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Introduction

Malaria is a common cause of serious illness in the returning traveller. Those from malaria-free regions travelling to areas where there is malaria transmission are highly vulnerable, as they have little or no immunity [1].

Military forces are regularly deployed for prolonged periods of time to areas where they are at risk of contracting the disease. Evidence suggests that there is an increased prevalence of malaria when military personnel are stationed in war zones, as a result of social disruption, urban damage and exposure to vectors when undertaking activities such as night time patrols [2,3]. During the 2003 Iraq war, service personnel from the UK Armed Forces deployed to southern Iraq, where there is a risk of contracting the Plasmodium vivax strain of malaria. For this area, a regimen of Chloroquine (with additional Proguanil if there is a risk of Chloroquine resistance is recommended) [4]. P. vivax, a strain of benign malaria, causes half of malaria cases in the Middle East, Asia, the Western Pacific, and Central and South America, and an estimated 70 to 80 million cases annually [5]. In Iraq, malaria is resurgent and although the 1957 WHO-assisted malaria control programme was successful, Iraq experienced a serious epidemic of P. vivax malaria after the 1991 Gulf war. Exact figures are unavailable but a WHO report from 2000 considered Iraq to have “a very serious malaria problem” with the low incidence level a result of “incomplete to nonexistent reporting of malaria cases”. [2]

Researchers investigating the level of awareness about malaria in the UK armed forces, found that knowledge regarding the seriousness of the disease and that protection could be achieved with chemoprophylaxis was high across the three services [6]. However, there appears to be a fatalistic attitude towards protection during deployment, perhaps due to risk taking and group behaviours with many accepting malaria exposure as an inevitable and unpreventable hazard on an operational tour [6]. Adverse or incorrect publicity may lead military personnel deployed to areas at risk to make incorrect attributions of the more severe risks associated with mefloquine to other anti-malarials. This suggests that increased awareness may not always affect behaviour positively if it is poorly understood [7].

Previous research has shown that a negative affect (typified by neurotic personality traits [8]) can affect symptom reporting, awareness of side effects to medical interventions and symptoms following environmental exposures. It is suggested that those with this neurotic personality are hyperaware of somatic changes and more likely to attribute these physical symptoms to the intervention or exposure [9-12]. We wanted to test whether there was a certain type of person who would report concerns, side effects and exposures, and if this could be explained by negative affect.

Methods

This study draws data from a cross sectional epidemiological study of the UK Armed Forces, examining the health of service personnel who had either deployed to the Iraq conflict since 2003 or not. These personnel were randomly selected and included all three services, Officers and other ranks, men and women, serving and ex-serving personnel and both regulars and reservists. Members of the reserve forces were over sampled at a ratio or 2:1. A detailed
description of the sampling, stratification and methods can be found in an earlier article [13]. For the purposes of this paper our analyses are restricted to participants who had been deployed to Iraq between 2003 and 2006; we have named this the Iraq War cohort. Malarial prophylaxis, Chloroquine and Proguanil, was offered to those individuals deploying areas where a risk of Malaria had been identified. Information on the study was provided to participants and they were informed that the study was entirely voluntary and they could withdraw at any time.

Between June 2004 and March 2006 participants were asked to complete a comprehensive questionnaire. Sections of the questionnaire contained questions on demographics, symptomatology and preparations for deployment. For this paper we used a measure of whether participants were offered and self reported uptake of malarial prophylaxis, participants were asked “whether you took them or not, did you have any concerns over taking them” and were given a free text box to record these concerns. In addition, the questionnaire included a measure of self reported exposure to a range of environmental hazards such as industrial chemicals, smoke from oil well fires and asbestos, a 53-item physical symptom checklist [14]. Common mental health problems were measured using the General Health Questionnaire 12 (GHQ-12), a five-item checklist of side effects attributed to anthrax vaccination and a seven-item checklist of side effects attributed to Nerve agent pre-treatment sets (NAPS tablets, used as an antidote against chemical weapons).

Individuals were defined as cases on the 53-item physical symptom checklist if they recorded 18 or more symptoms (a score above the 95th percentile) and the GHQ-12 if they scored four or above. Participants were recorded as being exposed to environmental hazards if they reported one or more hazard and attributing side effects to either the anthrax vaccination or NAPS tablets if they recorded one or more side effect. Whether individuals recorded concerns about malaria prophylaxis or not was coded in a binary variable.

Analysis

Chi squared analysis was used to compare the frequency of concerns with different demographics (sex, serving status, education and uptake of prophylaxis), as age was non parametric the Mann Whitney test was used to compare the age of those who reported a concern to those who did not. Logistic regression analysis was used to calculate odds ratios and 95% confidence intervals of associations between reporting concerns and reporting more physicial symptoms, common mental health problems (GHQ-12), environmental hazards and side effects attributed to other prophylactic treatment. Adjustment was made for potential confounders including age, sex, service (Royal Navy, Army or RAF), enlistment status (regular or reserve), education (based on highest qualification obtained) and fitness to deploy (a dichotomous marker of whether the individual was fit or not). Analyses were conducted with Stata 9 (StataCorp, College Station, TX). Weighted percentages were calculated to account for different sample ratios between regulars and reservists.

To further investigate the concerns experienced we carried out a qualitative analysis to see whether there were common themes occurring, and whether these themes could help explain the relationships explored above.

The content method of qualitative analysis was conducted on the free text responses where individuals reported concerns about taking malaria prophylaxis [15]. To avoid allocation bias a random sample of 585 answers was selected and the raw data from the free text section was broken down into segments of texts with similar themes and then grouped into initial sub categories, each containing data with similar themes which were constructed as recurring themes appeared in the data, these were then given a descriptive title. Further grouping of subcategories into common ideas was done to derive key themes.

Results

Iraq War cohort.

10272 (61%) of the contacted sample replied to the questionnaire, 160 (0.9%) refused to participate in the study. In an intensive follow-up study of non-responders already reported, non-response was largely due to our difficulty in finding people or participant inertia, with no significant differences between responders and non-responders in terms of health [13]. Furthermore there was no difference in rates of medical downgrading (a measure of overall general health between responders and non-responders [16]).

As mentioned above, the sample for the current study was restricted to 5302 participants who had deployed to the Iraq conflict since 2003. Within the 5302 participants, 92% were male, 14% were in the Navy, 67% in the Army and 19% in the Royal Air Force and 91% were regulars with 9% holding reservist status. In terms of highest qualification obtained, 8% left school with no qualifications, 46% with O levels, 30% with A-Levles, 11% had a degree and 5% had undertaken postgraduate qualifications. The median age was 32.3 with an interquartile range of 26.4-38.2. 78.0% had been offered anti malarials, of these 81.0% accepted and 26.0% reported experiencing side effects.

Quantitative analysis

Comparison of sociodemographic differences between individuals who reported a concern about anti-malarials and those who did not.

For the quantitative analysis, a dichotomous marker of zero or one was used for no concern or concern respectively. In our sample of 5302, respondents were significantly more likely to report a concern if they were female. Reporting concerns was associated with choosing not to take the malarial prophylaxis. There was no significant distinction between serving status, education and age and reporting a concern. [Table 1]

<table>
<thead>
<tr>
<th>Anti-malarials taken during deployment</th>
<th>Number reporting Concern</th>
<th>Weighted percentage*</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Took anti-malarial</td>
<td>727/2,651</td>
<td>27.0</td>
<td></td>
</tr>
<tr>
<td>Didn't take anti-malarial</td>
<td>357/1,075</td>
<td>33.1</td>
<td>0.0003</td>
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<thead>
<tr>
<th>Sex</th>
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</thead>
<tbody>
<tr>
<td>Male</td>
<td>1,025/3,793</td>
<td>26.8</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>130/556</td>
<td>36.1</td>
<td>0.0003</td>
</tr>
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<thead>
<tr>
<th>Service</th>
<th></th>
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</thead>
<tbody>
<tr>
<td>Navy</td>
<td>128/562</td>
<td>23.1</td>
<td></td>
</tr>
<tr>
<td>Army</td>
<td>794/2,765</td>
<td>28.3</td>
<td></td>
</tr>
<tr>
<td>RAF</td>
<td>233/822</td>
<td>28.4</td>
<td>0.0424</td>
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<thead>
<tr>
<th>Serving Status</th>
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</thead>
<tbody>
<tr>
<td>Regulars</td>
<td>938/3,445</td>
<td>27.2</td>
<td></td>
</tr>
<tr>
<td>Reservists</td>
<td>217/704</td>
<td>30.8</td>
<td>0.0525</td>
</tr>
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</table>

<table>
<thead>
<tr>
<th>Education</th>
<th></th>
<th></th>
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</thead>
<tbody>
<tr>
<td>Left School</td>
<td>292/407</td>
<td>24.2</td>
<td></td>
</tr>
<tr>
<td>O levels</td>
<td>1,605/2,260</td>
<td>26.3</td>
<td></td>
</tr>
<tr>
<td>A levels</td>
<td>1,034/1,470</td>
<td>29.0</td>
<td></td>
</tr>
<tr>
<td>Degree</td>
<td>440/568</td>
<td>27.1</td>
<td></td>
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<tr>
<td>Post grad</td>
<td>237/298</td>
<td>31.9</td>
<td>0.1824</td>
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</table>

<table>
<thead>
<tr>
<th>Age</th>
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</thead>
<tbody>
<tr>
<td>Median age</td>
<td>32.0</td>
<td>(26.6-38.0)</td>
<td></td>
</tr>
<tr>
<td>Did not report</td>
<td>32.8</td>
<td>(26.5-38.6)</td>
<td>0.1543</td>
</tr>
</tbody>
</table>

* Percentage adjusted to take account of sampling fraction.

Table 1. Sociodemographic difference between individuals who reported concerns vs individuals who did not report concerns.
Associations between reporting exposures/side effects between individuals who reported concerns about anti-malarials and those who did not.

Of the sample, 4,149 individuals responded to the question asking whether they had any concerns, of these, 1,155 (28%) replied in the positive. There was a significant association between those reporting concerns and those reporting physical symptoms (OR 2.11; 95% CI 1.80-2.47). The associations between reported side effects to NAPS and the anthrax vaccine and reported concerns were also significant, although less so for the anthrax vaccination (1.91;1.61-2.26) and (1.17; 1.00-1.36) respectively. Although the prevalence of those reporting exposure to environmental hazards was high for both groups, there was a strongly significant association between reporting being exposed to environmental hazards and reported concerns (3.10; 2.05-4.69).

These associations remained significant after adjusting for age, sex, service, education, fitness to deploy and serving status (Table 2). There was a significant association between reporting concerns and reporting common mental problems, measured by the GHQ-12 (1.90; 1.56-2.27).

<table>
<thead>
<tr>
<th></th>
<th>No concerns</th>
<th>Reported concerns</th>
<th>Unadjusted OR 95% CI</th>
<th>Adjusted OR 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Multiple Physical Symptoms</td>
<td>773/2,994</td>
<td>26</td>
<td>492/1,155</td>
<td>42</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>2.08</td>
<td>1.80-2.41</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>2.11</td>
<td>1.80-2.47</td>
</tr>
<tr>
<td>Side effects attributed Naps tablets</td>
<td>7752/409</td>
<td>32</td>
<td>427/888</td>
<td>47</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>1.92</td>
<td>1.63-2.25</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>1.91</td>
<td>1.61-2.26</td>
</tr>
<tr>
<td>Side effects attributed anthrax vaccination</td>
<td>1659/2,994</td>
<td>55</td>
<td>692/1,155</td>
<td>59</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>1.17</td>
<td>1.02-1.35</td>
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<td></td>
<td></td>
<td></td>
<td>1.17</td>
<td>1.00-1.36</td>
</tr>
<tr>
<td>Environmental exposures</td>
<td>2,700/2,962</td>
<td>91</td>
<td>1,092/1,130</td>
<td>97</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>2.87</td>
<td>2.00-4.06</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>3.10</td>
<td>2.05-4.69</td>
</tr>
<tr>
<td>GHQ Score</td>
<td>514/2975</td>
<td>17</td>
<td>321/1144</td>
<td>28</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>1.91</td>
<td>1.62-2.25</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>1.90</td>
<td>1.60-2.27</td>
</tr>
</tbody>
</table>

* Percentages adjusted to take account of sampling fractions.

Discussion

The principle findings of this study were as follows; those that reported concerns were more likely to also report multiple physical symptoms, side effects to NAPS tablets and the anthrax vaccine, and exposures during service to environmental hazards. Those reporting concerns were also more likely to report common mental health problems and were more likely to decline the malarial prophylaxis.

Concerns over Malaria Prophylaxis D Murphy, A Strong

**Key theme one: concern about safety**

“They made me ill and I was concerned about completing my duty”

“Not keen on taking tablets full stop [even aspirin]. Wasn’t willing to take something that could have side effects”

“In combination with NAPS, Gulf War syndrome”

“Concerned about all the drugs we were all supposed to take, too many in a short time scale”

**Key theme two: concern about trust**

“Concerned about all the drugs the military prescribed”

“The fact that we don't know what was in these”

“Taking all these tablets and vaccines, I felt there could have been an easier way to do it”

Box 1: Key Themes that emerged from qualitative analysis:

- **Concern about safety**
  - They made me ill and I was concerned about completing my duty.
  - Not keen on taking tablets full stop [even aspirin]. Wasn’t willing to take something that could have side effects.
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- **Concern about trust**
  - Concerned about all the drugs the military prescribed.
  - The fact that we don’t know what was in these things.
  - “Taking all these tablets and vaccines, I felt there could have been an easier way to do it.”

Effects. These included diarrhoea and mouth ulcers to nightmares, infertility and ‘Gulf war syndrome’. Despite the malaria risk, many were not willing to risk experiencing these side effects. Many were apprehensive about what the health effects of the combination of vaccines and drugs they were taking in preparation for their deployment would be for both short term side effects and longer lasting risks. The issue of a ‘cocktail’ of drugs was a recurrent theme, as were fears regarding ‘Gulf war syndrome’. These concerns were compounded by negative press in the media and accounts of experiences from other soldiers.

Concern about trust

There was a strong theme of mistrust about the amount of drugs that the military were giving them. Many respondents were critical of the way that medical countermeasures were administered. Respondents cited worries about the effects of having multiple medical countermeasures over a short period of time, or that they had not been administrated sufficiently in advance of their deployment. Some respondents doubted the effectiveness of the tablets and were concerned that they were not relevant to the area they were stationed or the conditions they were in.

**Table 2 Associations between reporting exposures/side effects between individuals who report concerns about anti-malarial tablets and those who did not report concerns**

**Qualitative analysis of concerns.**

We performed a constant comparative method of qualitative analysis on a random sample of 585 respondents. These were randomly from the 4,149 respondents who had reported concerns. Analysis was preformed to identify key themes that were evident in the data. Of the data sample, 407 (70%) responses contained a free text response, of these, 120 (29%) contained concerns about the anti-malarials medication. Analysis of these concerns generated six sub-categories, and two key themes emerged. The keys themes were ‘concern about safety’ and ‘concern about trust’. However, these were not mutually exclusive (Box 1).

**Concern about safety**

This was the most common category of concerns, incorporating the concerns about both long, and in particular, short term side effects to NAPS and the anthrax vaccine and reported concerns (1.90; 1.56-2.27).

**Key theme one: concern about safety**

“Not keen on taking tablets full stop [even aspirin]. Wasn’t willing to take something that could have side effects”

“In combination with NAPS, Gulf War syndrome”

“Concerned about all the drugs we were all supposed to take, too many in a short time scale”

**Key theme two: concern about trust**

“Concerned about all the drugs the military prescribed”

“The fact that we don’t know what was in these things”

“Taking all these tablets and vaccines, I felt there could have been an easier way to do it”

**Box 1: Key Themes that emerged from qualitative analysis**

- Concerns over Malaria Prophylaxis D Murphy, A Strong

- **Key theme one: concern about safety**
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  - In combination with NAPS, Gulf War syndrome.
  - Concerned about all the drugs we were all supposed to take, too many in a short time scale.

- **Key theme two: concern about trust**
  - Concerned about all the drugs the military prescribed.
  - The fact that we don’t know what was in these things.
  - “Taking all these tablets and vaccines, I felt there could have been an easier way to do it.”

**Effects.** These included diarrhoea and mouth ulcers to nightmares, infertility and ‘Gulf war syndrome’. Despite the malaria risk, many were not willing to risk experiencing these side effects. Many were apprehensive about what the health effects of the combination of vaccines and drugs they were taking in preparation for their deployment would be for both short term side effects and longer lasting risks. The issue of a ‘cocktail’ of drugs was a recurrent theme, as were fears regarding ‘Gulf war syndrome’. These concerns were compounded by negative press in the media and accounts of experiences from other soldiers.

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**Discussion**

The principle findings of this study were as follows; those that reported concerns were more likely to also report multiple physical symptoms, side effects to NAPS tablets and the anthrax vaccine, and exposures during service to environmental hazards. Those reporting concerns were also more likely to report common mental health problems and were more likely to decline the malarial prophylaxis.

The majority did not voice concerns regarding malarial prophylaxis, in those that did however, strong themes of unease regarding safety and trust emerged. Although women were more likely to be in this group, other sociodemographic differences didn’t influence this response.

The study had several strengths, the sample was large, randomly selected and representative of the wider armed forces including all three services, both officers and other ranks. The respondents were all deployed to the same area, during the same conflict, at similar times. Having the questions regarding health not linked to exposures and preventative measures may have minimised a framing effect.

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**Qualitative analysis of concerns.**

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**Concern about safety**

This was the most common category of concerns, incorporating the concerns about both long, and in particular, short term side
The main limitation of this paper was the reliance on retrospective data collection, and therefore vulnerable to recall bias. Recall of exposures can be unreliable; there is evidence of poor agreement between reporting events and the contemporaneous reports of the same events [17]. Ideally we would have objective independent records of environmental hazards, however due to the nature of war and the impossibility of recording all hazards to all personnel; this is unlikely to be possible. As the study was cross sectional, it was not possible to ascertain whether the association between poorer uptakes in the concern group was the reason for refusal of the prophylaxis, or whether the concerns were expressed following adverse responses to other preventative measures or before. We encountered problems regarding the answering of the free text question. It was not possible to know whether the concern described was a prospective concern or a report of an actually experienced side effect due to the retrospective nature of the questionnaire. Most respondents did not answer the question at all, and we could not and did not assume that non-response was a no. It is possible that those who chose to answer the question had a reason to do so, perhaps as a result of adverse events or increased anxiety.

Following the Gulf war and subsequent ill health of veterans, an atmosphere of distrust has evolved regarding health and medical counter measures [14, 18]. Despite the resounding success of chemoprophylaxis in the military, with infectious diseases, once the scourge of overseas military service, now a well controlled and preventable sideline, focus has shifted onto the risks of these measures rather than their benefits [19,20]. This shift is mirrored in the ongoing public concern regarding the since discounted link between the MMR vaccine and autism, where despite the overwhelming evidence to refute the link, uptake levels of the vaccine have dropped and cases of measles have risen as a result [21]. Studies investigating reasons for the reduced uptake of the vaccine have implicated concerns over the safety of the vaccine, the potential risks of the vaccine outweighing the risks of contracting the disease, negative publicity, and not trusting the advice given by health professionals and the government, partly as a consequence of GPs’ target payments for immunisation [22]. The results of our study support this suggestion that anxiety surrounding an efficient and widely used counter measure has resulted in a decreased uptake, with our results showing that those who convey apprehension over the malarial prophylaxis are less likely to take it. It is an interesting point that there are some military personnel, with a risk taking occupation, who are willing to go to war but not willing to take a licensed pharmaceutical.

Our data showed that those who reported concerns regarding taking the malarial prophylaxis were also more likely to report current non specific symptoms and side effects to other medical counter measures. This is consistent with the theory that the beliefs and expectations surrounding the intervention shape the noticing and reporting of symptoms. If the respondent was anxious about side effects before taking the tablets, they are likely firstly to be primed to notice any unusual physical symptoms, and secondly to interpret these sensations as an adverse reaction to the intervention. Exposure recall can be unreliable; however remembering more exposures over time is associated with worsening perception of health [17].

A study into reasons for poor compliance with chemoprophylaxis in the general population has shown that it was lowest amongst those who used a drug with a daily, as opposed to, a weekly dosing schedule, stayed in the malaria risk zone for more than 1 month, attributed an adverse health event to the chemoprophylaxis or feared one, and were less than 40 years of age [7]. In our study many of those concerned would fulfil much of these criteria, with tours lasting 6 months, an average age of 32.3 in the sample, a weekly dosing schedule and a high level of reporting of, and concern regarding side effects.

Conclusion
Our results showed that although the uptake of anti-malarial tablets was high prior to deployment to the Iraq war, many individuals reported concerns about taking them. Those with concerns were likely to follow neurotic personality patterns such as increased symptom awareness and attribution, and exposure recall. This theory of negative affect as a confounder is backed up by the recurring themes of mistrust and anxiety in the stated concerns. Due to the cross sectional and retrospective nature of the questionnaire it is not possible to confidently state that these concerns led to poor uptake in these groups, however it is clear that there is a strong association regarding anxiety and poor uptake of malarial prophylaxis.

References
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