The long term safety of anthrax vaccine, pyridostigmine bromide (PB) tablets, and other risk factors among Reserve Component Veterans of the First Persian Gulf War

Walter R. Schumm, PhD[1], Anthony P. Jurich, PhD, Stephan R. Bollman, PhD, Farrell J. Webb, PhD, and Carlos S. Castelo, PhD

[1]School of Family Studies and Human Services
Justin Hall, Kansas State University,
1700 Anderson Avenue
Manhattan, KS 66506-1403
Phone: +1 785 539-3641 (home) +1 785 532-1494 (office)
Fax: 785 532-5505 (FAX)
Email: Schumm@ksu.edu (work) WRSchumm@aol.com (home)

Abstract

Data from several hundred Reserve Component Persian Gulf War veterans were analyzed to assess associations between Gulf War illness as defined by both the CDC and Kansas classifications and a variety of potential risk factors. The most significant risk factors, in order of importance for their possible contributions to Gulf War illness were perceived exposure to nerve agent, ciprofloxacin pills, gum problems, insect repellant, anthrax vaccination, use of personal insecticide, reported reactions to vaccines, and botulim toxoid vaccine. Of those, PB tablets, gum problems, insect repellants, insecticide use, and anthrax vaccination were more significant statistically when veterans reported that they had experienced reactions to vaccines. Insect repellant and insecticide remained significantly related to Gulf War illness among veterans who remained in the United States during the war; among those non-deployed veterans, anthrax vaccine was associated with Gulf War illness (10% versus 4% for those with or without anthrax vaccine), but the relationship was not statistically significant if those who were "not sure" about their vaccination were removed from the analysis. For anthrax vaccine, Gulf War veterans needed only to report a "mild reaction" to maintain a significant relationship with Gulf War illness under the reaction condition. Anthrax vaccine seemed to be more reactive than other vaccines, especially for female veterans. A dose-response relationship was observed for PB tablets. Recall bias was reduced in several ways but may not have been eliminated. It is recommended that PB tablets, ciprofloxacin pills, as well as insect repellants and insecticides be used with caution, especially not exceeding recommended daily amounts. Anthrax vaccine should be administered on a voluntary basis only, given the long-term safety risks observed here, especially for those who experience even mild reactions.

Keywords: Gulf War illnesses, anthrax vaccine, pyridostigmine bromide, vaccine safety, insecticides, insect repellants, ciprofloxacin

1. Background

"Few meaningful conclusions for humans can be drawn from animal studies of the anthrax vaccine [1:280]." Thus, the Institute of Medicine acknowledged that human studies are desirable in assessing the efficacy and safety of anthrax vaccine. At the same time they noted that the U.S. military was now using a different strain of anthrax bacillus in the manufacturing process than was used for the vaccine used during the first Persian Gulf war [1:282]. Furthermore, the IOM also reaffirmed that "there were not enough cases of inhalation anthrax to determine if vaccination was effective against this [inhalation anthrax], the most lethal form of anthrax [1:283]. However, a later IOM report [2:77] while admitting that the Brachman et al. [3] study did not have enough cases to evaluate the efficacy of the vaccine against inhalational anthrax, still argued for the efficacy of the vaccine against inhalational anthrax.

From the above information, it is apparent that human studies are needed to follow up any possible long-term effects of anthrax vaccine, among others. Studies that address the anthrax vaccine used in the first Gulf War may not apply completely to the current anthrax vaccine being used by the U.S. military, but the similarities probably outweigh the differences because the targeted toxic protein (PA) is the same in both vaccines [1: 276, 282]. Finally, it appears that there remains controversy, even within the IOM, about the proven efficacy of anthrax vaccine against inhalational anthrax, particularly with respect to relative efficacy [2:77]. That is important because safety concerns would be magnified for a vaccine with uncertain efficacy. All vaccines involve a balance between the good they can do versus their inherent risks. A change in either efficacy or safety influences that balance, critical to decision-making about the extent of use of a vaccine. A vaccine that remains the only option, even if not completely effective, might be viable if it was completely safe. However, the same vaccine if found to be relatively unsafe, might be a viable option for only a few clients exposed to especially high risks from the pathogen. Moreover, the less safe a vaccine, the greater the desirability of making its application to most clients voluntary.

Previously, even though several studies in at least three nations that had revealed a correlation between either anthrax vaccination or vaccinations in general with subsequent self-reports of ill health [4, 5, 6, 7], the Institute of Medicine [2] had given the vaccine a nearly clean bill of health, basically discounting nearly all self-report research as later noted in a critique of their analysis of the survey conducted by U.S. Air Force Captain Jean Tanner [8].

In an attempt to resolve the self-report bias issue, Mahan et al. [9] tried to compare results from self-report data with results from vaccination records for Gulf War veterans. Of the 22

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health outcomes, they found 21 significant for self-report data and 9 for record data, leading them to conclude that most of the adverse effects observed for anthrax vaccination were caused by self-report bias. However, if both methods had involved the same statistical power, the vaccination record data would have yielded 16 significant results, not significantly different from the 21 found for self-report data [10].

2. Goals

A primary goal of this analysis was to evaluate long-term health consequences that might have been associated with anthrax vaccination and the consumption of pyridostigmine bromide (PB) tablets, within the context of a range of potential risk factors. A secondary goal of this analysis was to evaluate alleged health risk factors from the Gulf War as they might be related to health symptom clusters used to classify veterans as having Gulf War illnesses. A third goal was to control for as many spurious factors, such as recall bias, as possible to ensure that any results found would be robust (sustainable) with respect to many of the limitations noted in several IOM and other reports [1, 2, 7, 11, 12].

3. Methods

In 1996, the state of Ohio commissioned an independent study of the post-war health of Ohio's Gulf War veterans, through the Center for the Study of Veterans in Society (CSVS). Their goal was to investigate a variety of possible causes of the health complaints being voiced by Ohio veterans, inasmuch as the governor and legislature of Ohio had concerns about the costs of treatment for its veterans, concerns that were magnified by the slow progress being made at that time in understanding the nature and causes of Gulf War illnesses. More specifically, the CSVS contracted with Kansas State University researchers to conduct the study among a random sample of veterans who had lived in Ohio as of August 1990 or as of March 1996, a study that came to be known as the Ohio Desert Storm Survey Project. The Defense Manpower Data Center provided a list of such veterans, along with current, accurate addresses for about a third of the veterans on the list. Obtaining accurate addresses for the remaining sample proved to be a major challenge, but surveys were initially mailed to veterans in late 1996, a process that continued through the spring of 1997. Details of the project methodology have been explained in previous reports [13, 14]. Because of the 40-page length of the mailed survey and limited funding that restricted our follow-up process, response rates were limited to approximately 30 percent among Gulf War veterans and were lower among veterans who had not deployed to the Persian Gulf. Our initial efforts have focused on factors related to declines in self-reported subjective health [15, 16, 17, 18].

3. Limitations of past studies and how we have tried to minimize limitations in this study

Any study of health outcomes associated with participation in the first Gulf War must take into account the limitations of previous studies [1, 2, 7, 11, 12] and try to minimize them.

Recall bias is perhaps the most difficult problem because virtually no one has collected data from veterans longitudinally, beginning with the Gulf War. Consequently, almost all studies rely upon veterans' retrospective or recalled reports of both their exposures during the Gulf War and their previous or current constellations of symptoms, leaving open the possibility that those who experienced post-war problems will be more interested in their own minds in establishing a sense of causation between previous circumstances and their current health problems (i.e., I feel sick now, something must have caused this, what can I remember about the war that might have caused this?). It is also possible that some veterans are more sensitive to both what they are feeling now and what they felt in earlier times (e.g., I am more careful to assess my health than many others. I sense that I feel bad now, and I sensed that I felt bad after being exposed to something). Likewise, some veterans may simply have more difficulty recalling events or health concerns from the past, leading to more error in their reports of past events or health concerns than for other veterans. At the same time, it must be observed that Rand's study of recall bias yielded little support for the hypothesis that most Gulf War outcomes are nothing but recall bias [19: 107-122]. The Rand study concluded that even self-reported subjective health status was relatively unbiased [19: 113]. However, we chose to use that variable in this report because it seemed a good way to test the particular hypothesis that those who feel sick might be more likely to over-report or even imagine certain Gulf War exposures.

Since we collected data years after the war, it was impossible for us to describe our study as truly longitudinal. However, we did ask about each symptom for four different time periods – before the war as of August 1990, during the war, from after the war to 1995, and at the time of the survey, which depended on when respondents received and responded to the survey (1996-1997). We did for some items (vaccines) ask if they had been received at any time during or since the war and ideally we should have split the time period into during the war and since the war. Because our respondents were reservists on active duty for a limited time, we assumed that the vaccines most in question (e.g., for botulism) would in all probability have been given only just before or during the war.

However, it is unfair to treat longitudinal research as the "perfect" standard. Another serious limitation unique to military longitudinal research, though it may be far more important for future research on the current Gulf War, is that veterans may detect an association between admitting to symptoms and administrative action against them. In one unit, the first sergeant allegedly told his people that if they wanted to get home on time, they had better not admit to any sorts of combat stress or health problems again (in their first deployment in the current war, they had been honest and had been delayed as a consequence). The unit members were thus careful to report that they had no stress symptoms or other health concerns in order to avoid stigmatizing themselves and thus delaying their safe arrival home. Similarly, military aviators have admitted to not reporting medical symptoms for fear of being denied flight status, which denial would entail a significant loss of income (no more special, additional flight pay). Research that may minimize recall bias may instead become biased because of

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fears of the consequences of answering health research questions honestly while the veterans are still in theater or even once home as long as they fear indirect retribution for honest answers. We can imagine health researchers in the future wondering why members of certain units, being so free of symptoms in theater in 2005, developed so many poor health outcomes by 2015!

Some studies have not controlled for the number of tests performed, leaving open the possibility that some results that are reported as significant are actually still within the range of chance results. However, given that the concern here involves outcomes of alleged risk exposures, a medical safety issue, we will keep in mind the advice of the IOM [2:10] – "Expectations for the safety of vaccines are especially high because, in contrast to therapeutic agents, which are given when a disease is known to be present (or at least suspected), vaccines are usually given to people who are healthy to protect them against a disease that they may not be exposed to in the future." Later, the same IOM report [2:37-38] emphasized that "The burden of proof for the safety of vaccines is therefore even higher than the burden of proof for the safety of other medical interventions." Out of respect for the IOM's emphasis on the importance of vaccine safety, we will report unadjusted significance levels for all tests in order to minimize the chances of overlooking a valid safety issue.

Another limitation is that many studies failed to distinguish between specific and general risk factors; for example, they may have asked veterans about use of insecticides in general without asking about specific types of insect repellants (e.g., government-issued versus commercially available brands) or specific conditions under which they were exposed to insecticides (e.g., sources, frequency of exposure, and amounts of exposure). Some studies failed to assess risk factors in terms of levels of exposure that would permit dose-response relationships. With respect to the risk factors that seemed most likely to be valid (Pyridostigmine bromide tablets, insecticides, insect repellants, etc.) we asked either more than one related question or used multiple responses for questions that attempted to assess more than one aspect of the alleged risk factor. Thus, for some factors we were able to evaluate dose-response relationships.

Few studies have assessed genetic variations among veterans to help determine if some veterans are more susceptible to some risk factors because of such genetic variations. While we did not assess genetic variations, we may have found a proxy variable in terms of self-reported adverse reactions to vaccines, as many alleged risk factors were significantly related to health outcomes under the "reaction" condition but not the "no reaction" condition.

Some studies failed to compare risk exposures for both Gulf and non-Gulf veterans, although many such factors were not common to non-Gulf veterans. In this study, we assessed the apparent effects of insect repellant, insecticide, and anthrax vaccine for non-deployers who remained in the United States, but did not assess risk factors which were very infrequent among non-deployers (e.g., using PB tablets).

Another limitation of previous studies is that, even if they have found some relationship between worse health after the war and an alleged risk factor, they have not compared the outcomes for related risk factors in order to be confident that the outcome is related to a specific risk factor rather than related risk factors. For example, if one found a relationship between one vaccine and GWI, perhaps the real cause was other vaccines [2:153]. Just testing one vaccine means little unless all other vaccines are evaluated in the same way. Here we will test all vaccines, not just a particular one (i.e., anthrax vaccine), as recommended by the IOM [2:176].

Many studies of Gulf War health outcomes have featured relatively low response rates, which may involve selection effects as part of the explanation for observed results. Some studies have been population-based while others have relied upon data from one or more units that were or were not deployed to the Persian Gulf during the war. Our study was based on a population of veterans who had either lived in Ohio at the time of the war (even if they had moved since to other states) or veterans who had since moved into Ohio. Since we were funded by Ohio, we wanted to allow either group of veterans to recoup part of the tax money they had paid Ohio at some point by being allowed participation in the study about their postwar health. Our response rate was limited to about 30% for all those who deployed to the Persian Gulf and never exceeded about 50% for any subgroup of respondents. While our response rate is similar to that of some Gulf War studies, studies that have received far greater funding than ours [7, 9, 20], did obtain response rates much higher than ours.

One criticism of Gulf War research is that comparable groups of Gulf War veterans and non-Gulf War veterans were not assessed [19:13]. This criticism sounds valid except that it is essentially impossible to counter. Even if someone had sufficient valid data from those two groups, the groups would never be truly equivalent because the Gulf War group's multiple exposures and stresses, on average, were far more severe and unique compared to the control group. In addition, far fewer, if any, non-Gulf War veterans were given or consumed PB tablets, making a legitimate comparison between the two groups impossible. Therefore, the only realistically available comparison is among those who took fewer or more PB tablets among those who had deployed to the Gulf and shared in many of the same stressor events as others who also deployed to the Gulf.

4. Specific objectives of the study

The first objective of this analysis was to evaluate the bivariate relationship between numerous risk factors for Gulf War illness and both the CDC and Kansas classifications of Gulf War illness. When possible, we wanted to assess dose-response relationships, particularly with respect to PB, insect repellants, and insecticides. As noted by [1:12] as of 2000, no studies had been found that had been designed to assess a dose-response relationship for PB consumption among Gulf War veterans. IOM [1, 2, 11] reviews of the literature found nothing to support clear causal relationships between other potentially toxic exposures (e.g., insecticides, low-level sarin exposure, anthrax vaccine, multiple vaccinations within a brief period of time, or botulinum toxoid vaccine) and adverse long-term health outcomes. A recent retrospective study of health effects among Canadian forces found no relationship between numerous effects and anthrax vaccination [21]. Such outcomes would

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seem to make it very unlikely that our study would find any significant relationships between our measures of exposures and long-term health outcomes, other than by chance or the types of biases that might have occurred. However, our research was in a position to accomplish the research recommendation of the IOM [1:23] to study the long-term health effects of PB as might be related to genetic factors. Our study also would permit the assessment of interactive effects among numerous variables as recommended by the IOM [1:21], but that is outside the scope of this particular article due to space limitations.

The second objective was to challenge our own findings, however they turned out, by controlling for factors that might demonstrate that our initial bivariate findings were spurious.
As noted in the previous section, a variety of challenges to the validity of self-report data from Gulf War veterans have been proposed.

5. Methods

Measures. In our survey, veterans were asked to report their level of subjective health at several times, including before Desert Storm (before August 1990), during Desert Storm (August 1990 to June 1991), after Desert Storm (July 1991 to June 1995), during the past year and during the past month (both of which ranged between late 1995 and late 1997, depending on when they received their survey). Responses available for each time frame included five levels – poor, fair, good, very good, and excellent. Reaction to vaccines was measured by one item: "For any of the above vaccinations or injections, did you have an adverse reaction (unusual inflammation, swelling, redness, tenderness, etc.?) with response categories of "no," "yes, but only a mild reaction," "yes, a severe reaction but was not hospitalized," or "yes, you had to be hospitalized for your reaction."

Gulf War illness was measured by both the CDC [22] and the Kansas [7] classification methods. We had available 25 items assessing various aspects of cognitive impairments, 6 items on joint, muscle, and body pain symptoms, 6 items on fatigue symptoms, 8 items on skin problems, 3 items on respiratory symptoms, and 3 items on gastrointestinal issues.
To be classified as a GWI case, under the CDC definition, a veteran had to have two more symptoms (two at one time or one over two times) in two of the three areas of cognition, pain, or fatigue. To be classified under the Kansas classification, the veteran needed to report at least two symptoms in three of the six areas. We modified the Kansas definition because we did not ask questions about symptom severity, relying instead on veterans reporting at least two symptoms rather than only one severe symptom.

Risk factors included various vaccines and reactions to vaccines, including anthrax vaccine, a continuing source of controversy [23, 24, 25, 26, 27, 28, 29]; pyridostigmine bromide tablets, suspected to have been a problem by many [1, 16, 17, 30]; a variety of contacts with nerve agents, insecticides, and insect repellant [1, 11], and lastly inflamed, sore, or bleeding gums.

Because most of the risk factors were primarily associated with the Gulf War experience rather than reserve military duty in the United States, most of the analyses focused on veterans who had deployed to the Persian Gulf. However, we did analyze anthrax vaccination, use of personal insecticide, and use of DEET for veterans who served entirely within the United States during the war, in a military support role for the Gulf War.

Ideally, one should conduct a multivariate analysis of Gulf War health outcomes, taking into account multiple exposures among the predictor variables. However, multivariate analyses among Gulf War veterans present difficult challenges because of the high correlations among certain exposures and the possibility of overlooking interaction effects among critical variables. In our analyses here, we used primarily chi-squares tests, Pearson zero-order correlations, and partial correlations.

To control for self-report bias, several methods were applied. First, all those veterans who were classified with GWI before the war were not counted among those with GWI. In addition, individual symptoms used to classify veterans with GWI were not counted if they were reported before the war, thereby reducing the number of veterans classified as having GWI. Furthermore, we split subjects into two groups for each risk factor, a subgroup that had reported no reactions to vaccines and a subgroup that had reported at least some reactions to vaccines they had received.

6. Results

Results of the analyses are presented in Tables 1 through 33. Tables 1 to 9 involve analyses in which the CDC classification of Gulf War illness was applied, while Tables 10 to 30, except for table 19, involve predictions of the Kansas classification. Table 31 involves the CDC classification.

Tables 1 through 18 and 20 through 31 involve prediction of Gulf War illness. Tables 19, 32, and 33 involve the prediction of reactions to vaccines. Tables 24, 25, 26, 28, 32, and 33 use independent variables in which the "not sure" category has been deleted in order to reduce recall bias. Tables 29 to 31 involve only veterans who remained in the United States during the first Gulf War while all other tables concern deployed veterans who went to the Persian Gulf region.

6.1Bivariate results

Tables 1and 10 involve bivariate predictions of GWI, for the CDC and Kansas classifications, respectively, for the risk factors measured by "no," "not sure," and "yes." The strongest relationships with GWI in both tables were observed for PB tablet consumption, ciprofloxacin use, anthrax vaccination, and botulism toxoid vaccination.

Tables 2 through 9 and 11 through 18 concern bivariate relationships for risk factors measured with three or more levels other than "no," "not sure," and "yes." Only one variable was never significant—insecticide sprayed from the air. The strongest outcome was for perception of having been exposed to nerve agent. Other consistently significant outcomes occurred for reactions to vaccines, personal insecticide or insect repellants, and number of PB tablets consumed. Insecticide sprayed at ground level and geographic risks associated with the Khamisiyah depot's release of nerve agent yielded inconsistent results.

Table 19 shows that the more vaccines received during or since the Gulf War, the higher the rate of having reactions to

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vaccines. An independent samples t-test for those who did or did not have reactions featured mean scores of 3.84 vaccinations (SD = 1.90) for the former and 2.94 (SD = 2.01) for the latter with $t_{642} = 5.82$ ($p < .001$).

6.2 Role of vaccine reactions

Splitting the previously reviewed bivariate relationships on whether or not the veterans had any reactions to the vaccines they received proved to be important. Table 20 reports differences in relationships with GWI using reactions to vaccines as a splitting factor. Perceived exposure to nerve agent was the only factor that was highly significant ($p < .001$) under both conditions. Only one risk factor, ciprofloxacin, was more significant under the "no reactions" condition ($p < .001$) than under the "had reaction" condition ($p < .03$). However, use and number of PB tablets eaten, insecticide, DEET, and anthrax vaccination were more significant under the "had reaction" condition than under the "no reaction" condition.

Table 21 (compare to tables 9 and 18) shows that the effect of taking more PB tablets was more strongly related to GWI when the veterans had reported reactions to vaccines. Table 22 (compare to tables 7 and 16) shows the effect of vaccine reactions on the relationship between GWI and personal insecticide use. Table 23 (compare to tables 8 and 17) shows the similar role of vaccine reactions for insect repellant. Tables 24 and 25 show the role of vaccine reactions for PB tablets and anthrax vaccine, respectively; however, the "not sure" category is also omitted to reduce response bias.

Tables 21 through 25 indicate that the only time the risk factors of those variables are significant is under the "reactions" condition.

Table 26 reported a test of a variable that was, frankly, an after thought. Ideally, we would have tested for levels of mercury in a veteran's system after having a great deal of dental work done with mercury-based amalgams (dental fillings). Lacking such evidence, it was thought that a high amount of dental work done might either reflect poor dental health or a high number of fillings performed, which might be manifested in high rates of swollen or bleeding gums during the war itself. Either condition might be predictive of poor health later. The relationship of gum problems to GWI was significant under all conditions but more so under the "had reactions" condition.

6.3 Multivariate results

Although we have reservations about some aspects of multivariate analysis with Gulf War veteran data (because of highly correlated risk factors), we were interested in controlling for adverse reactions and for subjective health, both being attempted proxies for recall bias. First, in Table 27, because of the apparent importance of reactions to vaccines, we partialed out reactions from many of the risk factors to see if significant relationships could be explained away (i.e., reactions as a control variable might prove the other relationships to be spurious). However, very few of the relationships between risk factors and GWI were reduced in either substance or significance by controlling for reactions. Then, in Table 27, by controlling for the veteran's subjective health during the past month, we hoped to be controlling, in a different way, for recall bias. Overall, few risk factors became non-significant (geographical risk, ground sprayed insecticide) while one became more significant (total number of vaccines received).

6.4 Focus on other vaccinations

Table 28 controlled for reactions by deleting veterans who had not reacted to their vaccines and then controlled for bias by partial correlation of subjective health. The idea here was that we had already found anthrax vaccination to be related to GWI but that would mean little if all the other vaccines were also related to GWI. However, as shown in Table 28, the only vaccine related to GWI for both the zero-order correlation and the partial correlation (controlling for self-reported subjective health) was the anthrax vaccine. The results for anthrax vaccine are clearly different than for the other vaccines or injections. which would be an important finding according to the IOM [2 153].

6.5 Results for non-deployed veterans

Another objection to our results might be that it was the overall Gulf War stress that caused most of the observed relationships and that, accordingly, the observed relationships between the risk factors and GWI would not be found for those veterans who had remained in the United States. Most of the risk factors were essentially unique to veterans who deployed to the Gulf, as affirmed by few of the risk factors having any substantial numbers for those remaining in the United States. However, a few subjects reported anthrax vaccinations even though they had not deployed and some reported the use of insect repellant or personal insecticide. Tables 29, 30, and 32 indicate that anthrax vaccination, use of personal insect repellant, and use of personal insecticide were still significantly related to Kansas GWI classification, at least under the "had reaction" condition for insect repellant. There were too few cases of anthrax vaccination to permit a valid test for the anthrax vaccine under both reaction conditions. Even though those who said they had received anthrax vaccine were twice as likely to have GWI symptoms as those who denied receiving the anthrax vaccine, the results were no longer significant if the "not sure" category for anthrax vaccination was omitted in the analysis.

6.6 Predicting reactions to vaccines

Because of the importance of vaccine reactions, two more analyses were conducted. First, we looked at reactions (yes or no) as a function of receiving at least one anthrax vaccination. The reaction rate for those who received other vaccines but not anthrax vaccine was only 36.8% while those who may have received other vaccines along with the anthrax vaccine had a reaction rate of 55.4%. That difference was quite significant and reaffirms previous research in which anthrax vaccine was identified as having more reactions than most other vaccines [31].

It has also been noted that female veterans may react more often to anthrax vaccination than male veterans [2: 175]. From Table 33 it can be observed that female veterans were more

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likely to report having had vaccine reactions in general than were male veterans (61.7% versus 43.9%), even whether or not they had or did not have an anthrax vaccination. However, anthrax vaccination appeared to increase the gap between male and female veterans in terms of reactions, as their differences were significant when they had received anthrax vaccine but were not significant when they had not received the anthrax vaccine.

7. Discussion

Not all risk factors appeared to be correlated with Gulf War illness as defined by either the CDC or Kansas classifications. If recall bias or other spurious factors were entirely responsible for relationships between Gulf War illness and alleged risk factors, there should have been no such results. Clearly, most veterans, even those who are sick are not blaming *everything* for their current state of post Gulf War health.

7.1 Most Important Risk Factors. To assess the relative importance of the risk factors, we used the six tests performed for most of the variables, adding up the level and numbers of significant results for each variable. The only alleged risk factor that was very significant ($p < .001$) under all tests was the perception that the veteran had been exposed to nerve agent. It is likely that if this variable was used in a multivariate analysis, it would block out most other variables. Surprisingly, ciprofloxacin was the second most often significant risk factor. Notably, it was weakest when the veteran had reacted to vaccines. Tied for third were the number of PB tablets taken and having gum problems. Tied for fourth were the use of insect repellant and anthrax vaccination. At fifth was personal use of insecticide. At sixth was having reactions to vaccines. At seventh was botulism toxoid vaccine. Some risk factors were never significant – typhoid vaccine, yellow fever vaccine, and being sprayed from the air with insecticide. Other risk factors were significant for less than 50% of the tests performed—anti-malaria pills, gamma globulin injections, tetanus vaccine, hepatitis B vaccine, and geographical exposure to nerve agent from Khamisiyah.

7.2 Reactions to Vaccines

Anthrax vaccine, PB usage and numbers of tablets taken, use of insecticide, use of insect repellant, and gum problems were more significantly related to Gulf War illness under the "reaction" condition than they were under the "no reaction" (to vaccines) condition. The opposite situation was true for botulism toxoid vaccine and ciprofloxacin pills. It may be that "reactions to vaccines" serves as a proxy for genetic variances that make some veterans more susceptible to certain types of toxic exposures.

If self-report bias is operating, it would be an interesting mechanism to explain in terms of why it was stronger among those who reported reactions to vaccines for more but not all risk factors. The best explanation might be that veterans search their Gulf War experience for "things that went wrong" (like having reactions to vaccines) and hang any bad health issues in the present on such things. However, that idea fails to explain the diversity of outcomes that occurred when controlling for reactions to vaccines or for current subjective health.

We suspect that reactions to vaccines may serve as an important intervening variable as well as an interacting one if placed in a larger multivariate model. However, some risk factors would probably be so strong as to have a direct effect on health outcomes, regardless of their relationship to reactions to vaccines.

7.3 Comparisons of risk factors

Insecticide that is placed directly on the skin appears to be more risky than that which is sprayed from the ground or the air. Ground sprayed insecticide appears to be slightly more of an issue than insecticide sprayed from the air. It may just be a matter of relative frequency, though, with air sprayed insecticide being used less often. Anthrax vaccine turned out to be more strongly related to Gulf War health outcomes than any other vaccine assessed. In fact, most of the "control" vaccines had far less long-term safety issues than anthrax vaccine. Reactions to vaccines were more of an issue than the vaccines themselves, except in the case of anthrax vaccine. Finally, the perception of being exposed to nerve agent seemed to predict Gulf War illness better than self-reports of having been in certain geographical locations at the time of the Khamisiyah nerve agent releases.

7.4 Methodological Issues

Remarkably, the one risk factor that featured the lowest percentage of "not sure" responses was use of PB tablets. Anecdotally, the senior author recalls that most veterans he has encountered seemed to remember exactly how many PB tablets they received and consumed. There appears to have been much more confusion with regards to which vaccines or other pills had been received, a condition facilitated by the poor record keeping of vaccinations at the time. Having a "not sure" answer for vaccines was good in that it allowed veterans to express such an opinion but when they did so, such veterans gave away the fact they were uncertain. Uncertainty undoubtedly reflects confusion or memory weakening, but that tendency should operate to increase error variance, weakening the chances of finding significant relationships. It might be a "port of refuge" for a veteran who feels sick but can't pinpoint a cause. He or she may think, "I am sick. I don't think I had anthrax vaccine, but who knows, maybe it's why I am sick." Again, controlling for subjective health should have overcome that last objection, but most of the risk factors were not eliminated by such controls.

One regrettable limitation of this study was that a separate question was not asked about reactions to PB tablets; many veterans have anecdotally reported having reactions to PB tablets, often of a gastrointestinal nature. At the time we designed the survey, we did not expect veterans to be able to recall such details or to be able to determine if a reaction was associated with vaccines as opposed to pills or tablets. Having a question on the number of PB tablets taken was good, but it highlights that we did not have a similar question on the number of anthrax vaccinations received.

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By chance, we also found significant relationships between having gum problems and GWI but the cause/effect pattern is not clear. Did the reservists have an unusual amount of dental work done as part of their mobilization? Was there an unusual amount of fillings placed in their teeth, with a concurrent excess load of mercury? Was there some other underlying condition that led to gum problems and also later led to GWI? Our data do not allow us to decipher this issue because we failed to measure level of dental treatments or number of fillings completed as part of mobilization compared to prior or subsequent fillings.

7.3 Further work on PB/Anthrax Vaccine

We attempted to see if anthrax and PB tablets were correlated more with some symptom groups than others. We controlled for as much recall bias as possible by analyzing only subjects who had reacted to vaccines, deleting those subjects who responded "not sure" on the anthrax vaccine and PB questions, and partialing out past month's subjective health. The findings were remarkable. Even though using the Kansas Gulf War variable led to a significant partial correlation with anthrax vaccine in only two levels (yes and no), only two symptom groups remained significant as partial correlation ($pr = .20$, $p < .01$ for the pain symptom group; $pr = .13$, $p < .05$, one-tailed, for the fatigue symptom group). In contrast, the only symptom group that was not significant for PB was gastrointestinal ($pr = .10$), while all others were significant (neurological, $pr = .18$, $p < .05$; pain, $pr = .27$, $p < .001$; fatigue, $pr = .17$, $p < .05$; skin, $pr = .21$, $p < .01$; respiratory, $pr = .22$, $p < .01$).

We realized that controlling for reactions to vaccines by classifying subjects into "no" versus "some" reactions left open the question of "how much" of a reaction was needed to allow for a significant relationship between the Kansas classification of Gulf War illness and anthrax vaccination and consumption of PB tablets. Therefore, we selected only those veterans who reported that they had experienced "minor" reactions to their vaccines (e.g., soreness at the injection site, but not having to lose time at work or to be hospitalized). We continued to drop out the "not sure" category for both anthrax vaccination and use of PB tablets in order to minimize recall biases. Both anthrax ($r = .27$, $p < .01$) and PB tablets ($r = .31$, $p < .001$) remained significant. We further partialed out subjective health in the past month, which reduced the (partial) correlations to .18 ($p < .05$) and .22 ($p < .05$), respectively. In addition, we controlled for racial background by repeating the same analyses for white and minority veterans. Results were not significant for minority veterans. Results were stronger for white veterans, with $r = .30$ ($p < .001$) for anthrax vaccination and $r = .31$ ($p < .001$) for PB tablets predicting the Kansas classification of Gulf War illness. Controlling for subjective health yielded partial correlations of .20 ($p < .05$) for anthrax vaccination and .22 ($p < .05$) for PB tablets.

7.4 Implications

The dose-response relationships found here for PB tablets strongly suggests that the U.S. military should ensure that in future military operations that the use of PB tablets be kept to a minimum, as larger doses had more severe effects. The results for nerve agent exposure call for better rumor control so that veterans do not report exposures on the basis of guesswork. Future researchers must collect data on reactions to both vaccines and to PB tablets. Because the anthrax vaccine/Post Gulf War Health association was significant under at least some conditions, we think that the military should make the anthrax vaccine optional under informed consent, especially for those veterans who have only minor reactions [32]. No one should think that that will fix the problem because well over 50% of some groups had mild reactions, which as our testing showed, was a sufficient condition for health problems after the war. At the same time, it appears that veterans who do not react to the vaccine (or perhaps even PB tablets) when given may have little chance prospects of coming down with Gulf War illness. However, close watch needs to be maintained for other less well known risk factors, including ciprofloxacin, insect repellant and insecticides, and botulism toxoid vaccine.

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Table 1. Percentage of deployed Gulf War veterans reporting symptom clusters associated with Gulf War illness as defined by CDC classifications as a function of consumption of various risk factors

Risk factor	Response			Chi-Square Test (df = 2)
	No	Not Sure	Yes	
Anti-malaria pills	49.8% N=201	59.1% N = 181	54.5% N = 266	3.37
Typhoid vaccine	48.8% N = 43	51.8 N = 137	55.7% N = 467	1.21
Botulism toxoid	43.0% N = 165	56.4% N = 376	64.5% N = 107	13.58**
Gamma globulin	40.0% N = 30	60.0% N = 95	54.1% N = 523	3.72
Plague vaccine	49.7% N = 183	56.0% N = 327	56.5% N = 138	2.18
Meningococcus vaccine	45.3% N = 150	56.1% N = 394	60.6% N = 104	7.02*
Ciprofloxacin	44.1% N = 245	55.8% N = 292	73.0% N = 111	26.18***
Tetanus vaccine	37.3% N = 51	55.6% N = 117	55.8% N = 480	6.50*
Diphtheria vaccine	48.6% N = 109	50.9% N = 269	60.0% N = 270	6.18*
Hepatitis vaccine	47.0% N = 100	52.9% N = 225	57.6% N = 323	3.73
Yellow Fever vaccine	48.2% N = 83	55.2% N = 241	55.2% N = 324	1.44
Anthrax vaccine	41.5% N = 188	60.4% N = 149	59.1% N = 308	17.52***
Pyridostigmine Bromide tablets	39.7% N = 239	57.4% N = 54	63.5% N = 351	32.65***

Table 2. Percentage of deployed Gulf War veterans reporting symptom clusters associated with Gulf War illness as defined by CDC classifications as a function of severity of reactions to vaccines

Response ► Risk Factor ▼	None	Mild	Ssevere	Chi-square Test (df = 2)
Reactions to vaccines	43.2% N=338	63.8% N = 260	81.0% N = 42	38.32***

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Table 3. Percentage of deployed Gulf War veterans reporting symptom clusters associated with Gulf War illness as defined by CDC classifications as a function of severity of insecticide sprayed from the air in subject's billeting area

Risk factor ► Response ▼	Airspray
Never or don't know (N = 577)	53.2%
Once or twice (N = 26)	65.4%
Several times (N = 31)	61.3%
Two or three times a week (N = 7)	42.9%
Almost daily or more (N = 10)	70.0%
Chi-Square Test, df = 4	3.54

Table 4. Percentage of deployed Gulf War veterans reporting symptom clusters associated with Gulf War illness as defined by CDC classifications as a function of exposure to insecticide sprayed from the ground in subject's billeting area(s)

Risk factor ► Response ▼	Ground Spray
Not at all (N = 303)	47.5%
Occasionally (N = 289)	56.7%
Two or three times a week (N = 40)	72.5%
Almost every day (N = 14)	84.2%
Chi-Square Test, df = 3	18.49***

Table 5. Percentage of deployed Gulf War veterans reporting symptom clusters associated with Gulf War illness as defined by CDC classifications as a function of geographic location and risk associated with release of nerve agents from Khamisiya

Risk factor ► Response ▼	Ground Spray
Low risk (N = 482)	49.8%
Moderate risk (N = 90)	65.6%
High risk (N = 80)	67.5%
Chi-Square Test, df = 2	14.14**

Table 6. Percentage of deployed Gulf War veterans reporting symptom clusters associated with Gulf War illness as defined by CDC classifications as a function of perception of having been exposed to nerve agents from the release at Khamisiyahisiah

Risk factor ► Response ▼	Nerve Agent Exposure
Probably not exposed (N = 352)	36.9%
Possibly exposed (N = 291)	71.1%
Probably exposed (N = 82)	84.1%
Government informed subject of exposure (N = 3)	100.0%
Chi-Square Test, df = 3	98.79***

Table 7. Percentage of deployed Gulf War veterans reporting symptom clusters associated with Gulf War illness as defined by CDC classifications as a function of reported use of personal insecticide

Risk factor ► Response ▼	Insecticide
Not at all (N = 278)	42.1%
Only occasionally (N = 252)	59.1%
Small amounts daily (N = 81)	72.8%
Large amounts daily (N = 10)	100.0%
Chi-Square Test, df = 3	38.64***

Table 8. Percentage of deployed Gulf War veterans reporting symptom clusters associated with Gulf War illness as defined by CDC classifications as a function of reported use of personal insect repellant (DEET)

Risk factor ► Response ▼	Insect Repellant (DEET)
Not at all (N = 170)	38.2%
Only occasionally (N = 321)	55.5%
Small amounts daily (N = 138)	70.3%
Large amounts daily (N = 12)	66.7%
Chi-Square Test, df = 3	32.81***

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Table 9. Percentage of deployed Gulf War veterans reporting symptom clusters associated with Gulf War illness as defined by CDC classifications as a function of reported total consumption of Pyridostigmine Bromide (PB) tablets

Risk factor ► Response ▼	PB Tablets
None at all (N = 241)	39.8%
One or two (N = 54)	51.9%
Three to ten (N = 128)	58.6%
Eleven to twenty-one (N = 98)	71.4%
Twenty-two or more (N = 44)	75.0%
Several blister packs (N = 19)	68.4%
Chi-Square Test, df = 5	42.03***

Table 10. Percentage of deployed Gulf War veterans reporting symptom clusters associated with Gulf War illness as defined by Kansas classifications as a function of consumption of various risk factors

Response ► Risk Factor ▼	No	Not Sure	Yes	Chi-square Test (df = 2)
Anti-malaria pills	24.3% N=169	34.7% N = 147	30.8% N = 224	4.27
Typhoid vaccine	21.1% N = 38	33.3 N = 120	29.7% N = 381	2.11
Botulism toxoid	19.3% N = 145	31.7% N = 312	29.8% N = 83	13.12**
Gamma globulin	8.0% N = 25	39.2% N = 79	29.4% N = 436	9.08*
Plague vaccine	20.4% N = 152	33.2% N = 280	34.3% N = 108	9.01*
Meningococcus vaccine	18.8% N = 128	32.6% N = 325	35.6% N = 87	10.11*
Ciprofloxacin	19.4% N = 211	32.5% N = 249	48.8% N = 80	25.46***
Tetanus vaccine	19.0% N = 42	31.6% N = 98	30.5% N = 400	2.57*
Diphtheria vaccine	17.2% N = 93	31.3% N = 227	33.6% N = 220	8.84*
Hepatitis vaccine	17.1% N = 82	32.3% N = 189	32.0% N = 269	7.51*
Yellow Fever vaccine	20.0% N = 70	34.3% N = 201	29.0% N = 269	5.27+
Anthrax vaccine	17.8% N = 163	35.8% N = 123	34.3% N = 251	15.77***
Pyridostigmine Bromide tablets	18.2% N = 214	31.0% N = 42	38.4% N = 281	23.75***

Table 11. Percentage of deployed Gulf War veterans reporting symptom clusters associated with Gulf War illness as defined by Kansas classifications as a function of severity of short term reactions to vaccines and PB tablets

Response ► Risk factor ▼	None	Mild	Severe	Chi-square Test (df = 2)
Reactions after vaccines or PB tablets	23.2% N=302	36.6% N = 205	53.8% N = 26	18.02***

Table 12. Percentage of deployed Gulf War veterans reporting symptom clusters associated with Gulf War illness as defined by Kansas classifications as a function of severity of insecticide sprayed from the air in subject's billeting area

Risk factor ► Response ▼	Airspray
Never or don't know (N = 489)	29.4%
Once or twice (N = 15)	33.3%
Several times (N = 25)	24.0%
Two or three times a week (N = 6)	33.3%
Almost daily or more (N = 7)	57.1%
Chi-Square Test, df = 4	3.06

Table 13. Percentage of deployed Gulf War veterans reporting symptom clusters associated with Gulf War illness as defined by Kansas classifications as a function of exposure to insecticide sprayed from the ground in subject's billeting area(s)

Risk factor ► Response ▼	Ground Spray
Not at all (N = 258)	27.1%
occasionally (N = 138)	29.4%
Two or three times a week (N = 32)	40.6%
Almost every day (N = 14)	57.1%
Chi-Square Test, df = 3	7.70+

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Table 14. Percentage of deployed Gulf War veterans reporting symptom clusters associated with Gulf War illness as defined by Kansas classifications as a function of geographic location and risk associated with release of nerve agents from Khamisiyahisiah.

Risk factor ► Response ▼	Ground Spray
Low risk (N = 405)	27.2%
Moderate risk (N = 75)	40.0%
High risk (N = 63)	33.3%
Chi-Square Test, df = 2	5.47+

Table 15. Percentage of deployed Gulf War veterans reporting symptom clusters associated with Gulf War illness as defined by Kansas classifications as a function of perception of having been exposed to nerve agents from the release at Khamisiyah.

Risk factor ► Response ▼	Nerve agent exposure
Probably not exposed (N = 315)	16.5%
Possibly exposed (N = 158)	43.7%
Probably exposed (N = 56)	58.9%
Government informed subject of exposure (N = 3)	66.7%
Chi-Square Test, df = 3	66.36***

Table 16. Percentage of Deployed Gulf War Veterans Reporting Symptom Clusters Associated with Gulf War Illness as Defined by Kansas Classifications as a Function of Reported Use of Personal Insecticide.

Risk factor ► Response ▼	Insecticide
Not at all (N = 242)	21.9%
Only occasionally (N = 213)	32.4%
Small amounts daily (N = 59)	52.5%
Large amounts daily (N = 5)	40.0%
Chi-Square Test, df = 3	22.71***

Table 17. Percentage of deployed Gulf War veterans reporting symptom clusters associated with Gulf War illness as defined by Kansas classifications as a function of reported use of personal insect repellant (DEET).

Risk factor ► Response ▼	Insect repellant (DEET)
Not at all (N = 155)	18.1%
Only occasionally (N = 271)	29.5%
Small amounts daily (N = 100)	47.0%
Large amounts daily (N = 8)	37.5%
Chi-Square Test, df = 3	24.67***

Table 18. Percentage of deployed Gulf War veterans reporting symptom clusters associated with Gulf War illness as defined by Kansas classifications as a function of reported total consumption of Pyridostigmine tablets.

Risk factor ► Response ▼	Pyridostigmine Bromide tablets
None at all (N = 216)	18.1%
One or two (N = 50)	32.0%
Three to ten (N = 103)	29.1%
Eleven to twenty-one (N = 78)	47.4%
Twenty-two or more (N = 30)	50.0%
Several blister packs (N = 13)	53.8%
Chi-Square Test, df = 5	35.67***

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Table 19. Percentage of deployed Gulf War veterans reporting reactions to vaccines as a function of number of vaccines received

Risk factor ► Number of vaccines ▼	Percentage of veterans with reactions
None (N = 66)	22.7
One (N = 45)	28.9
Two (N = 70)	48.6
Three (N = 98)	42.9
Four (N = 86)	44.2
Five (N = 89)	51.7
Six (N = 39)	48.7
Seven (N = 24)	62.5
Eight (N = 16)	56.3
Mean = 3.35 SD = 2.12	43.3
Chi-Square Test (df = 8) = 23.72**	r = .18***

Table 20. Percentage of deployed Gulf War veterans reporting symptom clusters associated with Gulf War illness as defined by Kansas classifications as a function of reported risk factors for veterans who reported no reactions to vaccines versus those who reported some reactions

Risk factors	No reactions – was risk factor significantly related to GWI by Chi-Square Test?	Some reactions – was risk factor significantly related to GWI by Chi-Square Test?
Anti-Malaria pills	Yes ($p < .03$)	No
Typhoid vaccine	No	No
Botulism toxoid	Yes ($p < .05$)	No
Gamma globulin	Yes ($p < .02$)	No
Plague vaccine	No	No
Meningococcus vaccine	Yes ($p < .02$)	No
Ciprofloxin pills	Yes ($p < .001$)	Yes ($p < .03$)
Tetanus toxoid	No	No
Diptheria vaccine	No	No
Hepatitis B vaccine	No	No
Yellow Fever vaccine	No	No
Ground spray	Yes ($p < .04$)	No
Aerial spray	No	No
Nerve agent	Yes ($p < .001$)	Yes ($p < .001$)
Pyridostigmine Bromide tablets	No ($p < .06$)	Yes ($p < .001$)
Total PB tablets consumed	No ($p < .06$)	Yes ($p < .001$)
Insecticide use	No ($p < .07$)	Yes ($p < .02$)
Use of DEET	Yes ($p < .04$)	Yes ($p < .007$)
Anthrax vaccine	No ($p < .07$)	Yes ($p < .003$)
Summary of results below ▼		
Neither Column Significant	Typhoid Plague Tetanus Diptheria Hepatitis B Yellow Fever Aerial spray	
Both Columns Significant	Ciprofloxcin Nerve agent DEET	
Only Left Column Significant	Anti-Malaria Botulism Gamma globulin Ground spray	
Only Right Column Significant	PB tablets Insecticide use Anthrax vaccine	

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Table 21. Percentage of deployed Gulf War veterans reporting symptom clusters associated with Gulf War illness as defined by Kansas classifications as a function of consumption of PB tablets and of reported reactions to vaccines

PB tablets consumed	No reactions to vaccines	Some reactions to vaccines
None at all	17.0% (N = 141)	20.8% (N = 72)
One or two	27.6% (N = 29)	40.0% (N = 20)
Three to ten	18.4% (N = 49)	39.6% (N = 53)
Eleven to twenty-one	40.6% (N = 32)	53.3% (N = 45)
Twenty-two or more	33.3% (N = 15)	61.5% (N = 13)
Several blister packs	14.3% (N = 7)	100.0% (N = 6)
Chi-Square Test, df = 5	10.78+	25.99***

Table 22. Percentage of deployed Gulf War veterans reporting symptom clusters associated with Gulf War illness as defined by Kansas classifications as a function of reported personal use of insecticide and of reported reactions to vaccines

Insecticide use	No reactions to vaccines	Some reactions to vaccines
Not at all	18.6% (N = 161)	29.5% (N = 78)
Only occasionally	27.9% (N = 104)	37.4% (N = 107)
Small amounts daily	37.5% (N = 24)	61.8% (N = 34)
Large amounts daily	0.0% (N = 0)	40.0% (N = 5)
Chi-Square Test	5.84+ df = 2	10.52* df = 3

Table 23. Percentage of deployed Gulf War veterans reporting symptom clusters associated with Gulf War illness as defined by Kansas classifications as a function of reported personal use of insect repellant (DEET) and of reported reactions to vaccines

Personal use of insect repellant (DEET)	No reactions to vaccines	Some reactions to vaccines
No	17.1% (N = 105)	19.3% (N = 57)
Not sure	31.9% (N = 72)	40.4% (N = 47)
Yes	22.1% (N = 122)	46.5% (N = 127)
Chi-Square Test, df = 2	5.37+	12.34**

Table 24. Percentage of deployed Gulf War veterans reporting symptom clusters associated with Gulf War illness as defined by Kansas classifications as a function of reported PB use (omitting the "not sure" category) and of reported reactions to vaccines

PB usage	No reactions to Vaccines	Some reactions to vaccines	All subjects
No	17.3% N = 139	20.8% N = 72	18.2% N = 214
Yes	27.0% N = 115	48.6% N = 107	37.6% N = 226
Chi-Square Test, df = 1	3.48+	14.17***	20.41***

Table 25. Percentage of Deployed Gulf War Veterans Reporting Symptom Clusters Associated with Gulf War Illness as Defined by Kansas Classifications as a Function of Reported Anthrax Vaccination (omitting the "not sure" category) and of Reported Reactions to Vaccines.

Anthrax vaccination	No reactions to vaccines	Some reactions to vaccines	All subjects
No	17.1% N = 105	19.3% N = 57	17.8% N = 163
Yes	22.1% N = 122	46.5% N = 127	34.3% N = 251
Chi-Square Test, df = 1	0.88	12.31***	13.37***

Table 26. Percentage of deployed Gulf War veterans reporting symptom clusters associated with Gulf War illness as defined by Kansas classifications as a function of reported bleeding and swollenness of gums during Persian Gulf War anthrax vaccination and of reported reactions to vaccines

Sore, inflamed, or bleeding gums	All subjects	No reactions to vaccines	Some reactions to vaccines
No	27.8% (N = 521)	22.4% (N = 295)	35.5% (N = 7)
Yes	76.2% (N = 21)	57.1% (N = 7)	85.7% (N = 14)
Chi-Square Test, df = 1	22.61***	4.64*	14.01***

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Table 27. Zero-order and partial correlation between Kansas classification of Gulf War illness with selected risk factors, controlling for level of adverse reactions to vaccines and self-reported subjective health in past month

Risk factors	Zero-order Pearson correlations between Kansas classification of Gulf War illness and each risk factor	Partial correlations controlling for adverse reactions	Partial correlations controlling for self-reported subjective health in the past month
Anthrax Vaccine	.16**	.15**	.09+ (p < .05, one-tailed)
Pyridostigmine Bromide tablets consumed	.24***	.21***	.16**
Pyridostigmine tablets used	.21***	.18***	.13**
Insecticide	.20***	.16**	.09*
DEET repellant	.20***	.16**	.12**
Nerve agent	.34***	.31***	.21***
Geographical risk areas for nerve agent exsposure	.18**	.06	.00
Ground sprayed insecticide	.11*	.08+	.03
Air sprayed insecticide	.04	.02	.05
Total of eight vaccines	.06	.02	.09*
Swollen and bleeding gums	.24***	.22***	.16***
Ciprofloxacin	.21***	.18***	.19***
Anti-malaria pills	.06	.04	.06
Typhoid vaccine	.01	-.01	.04
Botulism Toxoid	.15**	.13**	.10*
Gamma Globulin	.02	.00	.06
Plague vaccine	.11*	.09*	.11*
Meningococcus vaccine	.12*	.11*	.10*
Tetanus Toxoid	.04	.02	.08
Diphtheria vaccine	.10*	.09*	.11*
Hepatitis vaccine	.08+	.06	.09+ (p < .05, one-tailed)
Yellow Fever vaccine	.02	.01	.06
Reactions to vaccines	.18**	N/A	.17***

Table 28. Zero-Order and partial correlations (controlling for subjective health) between vaccines and the Kansas classification of Gulf War illness among veterans who reported beactions to faccines after controlling for recall bias by eliminating"not sure" responses for all subjects (no controls for race)

Vaccines as risk factors	Zero-Order Pearson correlations	Partial correlations controlling for self-reported subjective health
Typhoid Vaccine	-.02	.04
Botulism Toxoid	.19	.12
Gamma Globulin	.07	.03
Plague Vaccine	.13	.14
Meningococcus Vaccine	.05	.06
Tetanus Vaccine	.02	.04
Diphtheria Vaccine	.15	.14
Hepatitis Vaccine	.13	.16*
Yellow Fever Vaccine	.09	.13
Anthrax Vaccine	.28***	.20**

* p < .05
** p < .01
*** p < .001

NOTE: Applying the same tests to Anti-Malaria pills yielded non-significant results under both conditions. However, with respect to ciprofloxacin pills, r = .23 (p < .05) and pr = .20 (p < .05).

Table 29. Percentage of deployed Gulf War veterans reporting symptom clusters associated with Gulf War illness as defined by Kansas classifications as a function of anthrax vaccination for all subjects who did not deploy or mobilize outside the U.S.

Anthrax vaccination	All subjects
No	4.3% (N = 256)
Not sure	20.0% (N = 30)
Yes	10.0% (N = 10)
Chi-Square Test, df= 2	11.87**

NOTE: Splitting the above analysis into "no reaction" and "reaction" subgroups was not feasible due to small cell sizes.

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Table 30. Percentage of Gulf War veterans who remained in the U.S. reporting symptom clusters associated with Gulf War illness as defined by CDC classifications as a function of reported usage of insect repellant (DEET) and of reported reactions to vaccines, split on nature of reactions to vaccines

Use of DEET	All subjects	No reactions to vaccines	Some reactions to vaccines
No use or only occasional use	10.7% (N= 290)	7.4% (N= 229)	25.5% (N = 55)
Used in small or large amounts daily	41.7% (N = 12)	14.3% (N = 7)	80.0%) (N = 5)
Chi-Square Test, df = 1	10.53**	0.45	6.49*
Pearson zero-order correlation	.19**	.04	.33*

NOTE: With the Kansas classification as the dependent variable there were no cases in the cell for "had GWI and used DEET more than occasionally."

Table 31. Percentage of Gulf War veterans who remained in the U.S. reporting symptom clusters associated with Gulf War illness as defined by CDC classifications as a function of reported usage of personal insecticide and of reported reactions to vaccines, split on nature of reactions to vaccines

Use of personal insecticide	All subjects	No reactions to vaccines	Some reactions to vaccines
No use or only occasional use	10.9% (N = 293)	7.0% (N= 229)	27.6% (N= 55)
Used in small or large amounts daily	44.4% (N = 9)	28.6% (N = 7)	100.0% (N = 2)
Chi-Square Test, df = 1	9.35**	4.49*	4.83*
Pearson zero-order correlation	.18**	.14*	.28*

NOTE: With the Kansas classification as the dependent variable, the percentages were 3.2 and 16.7 but the difference was not significant.

Table 32. Percentage of Gulf War veterans who deployed to the Gulf reporting reactions to vaccines as a function of receipt of anthrax vaccine

Percentage of subjects reporting reactions to vaccines by receipt of anthrax vaccine	No reactions	Did have reactions
No receipt of anthrax vaccine	63.2% (N = 120)	36.8% (N= 70)
Receipt of anthrax vaccine	44.6% (N = 137)	55.4% (N = 170)
Chi-Square Test, df = 1	16.14***	r = .18***

Table 33. Percentage of Gulf War veterans who deployed to the Gulf reporting reactions to vaccines as a function of gender and use of anthrax vaccine

Percentage of subjects reporting reactions to vaccines by gender	All subjects	No anthrax vaccination	Received anthrax vaccine
Males	43.9% (N = 529)	35.5% (N= 166)	51.7% (N = 230)
Females	61.7% (N = 115)	45.8% (N = 24)	66.2% (N = 77)
Chi-Square Test, df = 1	12.13***	0.95	4.91*

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