental health. Finally, the Cohort exhibited higher unadjusted means measured for SF-36V physical functioning, general health, vitality, social functioning, role emotional, and mental health, and lower unadjusted means for those components describing role limitations due to physical problems and bodily pain, suggesting a more functionally capable population when compared with the U.S. population [42].

The Millennium Cohort Study represents the first ever, comprehensive effort by any nation to prospectively evaluate health outcomes of military service. This project holds tremendous promise to help us better understand enigmatic problems, such as multisymptom illnesses experienced by Gulf War veterans. The Cohort will also identify and characterize the numerous, some as yet unidentified, benefits to health that may be common to our men and women in uniform, but not detected by previous study methodologies. The enrollment of more than 60,000 additional service members in subsequent panels will ensure that the Cohort remains relevant and representative of the military and their experiences with current and future deployments. Like other groundbreaking prospective studies, the value of the Millennium Cohort in defining causes of both health and disease is expected to have a resounding impact that grows over time.

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References

- [1] Gray GC, Coate BD, Anderson CM, et al. The postwar hospitalization experience of US veterans of the Persian Gulf War. *N Engl J Med* 1996;335(20):1505–13.
- [2] Gray GC, Smith TC, Knoke JD, Heller JM. The postwar hospitalization experience of Gulf War Veterans possibly exposed to chemical munitions destruction at Khamisiyah, Iraq. *Am J Epidemiol* 1999;150:532–40.
- [3] Kaiser KS, Hawksworth AW, Gray GC. Pyridostigmine bromide intake during the Persian Gulf War not associated with postwar handgrip strength. *Mil Med* 2000;165:165–8.
- [4] Smith TC, Heller JM, Hooper TI, Gackstetter GD, Gray GC. Are veterans of the Gulf War experiencing illness from exposure to Kuwaiti oil well fire smoke? Department of Defense hospitalization data examined. *Am J Epidemiol* 2002;155(10):908–17.
- [5] Smith TC, Gray GC, Weir JC, Heller JM, Ryan MAK. Gulf War veterans and Iraqi nerve agents at Khamisiyah. Postwar hospitalization data revisited. *Am J Epidemiol* 2003;158:456–67.
- [6] Smith TC, Corbeil TE, Ryan MA, Heller JM, Gray GC. In-theater hospitalizations of US and allied personnel during the 1991 Gulf War. *Am J Epidemiol* 2004;159(11):1064–76.
- [7] Gray GC, Kaiser KS, Hawksworth AW, Hall FW, Barrett-Connor E. Increased postwar symptoms and psychological morbidity among U.S. Navy Gulf War veterans. *Am J Trop Med Hyg* 1999;60(5):758–66.
- [8] Gray GC, Reed RJ, Kaiser KS, Smith TC, Gastanaga VM. The Seabee Health Study: self-reported multi-symptom conditions are common and strongly associated among Gulf War veterans. *Am J Epidemiol* 2002;155:1033–44.
- [9] Kroenke K, Koslowe P, Roy M. Symptoms in 18,495 Persian Gulf War veterans. *J Occup Environ Med* 1998;40(6):520–8.
- [10] Fukuda K, Nisenbaum R, Stewart G, et al. Chronic multisymptom illness affecting Air Force veterans of the Gulf War. *JAMA* 1998;280(11):981–8.
- [11] The Iowa Persian Gulf Study Group. Self-reported illness and health status among Persian Gulf War veterans: a population-based study. *JAMA* 1997;277(3):238–45.
- [12] Barrett DH, Gray GC, Doebbeling BN, Clauw DJ, Reeves WC. Prevalence of symptoms and symptom-based conditions among Gulf War veterans: current status of research findings. *Epidemiol Rev* 2002;24:218–27.
- [13] Segal M, Harris J. What we know about Army families. Special Report 21. Alexandria, VA: US Army Research Institute of the Behavioral and Social Sciences; 1993.
- [14] Pierce M, Luchsinger M. Psychological distress among Air Force wives. Colorado Springs, CO: US Air Force Academy; 1986.
- [15] Dlugosz LJ, Hocter WJ, Kaiser KS, et al. Risk factors for mental disorder hospitalization after the Persian Gulf War: U.S. Armed Forces, June 1, 1991–September 30, 1993. *J Clin Epidemiol* 1999;52:1267–78.
- [16] Hoge CW, Castro CA, Messer SC, McGurk D, Cotting DI, Koffman RL. Combat duty in Iraq and Afghanistan, mental health problems, and barriers to care. *N Engl J Med* 2004;351:13–22.
- [17] Schumm WR, Bell DB, Gade PA. Effects of a military overseas peacekeeping deployment on marital quality, satisfaction, and stability. *Psychol Rep* 2000;87(3 Pt 1):815–21.
- [18] Stuart JA, Halverson RR. The psychological status of U.S. Army soldiers during recent military operations. *Mil Med* 1997;162:737–43.
- [19] Litz BT, Orsillo SM, Friedman M, Ehlich P, Batres A. Posttraumatic stress disorder associated with peacekeeping duty in Somalia for U.S. military personnel. [Erratum: *Am J Psychiatry* 1997;154(5):722]. *Am J Psychiatry* 1997;154(2):178–84.
- [20] Orsillo SM, Roemer L, Litz BT, Ehlich P, Friedman MJ. Psychiatric symptomatology associated with contemporary peacekeeping: an examination of post-mission functioning among peacekeepers in Somalia. *J Trauma Stress* 1998;11(4):611–25.
- [21] Shigemura J, Nomura S. Mental health issues of peacekeeping workers. *Psychiatry Clin Neurosci* 2002;56(5):483–91.
- [22] Ford JD, Campbell KA, Storzbach D, Binder LM, Anger WK, Rohlman DS. Posttraumatic stress symptomatology is associated with unexplained illness attributed to Persian Gulf War military service. *Psychosom Med* 2001;63(5):842–9.
- [23] Hall DP Jr. Peacekeeping duty and PTSD. *Am J Psychiatry* 1997;154(10):1482–3.
- [24] Hall DP. Stress, suicide, and military service during Operation Uphold Democracy. *Mil Med* 1996;161(3):159–62.
- [25] Bartone PT, Adler AB, Vaitkus MA. Dimensions of psychological stress in peacekeeping operations. *Mil Med* 1998;163(9):587–93.
- [26] Murphy FM, Kang HK, Dalager NA, et al. The health status of Gulf War veterans: lessons learned from the Department of Veterans Affairs Health Registry. *Mil Med* 1999;164(5):327–31.
- [27] Smith TC, Smith B, Ryan MA, et al. Ten years and 100,000 participants later: occupational and other factors influencing participation in US Gulf War health registries. *J Occup Environ Med* 2002;44(8):758–68.
- [28] Smith TC, Jimenez DL, Smith B, et al. The postwar hospitalization experience of Gulf War veterans participating in US health registries. *J Occup Environ Med* 2004;46(4):386–97.
- [29] Secretary of Defense. Report to the Committee on National Security, House of Representatives, and the Armed Services Committee, U.S. Senate, on Effectiveness of medical research initiatives regarding Gulf War illnesses. Washington, DC: Department of Defense; 1998.
- [30] Committee on Measuring the Health of Gulf War Veterans, I.o.M. Gulf War veterans: measuring health. Washington, DC: National Academy Press; 1999.
- [31] Gray GC, Chesbrough KB, Ryan MAK, et al. The Millennium Cohort Study: a 21-year prospective cohort study of 140,000 military personnel. *Mil Med* 2002;167(6):483–8.
- [32] Dawber TR, Meadors GF, Moore FE. Epidemiological approaches to heart disease: the Framingham Study. *Am J Public Health* 1951;41:279–86.
- [33] Doll R, Hill HB. The mortality of doctors in relation to their smoking habits: a preliminary report. *BMJ* 1954;1:1451–5.

- [34] Belanger CF, Hennekens CH, Rosner B, Speizer FE. The Nurses' Health Study. *Am J Nurs* 1978;78(6):1039–40.
- [35] Criqui MH, Barrett-Connor E, Austin M. Differences between respondents and non-respondents in a population-based cardiovascular disease study. *Am J Epidemiol* 1978;108(5):367–72.
- [36] Dillman DA. Mail and telephone surveys: the total design method. New York: Wiley; 1978. xvi, 325.
- [37] Spitzer RL, Williams JB, Kroenke K, et al. Utility of a new procedure for diagnosing mental disorders in primary care. The PRIME-MD 1000 Study. *JAMA* 1994;272(22):1749–56.
- [38] Spitzer RL, Kroenke K, Williams JB. Validation and utility of a self-report version of PRIME-MD: the PHQ Primary Care Study. Primary care evaluation of mental disorders. *JAMA* 1999;282(18):1737–44.
- [39] Spitzer RL, Williams JB, Kroenke K, Hornyak R, McMurray J. Validity and utility of the PRIME-MD patient health questionnaire in assessment of 3000 obstetric-gynecologic patients: the PRIME-MD Patient Health Questionnaire Obstetrics-Gynecology Study. *Am J Obstet Gynecol* 2000;183(3):759–69.
- [40] Fann JR, Bombardier CH, Dikmen S, et al. Validity of the Patient Health Questionnaire-9 in assessing depression following traumatic brain injury. *J Head Trauma Rehabil* 2005;20(6):501–11.
- [41] Means-Christensen AJ, Arnau RC, Tonidandel AM, Bramson R, Meagher MW. An efficient method of identifying major depression and panic disorder in primary care. *J Behav Med* 2005;28(6):565–72.
- [42] Ware JE, Kosinski M, Gandek B. SF-36 Health Survey: manual and interpretation guide. Lincoln, RI: Quality Metric Incorporated; 2000.
- [43] Ware JE, Sherbourne CD. The MOS 36-item short-form health survey (SF-36): L conceptual framework and item selection. *Med Care* 1992;30:473–83.
- [44] Jones D, Kazis L, Lee A, et al. Health status assessments using the Veterans SF-12 and SF-36: methods for evaluating outcomes in the Veterans Health Administration. *J Ambul Care Manage* 2001;24(3):68–86.
- [45] Kang HK, Mahan CM, Lee KY, Magee CA, Murphy FM. Illnesses among United States veterans of the Gulf War: a population-based survey of 30,000 veterans. *J Occup Environ Med* 2000;42(5):491–501.
- [46] Ewing JA. Detecting alcoholism. The CAGE questionnaire. *JAMA* 1984;252(14):1905–7.
- [47] Weathers FW, Huska JA, Keane T. The PTSD Checklist Military Version (PCL-M). Boston, MA: National Center for PTSD; 1991.
- [48] Weathers FW, Litz BT, Herman DS, Huska JA, Keane TM. The PTSD Checklist (PCL): reliability, validity, and diagnostic utility. In *Paper presented at the Annual Meeting of International Society for Traumatic Stress Studies*, San Antonio, TX, 1993. Available at http://www.pdhealth.mil/library/downloads/PCL_ psychometrics.doc.
- [49] Lang AJ, Laffaye C, Satz LE, Dresselhaus TR, Stein MB. Sensitivity and specificity of the PTSD checklist in detecting PTSD in female veterans in primary care. *J Trauma Stress* 2003;16(3):257–64.
- [50] Brewin CR. Systematic review of screening instruments for adults at risk of PTSD. *J Trauma Stress* 2005;18(1):53–62.
- [51] American Psychiatric Association. Diagnostic and statistical manual of mental disorders 4th ed. DSM-IV. Washington, DC: American Psychiatric Association; 1994.
- [52] Blanchard EB, Jones-Alexander J, Buckley TC, Forneris CA. Psychometric properties of the PTSD Checklist (PCL). *Behav Res Ther* 1996;34(8):669–73.
- [53] Wright KM, Huffman AH, Adler AB, Castro CA. Psychological screening program overview. *Mil Med* 2002;167(10):853–61.
- [54] SAS Institute Inc. SAS/STAT® software version 9.0. Cary, NC: SAS Institute Inc.; 2002.
- [55] SAS Institute Inc. SAS/STAT® software: changes and enhancements through release 6.11. Cary, NC: SAS Institute Inc.; 1996. 1104.
- [56] Etter JF, Perneger TV. Analysis of non-response bias in a mailed health survey. *J Clin Epidemiol* 1997;50(10):1123–8.
- [57] Committee on Health Effects Associated With Exposures During the Gulf War. Gulf War and health volume 1. Depleted uranium, sarin, pyridostigmine bromide, vaccines. Division of Health Promotion and Disease Prevention, Institute of Medicine, 2000.
- [58] Institute of Medicine. Interactions of drugs, biologics, and chemicals in U.S. military forces. Washington, DC: National Academy Press; 1996.
- [59] Sato PA, Reed RJ, Smith TC, Wang L. Monitoring anthrax vaccine safety in US military service members on active duty: surveillance of 1998 hospitalizations in temporal association with anthrax immunization. *Vaccine* 2002;20(17–18):2369–74.
- [60] Grabenstein JD, Winkenwerder W Jr. US military smallpox vaccination program experience. *JAMA* 2003;289(24):3278–82.
- [61] U.S. Department of Health and Human Services. Healthy People 2010: understanding and improving health. 2nd ed. Washington, DC: U.S. Government Printing Office; 2000.
- [62] Division of Adult and Community Health National Center for Chronic Disease Prevention and Health Promotion Centers for Disease Control and Prevention. Behavioral Risk Factor Surveillance System Online Prevalence Data. Atlanta, GA, 2003. Available at <http://apps.nccd.cdc.gov/brfss/page.asp?yr=2003&state=All&cat=HA#HA>.
- [63] Barrett DH, Boehmer TK, Boothe VL, Flanders WD. Health related quality of life of US military personnel: a population based study. *Mil Med* 2003;168:941–7.
- [64] Trump DH, Brady PJ, Olsen CH. Self-related health and subsequent health care use among military personnel returning from international deployments. *Mil Med* 2004;169:128–33.
- [65] Gorham ED, Garland FC, Barrett-Connor E, Garland CF, Wingard DL, Pugh WM. Incidence of insulin-dependent diabetes mellitus in young adults: experience of 1,587,630 US Navy enlisted personnel. *Am J Epidemiol* 1993;138(11):984–7.
- [66] Murray CJ, Lopez AD. Alternative projections of mortality and disability by cause 1990–2020: Global Burden of Disease Study. *Lancet* 1997;1498–504.
- [67] The World Health Report 2001. Mental health: new understanding, new hope. Geneva: World Health Organization; 2001. p. 178.
- [68] Hoge CW, Lesikar SE, Guevara R, et al. Mental disorders among U.S. military personnel in the 1990s: association with high levels of health care utilization and early military attrition. *Am J Psychiatry* 2002;1576–83.
- [69] Bray RM, Hourani LL, Rae KL, et al. 2002 Department of Defense Survey of Health Related Behaviors Among Military Personnel. Research Triangle NC: Research Triangle Institute; 2003.