

Gulf War Syndrome: Evidence Based on the National Survey of Veterans*

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Abstract: The 2001 National Survey of Veterans, conducted ten years after the end of the Gulf War, provides invaluable information on the long time chronic health effects of the war. Using the semi-parametric Generalized Additive Model to control for different age distributions in our study sub-populations, we find that it is not the Gulf War deployment or combat *per se*, but the exposure to toxic chemicals that is the root cause of the myriad of health problems faced by many gulf war veterans. The simultaneous presence of multiple ailments for these veterans, known as the Gulf War syndrome, is also confirmed. Our study provides important additional evidence on the complexity in identifying the genuine health problems faced by the Gulf war veterans that came from widely varying socio-economic backgrounds.

Key words Gulf war veterans, Generalized Additive Model, Chemical exposure

JEL Classification I12, I18, C49

** This research was supported by the National Center on Minority Health and Health Disparities, National Institutes of Health (grant number P20MD003373). The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Center on Minority Health and Health Disparities or the National Institutes of Health. We thank John Jones, Terrence Kinal and Zulkarnain Pulungan for many comments and suggestions.*

Gulf War Syndrome: Further Evidence Based on the National Survey of Veterans

1 Introduction

The past twenty years have witnessed a compelling story of suffering by veterans who served in the 1990-1991 Persian Gulf War. The conditions affecting Gulf War veterans, like many wars before it, appear to be complex, involving diverse debilitating symptoms associated with multiple organs and physiological systems. The traditional scientific consensus in the years immediately following the war was that psychiatric illness, combat experience, or other deployment-related stressors are the likely reasons for the Gulf War ailments. However, many observers were unconvinced that wartime stress can adequately explain the symptoms of the Gulf war veterans. This is because the war only had four days of ground combat and most of the veterans were never in the combat area. The U.S. Department of Veterans Affairs (VA) has been under increasing pressure from the veterans groups to de-emphasize the view that stress and trauma were chief drivers of Gulf War illness. The Clinton administration passed a law in 1998 to conduct an extensive research on Gulf War symptoms. In accordance with this law, Congress and the VA established the Research Advisory Committee on Gulf War Veterans' Illnesses in 2002. One of the prominent findings of this federal panel is a conclusion, based on recent epidemiologic studies, that there is a "probable link" between toxic chemical exposure such as sarin gas and the mysterious ailments that continues to inflict the Gulf war veterans. This conclusion departs from the past official consensus that stress is the possible explanation for Gulf war illnesses. The proponents of the stress theory maintain that it is too early to rule out any specific cause since it is difficult to

determine which troops were exposed to what chemicals. Despite recent advances in their understanding of the long term effect of some of these chemicals, the federal panel concluded that their finding is inconclusive due to the lack of objective government data on Gulf War veterans. They recommended that government should give priority to research studies capable of “making full use of existing federal data resources related to Gulf War veterans’ health and military service”, and that there is an “urgent need” for additional studies to “reevaluate the association of combinations of neurotoxic exposures with chronic illness in Gulf War veterans”. Due to the obvious relevance of the Gulf War experience to recent Iraq and Afghanistan wars, future deployments and homeland security, the report also recommended that the VA invest at least \$60 million over the next 4 years for additional Gulf War illness research. Because of the limitations in the scope of previous research and the lack of effective follow-up study on long term chronic health problem for Gulf War veterans, the etiologic basis and clinical significance of Gulf war veterans remain unclear.

The 2001 National Survey of Veterans (*NSV2001*), the latest comprehensive national survey of veterans, deserves special attention. It provides rich information on Gulf War veterans’ health and socio-economic status 10 years after the war. Since most studies on Gulf War veterans are based on data collected in 1990s, this 2001 veteran’s data will extend previous research to reveal the long time potential effects of Gulf War. Quite surprisingly, a preliminary analysis of the *NSV2001* data revealed that the Gulf war veterans are systematically better in self-reported health status and in terms of the incidence of typical Gulf war related ailments than the non-Gulf war veterans. However, the age distribution and the socio-economic status of the two groups are quite different. Thus, unless the effects of these confounders are

appropriately and adequately controlled for, the true health effects of the Gulf war deployment cannot be delineated.

The analysis presented here utilizes semiparametric estimation approach to unravel the complexity of Gulf war veterans' health problems using a very comprehensive nationally representative data on all veterans. We study if the veterans who were deployed in the Gulf war have significantly more health problems than other veterans, and whether chemical exposure can be related to the typical Gulf war symptoms.

Our study contributes to the existing literature in two ways: We provide epidemiological evidence on the prevalence and nature of Gulf war illnesses. Methodologically, we use Generalized Additive Model (GAM) to control for the age heterogeneity in our national sample of all veterans that would otherwise confound the true effect of chemical exposure on the Gulf war veterans.

2 Study Motivation and the Data

2.1 The national Survey of veterans

NSV2001 is the fifth in a series of comprehensive nationwide surveys designed to investigate the demographic profile of US veterans, and to help the Department of Veterans Affairs (VA) to plan its future programs and services for veterans. Data collection began February 12, 2001, and ended November 12, 2001. A total of 19,961 interviews enter our analysis, consisting of 2,267 Gulf War veterans (11.36%) and 17694 non-Gulf War veterans (88.64%).

2.2 Early surprise: Preliminary Results from the Survey Data

The main objective for our study is to evaluate the health status of Gulf War veterans and compare them with non-Gulf war veterans. Table 1 provides percent

distribution of self-reported health status reported by veterans from our data. Surprisingly, more Gulf War veterans evaluated their health status as “excellent” (15.70% vs. 12.13%), “very good” (28.28 vs. 22.32) and “good” (31.27 vs. 28.72) than non-Gulf war veterans. Much lower percent of Gulf war veterans report poor health compared with other veterans. The p-value for χ^2 test is less than 0.0001, indicating a very significant difference between these two groups. Furthermore, for the typical Gulf War syndromes (*viz.*, gastrointestinal, depression, fatigue, chronic pain, ENT and concentration problems), Figure 1 indicates that the percentage of Gulf War veterans who have multisymptoms is almost the same as non-Gulf War veterans (39.35 vs. 38.32). For typical Gulf War symptoms, especially for depression, fatigue and concentrating problems, Gulf War veterans are significantly less likely to develop these ailments (Table 2). The better health status of Gulf War veterans is further confirmed by the comparison of common medical problems such as cancer, high blood pressure, diabetes, stroke, heart disease, and arthritis. In addition, Table 3 shows that Gulf War veterans have smaller possibility to have all of these common medical problems, including PTSD, one of the main contributing factors for Gulf War illnesses supported by some researchers.

As a first look, these results from the 2001 survey contradict the previous findings on the relative health status of Gulf war veterans, and raise the essential question: “Are Gulf War veterans truly more ill compared with other veterans?” The question merits a deeper look into the data.

2.3. Characteristics of 2001 NSV Data

As we mentioned, *NSV2001* is the latest series of nationwide surveys. Unlike previous research in the Gulf War veterans, this data is a comprehensive survey and is aimed at providing an overall look at all veterans’ health problems in their socio-

economic context. It is not specially designed for studying Gulf war illnesses. Therefore, for finding the true effects of Gulf War deployment using this survey, we have to control for potential confounders like the age distributions of the respective sub-populations. Previous studies on Gulf War veterans were based on data concentrating on Gulf war veterans and considered possible confounding effects during data collection design. For example, Kang *et al.* (2000, 2002), Steele (2000) and Cherry *et al.* (2001) chose the veterans who served in non-Gulf locations during the same period time of Gulf war as comparison group. The demographic characters of the two comparison groups are, as a result, similar or matched. The *NSV2001* includes veterans from all periods. One advantage of this comprehensive data set is that we have information on the health status of many non-Gulf War veterans who were exposed to chemicals, and also on many Gulf War veterans who were not exposed to chemicals.

Table 4 provides sociodemographic characteristics of *NSV2001* sample of veterans. Compared to non-Gulf veterans the Gulf War veterans are much younger (40.8 vs. 61.6 years). This is not surprising, given the general design for the survey; Gulf War was the final war period surveyed in *NSV2001*. Figures 2 and 3 provide direct comparison of the age distributions of Gulf War and non Gulf war veterans respectively. We see that less than 10 percent Gulf War veterans are older than 55, whereas the majority of the non-Gulf War veterans are over age 50. As a result, finding from *NSV2001* might be affected by the “age effect” that arises from the fact that younger veterans tend to be healthier and less likely to develop illnesses than older veterans.

The education level and the economic status of the Gulf war veterans are also much higher than the non-Gulf veterans. The percentage of whites compared to other

rates is also significantly smaller for Gulf veterans. (72.08% vs. 83.69%). We also find that relatively more number of females is Gulf veterans compared to other veterans (16.85% vs. 5.06%). It is clear that unless we control for these confounders, the effect of chemical exposure on the Gulf War veterans can not be properly ascertained.

3 The Logistic Model

With a binary dependent variable (health problem = 1, otherwise 0) the most widely used method to control for potential confounders is the logistic model with multiple covariates:

$$\log\left[\frac{p(X)}{1-p(X)}\right] = \beta_0 + \beta_1 X_1 + \dots + \beta_p X_p,$$

where $p(X) = \text{Pr ob}(Y = 1|X)$

The assumption behind this model is that logit $p(X)$ is a linear function of a set of covariates X_1, X_2, \dots, X_p . The parameters of the linear function are then estimated by maximum likelihood method. In our analysis, the logit of probability of developing specific illness is modeled as a linear function of Gulf war dummy and other explanatory variables like age, education, race, and others. Two likely factors proposed by various researchers - chemical exposure and PTSD - are also included in the explanatory variables.

In order to better capture the age effect in our data, we added an interaction variable - age times gulf war veterans (age*gulf) - in our regression. The other cross variable used on the right hand side of logistic regression is gulf war dummy times chemical exposure (gulf*chem) to capture the effect of the specific types of chemicals that the Gulf veterans were exposed as compared with other veterans. Relatively more

number of Gulf veterans report having exposed to chemicals than other veterans (34.10 vs. 21.67%). The logistic regression results are shown in Tables 5a - 10a.

We evaluate six typical Gulf War illnesses: Chronic pain, Gastrointestinal, Depression, Fatigue, Concentration and ENT problems. Despite specifying age and other potential confounders on the explanatory side of the model, logistic model estimates provide almost the same conclusion as the preliminary analysis of the data. Gulf war veterans show lower possibility to develop four of the six typical symptoms: chronic pain (OR=0.283), Gastrointestinal (OR=0.291), depression (OR= 0.633), and concentration (OR=0.474). For fatigue and ENT the odds ratios were not statistically different from one. One interesting finding is that the interaction variable age*gulf has odds ratios significantly over one for Chronic pain, Gastrointestinal and Concentration problems suggesting that with comparable age as other veterans, the Gulf veterans have a higher probability of getting these health problems. Veterans who have relatively better socio-economic status (income and education) and are white have less likelihood of suffering from all these symptoms, possibly because they can receive better treatment and management of their health problems. The variable Gulf*Chem is significant for Depression and Fatigue, but not for other ailments. The variable Chem_Exposure is very significant for all symptoms and the odds ratios are always in excess of 1.5. However, since the Gulf dummy comes out to be significantly negative for all symptoms except ENT (for which it was statistically insignificant), the question still remains if we are adequately controlling for the differential age distributions between these two groups.

4 The Generalized Additive Model (GAM)

4.1 Limitations of Logistic Model for controlling age effect

The logistic model is limited in controlling age effects since it assumes a rather simple relationship between the transformation of the response variable and independent variables. If the independent variable is related to the response variable in a complicated nonlinear fashion then the linearity assumption is not reasonable and the logistic model can yield misleading coefficients for all explanatory variables. Based on the Generalized Additive model (that we will explain shortly) Figures 4 - 9 give plots of the partial effects of age on the possibility of developing the six typical Gulf War symptoms with a 95 percent confidence interval. Except for the ENT case, none of effects look linear. This highly nonlinear relationship between age and response variable is the key to understand why our logistic model provides little control for the age heterogeneity in the two samples.

4.2 Methodology for Generalized Additive Model

One approach to model an unknown nonlinear relation between dependent and independent variables is nonparametric regression. Nonparametric regression relaxes the usual assumption of linearity and enables one to explore the data more flexibly, uncovering structure in the data that might otherwise be missed. However, many forms of nonparametric regression do not perform well when the number of independent variables in the model is large. The sparseness of data in this setting causes the variances of the estimates to be unacceptably large. The problem of rapidly increasing variance for increasing dimensionality is referred to as the "curse of dimensionality." Interpretability is another problem with nonparametric regression based on kernel and smoothing spline estimates. The information these estimates

contain about the relationship between the dependent and independent variables is often difficult to comprehend.

To overcome these difficulties, Stone (1985) proposed Additive models. These models estimate an additive approximation to the multivariate regression function. The benefits of an additive approximation are at least twofold. First, since each of the individual additive terms are estimated using a univariate smoother, the curse of dimensionality is avoided, at the cost of not being able to approximate universally. Second, estimates of the individual terms explain how the dependent variable changes with the corresponding independent variables.

To extend the additive model to a wide range of distribution families, Hastie and Tibshirani (1990) proposed Generalized Additive models. These models enable the mean of the dependent variable to depend on an additive predictor through a nonlinear link function. The models permit the response probability distribution to be any member of the exponential family of distributions. Many widely used statistical models belong to this general class; they include additive models for Gaussian data, nonparametric logistic models for binary data, and nonparametric log-linear models for Poisson data.

For response random variable Y and a set of predictors X_1, X_2, \dots, X_p , instead of defining

$$Y = \beta_0 + \beta_1 X_1 + \dots + \beta_p X_p + \text{Error}$$

the additive model generalizes the linear model by modeling the conditional expectation as

$$Y = S_1(X_1) + S_2(X_2) + \dots + S_p(X_p) + \text{Error}$$

where $s_i(X)$, $i = 1, 2, \dots, p$ are smooth functions. In order to be estimable, the smooth functions s_i have to satisfy the standardized conditions, viz., $Es_j(X_j) = 0$.

Since our analysis includes potentially a large number of explanatory variables, we specified a semiparametric generalized additive model with logit link:

$$g(p) = \log[p(X)/(1-p(X))] = \beta_0 + \beta_1 X_1 + \dots + \beta_{p-1} X_{p-1} + S(\text{age})$$

where X_1 to X_{p-1} stand for other independent variables such as gender, education, chemical exposure etc. Age is the main variable of interest we try to control with semiparametric specification. There are many ways to estimate generalized additive models. We estimate the parameters with the local scoring algorithm suggested by Hastie and Tibshirani (1986).

Figures 2 and 3 indicate that between ages 28 and 60 the most part of Gulf War veterans overlapped with non Gulf veterans. Also, between ages 28 and 60, the non-linear relation between age and the incidence of the health problems can reasonably be approximated by a quadratic function. The confidence interval of beyond 60 is also very wide implying less precise approximation. So we have good reasons to restrict our sample to all veterans who are between 28 and 60 years old. Another reason for restricting veterans in our sample to be older than 28 is that a Gulf war veterans can not possibly be less than 28 years old when the survey was taken.

4.3 Results from GAM Estimation

The last two columns of results from Tables 5b - 10b provide regression results from the GAM model with the sample restricted to ages 28-60. The first two columns show the results from logistic regression with age, age^2 and other covariates. Not

surprisingly, logistic regression and GAM provide almost the same results due to the quadratic age specification in the former as diagnosed by GAM. The nonparametric age specification is significant in five of the six typical Gulf war symptoms, with p-value less than 0.05. As expected from the corresponding graph, ENT is the only symptom with insignificant nonlinear age effect. For this problem, logistic model without age square specification provides very similar results with that from GAM. This regression results further confirm the value of GAM in controlling for the age confounder.

Most prominently and consistently, chemical exposure remains the chief driver for all these medical problems, even after we control the effect of stress factor PTSD. Especially for the Gulf veterans who have been exposed to the toxic exposure (gulf*chem_exposure), the odds ratios are always significantly above 1 for five of the six symptoms. Although PTSD is also a significant contributor to all the problems we evaluated, it can not explain the incidence of the individual medical problems we are analyzing. Studies of veterans from different wars have consistently found that patients with PTSD generally have more symptomatic complaints than those without PTSD. Also only a small fraction of veterans (6.79%) report PTSD in our sample. The reason is that the war was short, requiring only four days of ground combat to achieve a decisive victory. Casualty rates were very low, and the vast majority of veterans was never in combat areas and did not witness any deaths during deployment. VA has also reported that less than four percent of veterans examined in its Gulf War registry have either a primary or secondary diagnosis of PTSD. Similarly, a RAND report commissioned by the Department of Defense to review the scientific evidence concerning stress and Gulf War illnesses concluded that overall rates of PTSD are low in Gulf War veterans. As noted, the chemical exposure remains significant even after

we control for the presence of PTSD problem in both logistic and GAM specifications. This consensus between the two model specifications demonstrates that at least, deployment stress is not enough to explain the relative health status of Gulf war veterans.

Remarkably, for Chronic pain and Gastrointestinal problems, the OR for the Gulf dummy changes from significantly less than one to significantly greater than one in GAM estimation implying that once age is properly accounted for, Gulf veterans indeed have more incidence of these problems. For Depression and Fatigue problems OR for Gulf dummy increased significantly, but did not exceed the value of one. However, for these ailments, the Gulf*Chem dummy is significantly more than one. This variable together with Chem_exposure implies that chemical exposure in the Gulf war increased the odds of being inflicted with these ailments. For concentration problem, the Gulf dummy in GAM estimation again increased in OR, but did not exceed one. The Gulf*Chem variable is also not statistically significant. For this medical problem, the only evidence of the Gulf War comes via the Chem_exposure variable. For ENT, GAM and the logistic model with linear and quadratic age terms estimations, as expected, are very similar because our non-parametric estimation identified the age effect as close to being linear. For this medical problem (i.e., ENT), Gulf dummy is always positive and highly significant. Thus the preponderance of the evidence is that once the effects of the cofounders, most notably that of age, is appropriately taken care off, the gulf war veterans, due to their exposure to chemicals, have significantly higher odds in developing these chronic medical problems that did not fade away even 10 years after the exposure.

However it is the occurrence of multiple symptoms that distinguishes Gulf War veterans from other veterans. Table 11 indicates that Gulf War veterans are significantly more likely to have more than three of the six typical symptoms all simultaneously; this is especially true for Gulf War veterans who had toxic exposure. This finding supports the conclusion of the recent report released by the federal Committee: “A similar proportion of Gulf and non Gulf veterans reported a relatively low level of symptoms ---- that is, symptoms in just one or two of the six defined symptom groups.” However, more Gulf War veterans “reported having moderate-to-severe symptoms in three or more of the symptom domains”.

Generally speaking, our results indicate that the pattern of symptoms in Gulf War veterans is unique in terms of the occurrence of multiple symptoms. To be a Gulf War veteran may not result in worse health with respect to only one medical condition. The Gulf War veterans who were exposed to chemical exposure during the war are most likely to be troubled by a multitude of symptoms. Therefore, after reevaluating the data, we reach the conclusion that many Gulf War veterans are ill in a special way in that they are inflicted by multiple problems, and the likely causal link to this syndrome is the toxic chemical exposure.

This conclusion is further confirmed when we restrict our analysis to a sample of only Gulf War veterans. We compare gulf war veterans who had experienced toxic exposure during the war with those who did not report chemical exposure. Table 12 indicates that veterans with chemical exposure suffer from worse self-report health status, more service-connected disability, higher outpatient and inpatient hospitalizations and abnormally higher rate of the typical Gulf war symptoms. Moreover, Table 13 and Figure 11 show that a similar proportion of chemically

exposed and non-exposed Gulf war veterans reported a relatively low number of symptoms—for instance, only one medical problem out of the six defined symptom groups. However, over 50 percent of exposure veterans reported symptoms in two or more of the symptom domains, compared to less than 30 percent of the comparison group. Thus, the Gulf War veterans experiencing chemical exposure have worse health status, in terms of frequency, severity, duration, and the occurrence of multiple-symptom health problems. In table 14, we report an ordered probit regression of self-reported health status on chemical exposure with controls for race, gender, education, age and income. Based on this regression, Figure 12 depicts a significant left shift of the distribution of the predicted probabilities of falling into different self-reported health groups for these two Gulf veterans groups. This graph shows that for chemically exposed Gulf veterans, the probabilities of reporting poor and fair health are higher, and those for very good and excellent health, they are lower compared to Gulf veterans who were not exposed to the chemicals. In table 15, we report a logistic regression of having three or more Gulf illness syndromes as a function of Chemical exposure, gender, race, education income and age. Again, the effect of Chem_exposure is found to be very significant with an odds ratio in excess of 3. Based on this regression, Figure 13 reveals that a gulf veteran's probability for having three or more health symptoms increases substantially after exposure to chemicals. The vertical difference between the two lines depicts the marginal effect of chemical exposure as a function of age; we find that this difference also increases with age.

These regressions clearly show that our analysis of the NSV2001 data overwhelmingly supports the conclusion of the federal panel that chemical exposure during the Gulf war is the principal driver of the much documented Gulf War illnesses.

5 Conclusions

Despite recent research breakthroughs in research on the effects of clinical exposure on Gulf War illnesses, the etiologic basis and clinical significance of Gulf war veterans still remain unclear. Due to the lack of objective long term follow-up data, there has been no conclusive answer to the fundamental question related to the pattern and nature of these mysterious and often debilitating ailments. In their latest 2004 report, the Research Advisory Committee on Gulf War Veterans' Illnesses, appointed by Congress and the VA, recommended that important social priority should be given to expansive studies capable of reevaluating the possible reasons of the Gulf War illnesses. The 2001 National Survey of veterans, conducted 10 years after the Gulf War, provides invaluable information for long time chronic health effect of the war and deserves special investigation. Our preliminary data analysis, contrary to previous evidence on the relative health for Gulf War veterans, indicates better health for Gulf War veterans compared to other veterans. Using this data and appropriate statistical methods, we assessed the health of Gulf war veterans, compared their health to veterans who did not served in Persian Gulf, and reevaluated the probable link between chemical exposure and Gulf War illnesses.

Since 2001 NSV is a comprehensive dataset where Gulf veterans represent only a small part of it, we showed that age distribution of veterans in different sub-populations is an extremely important confounding factor that can yield misleading regression results unless it is appropriately controlled for. The widely used logistic model contributes little in controlling age effect due to its simplifying assumption. We show that the marginal effect of age in our sample is highly non-linear requiring a more flexible specification of the effect of age on health. We used the semi-

parametric Generalized Additive Model and estimated it using local scoring algorithms. The results are striking. After successfully controlling the effect of age with GAM specification, we could unravel the true underlying causes of the special health problems of Gulf war veterans. Gulf War deployment, by itself, is not the root cause of the myriad of health problems faced by some of the gulf war veterans. Only the Gulf War veterans who were exposed to toxic chemicals are found to be strongly associated with an abnormally high risk of the typical gulf war illnesses. Moreover, an important feature of the health problems of Gulf War veterans is the presence symptoms for a number of ailments.

We also reevaluated the two possible contributors to the ill health of Gulf war veterans: deployment stress and chemical exposure. Since the war was short and the overall rate of PTSD in Gulf war veterans is low, PTSD is less likely to be the main factor causing health problems in Gulf war veterans. Instead, both logistic regression and GAM specifications indicate significant contribution of chemical exposure even after we control the deployment stress factor. This finding suggests a strong association between the higher prevalence of Gulf syndromes and the toxic exposure specific to the Gulf war.

Our study provides important additional evidence on the complexity of Gulf war veterans' health problems. Methodologically, we addressed the potential confounding effect of different age distributions in study sub-samples with a semi-parametric statistical approach that will, hopefully, help future empirical studies.

Reference:

1. Australian Commonwealth Department of Veterans' Affairs. Australian Gulf War Veterans' Health Study Report. *ACDVA*. 2003.
2. Chemicals Sickened Gulf War Veterans, Latest Study Finds, *New York Times*, October 15, 2004
3. Cherry N, Creed F, Silman A et al. Health and exposures of United Kingdom Gulf War veterans. Part II: The relation of health to exposure. *Occup Environ Med* 2001;58:299-306.
4. Gray GC, Smith TC, Kang HK, et al. Are Gulf War veterans suffering war-related illnesses? Federal and civilian hospitalizations examined, June 1991 to December 1994. *Am J Epidemiol* 2000;151:63-71.
5. Hastie, T.J. and Tibshirani, R.J. (1986), "Generalized Additive Models (with discussion)," *Statistical Science*, 1, 297 - 318.
6. Hastie, T.J. and Tibshirani, R.J. (1990), *Generalized Additive Models*, New York: Chapman and Hall.
7. Hotopf M, David AS, Hull L, Ismail K, Unwin C, Wessely S. The health effects of peacekeeping (Bosnia, 1992-1996): a cross-sectional study - comparison with nondeployed military personnel. *Mil Med*. 2003;168:408-413.
8. Hotopf M, David AS, Hull L, Nikalaou V, Unwin C, Wessely S. Gulf war illness - better, worse, or just the same? A cohort study. *BMJ*. 2003;327:1370-1374.
9. Hyams KC, Signall FS, Roswell R. War syndromes and their evaluation: from the U.S. Civil War to the Persian Gulf War. *Ann Intern Med* 1996;125:398-405.

10. Iowa Persian Gulf Study Group. Self-reported illness and health status among Gulf War veterans—a population-based study. *JAMA* 1997;277:238-45.
11. Ishoy T, Suadicani P, Guldager B, Appleyard M, Hein HO, Gyntelberg F. State of health after deployment in the Persian Gulf: The Danish Gulf War Study. *Dan Med Bull.* 1999;46:416-419.
12. Kang HK, Mahan CM, Lee KY. Illnesses among United States veterans of the Gulf War: a population-based survey of 30,000 veterans. *J Occup Env Med* 2000;42:491-501.
13. Landrigan PJ. Illness in Gulf War veterans: causes and consequences. *JAMA* 1997;277:259-61.
14. Lange G, Tiersky L, DeLuca J, et al. Psychiatric diagnoses in Gulf War veterans with fatiguing illness. *Psychiatry Research* 1999;89:399-48.
15. Murphy FM. Gulf War syndrome: there may be no specific syndrome, but troops suffer after most wars. (Editorial). *BMJ* 1999; 318:274-5.
16. Presidential Advisory Committee on Gulf War Veterans' Illnesses: final report. Washington, DC: US Government Printing Office, 1996.
17. SAS Institute Inc. (2000), *SAS/STAT User's Guide, Version 9*, Cary, NC: SAS Institute Inc
18. Stone, C.J. (1985), "Additive Regression and Other Nonparametric Models," *Annals of Statistics*, 13, 689 - 705.
19. Scientific Progress in Understanding Gulf War veterans' Illnesses: Report and Recommendations, Research Advisory Committee on Gulf War Veterans' Illness, September, 2004

20. Steele L. Prevalence and patterns of Gulf War illness in Kansas veterans: association of symptoms with characteristics of person, place, and time of military service. *Am J Epidemiol* 2000;152:991-1001.
21. VA Advisers Link Gulf War Illnesses to Neurotoxins, *Science* 2004 306: 26-27
22. Verbrugge LN, Ascione FJ. Exploring the iceberg: common symptoms and how people care for them. *Med Care* 1987;25:539-63.
23. Wolfe J, Proctor SP, Erickson DJ, et al. Relationship of psychiatric status to Gulf War veterans' health problems. *Psychosom Med* 1999;61:532-40.

Table 1. Distribution of General Health Status by Veterans*

Self-evaluated Health Status	Gulf War Veterans (n = 2267)	Non-Gulf War Veterans (n = 17694)
Excellent	15.70	12.13
Very Good	28.28	22.32
Good	31.27	28.72
Fair	18.31	20.19
Poor	6.18	12.72

* The hypothesis of independence of deployment status and perceived health status is rejected at 5% level of significance, $\chi^2 = 215.0868(p < 0.0001)$.

Figure 1. U.S. Gulf War Veterans Reporting Typical Symptoms (%)

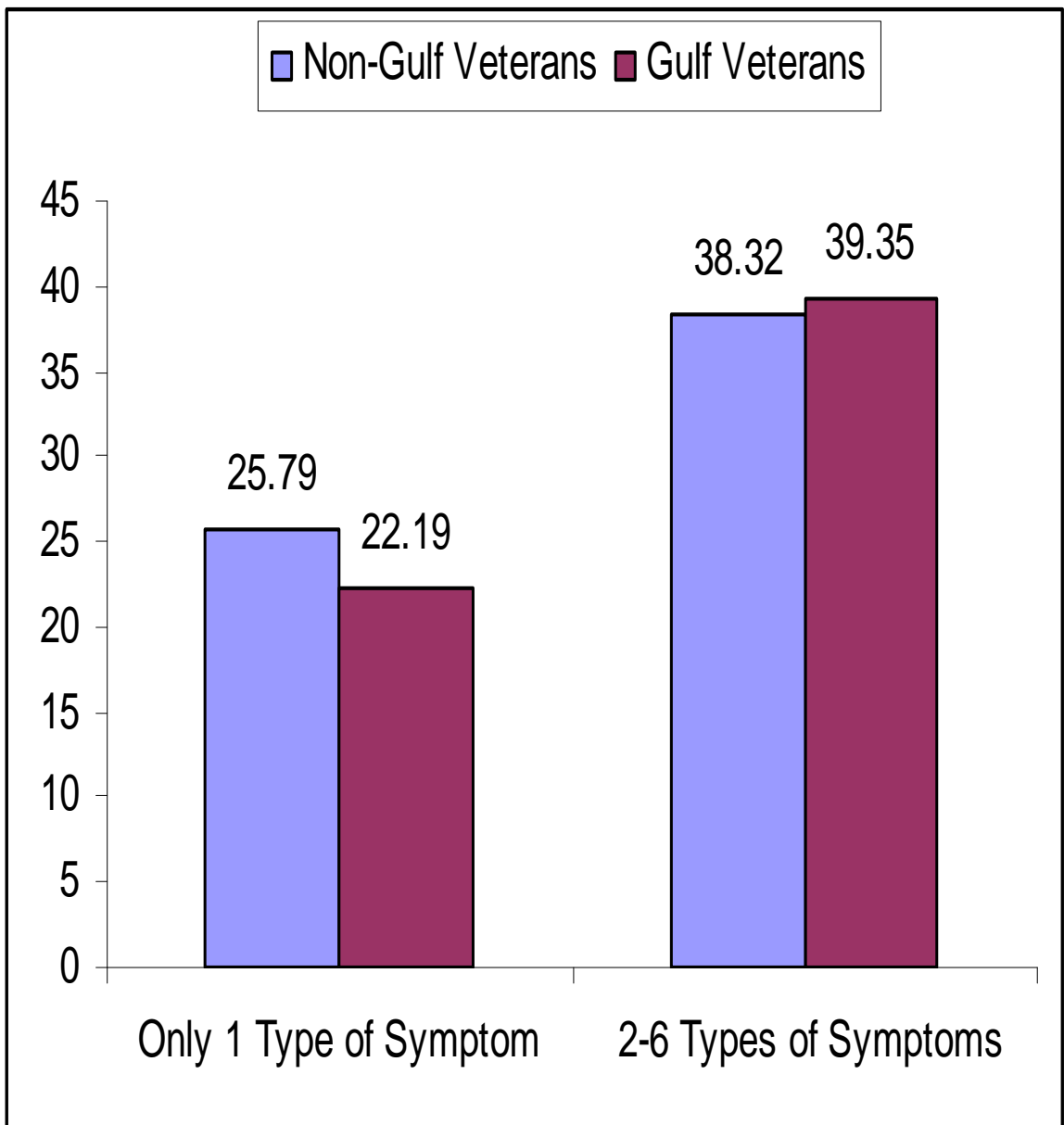


Table 2. Gulf War Veterans Reporting Typical Gulf War Syndromes (%)

	Gulf War Veterans	Non-Gulf Veterans	p-value
Fatigue	39.13	45.24	<0.0001
Depression	23.95	26.40	0.0125
Difficulty concentrating	14.16	16.92	0.0009
Gastrointestinal	19.14	17.33	0.0323
ENT Problem	20.56	15.51	<.0001
Chronic Pain	25.89	21.62	<.0001

Table 3. Prevalence Rate (%) of U.S. Gulf War Veterans Reporting Common Medical Problems

	Gulf War Veterans	Non-Gulf Veterans	p-value
Diabetes	3.75	14.98	<0.0001
Kidney problem	8.43	14.41	<0.0001
Stroke	0.79	4.33	<0.0001
Heart Disease	7.41	21.36	<0.0001
Cancer	2.78	9.67	<0.0001
High Blood Pressure	18.00	42.11	<0.0001
Lung Problem	7.85	12.63	<0.0001
Arthritis	23.82	34.71	<0.0001
Liver	2.16	2.45	0.2058
PTSD	6.79	7.31	0.3605

Table 4. Distribution of Sociodemographic Characteristics in 2001

National Survey of Veterans

Characteristics	Gulf War veterans (n = 2267)	Non-Gulf War veterans (n = 17694)	P-Value
Age (mean age in years in 2001)	40.8	61.6	<0.0001
Gender			<0.0001
Male	83.15	94.94	
Female	16.85	5.06	
Education Level			<0.0001
Less than HS	1.76	13.90	
HS diploma	22.45	29.24	
Post HS training	44.55	32.02	
BA degree or higher	31.14	24.60	
Financial Income			<0.0001
\$0-\$10,000	3.79	8.53	
\$10,001-\$20,000	7.72	18.14	
\$20,001 to \$30,000	12.53	17.66	
\$30,001 to \$40,000	15.88	13.33	
\$40,001 to \$50,000	15.00	10.87	
Over \$50,000	45.08	31.46	
Race			<0.0001
White	72.08	83.69	
Black	16.63	7.86	
Other	11.29	8.45	
Chemical Exposure	34.10	21.67	<0.0001

Figure 2. Age Distribution of Gulf War Veterans in 2001 NSV

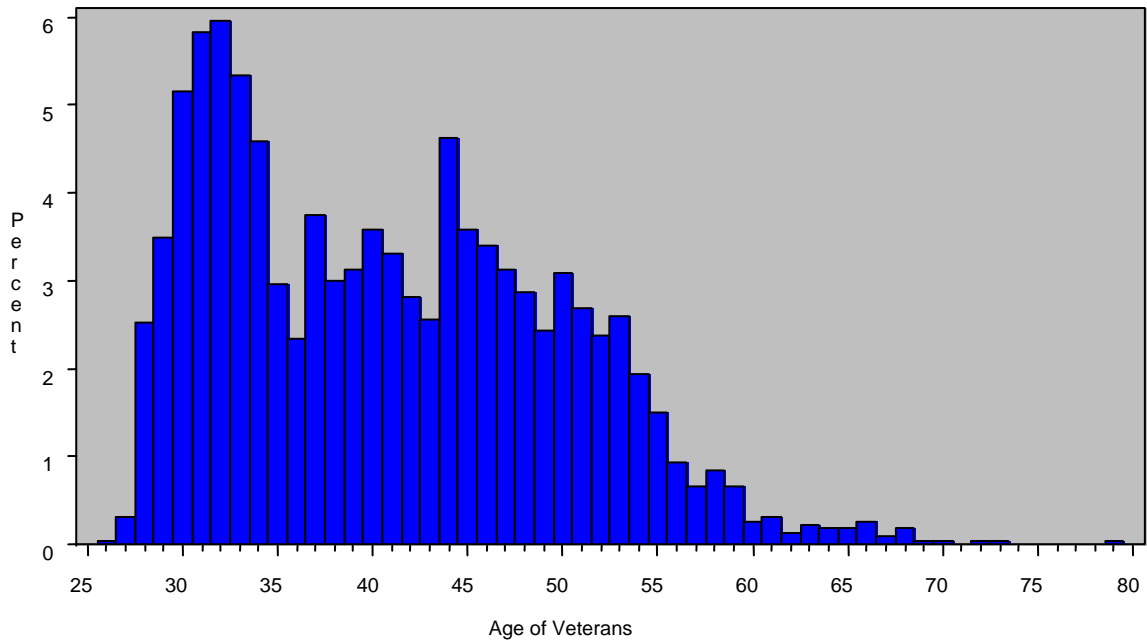


Figure 3. Age Distribution of Non Gulf War Veterans in 2001 NSV

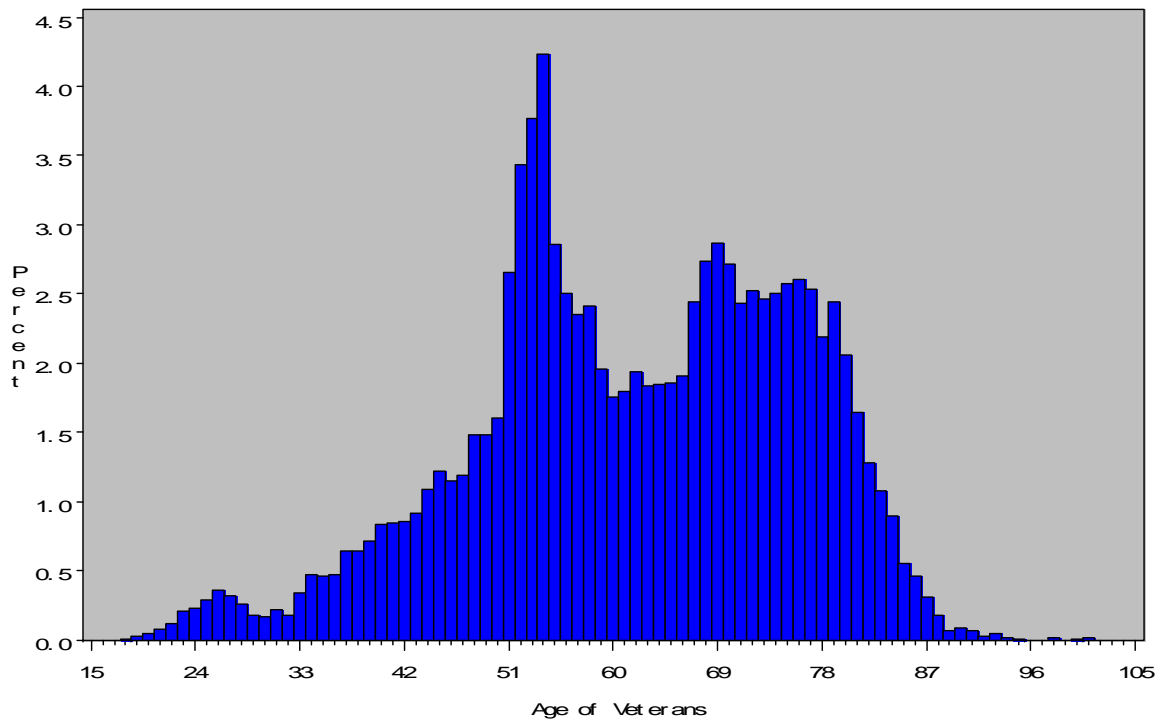


Table 5a. Logistic Model for Chronic Pain Problem

	Odds Ratio	P-Value
Male	0.594	<.0001
Gulf	0.283	<.0001
Chemi_exposure	1.952	<.0001
White	0.785	<.0001
Edu ≥ HS	0.817	0.0002
Income ≥ 10K	0.614	<.0001
PTSD	4.905	<.0001
Gulf*Chemi	1.055	0.6327
Age*Gulf	1.035	<.0001
Age	1.003	0.0231

Table 5b. Logistic Model and GAM for Chronic Pain Problem
(Age: 28-60)

	Logistic Odds Ratio	Logistic P-Value	GAM Odds Ratio	GAM P-Value
Male	0.576	<.0001	0.589	<.0001
Gulf	1.276	0.0036	1.278	0.0033
Chemi_exposure	1.778	<.0001	1.843	<.0001
White	0.799	<.0001	0.805	0.0002
Edu ≥ HS	0.747	0.0040	0.748	0.0042
Income ≥ 10K	0.483	<.0001	0.486	<.0001
PTSD	4.610	<.0001	4.689	<.0001
Gulf*Chemi	1.211	0.1080	1.173	0.1815
Age	1.223	<.0001	1.013	0.0004
Agesquare	0.998	<.0001	.	.

* χ^2 test for nonparametric age effect in GAM model is 61.1960 (p<0.0001)

Table 6a. Logistic Model for Gastrointestinal Problem

	Odds Ratio	P-Value
Male	0.723	<.0001
Gulf	0.291	<.0001
Chemi_exposure	1.638	<.0001
White	0.983	0.7411
Edu ≥ HS	0.761	<.0001
Income ≥ 10K	0.803	0.0009
PTSD	3.369	<.0001
Gulf*Chemi	1.110	0.3901
Age*Gulf	1.036	<.0001
Age	1.011	<.0001

Table 6b. Logistic Model and GAM for Gastrointestinal Problem
(Age: 28-60)

	Logistic Odds Ratio	Logistic P-Value	GAM Odds Ratio	GAM P-Value
Male	0.730	0.0007	0.742	0.0014
Gulf	1.392	0.0004	1.393	0.0003
Chemi_exposure	1.539	<.0001	1.574	<.0001
White	0.922	0.1992	0.926	0.2232
Edu ≥ HS	0.882	0.2576	0.881	0.2547
Income ≥ 10K	0.656	<.0001	0.659	<.0001
PTSD	3.134	<.0001	3.169	<.0001
Gulf*Chemi	1.217	0.1290	1.191	0.1771
Age	1.289	<.0001	1.021	<.0001
Agesquare	0.997	<.0001	.	.

* χ^2 test for nonparametric age effect in GAM model is 45.1556 (p<0.0001)

Table 7a. Logistic Model for Depression Problem

	Odds Ratio	P-Value
Male	0.867	0.0432
Gulf	0.633	0.0833
Chemi_exposure	1.466	<.0001
White	0.662	<.0001
Edu ≥ HS	0.693	<.0001
Income ≥ 10K	0.459	<.0001
PTSD	8.127	<.0001
Gulf*Chemi	1.393	0.0043
Age*Gulf	1.002	0.6919
Age	0.997	0.0195

Table 7b. Logistic Model and GAM for Depression Problem (Age: 28-60)

	Logistic Odds Ratio	Logistic P-Value	GAM Odds Ratio	GAM P-Value
Male	0.789	0.0048	0.786	0.0041
Gulf	0.713	<.0001	0.708	<.0001
Chemi_exposure	1.575	<.0001	1.568	<.0001
White	0.656	<.0001	0.656	<.0001
Edu ≥ HS	0.723	0.0011	0.723	0.0011
Income ≥ 10K	0.344	<.0001	0.344	<.0001
PTSD	8.510	<.0001	8.480	<.0001
Gulf*Chemi	1.262	0.0571	1.273	0.0476
Age	1.119	0.0005	1.000	0.9389
Agesquare	0.999	0.0005	.	.

* χ^2 test for nonparametric age effect in GAM model is 28.1370 (p<0.0001)

Table 8a. Logistic Model for Fatigue Problem

	Odds Ratio	P-Value
Male	0.689	<.0001
Gulf	0.826	0.3966
Chemi_exposure	1.644	<.0001
White	0.830	<.0001
Edu ≥ HS	0.735	<.0001
Income ≥ 10K	0.464	<.0001
PTSD	4.645	<.0001
Gulf*Chemi	1.267	0.0206
Age*Gulf	1.003	0.6247
Age	1.015	<.0001

Table 8b. Logistic Model and GAM for Fatigue Problem
(Age: 28-60)

	Logistic Odds Ratio	Logistic P-Value	GAM Odds Ratio	GAM P-Value
Male	0.702	<.0001	0.702	<.0001
Gulf	0.940	0.3828	0.937	0.3576
Chemi_exposure	1.745	<.0001	1.748	<.0001
White	0.796	<.0001	0.796	<.0001
Edu ≥ HS	0.656	<.0001	0.657	<.0001
Income ≥ 10K	0.395	<.0001	0.395	<.0001
PTSD	5.723	<.0001	5.721	<.0001
Gulf*Chemi	1.175	0.1389	1.174	0.1393
Age	1.151	<.0001	1.013	<.0001
Agesquare	0.999	<.0001	.	.

* χ^2 test for nonparametric age effect in GAM model is 28.1370 (p<0.0001)

Table 9a. Logistic Model for Concentration Problem

	Odds Ratio	P-Value
Male	0.859	0.0803
Gulf	0.474	0.0250
Chemi_exposure	1.789	<.0001
White	0.625	<.0001
Edu ≥ HS	0.565	<.0001
Income ≥ 10K	0.435	<.0001
PTSD	10.244	<.0001
Gulf*Chemi	1.034	0.8152
Age*Gulf	1.013	0.0935
Age	1.002	0.1916

Table 9b. Logistic Model and GAM for Concentration Problem
(Age: 28-60)

	Logistic Odds Ratio	Logistic P-Value	GAM Odds Ratio	GAM P-Value
Male	0.784	0.0176	0.783	0.0170
Gulf	0.870	0.1993	0.861	0.1654
Chemi_exposure	1.796	<.0001	1.807	<.0001
White	0.637	<.0001	0.638	<.0001
Edu ≥ HS	0.619	<.0001	0.620	<.0001
Income ≥ 10K	0.354	<.0001	0.355	<.0001
PTSD	11.086	<.0001	11.092	<.0001
Gulf*Chemi	0.985	0.9210	0.989	0.9398
Age	1.225	<.0001	1.013	0.0044
Agesquare	0.998	<.0001	.	.

* χ^2 test for nonparametric age effect in GAM model is 34.9559 (p<0.0001)

Table 10a. Logistic Model for ENT Problem

	Odds Ratio	P-Value
Male	0.557	<.0001
Gulf	1.290	0.3519
Chemi_exposure	1.744	<.0001
White	1.074	0.1719
Edu ≥ HS	0.941	0.3213
Income ≥ 10K	0.922	0.2495
PTSD	2.286	<.0001
Gulf*Chemi	1.036	0.7645
Age*Gulf	1.003	0.6126
Age	1.009	<.0001

Table 10b. Logistic Model and GAM for ENT Problem
(Age: 28-60)

	Logistic Odds Ratio	Logistic P-Value	GAM Odds Ratio	GAM P-Value
Male	0.519	<.0001	0.524	<.0001
Gulf	1.400	0.0002	1.402	0.0002
Chemi_exposure	1.648	<.0001	1.667	<.0001
White	1.090	0.1884	1.092	0.1769
Edu ≥ HS	0.976	0.8342	0.975	0.8319
Income ≥ 10K	0.994	0.9551	0.996	0.9688
PTSD	2.152	<.0001	2.168	<.0001
Gulf*Chemi	1.123	0.3574	1.109	0.4092
Age	1.009	0.0178	1.009	0.0213
Agesquare				

* χ^2 test for nonparametric age effect in GAM model is 2.9308 (p=0.4024)

Figure 4. Partial Effect of Age on Depression Problem

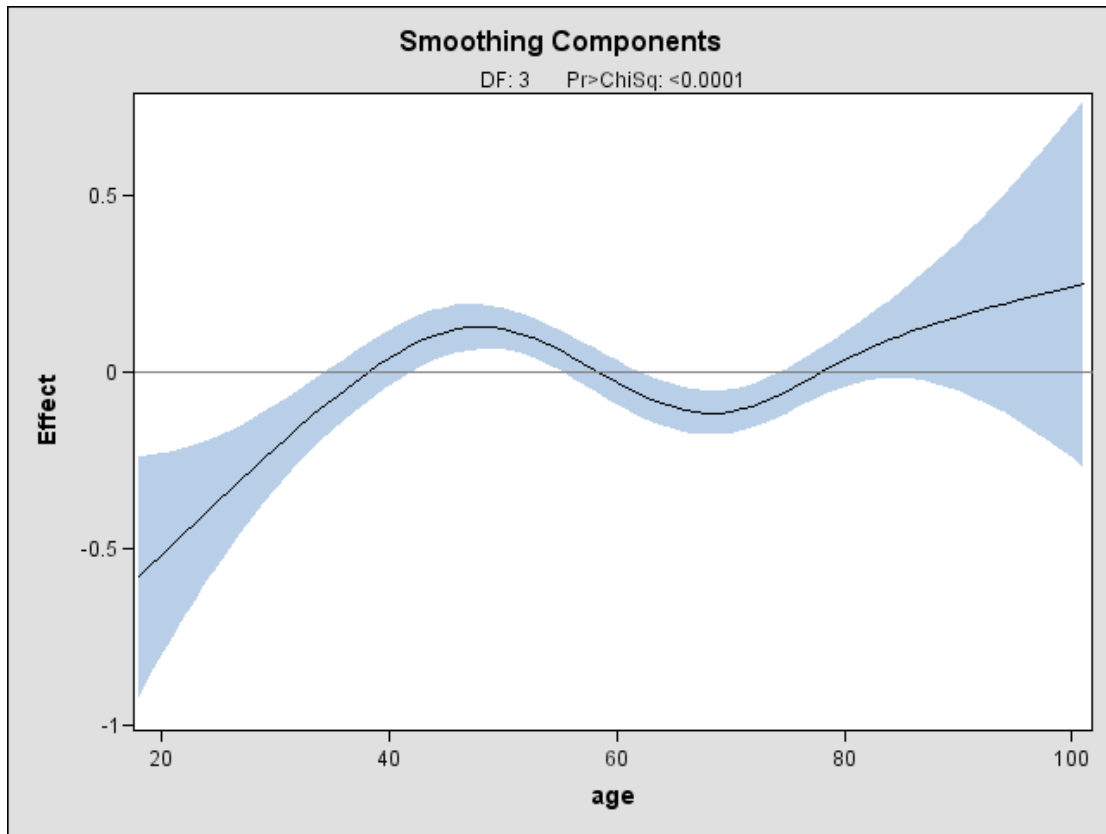


Figure 5. Partial Effect of Age on ENT Problem

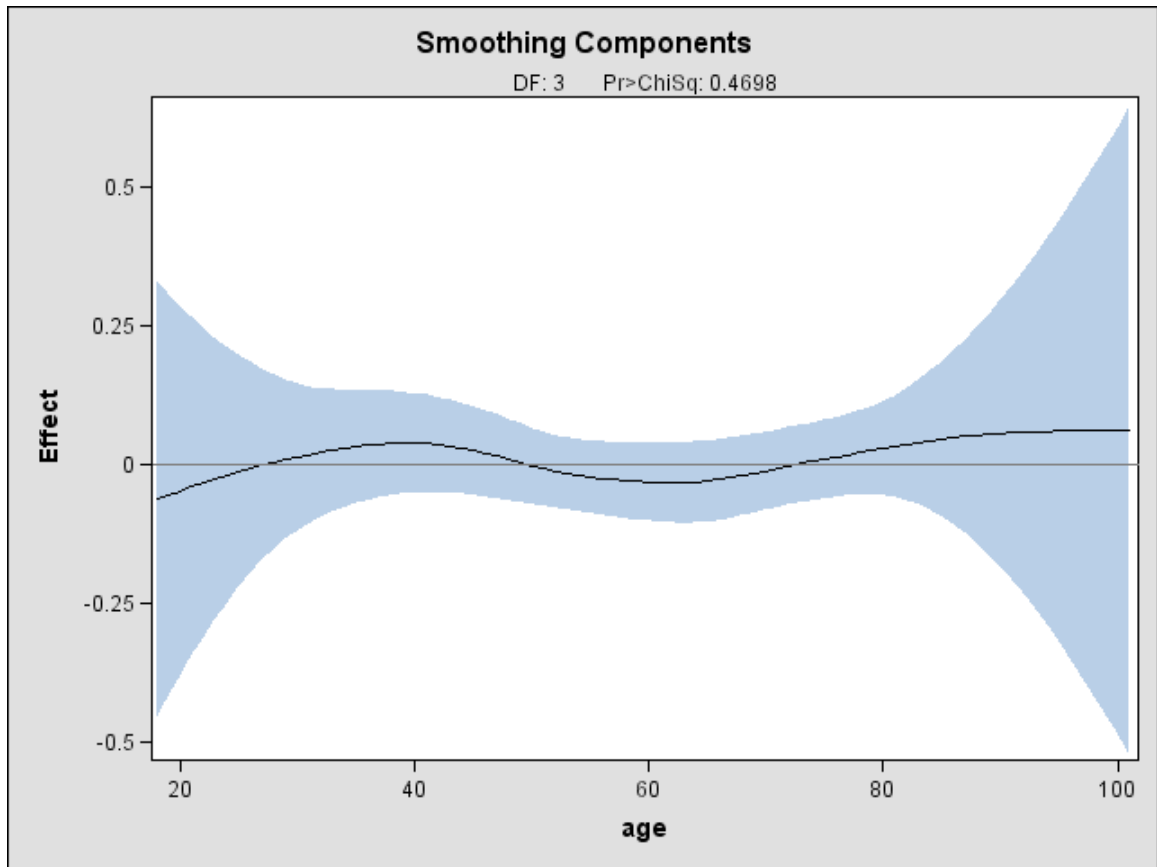


Figure 6. Partial Effect of Age on Chronic Pain Problem

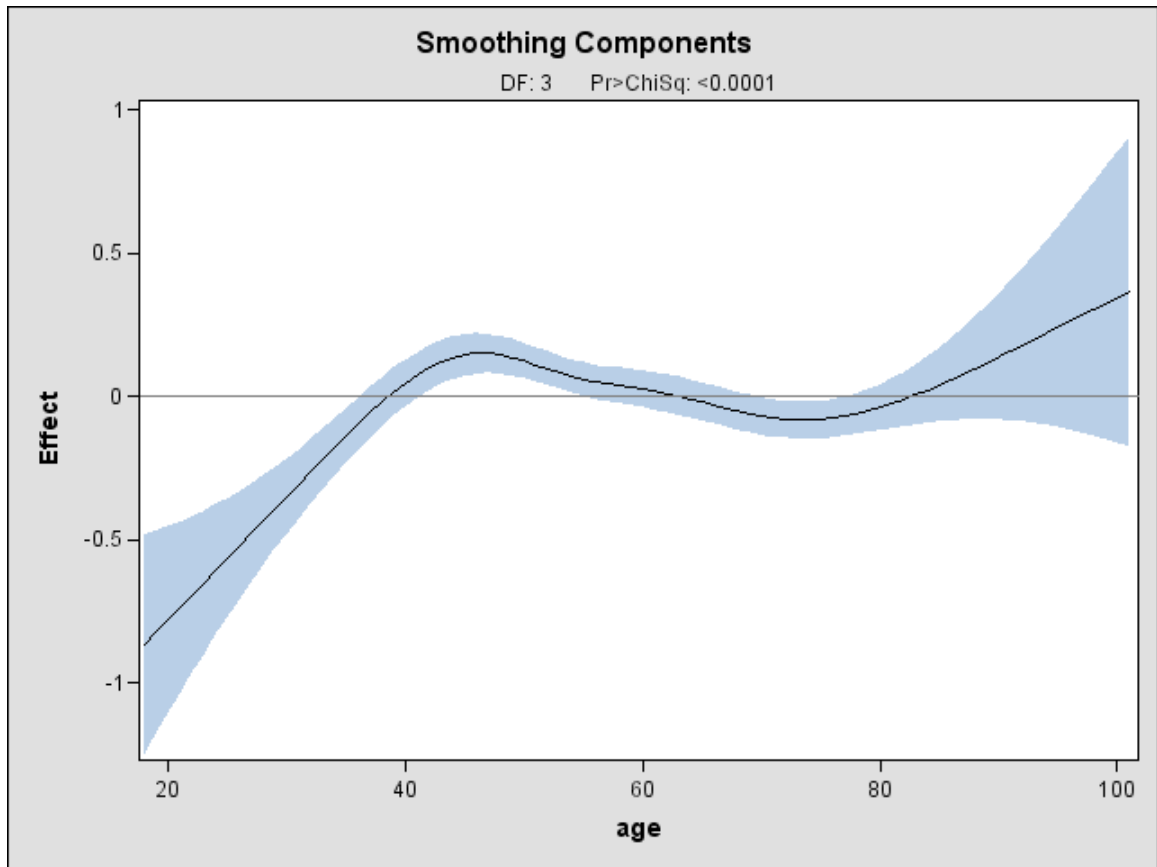


Figure 7. Partial Effect of Age on Fatigue Problem

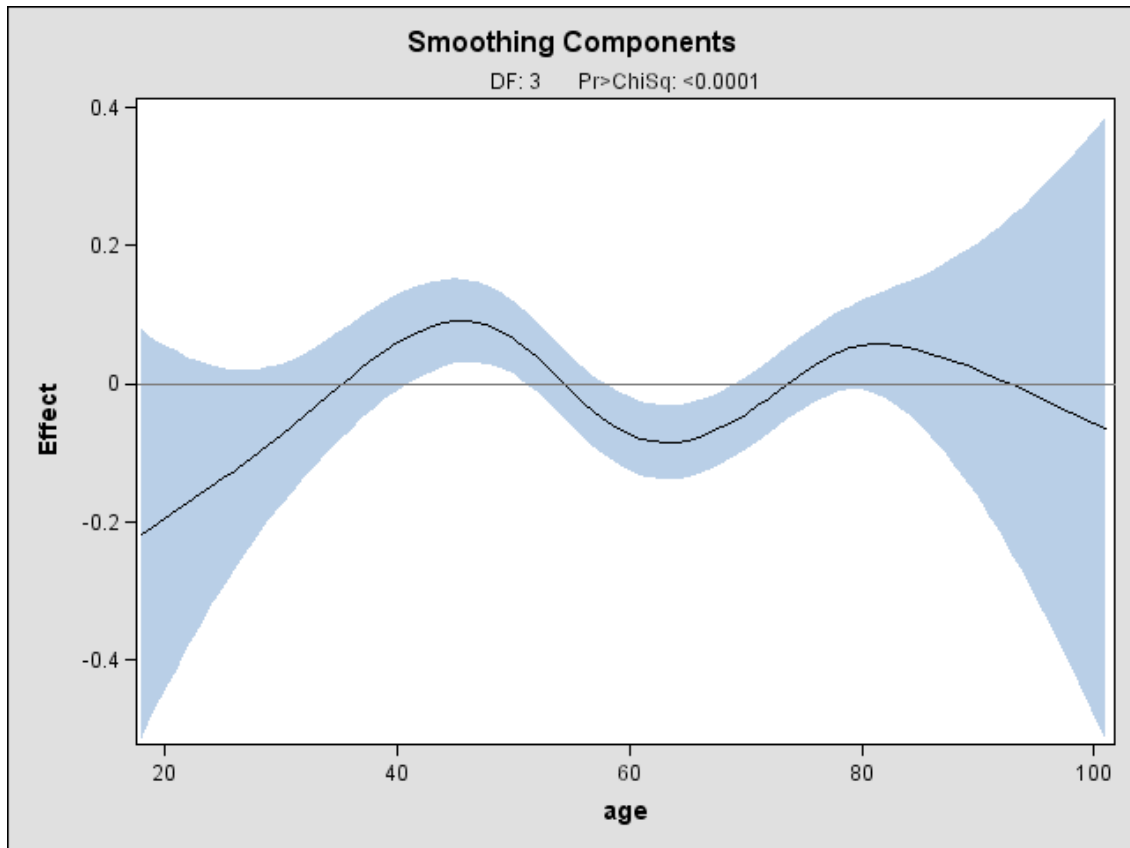


Figure 8. Partial Effect of Age on Gastrointestinal Problem

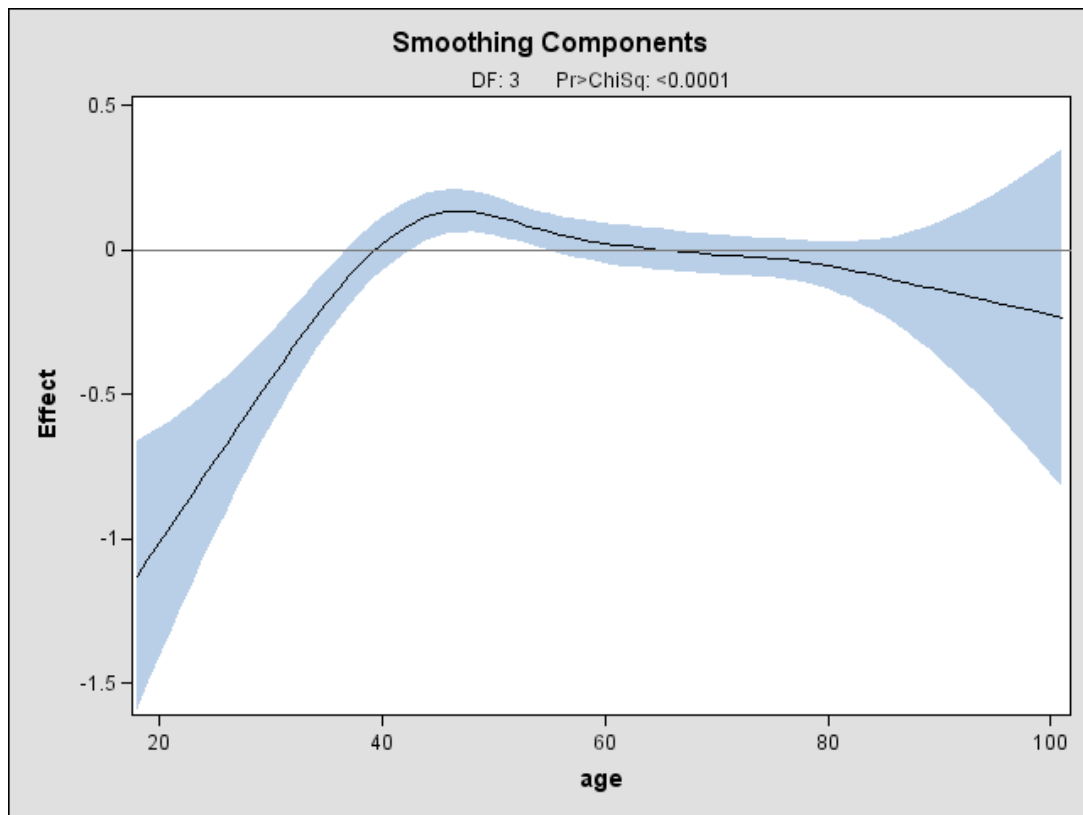


Figure 9. Partial Effect of Age on Concentration Problem

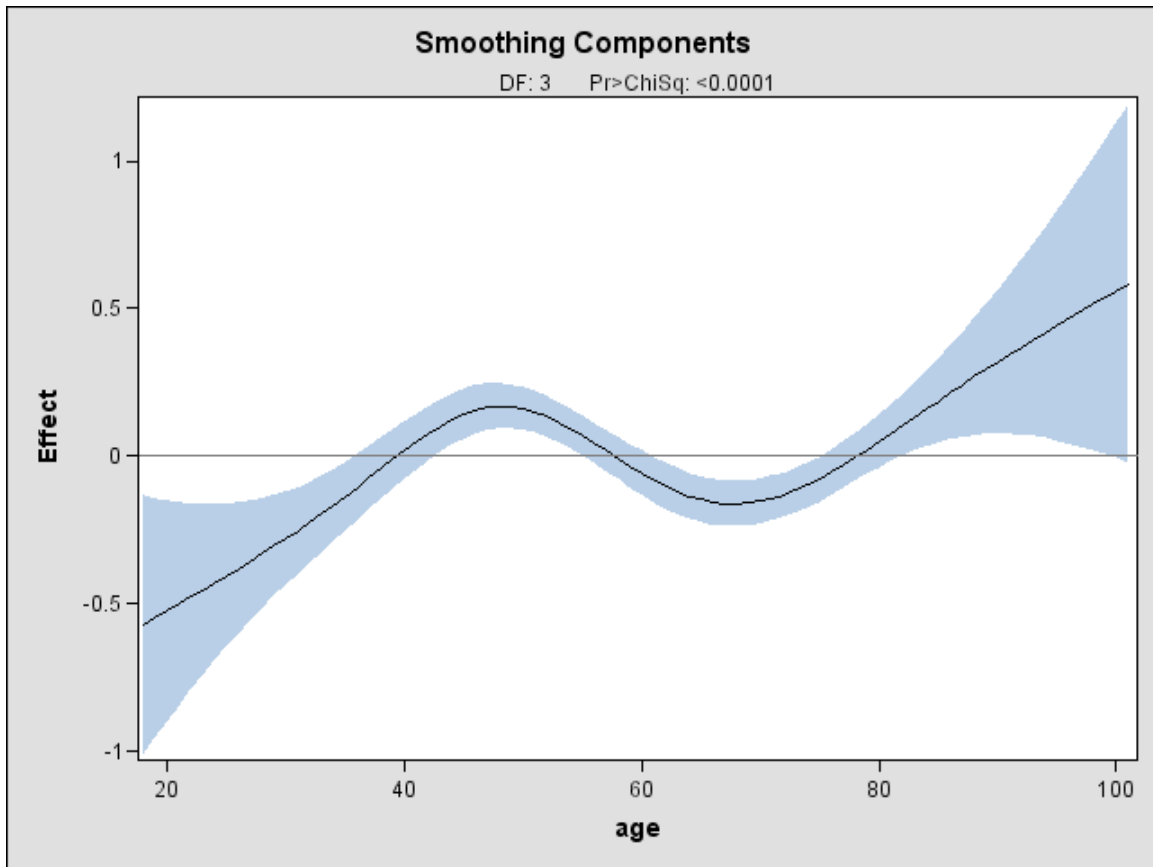


Table 11. Logistic and GAM Analysis for Having More than Three Typical Symptoms

	Logistic Odds Ratio	Logistic P-Value	GAM Odds Ratio (28-60)	GAM P-Value (28-60)
Male	0.624	<.0001	0.614	<.0001
Gulf	0.235	<.0001	1.202	0.0819
Chem_exposure	2.131	<.0001	2.097	<.0001
White	0.750	<.0001	0.755	<.0001
Edu ≥ HS	0.691	<.0001	0.615	<.0001
Income ≥ 10K	0.566	<.0001	0.452	<.0001
PTSD	7.954	<.0001	8.232	<.0001
Gulf*Chem	1.210	0.1505	1.269	0.0924
Age*Gulf	1.037	<.0001	.	.
Age	1.008	<.0001	1.020	<.0001

* χ^2 test for nonparametric age effect in GAM model is 69.5561 (p<0.0001)

Figure 10. Partial Effect of Age for Having More than Three Symptoms

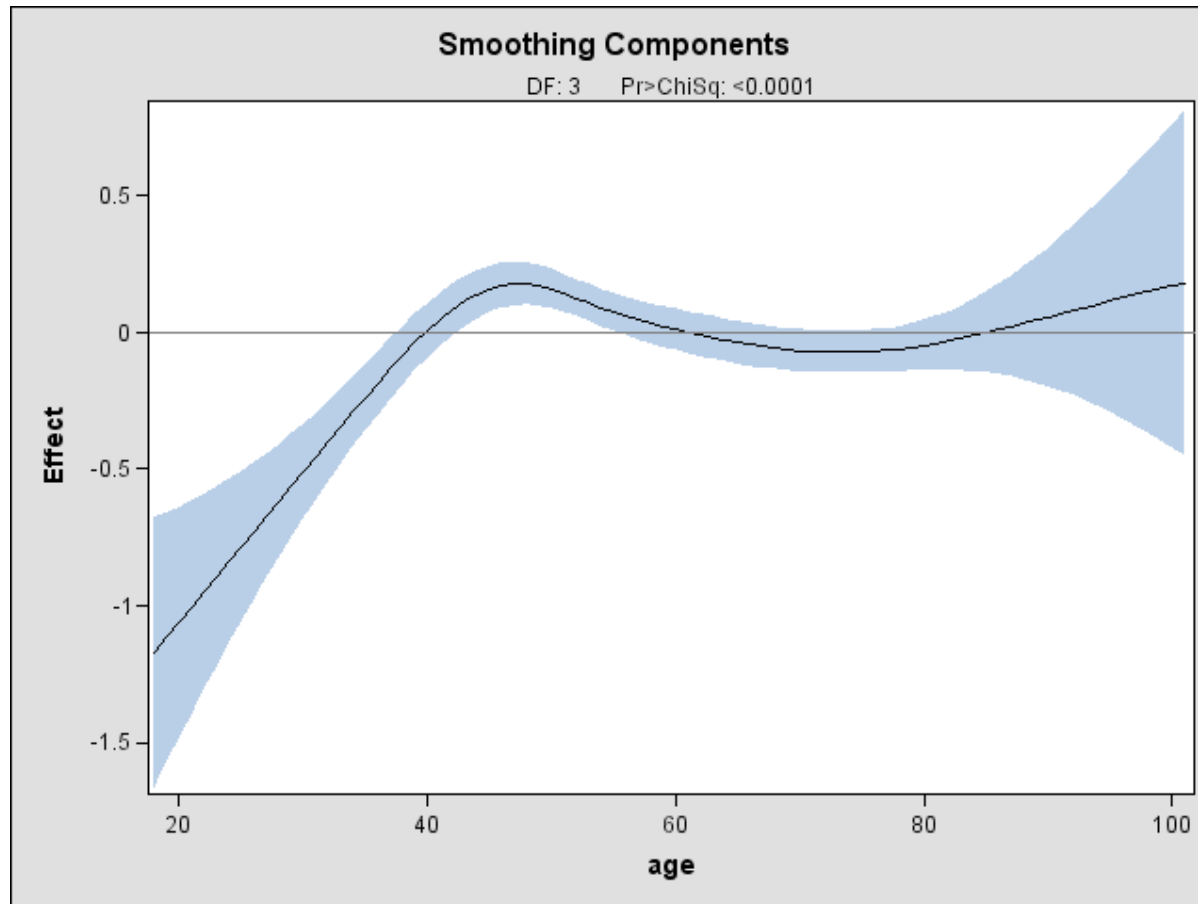


Table 12. General Health Status of Gulf-War Veterans

	Chemical Exposure	No Chemical Exposure	p-value
Self-evaluated Health Status			
Excellent	9.44%	18.94%	<.0001
Very Good	20.05%	32.53%	
Good	32.99%	30.39%	
Fair	26.52%	14.06%	
Poor	10.61%	3.88%	
Service-Connected Disability	60.03%	39.89%	<.0001
Number of Outpatient Visits	8.49	4.92	<.0001
Usage of Emergency Service	32.99%	26.57%	0.0069
Usage of Inpatient Service	8.15%	6.36%	0.2885
ENT Problem	28.07%	16.67%	<.0001
Chronic Pain	37.77%	19.75%	<.0001
Fatigue	52.78%	32.06%	<.0001
Depression	35.06%	18.21%	<.0001
Concentrating Problem	21.99%	10.11%	<.0001
Gastrointestinal	27.81%	14.66%	<.0001

Table 13. Proportion of U.S. Gulf War Veterans Reporting Typical Symptoms

Number of Symptoms	Chemical Exposure (%)	No Chemical Exposure (%)	p-value
0	25.10	45.38	<.0001
1	20.44	23.09	
2	18.37	15.86	
3	13.84	8.63	
4	9.96	4.75	
5	8.80	1.94	
6	3.49	0.33	

Figure 11. Proportion of U.S. Gulf War Veterans Reporting Typical Symptoms

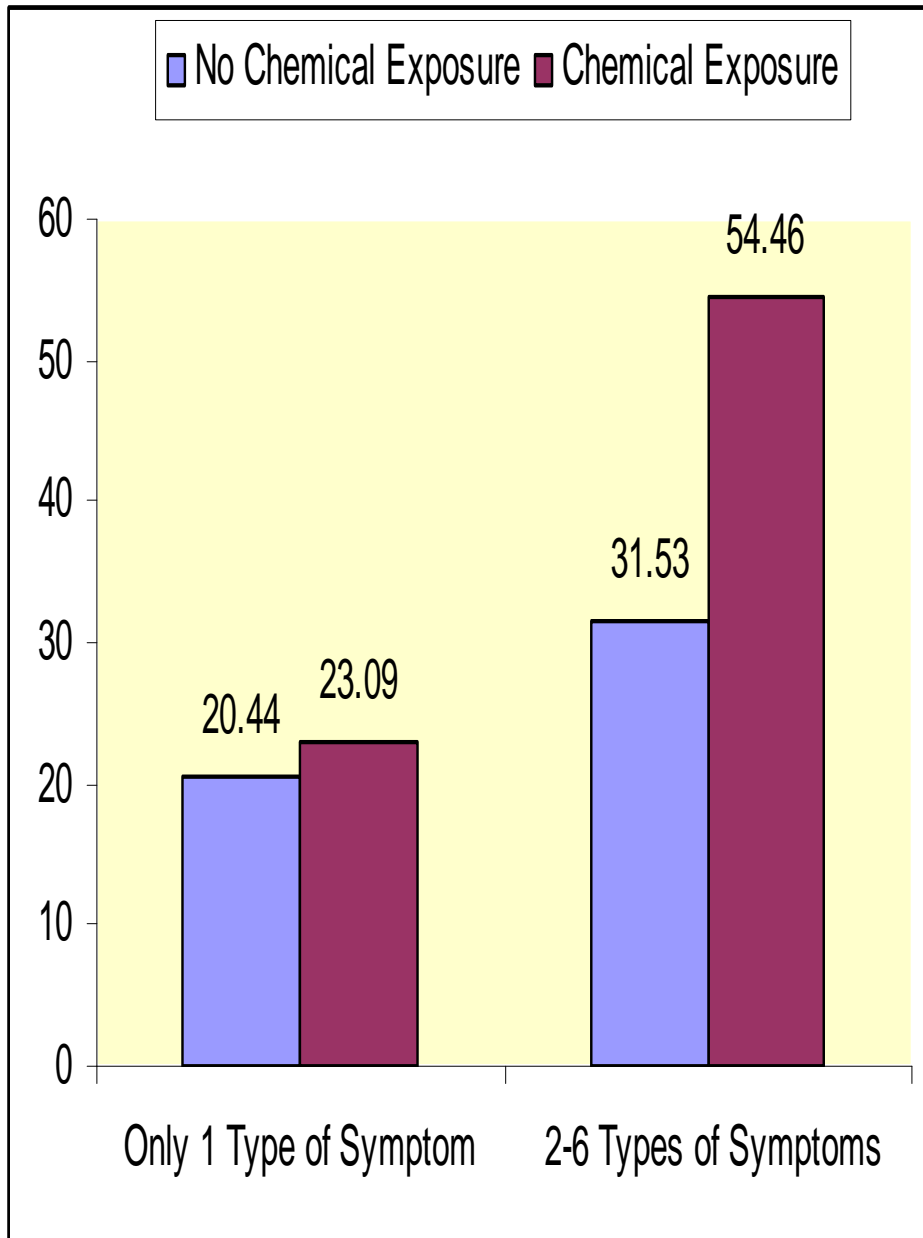


Figure 12. Effects of Chemical Exposure on Predicted Probabilities of Self-Report Health for Gulf Veterans

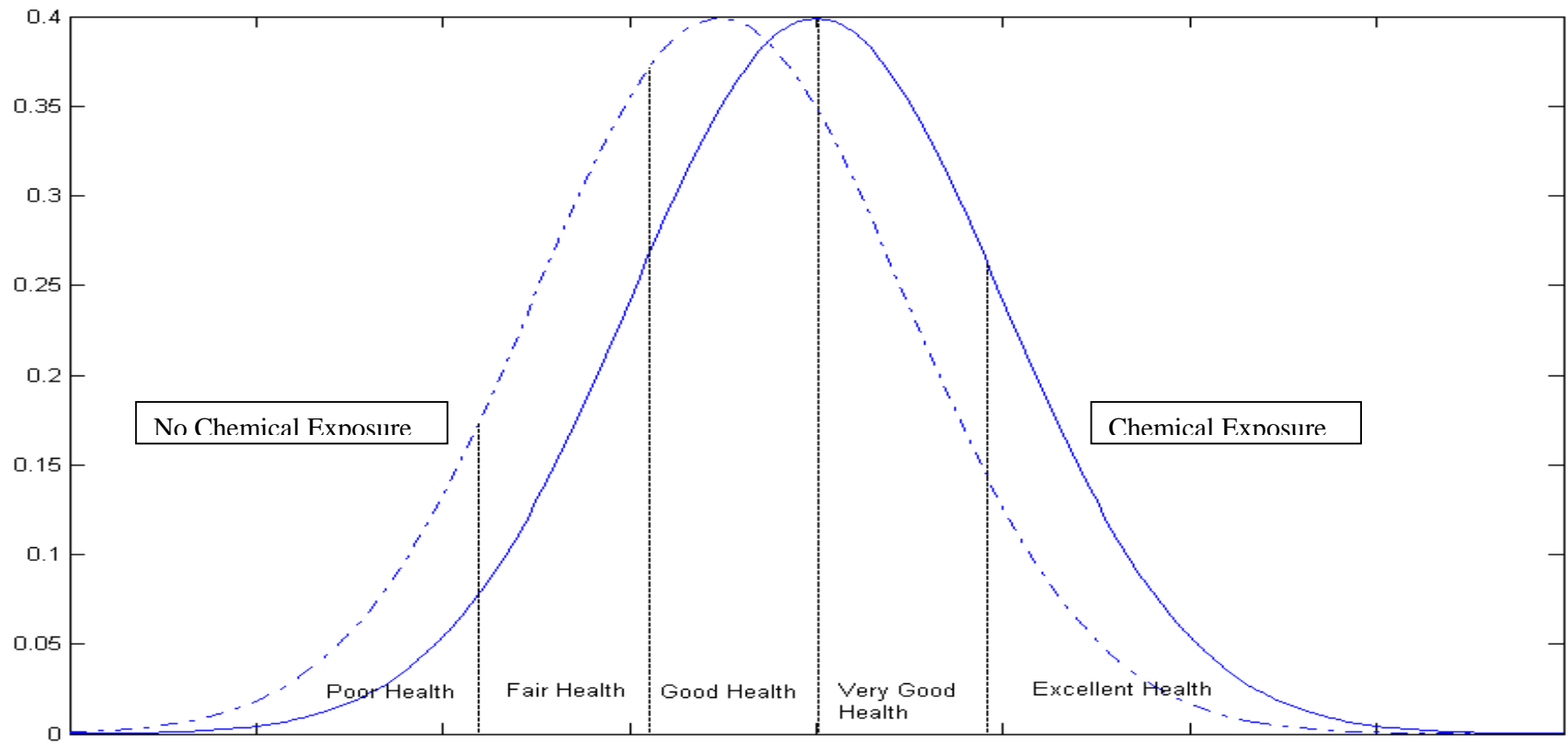


Table 14. Ordered Probit Model for Self-reported Health Status
(Gulf Veterans Only)

	Marginal Effect for Health = Poor	Marginal Effect for Health = Fair	Marginal Effect for Health = Good	Marginal Effect for Health = Very Good	P Value
Chem_exposure	0.0535	0.1053	0.0467	- 0.0885	0.0000
White	-0.0344	-0.0676	-0.0300	0.0568	0.0000
Male	-0.0124	-0.0243	-0.0108	0.0205	0.0458
Age	0.0020	0.0039	0.0017	-0.0033	0.0000
Edu ≥ HS	- 0.0264	- 0.0520	- 0.0230	0.0437	0.1400
Income ≥ 10K	- 0.0627	- 0.1234	- 0.0547	0.1038	0.0000

* $\mu_1 = 0.9120323174$ $\mu_2 = 1.81376483$ $\mu_3 = 0.723154216$

Table 15. Logistic Regression for having More than three Problems
(Gulf Veterans Only)

	Odds Ratio	P-Value
Male	0.543	<.0001
Chem_Exposure	3.066	<.0001
White	0.705	0.0022
Edu ≥ HS	0.499	0.0518
Income ≥ 10K	0.354	<.0001
Age	1.034	<.0001

Figure 13. Effect of Chemical Exposure on the Probability of Having More Than Three Typical Gulf War Syndromes

