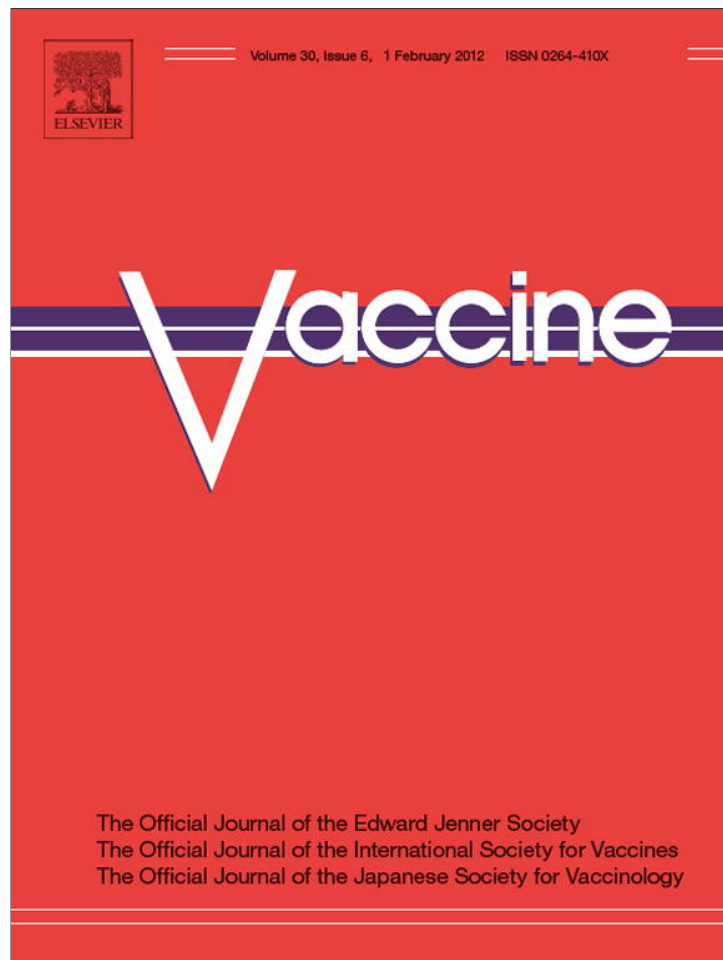


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## A longitudinal study of UK military personnel offered anthrax vaccination: Informed choice, symptom reporting, uptake and pre-vaccination health

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### ABSTRACT

**Aim:** To determine longer term health outcome in a cohort of UK service personnel who received the anthrax vaccination.

**Method:** We conducted a three year follow up of UK service personnel all of whom were in the Armed Forces at the start of the Iraq War. 3206 had been offered the anthrax vaccination as part of preparations for the 2003 invasion of Iraq. A further 1190 individuals who did not deploy to Iraq in 2003 were subsequently offered the vaccination as part of later deployments, and in whom we therefore had prospective pre-exposure data.

**Results:** There was no overall adverse health effect following receipt of the anthrax vaccination, with follow up data ranging from three to six years following vaccination. The previous retrospective association between making an uninformed choice to receive the anthrax vaccination and increased symptom reporting was replicated within a longitudinal sample where pre-vaccination health was known.

**Conclusions:** Anthrax vaccination was not associated with long term adverse health problems. However, symptoms were associated with making an uninformed choice to undergo the vaccination. The results are important both for the safety of the vaccine and for future policies should anthrax vaccination be required in either military or non military populations.

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### 1. Introduction

In the build-up to the 2003 Iraq War, the UK Ministry of Defence (MoD) offered the anthrax vaccination as part of the preparation of service personnel prior to deployment. The anthrax vaccination was offered on a voluntary basis supported by a Vaccine Information Programme (VIP), which consisted of video and written information, intended to facilitate informed choices. Personnel were then given a “cooling off” period before being invited to sign a consent form. This move reflected changes in society away from medical paternalism and towards medical consumerism, underpinned by informed choice, and was intended to increase confidence in the anthrax vaccination programme. It was also a response to the problems associated with the vaccination following the 1991 Gulf War.

We previously showed that receiving an anthrax vaccination was not associated with adverse health outcome in members of the UK Armed Forces who received the vaccine as part of the medical counter measures used prior to the 2003 invasion of Iraq

[1]. This was an important finding given the previous associations that we and others had found between anthrax vaccination and ill health after the 1991 Gulf War [2–4]. However we did find a link between making an uninformed choice to receive the vaccination and increased symptom reporting [1]. The cross-sectional nature of the study however made it difficult to determine the direction of causality. In particular, we could not exclude a confounding effect of pre-vaccination psychological or symptomatic health on recall of choice and experience of symptoms.

The current study adds to these findings in two ways. Firstly, by conducting a follow up study it allows assessment of adverse effects of the vaccination over a longer time frame; and secondly, by using the prospective design to identify individuals who received the vaccination between the two time points of the study, it is possible to assess the influence of pre-vaccination health on post-vaccination symptoms and recollection of choice. In addition, the opportunity was taken to replicate previous findings that personnel accurately report receipt of the anthrax vaccination although this does not extend to recollection of the number of times they received the vaccination [1,5,6]. We were unable to verify the number of vaccinations personnel received in total. Research within American samples suggests that fewer than one in five personnel complete the full series of five doses of anthrax vaccinations that are required for full immunity [7].

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The cohort had been contacted for the first time as part of a longitudinal study exploring health and well being in the UK Armed Forces after the 2003 Iraq conflict [8]. The data used in this paper come from a second wave of data collection carried out approximately three years later [9].

## 2. Methods

### 2.1. Procedure

Data for this study were drawn from the second stage of an ongoing longitudinal study of the health and well being of UK military personnel conducted by King's College, London [9]. The study was set up following the UK military's participation in the 2003 invasion of Iraq.

Stage one of the study took place between the end of 2003 and 2005 and consisted of two randomly selected groups. The first comprised approximately 10% of the UK Armed Forces that deployed during the 2003 invasion of Iraq. The second group included individuals who were in the UK Armed Forces at the time of the invasion but had not deployed to Iraq. There were many reasons why personnel may not have deployed during the 2003 war in Iraq. Principal among these were that they were not members of units selected to deploy. Importantly, we have reported that there were no differences in terms of medical downgrading between those who deployed and those who did not [10]. In total, the sample comprised 17,698 individuals and included full-time regulars and reservists, men and women, Officer and other rank, all three services (Royal Navy, Army and the RAF), currently serving and those that had left the military by the time the sample was recruited. Data were collected via questionnaires that were either distributed directly to participants through a three-stage postal survey or by visiting military bases across the UK, Germany and Cyprus. A variety of techniques was employed to contact participants who had not responded to the recruitment attempts described above. These included telephone tracing via directory enquires and seeking alternative address information available through the NHS tracing services or the electoral registry. 10,272 (58.0%) participants responded to the first stage. An intensive follow up of non-responders concluded that no health differences were present between those who returned completed questionnaires and those who did not and that non-response was most likely due to poor quality contact information. Full details of this stage of the study have been published previously [8].

The second stage of data collection was carried out between July 2007 and November 2009 and employed a similar method of data collection as described above. Of the 10,272 participants who responded at stage one, 9395 were followed up in this second stage. 914 participants were excluded from the second stage of data collection (733 had not consented to follow up, 29 had died and 152 were no longer eligible or we had insufficient address information to make re-contacting them possible) and an additional 37 were added (these had returned completed questionnaires beyond the cut-off date for inclusion in stage one but were later added to the dataset).

### 2.2. Sample

The service personnel in the study is divided into two groups. The first group includes all those who had already received the anthrax vaccine before the first wave of data collection, i.e. those who had been vaccinated before the original 2003 deployment to Iraq [8]. This group thus provided the majority of the person years of post-vaccination exposure. The second sample used for this paper consists of those who had not been offered the anthrax vaccination

during the first wave of data collection (because they did not deploy to Iraq or Afghanistan during the early stages of the conflict), but who did deploy to either theatre between the two waves of data collection, and who were at that point offered the vaccination prior to their deployment.

### 2.3. Measures

#### 2.3.1. Health

A strength of the follow up study was that the principal measures were unchanged from stage one. Thus the same four self reported measures of well being were used at follow up. These included the following measures:

- (a) of self-rated health from the SF-36 (to score as a case participants had to rate their health as 'fair' or 'poor') [11];
- (b) a 53-item physical symptom checklist (to meet case criteria for the physical symptoms participants had to report 18 or more symptoms (above the 95th percentile)) [8];
- (c) symptoms of common mental health disorders were measured using the 12-item General Health Questionnaire (GHQ-12) (a score of four or more indicated case criteria) [12];
- (d) symptoms of post traumatic stress disorder using the 17-item National Centre for PTSD checklist (PCL-C) (where a score of 50 or more indicated meeting case criteria) [13].

#### 2.3.2. Vaccination status

A separate section of the questionnaire was concerned with the anthrax vaccination. Questions included whether participants had been offered the vaccination, whether they had accepted the vaccination. In addition, within this section, participants were asked whether they had experienced any side effects that they attributed to the vaccination.

#### 2.3.3. Informed choice

This was measured using three items that were combined to form a binary classification: informed vs. uninformed. These were (a) whether participants felt pressure to receive the vaccination, (b) if participants were satisfied with their decision and (c) if they would repeat their decision in the future. A full description of this measure has been described previously [1].

#### 2.3.4. Demographic characteristics

A separate section of the questionnaire asked participants to record demographic characteristics. These included, age, sex, service (Royal Navy, Army or RAF), enlistment status (full-time regular or reservist e.g. Territorial Army) and rank (Officer or other rank).

### 2.4. Analysis

The first phase of the analysis was restricted to the first group who had been offered the anthrax vaccination prior to the 2003 Iraq conflict. Logistic regression modelling was conducted to generate odds ratio for associations between uptake of the anthrax vaccination at stage one and follow up health at stage two of data collection. Models were then fitted between informed choice at stage one and follow up health at stage two. In both sets of analyses four models were fitted. The first was unvaried; the second adjusted for demographic characteristics from stage one; and the third adjusted for demographic characteristics and stage one health status. The final model excluded individuals who had met case criteria for the health outcome under investigation and adjusted for demographic characteristics.

Analyses were then conducted on the second group of participants who had been offered the vaccination between stages one

and two of data collection. We previously showed that participants who had been offered the vaccination recalled whether or not they had received the anthrax vaccination with considerable accuracy (Kappa 0.81; 95% CI 0.73–0.90) [1]. We used the opportunity afforded by the second group of participants, to replicate the previous finding. Within this group a 10% sub-sample was randomly selected and medical records were accessed. This was done by randomly assigning a number to all participants and then selecting the first 10% of these numbers. Kappa statistics were used to assess agreement between receipt of the anthrax vaccination from self-report and receipt from participants' medical records.

Logistic regression was used to determine associations between receipt of the anthrax vaccination and health, both at stage two. Next, models were fitted to explore if stage one health or demographic characteristics predicted making informed or uninformed choices to accept the vaccination or not at stage two. The next set of analyses was to observe the relationship between making an uninformed choice to receive the anthrax vaccination and adverse health. These analyses were further adjusted for stage two demographics and stage one health status. The final analysis built up models to explore the strongest predictors of stage two health outcomes.

Demographic characteristics used for adjustment include age, sex, service (Royal Navy, Army, or RAF), Officer or other rank, and enlistment status (either full-time regular or a member of the reserve forces). Sampling and response weights were used for all analyses presented. Analyses were conducted using STATA 9 (Stata Corporation, College Station, TX, USA). Ethical approval was granted for the epidemiological study by both the King's College Research Ethics Committee LREC (ref. 150/034) and the MoD Naval Research Ethics Committee MoD(N)PREC (ref. 11-03-219).

### 3. Results

6429 (68.4%) returned completed questionnaires. Differences were found in demographic characteristics between completers and non-completers of the questionnaire. Older participants, women, and those holding a higher rank were more likely to return completed questionnaires. These differences were taken into account by applying sampling and response weights in the analyses. A further mailing to non-responders of the second stage, with a shortened version of the questionnaire, concluded there were no health differences between participants who responded and those that did not, using measures identical measures of fatigue, GHQ-12 and PTSD. Importantly, no stage one health differences were present between participants who returned completed stage two questionnaires and those that did not. Further details have been described elsewhere. [9].

The total sample for this study was 4396. This include 3206 participants who had been offered the anthrax vaccination before stage one, and 1190 participants who had been offered the vaccination for the first time after the end of data collection at stage one.

The first sets of analyses were restricted to the 3206 participants who had been offered the anthrax vaccination at stage one and had been followed up at stage two (response rate: 60.5%). 11% were in the Royal Navy, 68% were in the Army and 21% the RAF. 19% were Officers, 91% male, 89% regulars and the mean age was 36.4. No significant differences were observed between those participants who returned completed questions and those offered that did not within this sample frame.

The relationship between uptake of the anthrax vaccination at stage one and health is explored in Table 1. In all four models there were no significant associations between receiving the vaccination and subsequent adverse health. Table 2 reports associations between participants making uninformed choices to receive the

vaccination at stage one and health outcomes at stage two. Model two shows a significant relationship between meeting case criteria for three of the four health outcomes at stage two (GHQ-12, multiple physical symptoms and health perception) if participants had reported making an uninformed choice to accept the vaccination at stage one. These associations lost significance in models three and four where either further adjustment had been made for stage one health status (model three) or alternatively where removing those individuals who already met case criteria for any of the four outcomes at stage one (model four).

The second set of analyses restricted the 1190 participants who had been offered the anthrax vaccination for the first time after the completion of stage one data collection. Firstly, medical records were assessed for a randomly selected 10% sub sample. In total, the records of 120 participants were checked. Substantial agreement (Kappa = 0.75; 95% CI 0.64–0.97) was found between questionnaire self-report and written medical records recording anthrax vaccinations. The observed level of agreement was 89%. The positive agreement for accepting the vaccination was 92%, and the negative was 80%, thus justifying the use of self-reported vaccination in the analysis.

1190 participants were offered the anthrax vaccination for the first time at stage two. Uptake of the vaccination was low at 15% and of these, 19% reported making an uninformed choice to receive the vaccination. 54% of the sample was in the Army, 32% in the RAF and 14% in the Royal Navy. 20% were Officers, 92% male, 94% regulars and the mean age was 32.2.

Within this sample no significant associations were observed between uptake of the vaccination at stage two and health (Table 3).

Turning now to the issue of informed choice, there were significant stage one health differences between participants who later made informed or uninformed choices at stage two. Participants making uninformed choices were more likely to report symptoms of common mental health problems (GHQ-12) and rate their health as fair or poor at stage one (Table 4). Few demographic differences were present. Participants who were in the RAF at stage one, were less likely to report making uninformed choices at stage two. The odds ratio for other ranks being more likely to later report uninformed choices approached but did not reach conventional statistical significance (OR 2.77; 95% CI 0.95–8.09).

Table 5 reports the relationship between making an uninformed choice to receive the vaccination at stage two and concurrent health status at stage two. These analyses were restricted to 15% ( $n = 166$ ) of participants who had both been offered and had accepted the vaccination for the first time at stage two. The outcome measures included validated health outcomes from a separate section of the questionnaire and side effects directly attributed to the vaccination. Model one reports associations between uninformed choice and health adjusted for demographics. Participants who reported making uninformed choices were more likely to meet case criteria on the GHQ-12, report 18 or more physical symptoms, perceive their health as worse, and report flu-like symptoms attributed to the vaccination. These associations remained significant in model two after further adjustment for pre-vaccination health status (stage one health observed in Table 4). However, these effect sizes decreased.

Table 6 shows uptake rates of the anthrax vaccination, and rates of participants making informed or uninformed choices to accept the vaccination. The first finding is that uptake of the vaccination dropped dramatically between stages one and two of the study. Within participants who received the vaccination, significantly fewer reported making an uninformed choice to do so at stage two.

The final analysis in Table 7 reports variables associated with meeting case criteria for a range of health outcomes at stage two. It is clear that for a specific health outcome, stage one health status has the biggest effect size for explaining health status at stage two.

**Table 1**  
Health outcomes at follow up for individuals who reported receiving the anthrax vaccination at stage one.

	Model one <sup>a</sup>		Model two <sup>b</sup>		Model three <sup>c</sup>		Model four <sup>d</sup>	
	Odds ratio	(95% CI)	Odds ratio	(95% CI)	Odds ratio	(95% CI)	Odds ratio	(95% CI)
GHQ-12	0.90	(0.71–1.14)	0.86	(0.67–1.10)	0.86	(0.66–1.12)	0.84	(0.61–1.17)
PCL-C	0.97	(0.62–1.52)	0.97	(0.60–1.57)	0.94	(0.57–1.55)	0.90	(0.52–1.53)
Multiple symptoms	1.28	(0.92–1.78)	1.32	(0.93–1.87)	1.25	(0.86–1.81)	1.23	(0.63–2.39)
Health perception	0.97	(0.74–1.27)	1.00	(0.75–1.34)	0.90	(0.66–1.22)	0.93	(0.65–1.34)

<sup>a</sup> Model one – unadjusted.

<sup>b</sup> Model two – adjusted for age 10, sex, service, rank, fitness to deploy and regular/reservist status.

<sup>c</sup> Model three – adjusted for age 10, sex, service, rank, fitness to deploy and regular/reservist status & health outcome status at baseline.

<sup>d</sup> Model four – adjusted for age 10, sex, service, rank, fitness to deploy and regular/reservist status & individuals removed from analysis that scored positive to respective health outcome at baseline.

**Table 2**  
Health outcomes at follow up for individuals who made an uninformed choice to receive the anthrax vaccination at stage one.

	Model one <sup>a</sup>		Model two <sup>b</sup>		Model three <sup>c</sup>		Model four <sup>d</sup>	
	Odds ratio	(95% CI)	Odds ratio	(95% CI)	Odds ratio	(95% CI)	Odds ratio	(95% CI)
GHQ-12	1.42	(1.10–1.85)	1.32	(1.01–1.74)	1.11	(0.82–1.50)	1.22	(0.83–1.79)
PCL-C	1.70	(1.04–2.80)	1.40	(0.84–2.33)	1.15	(0.67–1.98)	1.38	(0.78–2.46)
Multiple symptoms	1.69	(1.21–2.34)	1.54	(1.10–2.16)	1.09	(0.75–1.57)	1.24	(0.59–2.62)
Health perception	1.59	(1.18–2.15)	1.47	(1.06–2.02)	1.20	(0.86–1.69)	1.20	(0.79–1.82)

<sup>a</sup> Model one – unadjusted.

<sup>b</sup> Model two – adjusted for age 10, sex, service, rank, fitness to deploy and regular/reservist status.

<sup>c</sup> Model three – adjusted for age 10, sex, service, rank, fitness to deploy and regular/reservist status & health outcome status at baseline.

<sup>d</sup> Model four – adjusted for age 10, sex, service, rank, fitness to deploy and regular/reservist status & individuals removed from analysis that scored positive to respective health outcome at baseline.

**Table 3**  
Associations between receipt of the anthrax vaccination at stage two and health (restricted to only individuals who did not receive vaccine at stage one and were offered vaccine at stage two).

	No anthrax vaccine		Anthrax vaccine		Unadjusted odds ratio		Adjusted odds ratio <sup>b</sup>	
	n	(%) <sup>a</sup>	n	(%) <sup>a</sup>	OR	(95% CI)	OR	(95% CI)
GHQ-12	212/1014	(22)	38/170	(21)	0.96	(0.63–1.45)	0.93	(0.60–1.44)
Physical symptoms	89/953	(10)	15/156	(10)	0.98	(0.54–1.77)	0.89	(0.48–1.67)
Health perception	141/1020	(14)	28/170	(16)	1.14	(0.71–1.82)	1.08	(0.66–1.75)
PCL-C	43/1018	(4)	6/170	(4)	0.82	(0.32–2.09)	0.73	(0.29–1.86)

<sup>a</sup> Percentages adjusted to take account of sampling and response fractions.

<sup>b</sup> Model 1: adjusted for stage two variables age 10, sex, service, rank, regular/reservist status.

**Table 4**  
Stage one demographic characteristics associated with making an uninformed choice to receive the anthrax vaccination at stage two.

	Informed choice		Uninformed choice		Unadjusted odds ratio		Adjusted odds ratio <sup>b</sup>	
	n	(%) <sup>a</sup>	n	(%) <sup>a</sup>	OR	(95% CI)	OR	(95% CI)
<b>Demographics</b>								
<b>Sex</b>								
Male	1003/1045	(96)	42/1045	(4)	1.00		1.00	
Female	97/99	(98)	2/99	(2)	0.55	(0.13–2.35)	0.80	(0.20–3.12)
<b>Ranks</b>								
Officer	259/269	(96)	10/269	(4)	1.00		1.00	
Other rank	841/875	(96)	34/875	(4)	1.04	(0.50–2.35)	2.77	(0.95–8.09)
<b>Service</b>								
Army	528/552	(95)	24/552	(5)	1.00		1.00	
RAF	427/439	(97)	12/439	(3)	0.65	(0.31–1.36)	0.38	(0.16–0.92)
Navy	145/153	(96)	8/153	(4)	0.86	(0.35–2.09)	0.88	(0.35–2.24)
<b>Enlistment status</b>								
Regular	1028/1070	(96)	42/1070	(4)	1.00		1.00	
Reserve	72/74	(97)	2/74	(3)	0.71	(0.17–3.02)	1.51	(0.47–4.85)
<b>Age</b>								
Mean age	34.0 years old		31.5 years old		0.92	(0.54–1.57)	0.95	(0.52–1.73)
<b>Pre-vaccination health</b>								
GHQ-12	223/1091	(22)	16/44	(37)	2.12	(1.09–4.11)	2.15	(1.11–4.19)
Physical symptoms	300/1100	(28)	17/44	(37)	1.51	(0.79–2.90)	1.52	(0.81–2.84)
Health perception	90/1092	(9)	9/44	(24)	3.13	(1.41–6.95)	3.03	(1.31–7.02)
PCL-C	38/1089	(4)	4/44	(10)	2.98	(0.97–9.17)	2.80	(0.90–8.76)

<sup>a</sup> Percentages adjusted to take account of sampling and response fractions.

<sup>b</sup> Model 1: adjusted for stage two variables age 10, sex, service, rank, regular/reservist status.

**Table 5**  
Associations between making an uninformed choice to receive the anthrax vaccination and adverse health at stage two.

	Informed choice		Uninformed choice		Unadjusted OR		Model one <sup>b</sup>		Model two <sup>c</sup>	
	n	(%) <sup>a</sup>	n	(%) <sup>a</sup>	Odds	(95% CI)	Odds	(95% CI)	Odds	(95% CI)
<b>Follow-up health</b>										
GHQ-12	24/134	(17)	14/32	(42)	3.59	(1.48–8.72)	3.53	(1.41–8.87)	2.89	(1.08–7.79)
Physical symptoms	8/123	(6)	7/29	(25)	4.70	(1.48–14.9)	5.66	(1.72–18.7)	4.24	(1.28–14.1)
Health perception	17/134	(12)	11/32	(33)	3.59	(1.38–9.35)	3.89	(1.44–10.5)	3.49	(1.13–10.8)
<b>Attributed to vaccine</b>										
Flu-like	33/134	(24)	18/32	(60)	4.63	(1.96–10.9)	4.92	(1.97–12.3)	4.34	(1.71–11.0)
Tired	32/134	(25)	14/32	(44)	2.35	(0.99–5.57)	2.43	(0.93–6.34)	1.98	(0.74–5.35)
Sore arm	65/134	(47)	21/32	(66)	2.17	(0.92–5.10)	2.03	(0.83–4.98)	1.90	(0.77–4.72)

<sup>a</sup> Percentages adjusted to take account of sampling and response fractions.

<sup>b</sup> Model 1: adjusted for stage two variables age 10, sex, service, rank, regular/reservist status.

<sup>c</sup> Model 2: adjusted for variables in Model 1 and baseline health (Stage one GHQ-12, health perception and physical symptoms).

**Table 6**  
Uptake rates of the anthrax vaccination at stage one and stage two and rates of quality of choice.

Uptake rates	Informed choice to receive anthrax vaccination		Uninformed choice to receive anthrax vaccination	
	%	(95% CI) <sup>a</sup>	%	(95% CI) <sup>a</sup>
Stage one (72%)	73	(71–74)	27	(26–29)
Stage two (14%)	81	(75–87)	19	(13–25)

<sup>a</sup> Binomial Wald 95% confidence intervals.

For example, meeting case criteria for GHQ-12 at stage one, means individuals have an odds ratio of 4.59 of being a case at stage two. Nevertheless, even taking into account these powerful associations, making an informed choice around vaccination receipt did still have some influence on symptom reporting.

**4. Discussion**

We report that receipt of the anthrax vaccination has not resulted in any long term adverse health effects. This supports previous work [4,14–16] but goes further by following participants over a longer time period. One consequence of this is that it may now be necessary to reinterpret the two studies, including one from our group at King's, that reported a link between the anthrax vaccination and increased multiple physical symptoms in veterans of the 1991 Gulf War [3,4]. Our new findings, using improved exposure data that followed better record keeping after 2003, and now

having both earlier outcome data and now longer outcome data, collectively suggest anthrax vaccination was not associated with short or long term health effects in those vaccinated in and after 2003. By implication this also sheds some doubt on the previous assertions that the anthrax vaccination was associated with the subsequent ill health of Gulf War veterans. Instead the focus should shift away from the anthrax vaccine per se, and towards how it was administered during the Gulf War. This shift in focus is suggested because, within the UK Military, changes have been made to how the anthrax vaccination was administered following the 1991 Gulf War, to increase the time interval between injections (the anthrax vaccination require four injections and a yearly booster) and limiting the administration of the vaccination to before, and not during deployment, which was often the case in the 1991 Gulf War [17,18]. However, the current study did not explore the effect of dose interval on health status.

In this paper we report an association between making an uninformed choice to receive the vaccination and an increased

**Table 7**  
Exploring factors that predict stage two health.

	GHQ-12 (ORs)			Multiple physical symptoms (ORs)			Health perception (ORs)		
	Model 1	Model 2	Model 3	Model 1	Model 2	Model 3	Model 1	Model 2	Model 3
<b>Baseline health</b>									
GHQ-12	3.65 <sup>*</sup>	3.83 <sup>*</sup>	4.59 <sup>*</sup>	1.08	1.10	2.25	1.92	2.25 <sup>*</sup>	1.26
PCL-C	0.40	0.40	0.37	5.32 <sup>*</sup>	5.51 <sup>*</sup>	6.58	2.61	2.75	1.77
Physical symptoms	2.41 <sup>*</sup>	2.33 <sup>*</sup>	1.47	5.60 <sup>*</sup>	6.52 <sup>*</sup>	5.29 <sup>*</sup>	1.38	1.16	1.29
Health perception	2.71 <sup>*</sup>	2.92 <sup>*</sup>	2.22	1.58	1.56	0.60	9.60 <sup>*</sup>	9.45 <sup>*</sup>	10.4 <sup>*</sup>
R <sup>2</sup> <sup>a</sup>	14.6%			33.3%			22.6%		
<b>Demographics</b>									
Age 10 <sup>b</sup>		1.01	1.02		0.99	1.06		1.04	1.02
Regular vs. reserve		1.30	3.79		1.25	0.87		0.78	1.65
Officer vs. rank		0.97	1.04		0.96	0.97		1.35	0.89
Army		1.00	1.00		1.00	1.00		1.00	1.00
RAF		1.23	1.66		0.56	0.75		1.35	0.99
Navy		1.61	1.81		0.88	0.90		0.69	0.89
R <sup>2</sup> <sup>a</sup>		15.2%			34.0%			23.6%	
<b>Uninformed choice</b>									
R <sup>2</sup> <sup>a</sup>			2.90 <sup>*</sup>			3.45 <sup>*</sup>			3.62 <sup>*</sup>
			17.9%			34.7%			23.9%

<sup>a</sup> Variance explained by logistic regression model adjusted for the variables above.

<sup>b</sup> Age 10 is age divided by 10 to make one unit equals to a 10 year age gap.

<sup>\*</sup> P-Value < 0.05.

likelihood of reporting symptoms of ill health on a range of health outcomes and symptoms directly attributed to the vaccination. The mechanism for this relationship is unknown, but we hypothesise that it may be mediated by anxiety. We hypothesise that individuals who report making an uninformed choice may be more anxious about the consequence of this choice, given the controversial history of the vaccination, especially in the context of 'Gulf War Syndrome' [2–4,19]. It has previously been demonstrated that anxiety following medical interventions increases symptom reporting [20,21], and that this may be due to processes of increased sensitivity to symptoms and symptom monitoring [22]. What we do not know is whether higher levels of anxiety lead to the reporting of a lower quality of decision or whether the experiences of a lower quality decision increase anxiety.

Participants who made an uninformed choice at stage one, but whose health was unaffected, were not at increased risk of developing ill health at stage two. This finding needs to be interpreted carefully. One possibility could be that quality of choice affects health, but that this effect has to occur in a relatively short time frame. Individuals who make uninformed choices, but whose health in the short term is unaffected, are not put at increased risk of ill health in the future as a consequence of the quality of their choice. This makes intuitive sense if, as hypothesised, anxiety mediates the association between uninformed choice and symptom reporting. This is because if an uninformed choice has not resulted in anxiety and increased symptom reporting at stage one, there would be no cause for ill health to develop at stage two. Alternatively, the above finding could be evidence of reverse causality, in that participants who were ill at stage one (for unrelated reasons) simply recalling their decisions as less informed.

Analyses restricted to participants who had received the vaccination for the first time at stage two shed further light on this. No demographic variables from stage one predicted whether participants made informed or uninformed choices at stage two, but several health outcomes did. Participants who made uninformed choices at stage two were more likely to have previously met case criteria for common mental health problems (GHQ-12) and rated their health as worse. Reporting of informed choices may be confounded by prior psychological ill health. Nevertheless, after adjustment for these pre-choice health outcomes the association remained significant between choice and health.

The current findings demonstrate a dramatic drop in the uptake of the anthrax vaccination, whilst at the same time an increase in the proportion of those making an informed choice to accept it. This supports our previous finding that when a perceived threat decreases, uptake decreases correspondingly [23]. The second finding, of an increase in the proportion making informed choices, is encouraging as evidence presented shows a significant association between poorly informed choices and subsequent ill health. It is also possible that as threat levels have decreased, coercion (and in turn, perceived coercion) has also decreased, as there is no longer an operational need to ensure high coverage rates of the vaccination.

A limitation of this paper is that the measure of informed choice was self reported retrospectively. This means, as discussed above, that causality cannot easily be inferred. Receipt of the anthrax vaccination was reliant on self report. However, this was found to have a high level of agreement with uptake extracted from participants' medical records for both samples involved in the analyses. Another limitation was that we were unable to control our analyses for deployment-related experiences. However, epidemiological evidence that we have previously published within this cohort did not report a deployment effect on health within this cohort [8].

The current study benefited from several strengths. The sample was randomly selected and representative of the UK Armed Forces. The cohort is the first of its kind within the UK Armed Forces, allowing longitudinal analysis of health to be conducted between four

and six years after the anthrax vaccination had been administered. Unlike past studies [3,4] self reported receipt of the vaccination had been validated against receipt from participants' medical records. Pre-vaccination health data were available for participants who were followed up at stage two. Confounding by reverse causality between uninformed choice and ill health was reduced by adjustment, although the possibility of residual confounding cannot be excluded.

Participants who had received the vaccination for the first time at stage two allowed for a replication study of previous work to be completed within a distinct sample. With causality difficult to interpret, this was an important step in providing evidence against confounding by recall bias. No stage one health differences were observed between participants who returned completed questionnaires at the second wave of data collection and those who did not. This suggests an absence of any health bias related to participation in the second phase, and that the cohort remains representative.

## 5. Conclusions

Receipt of the anthrax vaccination offered to the UK Armed Forces since 2003 has yet to result in long term health problems. However, those making uninformed choices to receive the vaccination were more likely to report symptoms, an association that persisted over the follow up period. Individuals' health prior to being offered the vaccination was the biggest predictor of health status following receipt of the vaccination, meaning that prior health status remains the strongest predictor of current health status. However, making an uninformed choice when controlling for prior health status remained a significant, albeit lesser, predictor of poor health.

Both civilian and military personnel who are offered the anthrax vaccination in the future can be reassured about its safety. However, it is also important to emphasise and respect choice if the risk of symptomatic side effects is to be avoided.

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