Papers

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Incidence of cancer among UK Gulf war veterans: cohort study

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Abstract

Objectives To determine whether incidence rates of cancer are higher in UK service personnel who were deployed in the Gulf war than in those not deployed and whether any increased risk of cancer is related to self reported exposures to potentially hazardous material during the period of deployment.
Design A cohort study with follow up from 1 April 1991 (the end of the Gulf war) to 31 July 2002.
Participants 51 721 Gulf war veterans and 50 755 service personnel matched for age, sex, rank, service, and level of fitness who were not deployed in the Gulf (the Era cohort).
Main outcome measures Incident cancers, identified on the NHS central register.
Results There were 270 incident cancers among the Gulf cohort and 269 among the Era cohort (incidence rate ratio 0.99, 95% confidence interval 0.83 to 1.17). There was no excess in site specific cancers among the Gulf cohort. Adjustment for lifestyle factors (smoking and alcohol consumption) did not alter these results. In the Gulf cohort, risk of cancer was not related to multiple vaccinations or exposure to pesticides or depleted uranium during deployment.
Conclusion There is no current excess risk of cancer overall nor of site specific cancers in Gulf war veterans. Specific exposures during deployment have not resulted in a subsequent increased risk of cancer. The long latent period for cancer, however, necessitates the continued follow up of these cohorts.

Introduction

Studies among UK veterans of the Gulf war have shown an excess of self reported morbidity compared with that seen in members of the armed forces who were serving at the time of the Gulf war (1991) and were fit for active service but were not deployed.[1 2] The excess is evident across all types of morbidity, but there are no unusual clusters of symptoms.[2 3] The symptoms most commonly reported are non-specific, such as fatigue, stiffness, sleep disturbance, sudden changes of mood, irritability, and poor memory.

There has been concern about a possible link between service in the Gulf and an increased risk of cancer, particularly in relation to personnel who were exposed to depleted uranium. A review of the evidence, however, concluded that, except in extreme circumstances, any excess risk is likely to be small.[4] A US study among a sample of Gulf war veterans found an excess of testicular cancer in the short term,[5] while a study of admissions to hospital among US Gulf War veterans found excess admissions for cancers (mostly benign) during 1991. Mortality studies of US[6] and UK veterans,[7] however, found no increased risk of death from cancer.

We examined whether UK Gulf veterans have experienced increased incidence rates of cancer in the 11 years since the end of the war compared with service personnel not deployed; whether any excess risk, if found, could be explained by the possible confounding effects of lifestyle factors (such as cigarette smoking and alcohol consumption); and whether risk of cancer is related to self reported exposures to potentially hazardous material during the period of deployment.

Methods

We carried out a cohort study of all UK armed forces personnel who served in the Gulf area sometime between September 1990 and June 1991 (the "Gulf" cohort). Specific details of the "Gulf area" as defined for this study have previously been described.[7] A comparison group of the same size was randomly selected from members of the armed forces who were in service on 1 January 1991 but who were not deployed to the Gulf area (the "Era" cohort). This comparison group was stratified to match the Gulf cohort on age, sex, service branch and rank, and (for the army and air force) level of fitness for active service. Staff from the Gulf Veterans' Illnesses Unit of the Ministry of Defence identified Gulf cohort members and selected Era cohort members.

Details of all members of the two cohorts were sent to National Statistics for identification on the NHS central register. This register was established in 1939 and contains an entry for everyone in the United Kingdom who has ever been registered with a general practitioner and all people born in, or who have immigrated to, the United Kingdom. The register contains information on cancers diagnosed, including date of diagnosis and information on site of cancer, coded according to ICD-10 (international classification of diseases, 10th revision). Information is also available (with dates) on deaths and on people emigrating from the United Kingdom.

Over 96% of members of both cohorts were identified and "flagged" on the NHS central register and are included in the current analysis. We included information on the first diagnoses of malignant cancer (ICD-10 codes C00-C95) registered on the NHS central register with date of diagnosis before 31 July 2002. We calculated person years at risk for cancer from 1 April 1991 (the nominal end of the Gulf War) until the earliest of either date of emigration from the United Kingdom, date of death, date of first diagnosis of cancer, or 31 July 2002.

We analysed the data with a Cox proportional hazards model with adjustment for sex, age group, service branch and rank, and a comparison between Gulf and Era veterans, that is, expressed as an incidence rate ratio (equivalent to the hazard ratio) with 95% confidence interval. To determine whether the incidence rate ratio changed with time, it was calculated separately for the periods before (inclusive) and after December 1997 (this date

Table 1 Morbidity surveys among Gulf War veterans and service personnel who were not deployed in the Gulf (Era cohort)

Survey	Reference	Date of survey	No of participants	
			Gulf	Era cohort
1	Unwin, 1999[1]	Sept 1997 - Nov 1998	2 735	2 422
2	Cherry, 2001[2]	Dec 1997 - Sep 1999	8 081	3 935
3	Maconochie, 2003[8]	Aug 1998 - Mar 2001	25 084	19 003

Table 2 Demographic and military characteristics of cohort members eligible for follow up according to whether they served in the Gulf. Figures are numbers (percentages) of members

	Gulf cohort (n=51 721)	Era cohort (n=50 755)	Total
Men	50 637 (98)	49 685 (98)	100 322 (98)
Women	1 084 (2)	1 070 (2)	2 154 (2)
Age (years):			
<20	6 165 (12)	6 038 (12)	12 203 (12)
20-24	18 390 (35)	17 880 (35)	36 270 (35)
25-29	12 463 (24)	12 287 (24)	24 750 (24)
30-34	7 648 (15)	7 569 (15)	15 217 (15)
35-39	4 197 (8)	4 173 (8)	8 370 (8)
>39	2 858 (6)	2 808 (6)	5 666 (6)
Rank:			
Officer	5 779 (11)	5 626 (11)	11 405 (11)
Other ranks	45 942 (89)	45 129 (89)	91 071 (89)
Service branch:			
Army	36 272 (70)	35 324 (70)	71 596 (70)
Navy	5 738 (11)	5 706 (11)	11 444 (11)
Air Force	9 711 (19)	9 725 (19)	19 436 (19)

Table 3 Occurrence of cancer among cohort members according to whether they served in the Gulf: demographic and military characteristics

	Gulf cohort (n=51 721)	Era cohort (n=50 755)	Incidence rate ratio (95% CI)
All cancers	270	269	0.99 (0.83 to 1.17)
Men	257	256	0.99 (0.83 to 1.17)
Women	13	13	0.98 (0.47 to 2.12)
Age (years):			
<20	11	12	0.90 (0.40 to 2.03)
20-24	39	48	0.79 (0.52 to 1.21)
25-29	46	41	1.11 (0.73 to 1.69)
30-34	41	40	1.02 (0.66 to 1.57)
35-39	52	38	1.37 (0.90 to 2.08)
>39	81	90	0.89 (0.66 to 1.20)
Rank:			
Officer	77	64	1.18 (0.84 to 1.64)
Other ranks	193	205	0.93 (0.76 to 1.13)
Service branch:			
Army	170	175	0.95 (0.77 to 1.17)
Navy	38	26	1.46 (0.88 to 2.40)
Air Force	62	68	0.92 (0.65 to 1.29)

was chosen to give the same number of incident cancers in the two time periods).

The Gulf and Era cohorts also acted as a sampling frame for three morbidity surveys conducted between 1997-2001.[1 2 8] The first two surveys, both surveys of general health, drew random samples from each of the cohorts (using non-overlapping samples) while the third survey, a study of reproductive and child health, included all people in both cohorts (table 1). These studies collected information in a consistent way about tobacco smoking (current smoker, previous smoker, never smoker), alcohol intake at the time of the survey, and, in the Gulf cohort, exposures to potentially hazardous material during service in the Gulf. We used information from the third study if possible (n=40 853) and otherwise from studies 1 and 2 (n=8494). Among people participating in at least one of these three morbidity surveys, we compared the incidence of cancer between Gulf and Era cohort members, additionally adjusting for the effects of tobacco smoking and alcohol intake using a Cox proportional hazards model. Secondly, we compared cancer incidence according to certain exposures during the time in the Gulf. Effects are again reported as incidence rate ratios and 95% confidence intervals.

Results

Both cohorts initially comprised 53 462 members. We excluded from follow up 44 from the Gulf cohort and 10 from the Era cohort who had died, two from each cohort who had emigrated, 29 from the Gulf cohort and 52 from the Era cohort who had had cancer diagnosed before 1 April 1991, and five in each cohort who were recorded as having had cancer diagnosed but without a date. A further 3987 people (1653 Gulf and 2334 Era) could not be identified on the NHS central register. Further information from the Ministry of Defence resulted in the exclu-

Table 4 Occurrence of site specific cancer among cohort members according to whether they served in the Gulf

Cancer type	(ICD-10 code)	Gulf	Era	Incidence rate ratio
All cancers	C00-97	268	265	0.98 (0.82 to 1.18)
All excluding non-melanoma skin cancer	All except C44	213	215	0.97 (0.81 to 1.18)
Oral cavity	C00-14	9	8	1.11 (0.43 to 2.87)
Upper digestive tract	C15-17	9	6	1.47 (0.53 to 4.14)
Lower digestive tract	C18-21	13	18	0.71 (0.35 to 1.45)
Bronchus, lung, and trachea	C33-34	14	18	0.76 (0.38 to 1.54)
Malignant melanoma skin	C43	14	10	1.38 (0.61 to 3.10)
Other skin	C44	55	50	1.08 (0.74 to 1.59)
Breast	C50	6	10	0.59 (0.21 to 1.62)
Prostate	C61	7	6	1.15 (0.39 to 3.41)
Testis	C62	39	46	0.83 (0.54 to 1.28)
Urinary tract	C64-8	13	9	1.42 (0.61 to 3.32)
Central nervous system	C69-72	21	25	0.83 (0.46 to 1.48)
Lymphoid and haematopoietic	C81-96	45	34	1.30 (0.83 to 2.03)
All other sites	Various*	23	25	0.90 (0.51 to 1.59)
ICD code unavailable		2	4	

*C22-32, 35-42, 45-49, 51-60, 63, 73-80, 97.

Table 5 Occurrence of site specific cancer among cohort members according to whether they served in the Gulf: adjusted for smoking and alcohol consumption

				Incidence rate ratio	
Cancer type	ICD-10 code	Gulf (n=28 518)	Era (n=20 829)	Unadjusted	Adjusted
All cancers	C00-97	144	95	1.11 (0.86 to 1.44)	1.12 (0.86 to 1.45)
All excluding non-melanoma skin cancer	All except C44	109	75	1.06 (0.79 to 1.43)	1.07 (0.79 to 1.43)
Oral cavity	C00-14	4	5	0.59 (0.16 to 2.18)	0.58 (0.16 to 2.16)
Upper digestive tract	C15-17	2	2	0.73 (0.10 to 5.19)	0.69 (0.10 to 4.93)
Lower digestive tract	C18-21	6	6	0.73 (0.24 to 2.27)	0.73 (0.24 to 2.27)
Bronchus, lung, and trachea	C33-34	3	5	0.49 (0.10 to 1.84)	0.41 (0.10 to 1.73)
Malignant melanoma skin	C43	10	5	1.46 (0.50 to 4.28)	1.50 (0.51 to 4.40)
Other skin	C44	35	20	1.28 (0.74 to 2.22)	1.30 (0.75 to 2.26)
Breast	C50	5	4	0.91 (0.25 to 3.41)	0.98 (0.26 to 3.64)
Prostate	C61	4	3	0.98 (0.22 to 4.36)	1.03 (0.23 to 4.62)
Testis	C62	24	15	1.17 (0.61 to 2.23)	1.17 (0.61 to 2.23)
Urinary tract	C64-8	7	4	1.28 (0.37 to 4.37)	1.29 (0.38 to 4.41)
Central nervous system	C69-72	12	8	1.10 (0.45 to 2.68)	1.08 (0.44 to 2.65)
Lymphoid and haematopoietic	C81-96	24	11	1.60 (0.78 to 3.26)	1.60 (0.79 to 3.28)
All other sites	Various*	8	7	0.84 (0.30 to 2.31)	0.84 (0.30 to 2.32)
ICD code unavailable		2	0		

*C22-32, 35-42, 45-49, 51-60, 63, 73-80, 97.

sion of eight from the Gulf cohort and 304 from the Era cohort who did not meet the entry criteria. Table 2 gives the demographic characteristics of the 51721 and 50755 cohort members who were followed up.

During follow up cancer was diagnosed in 270 Gulf veterans and 269 Era veterans (incidence rate ratio 0.99, 95% confidence interval 0.83 to 1.17) (table 3). There was no large or significant excess of cancers in either men or women or in any service branch, rank, or age group. The incidence rate ratio did not differ significantly between the period up to and including 1997 (1.04, 0.82 to 1.32) and the later period (0.93, 0.74 to 1.19). After exclusion of non-melanoma skin cancers and cancers for which site information was unavailable, there were a total of 213 and 215 Gulf and Era veterans, respectively, in whom cancer was diagnosed (0.97, 0.81 to 1.18) (table 4).

A comparison of incidence rates of cancer among subgroups of cohort members who participated in one of the morbidity surveys and provided information on smoking and alcohol similarly showed no significant excess of cancers among the Gulf veterans (1.11, 0.86 to 1.44). This incidence rate ratio was slightly, but not significantly, higher than that among cohort members who did not take part in one of the morbidity surveys (0.95, 0.75 to 1.19). Among cohort members who did participate in a morbidity survey, the incidence rate ratio did not change (1.12, 0.86 to 1.45) after we adjusted for smoking status (current, past, never smoker) and for the usual intake of alcohol at the time they completed the questionnaire (table 5). This additional adjustment for tobacco and alcohol intake also resulted in little or no change in any of the risks for site specific cancers (table 5). Finally, among the Gulf veterans who participated in at least one of the morbidity surveys we examined the incidence of cancer with respect to some of the exposures reported during deployment to the Gulf. Neither exposure to pesticides (through handling, personal use, or sprayed accommodation) nor multiple vaccination against anthrax, plague, and pertussis nor reported exposure to depleted uranium was associated with any subsequent significant excess risk of cancer, either overall (table 6) or for site specific cancers (data not shown).

Discussion

Our study of 102 476 veterans has shown that the incidence of cancer in those who served in the Gulf was similar to that in veterans who were fit for active service but were not deployed. This

Table 6 Risk of any cancer by exposure agent among cohort members who served in the Gulf

Exposure agent	Not exposed		Exposed		Incidence rate ratio (95% CI)
	Total	Cancers	Total	Cancers	
Multiple vaccination (anthrax, plague, pertussis)	21 313	107	7 205	39	1.08 (0.75 to 1.56)
Used personal pesticides or insecticides	13 125	82	15 393	64	0.66 (0.48 to 0.92)
Handled pesticides	26 467	134	2 051	12	1.16 (0.64 to 2.09)
Living quarters treated with pesticides	22 251	115	6 267	31	0.96 (0.64 to 1.42)
Depleted uranium	26 426	139	2 092	7	0.63 (0.30 to 1.36)

What is already known on this topic

Veterans of the 1990-1 Gulf war have an excess of self reported symptoms

Their mortality experience (including cancer mortality) is similar to that seen in military personnel who were serving at the same time but who were not deployed in the Gulf

What this study adds

Incidence of and mortality from cancer in Gulf War veterans is almost identical to that seen in veterans who were not deployed in the Gulf

This comparison takes account of lifestyle factors (smoking and alcohol consumption), which are known to influence cancer risk

The risk of cancer was no higher in Gulf war veterans who reported exposure to specific substances such as depleted uranium or pesticides

result did not change when we took into account the effects of lifestyle (smoking and alcohol consumption) among a subgroup who participated in one of the UK morbidity surveys. In this subgroup there was no significant excess risk of cancer associated with reported exposure to pesticides, multiple vaccination against anthrax, plague and pertussis, or exposure to depleted uranium.

There are several methodological considerations regarding the current study. Firstly, though we excluded the small number of cohort members who could not be traced through the NHS central register, some information was available on diagnoses of cancer in these people from alternative sources. Among them the number of cancers was higher in the Era cohort (n = 11) than in the Gulf cohort (n = 3). Secondly, information on lifestyle habits was obtained only at the time of the morbidity surveys, 6-10 years after the Gulf war. These data show that the proportion who were current smokers and the amount of alcohol drunk in a week were similar in the two cohorts,[1 2] and thus the estimates of rate ratios are little changed with adjustment for these factors. We will have underestimated the relative risk of cancer in Gulf war veterans only if they habitually smoked less or drank less alcohol and had recently increased consumption (or vice versa in relation to Era veterans). Neither seems plausible. Finally, the "exposures" reported at the time of the Gulf are, in the absence of any objective measure of individual exposure, based on self report. The concern about self reported exposures is that people who develop an adverse health outcome may differentially recall past events. This is most likely to result in ill people over-reporting past exposures and well people under-reporting (that is, forgetting) them. With either scenario, the observed effect of an exposure on health will be overestimated and therefore this could not explain our failure to detect true adverse effects of any of these exposures if they were to exist.

Relatively little information has been published on cancers among Gulf war veterans. The mortality study among the same group of UK Gulf and Era veterans showed only a small non-significant increased risk of death from cancer nine years after the end of the conflict (mortality rate ratio 1.11, 0.73 to 1.67).[7] A mortality study among US veterans also failed to show an increased risk of death from cancer seven years after the end of the conflict (0.90, 0.81 to 1.01, for men; 1.11, 0.78 to 1.57 for women).[6] In the US study there was no increased risk of death from cancer among Gulf War veterans who were potentially exposed to nerve gas as a result of US troops exploding abandoned Iraqi munitions (0.95, 0.69 to 1.30). An early report of an increased risk of testicular cancer in the period immediately after deployment was no longer evident on further follow up. It was concluded that the original observed excess was because healthy serviceman were selected for deployment and care was deferred during deployment.[5]

In summary, our results confirm that there is no overall increase in incidence of or mortality from cancer among UK Gulf veterans. Neither was the incidence of cancer higher among those veterans who reported specific exposures during their deployment. Although this study should provide some reassurance of a lack of association between deployment to the Gulf and increased risk of cancer, the long latent period for cancer requires that these cohorts should continue to be followed up and their experience of cancer monitored.

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