

## Multiple vaccinations, health, and recall bias within UK armed forces deployed to Iraq: cohort study

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### ABSTRACT

**Objective** To assess the relation between self reported number of vaccinations received and health, and between numbers of vaccinations recorded from individuals' medical records and health.

**Design** First phase of a cohort study.

**Setting** UK armed forces personnel.

**Participants** 4882 randomly selected military personnel deployed to Iraq since 2003 and a subset of 378 whose vaccination records were accessed.

**Main outcome measures** Psychological distress, fatigue, symptoms of post-traumatic stress disorder, health perception, and multiple physical symptoms.

**Results** Personnel who reported receiving two or more vaccinations on a single day were more likely to report symptoms of fatigue (adjusted risk ratio 1.17, 95% confidence interval 1.05 to 1.30), show caseness according to the general health questionnaire (1.31, 1.13 to 1.53), and have multiple physical symptoms (1.32, 1.08 to 1.60). These associations were no longer significant when number of vaccinations recorded in individuals' medical records was used as the independent variable.

**Conclusions** Multiple vaccinations given to personnel in the UK armed forces in preparation for deployment to Iraq are not associated with adverse health consequences when vaccinations are recorded objectively from medical records. Adverse health consequences associated with self reported multiple vaccinations could be explained by recall bias.

### INTRODUCTION

Several studies have found an association between self reported multiple vaccinations in service personnel deployed to the 1991 Gulf war and ill health in Gulf war veterans.<sup>1-6</sup> While multiple vaccinations were associated with the onset of symptoms, they were not a risk factor for the continuation of poor health.<sup>7</sup> Researchers, however, did not have contemporaneous vaccination records. Other studies that did not find such an association<sup>8,9</sup> have led to concern over the validity of earlier findings. It is argued that the sample examined might not have been representative, that there could have been over-reporting of vaccinations,<sup>10</sup> that other exposures could not be adequately controlled for,<sup>11</sup>

and that recall bias was responsible for the results. Retrospective recall of symptoms can be affected by recall bias.<sup>12</sup>

We examined the impact of receiving multiple vaccinations on health within two samples: one in which receipt of vaccinations was self reported and the other (a subset of the first) in which vaccinations were confirmed from individuals' medical records. This allowed us to observe the effects on health of receipt of multiple vaccinations and the influence of recall bias.

### METHODS

#### Sampling

We conducted a cross sectional study of the UK armed forces from June 2004 to March 2006. Two groups of personnel randomly selected from UK armed forces were surveyed: the first had deployed to the 2003 Iraq war, and the second group had not. Details of sampling and methods of data collection are described elsewhere.<sup>13</sup>

We restricted the current analyses to participants who had deployed either during the Iraq war or had subsequently deployed to Iraq. Data were collected through detailed questionnaires. Participants were asked "What was the maximum number of any vaccines that you received in one day in preparation for your deployment?" Examples of the vaccinations administered to service personnel include those against anthrax, tetanus, typhoid, and yellow fever. All such vaccines, with the exception of the anthrax vaccination, were administered routinely. The anthrax vaccination was offered under a separate programme that included information and written consent.

#### Health measures

Our outcome variables included a range of health measures: a 13 item fatigue scale,<sup>14</sup> a general health questionnaire (GHQ-12),<sup>15</sup> a 53 item physical symptom checklist,<sup>2</sup> self perception of health with a single item from the SF-36,<sup>16</sup> and symptoms of post-traumatic stress disorder measured with a 17 item checklist (PCL-C).<sup>17</sup> Table 1 describes case definitions. Over 95% of participants gave us permission to access their medical records.

**Table 1** | Case definitions according to follow-up health outcomes

Scale	Case definition
Fatigue scale	Score of $\geq 4$
GHQ-12	Score of $\geq 4$
Health perception	Rating health as "fair" or "poor"
53 item symptom checklist	$\geq 18$ ( $\geq 90$ th centile)
PTSC (PCL-C)	Score of $\geq 50$

GHQ=general health questionnaire; PTSC=post-traumatic stress centre checklist.

#### Receipt of vaccinations taken from medical records

We randomly selected a subset of 10% of our sample to assess agreement between the number of self reported vaccinations received on a single day and what was recorded in their medical records. A member of the research team visited military medical centres, collected data on vaccination, and recorded the maximum number of vaccinations received on a single day before deployment from 31 July 2002 to 31 March 2006. To avoid missing data, we accessed deployment medical records as well as standard medical records.

#### Analysis

We used weighted  $\kappa$  statistics to assess the level of agreement between self reported number of vaccinations received during one day and the number recorded within a participant's medical records. We used  $\chi^2$  test for categorical data and Mann-Whitney U test for continuous data to identify sociodemographic differences between those whose records were checked and those in the full sample. Logistic binomial regression models were fitted to calculate risk ratios (with 95% confidence intervals) between health outcomes and self reported receipt of multiple vaccinations on one day and health outcomes and receipt of multiple vaccinations on one day according to medical records. This analysis was repeated between self reported receipt and health in the subsample whose records had been accessed. Analyses were weighted according to sampling fractions and adjusted for service (navy, army, and air force), rank (officer or not), sex, age, medical fitness (a dichotomous marker that indicated whether fit to deploy or not, and enlistment status (regular or reserve). Analyses were conducted with Stata 9 (StataCorp, College Station, TX).

#### RESULTS

The participation rate was 61% ( $n=10\,272$ ). Some 4882 participants had deployed either during the invasion of Iraq or on subsequent operations to Iraq and had answered the question pertaining to the maximum number of vaccinations received on one day. Of these, 14% were in the navy, 68% in the army, and 18% in the air force; 16% were officers; 8% were women; and 10% were in the reserves. The median age was 32.2 years (interquartile range 26.4-38.2). An intensive follow-up study of non-responders found no significant differences in health between responders and non-responders.<sup>13,18</sup>

From our selected subsample we were able to access the records of 420 individuals. The medical records for 378 of these individuals recorded that they had

received one or more vaccinations and form the basis of our analysis. Within this group, for 303 individuals we had both self reported and medical records vaccination data. For these 303 individuals we assessed the level of agreement between self reported receipt of multiple vaccinations received on one day and what was recorded in the medical records. The  $\kappa$  score was 0.04 (95% confidence interval -0.02 to 0.12), indicating poor agreement. Table 2 shows the number of self reported vaccinations against the number recorded within medical records.

There were differences in sociodemographic variables between the sample whose records were checked and the full sample (table 3). Among individuals whose records were checked, more were in the army and nearly all were regular personnel compared with the full sample, in which 90% were regular personnel. Also, individuals whose records were checked were marginally younger. We investigated the relation between self reported receipt of no more than one vaccination or two or more vaccinations on one day and adverse health (table 4). After adjustment, we found significant associations between receipt of two or more vaccinations on one day and caseness for fatigue (odds ratio 1.17, 95% confidence interval 1.05 to 1.30), common mental disorder (1.31, 1.13 to 1.53), and multiple physical symptoms (1.32, 1.08 to 1.60).

We repeated the analysis using the number of vaccinations recorded from participants' medical records (table 4). Without exception, we found no health differences between individuals whose medical records indicated they had received no more than one and those who had received two or more vaccinations on a single day.

Table 4 also shows results of the analysis between health and self reported number of vaccinations restricted to those individuals whose records had also been checked. After adjustment, we found significant associations between receipt of two or more vaccinations and caseness for fatigue (1.57, 1.06 to 2.33) and common mental disorder (1.89, 1.08 to 3.30).

#### DISCUSSION

In this study of personnel deployed to Iraq we found that recall of the number of vaccinations received on a single day cannot be considered reliable. This is not the case for individual vaccinations—for example, self reported uptake of the anthrax vaccinations by UK and US military personnel is highly reliable.<sup>19,20</sup> Recall bias

**Table 2** | Number of self reported vaccines against number of vaccines recorded in medical records (for individuals who received one or more vaccinations)

Self report	Medical records			
	1	2	3	$\geq 4$
1	68	38	9	4
2	70	26	13	1
3	24	15	14	0
$\geq 4$	11	6	1	3

**Table 3** | Demographic characteristics between those whose medical records were checked and those whose records were not checked. Figures are numbers (percentages\*) of participants unless stated otherwise

	Self reported vaccination (n=4882)	Medical records checked (n=420)	P value†
<b>Service:</b>			
Navy	669 (14)	44 (11)	<0.001
Army	3376 (68)	212 (50)	
Air force	837 (18)	164 (39)	
<b>Rank:</b>			
Officer	825 (16)	57 (13)	0.126
Other ranks	4057 (84)	363 (87)	
<b>Sex:</b>			
Male	4436 (92)	388 (92)	0.579
Female	446 (8)	32 (8)	
<b>Enlistment status:</b>			
Regular	3981 (90)	419 (100)	<0.001
Reservist	901 (10)	1 (0)	
Mean age (95% CI)	32.9 (32.7 to 33.14)	31.8 (31.1 to 32.5)	0.005

\*Percentages adjusted to take account of sampling fractions.

†P values from  $\chi^2$  except for age, which is from Mann-Whitney.

seems to mediate an association between self reported uptake of multiple vaccinations and experiencing poorer health. Such associations were no longer significant, however, when we repeated the analyses using receipt of vaccinations recorded from an individual's medical records rather than self report. In view of these findings, we conclude that there is no evidence that receiving multiple vaccinations has resulted in adverse health for UK service personnel deployed to Iraq since 2003.

What do these findings tell us about multiple vaccines and earlier studies on illness after the 1991 Gulf war? Important differences exist in the administration of medical countermeasures between the two wars. In general, vaccinations administered to UK service personnel deployed to Iraq since 2003 were administered before their deployment; this was not the case during the 1991 Gulf war when many personnel received vaccinations while on deployment. Pertussis was not offered to service personnel in 2003 but was used as an adjuvant for the anthrax vaccination in 1991 and was proposed as a possible cause of symptoms.<sup>21</sup> The total number of vaccines reportedly received in UK Gulf war veterans was considerably higher than in 2003, and most of the studies were not limited to total vaccines received on a single day but before and during deployment. In these earlier studies many participants reported receiving six or more vaccines, and the association was concentrated in those in this extreme group. Furthermore, while there was a health effect to be explained after the 1991 Gulf war, there has not been evidence of a new "Iraq war syndrome."<sup>13,22</sup>

#### Strengths and weaknesses

One strength of this study was that we were able to analyse data from both self reported measures and medical records about the number of vaccinations received. This allowed us to ascertain both the effects of vaccinations on health and the possible impact of recall bias. Our sample was randomly selected and representative of the UK armed forces.

There were sociodemographic differences between the full sample and the subset of people whose medical

**Table 4** | Health comparisons between individuals according number of vaccinations received on single day and self reported vaccination, vaccination in medical records, and subsample of self reports with medical records also checked. Figures are numbers (percentage\*) of participants

	Received no more than 1 vaccination on 1 day	Received $\geq 2$ vaccinations on 1 day	Risk ratio (95% CI)	
			Unadjusted	Adjusted†
<b>Self reported vaccination</b>				
Fatigue case	366/1266 (29)	1036/2893 (35)	1.23 (1.11 to 1.35)	1.17 (1.05 to 1.30)
Common mental disorder (GHQ-12)	199/1272 (16)	635/2901 (21)	1.37 (1.18 to 1.58)	1.31 (1.13 to 1.53)
Multiple physical symptoms	125/1289 (10)	406/2924 (14)	1.41 (1.17 to 1.71)	1.32 (1.08 to 1.60)
Health perception	134/1277 (10)	359/2914 (12)	1.13 (0.94 to 1.37)	1.02 (0.84 to 1.24)
PTSD (PCL-C)	43/1265 (3)	130/2893 (4)	1.23 (0.87 to 1.73)	0.98 (0.69 to 1.39)
<b>Medical records of vaccination</b>				
Fatigue case	66/216 (31)	45/158 (29)	0.94 (0.68 to 1.29)	0.92 (0.66 to 1.28)
Common mental disorder (GHQ-12)	49/217 (23)	24/159 (15)	0.67 (0.43 to 1.04)	0.73 (0.47 to 1.14)
Multiple physical symptoms	21/218 (10)	15/160 (9)	0.98 (0.52 to 1.84)	1.07 (0.58 to 1.97)
Health perception	28/216 (13)	10/159 (6)	0.49 (0.24 to 0.97)	0.54 (0.27 to 1.08)
PTSD (PCL-C)	11/214 (5)	6/158 (4)	0.74 (0.28 to 1.96)	0.81 (0.31 to 2.15)
<b>Self report and medical records</b>				
Fatigue case	26/118 (22)	63/181 (35)	1.58 (1.07 to 2.35)	1.57 (1.06 to 2.33)
Common mental disorder (GHQ-12)	14/118 (12)	41/183 (22)	1.89 (1.07 to 3.32)	1.89 (1.08 to 3.30)
Multiple physical symptoms	7/119 (6)	19/184 (10)	1.76 (0.70 to 4.06)	1.81 (0.79 to 4.15)
Health perception	9/117 (8)	21/183 (12)	1.50 (0.71 to 3.16)	1.46 (0.69 to 3.13)
PTSD (PCL-C)	3/116 (3)	8/182 (4)	1.70 (0.46 to 6.31)	1.60 (0.44 to 5.55)

GHQ=general health questionnaire; PTSC=post-traumatic stress checklist.

\*Percentages adjusted to take account of sampling fractions.

†Adjusted for age, sex, service, rank, fitness to deploy, and regular/reservist status.

### WHAT IS ALREADY KNOWN ON THIS TOPIC

Several studies have implicated multiple vaccinations as a risk factor for the excess ill health observed in Gulf war veterans

Previous studies have relied on retrospective self report of vaccination

### WHAT THIS STUDY ADDS

Although self reported multiple vaccines were associated with illness, there was no such association when multiple vaccinations were ascertained from contemporaneous medical records  
Earlier associations between self reported receipt of multiple vaccinations and illness were probably caused by recall bias

records were accessed. In particular, the medical records that were checked were almost exclusively those of regular personnel. We have previously found that reservists were at increased risk of ill health after deployment to Iraq,<sup>13</sup> and we adjusted our current analyses for regular or reserve status. Finally, we recognise the self reported measure of multiple vaccinations used in this paper was crude (one question), and data were collected between two and three years after participants had received vaccinations. This might mean that individuals' responses about receipt of multiple vaccinations were more prone to recall bias than one might normally expect. While this might limit our findings that used self reported measures of vaccination uptake, data collected from medical records would be unaffected.

Evidence from Gulf war veterans indicates that recall of exposures was associated with current rating of health. Reporting new exposures was associated with a worsening of health.<sup>23</sup> Within Gulf war veterans most exposures were associated with most outcomes, which points to evidence of recall bias.<sup>24</sup>

### Conclusions

Receipt of multiple vaccinations in UK armed forces personnel before the 2003 Iraq war has not resulted in adverse health. Recall bias was evident with self reported measures of receipt of vaccinations. It is difficult to quantify the extent to which similar processes might have accounted for the reported associations between self reported multiple vaccinations and illness after the 1991 Gulf war.

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