The Centre for Military and Veterans' Health

The Middle East Area of Operations (MEAO)

Mortality and Cancer Incidence Study

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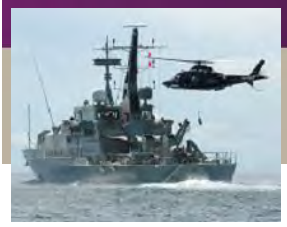



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Executive Summary

The Middle East Area of Operations (MEAO) mortality and cancer incidence study is part of a series of studies conducted by the Centre for Military and Veterans' Health (CMVH) to investigate the health and well-being of the Australian Defence Force (ADF) veterans who have deployed on active service to the Middle East. The deployment to the MEAO included operations within Iraq, Afghanistan, Gulf States and the maritime environment in the vicinity of the Arabian Gulf. CMVH has previously conducted mortality and cancer incidence studies of deployments to the Near North of Australia (Solomon Islands, Bougainville and East Timor).

This report presents the rates of mortality and cancer incidence in those deployed to the MEAO (the MEAO veterans group) and in a group of ADF personnel who did not deploy to the MEAO (the comparison group). One of the main questions of interest is whether those who deployed to the MEAO have higher rates of mortality or cancer compared with the comparison group. The other main question is how these rates compare to those of their Australian contemporaries.

The MEAO veterans group was derived from 33,571 ADF personnel deployed to the Middle East at some stage during the period 23 February 2000 to 25 January 2012. The comparison group was a stratified random sample of 16,765 drawn from ADF members who served in this period and was similar to the MEAO veterans group on the basis of service (Navy, Army, Air Force), service type (regular or reserve), sex and the date of enlistment (before 2001, 2001-2005 and 2005 onwards). The rates of mortality and cancer incidence in each group were calculated as the total number of events divided by the total time at risk within the follow-up period. Relative rates (RRs) and 95% confidence intervals (CI) were calculated for the MEAO veterans group relative to the comparison group.

Standardised mortality ratios (SMRs) and standardised incidence ratios (SIRs) were used to compare mortality and cancer rates respectively in the MEAO veterans and comparison groups to Australian norms. The number of observed events in the ADF group was divided by the number of events expected based on Australian rates for the various age strata and multiplied by 100 to obtain these standardised ratios.

Linkage with the National Death Index identified 105 deaths in the MEAO veterans group and 145 deaths in the comparison group between the start of follow-up and 31 December 2011.

Cause of death data were available up to 31 May 2010. The overall death rate in the MEAO veterans group was significantly lower than that observed in the comparison group (RR 0.40 95% CI (0.31, 0.51)). Lower death rates among the MEAO veterans group were also observed when deaths from specific causes were assessed. It is likely that this deficit of deaths is due in part to a strong "healthy warrior effect".

All-cause mortality was lower among MEAO veterans than in the Australian population of the same age (SMR 52.1, 95%CI (37.4, 72.6)). In contrast, the comparison group of ADF personnel had a higher all-cause death rate (SMR 172.4, 95%CI (137.7, 215.8)).

Cancer data were available from the National Cancer Statistics Clearing House up to 31 December 2008. There were 102 cancers (1.23 per 1000 person-years at risk) in the MEAO veterans group and 89 cancers (2.16 per 1000 person-years) in the comparison group between the start of follow-up and 31 December 2008. After adjusting for age group and sex, there was no clear difference in the cancer incidence rate between the MEAO veterans group and the comparison group (RR 1.05,

95% CI (0.77, 1.43)). However, the rate of cancers in male urogenital organs was higher in the MEAO group compared to the comparison group (adjusted RR 1.99, 95% CI (1.09, 3.64)).

The MEAO veterans group and the comparison group had cancer incidence rates similar to those observed in the Australian population of the same ages (SIRs 106.6, 95% (87.8, 129.4) and 107.6, 95% CI (87.4, 132.5) respectively). MEAO veterans had higher rates of prostate cancers than expected based on rates in the Australian population (SIR 231.9, 95% CI (144.1, 373.0)).

All results presented in this report are based on a short average follow-up period (approximately 3 years follow-up for cancer incidence results and between 4 and 5 years for the analysis of mortality). Because of the short follow-up period it may be premature to interpret the results without resorting to speculation. The latency period, between exposure to a carcinogen and a cancer presenting, is likely to be longer than the follow-up time accrued to date. Therefore, the cancer statistics presented in this report should be interpreted with caution.

Continued follow-up of the MEAO study population will allow the inclusion of everyone who served in the MEAO (and a relevant comparison group). With increasing time the number of deaths and cancers that develop in the post deployment period will increase. The increased statistical power gained from a longer period of follow-up will also enable the identification of specific groups at increased risk of cancer and mortality. This study has provided a sound baseline and established the methodology to enable continued regular follow-up, allowing a clearer picture of the health outcomes of MEAO veterans to emerge.

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1 Introduction and research aims

The Middle East Area of Operations (MEAO) Mortality and Cancer Incidence Study is part of a series of studies that aim to examine the health and well-being of Australian Defence Force (ADF) veterans who have deployed on active service overseas. It is being conducted by the Centre for Military and Veterans' Health (CMVH) at the University of Queensland. CMVH has previously conducted mortality and cancer incidence studies of military deployments to Australia's Near North Area of Influence (Solomon Islands, Bougainville and East Timor).

One of the main questions of interest is whether veterans are at an increased risk of death or illness compared to their Australian contemporaries. Deployment may increase the risk of ill health in a number of ways. A psychological trauma may lead to a later suicide; a physical trauma may lead to a chronic disease that reduces life expectancy; development of post-traumatic stress disorder, or known or unknown environmental toxins, may lead to death or cancer. Differences in diet and in the prevalence of smoking and alcohol consumption whilst on deployment may also lead to an increased risk of cancer or other conditions.

1.1 Aims and objectives

The aims of the MEAO Mortality and Cancer Incidence Study are to determine the rates of mortality and cancer incidence among ADF personnel previously deployed to the MEAO.

The MEAO Mortality and Cancer Incidence Study is designed to assess health outcomes over an extended period of time. With sufficient follow-up, the study will be able to address the following questions.

i) Is mortality higher among MEAO veterans than in a comparison group of ADF personnel not deployed to the MEAO and how do these groups compare with the general population?

Post-conflict syndromes have followed wars since at least the United States Civil War [9] and the Boer war [10]. Focus on the psychological and physical ill health of veterans in the United States became acute following the Vietnam conflict when the first five year period of separating from the military was associated with an increased risk of dying from motor vehicle accidents, suicide, homicide and accidental poisoning [3]. More recent studies of British and American veterans of the 1990-1991 Gulf War have also found increased mortality rates due to external causes in the years immediately following return from deployment [11, 13].

Comparisons of rates of mortality and cancer incidence between MEAO veterans and the Australian population provides a relative estimate for the deployed group ; however, there may be systematic biases. The Healthy Worker Effect refers to the well-established finding that individuals who are in the workforce are healthier than the average population: the "sicker" or "unhealthier" components of the population are unable to work [18]. Therefore a comparison of mortality or cancer incidence for an occupational group relative to the general population may give the appearance of "better health" in the group of workers. This phenomenon has been extended to the "Healthy Soldier Effect". The recruitment processes and enlistment requirements of a Defence force such as the ADF ensure that members are "healthier" than other workers [18]. More recently the "Healthy Warrior Effect" has been observed [7] as Defence personnel who undertake operational deployments are required to be at the highest level of fitness, and have undergone another level of health screening beyond those for military personnel not deployed.

Therefore for the MEAO Mortality and Cancer Incidence Study, comparisons were made between deployed personnel and a comparison group of ADF members who were not deployed to the MEAO, as well as comparisons with the Australian population.

i) Is cancer incidence higher among MEAO veterans than in a comparison group of ADF personnel not deployed to the MEAO and how do these groups compare with the general population?

A study of Australian veterans of the Korean War has shown higher than expected incidence of cancer compared with the Australian community [17]. While studies of British veterans of the first Gulf War had not shown elevated rates of cancer after one decade [14], a more recent study of United States Gulf War veterans found an increased risk of lung cancer [19].

ii) Do mortality and cancer incidence rates differ based on timing of deployment?

Investigation into the health of UK veterans of the Gulf and Iraq Wars has noted that research in the military tends to focus on comparisons between deployed and non-deployed personnel, not temporal trends [8]. However, recent research on military personnel deployed to the Middle East provides evidence of changes over time in factors such as the severity of injuries sustained [12] and symptom reporting [8]. Over a longer time period than covered in this present report it will be possible to compare mortality and cancer incidence rates between those who deployed at different stages of the conflict.

iii) How does mortality and cancer incidence compare between subgroups within those deployed to the MEAO?

In the longer term, the study has the potential to compare mortality and cancer incidence between different groups of MEAO veterans. For example, the health outcomes of those deployed to Iraq and Afghanistan may be different and those who served in a particular role on deployment may be at higher risk of specific outcomes. For subgroups of the MEAO veterans it will also be possible to assess whether certain self-reported risk factors (e.g., exposures and experiences on deployment) are associated with higher mortality or cancer rates. Those who went to the MEAO may have been stationed in one of four distinct areas: Afghanistan, Iraq, Gulf States and the maritime environment in vicinity of Arabian Gulf. Comparisons between these groups may also be possible.

This report presents outcomes for mortality and cancer incidence. Due to the short period of follow-up observed to date, the focus is on research questions i) and ii):

ii) *Is mortality higher among MEAO veterans than in a comparison group of ADF personnel not deployed to the MEAO and how do these groups compare with the general population?*

iii) *Is cancer incidence higher among MEAO veterans than in a comparison group of ADF personnel not deployed to the MEAO and how do these groups compare with the general population?*

Mortality and cancer incidence rates by broad demographic subgroups within the MEAO veterans and the comparison groups are also presented.

1.2 Background

Following the September 11 attacks on the United States in 2001, Australia announced an ADF contribution to coalition operations against terrorism. The ADF has deployed members of the Royal Australian Navy, Australian Army and Royal Australian Air Force (RAAF) to the MEAO since October 2001 on various operations in Afghanistan, the "coalition of the willing" in Iraq, and other classified locations.

Operations in Iraq included BASTILLE, FALCONER, CATALYST, and KRUGER. More than 20,000 ADF personnel served in Iraq as part of Operation CATALYST between 2003 and 2009, with Australia formally concluding its military commitment to the rehabilitation of Iraq on 31 July 2009. The ADF's Security Detachment, which provided personal protection and physical security in Iraq, remained in Baghdad until complete transfer of security capabilities from the ADF to a civilian contractor in late July 2011.

Under Operation SLIPPER in Afghanistan, which commenced in October 2001, Australian forces contribute to the International Security Assistance Force operations in Afghanistan led by the North Atlantic Treaty Organization (NATO), to maritime security in the MEAO and counter piracy operations in the Gulf of Aden. The deployment to Afghanistan is still ongoing.

The MEAO Census study has collected self-reported information on psychological, environmental and chemical exposures from MEAO veterans. Such exposures have the potential to increase the risk of mortality from specific causes and the incidence of certain types of cancer. This study is designed to document mortality and cancer incidence rates among those deployed to the MEAO and to identify high risk groups over an extended period of follow-up.

2 Methods

2.1 Study design

The MEAO Cancer and Mortality Study is a cohort study designed to analyse the mortality and cancer incidence of ADF personnel over the long term, both while they are currently serving members and once they leave the ADF. The mortality and cancer incidence rates of veterans who deployed to the MEAO are compared with those of a group of ADF personnel who served over the same interval but who did not deploy to the Middle East. In addition, mortality and cancer incidence in both military cohorts is compared with those in the general Australian population.

Information on mortality and cancer incidence in the Australian population was obtained from the National Death Index (NDI) and the National Cancer Statistics Clearing House (NCSCH) held by the Australian Institute of Health and Welfare (AIHW).

2.2 Study population

The list of ADF personnel deployed to the MEAO was obtained from PMKeyS, which is the human resource system used by the Department of Defence for all aspects of personnel management. This nominal roll comprised 33,571 ADF personnel deployed to the Middle East between 23 February 2000 and 25 January 2012. The MEAO deployment is ongoing so those deploying for the first time after 25 January 2012 are not currently included in the MEAO nominal roll used in this study. All personnel on the nominal roll form the MEAO veterans group for this study.

The comparison group for the MEAO Mortality and Cancer Incidence Study includes ADF personnel who were not deployed to the Middle East, but were potentially eligible for deployment. This group was selected using random sampling with frequency matching on potential confounding variables. Given the large scale of the MEAO deployment it was not feasible to select a comparison group as large and with similar characteristics from the remaining non-deployed personnel. Therefore, a comparison group half the size of the veterans group was selected (N=16,765). Individuals were eligible for inclusion in the comparison group if they were members of the ADF at some time between November 2001 and January 2012, but they had not deployed to the MEAO. The study was designed so that the MEAO veterans group and the comparison group were as similar as possible, except for the fact that the MEAO veterans group deployed to the MEAO. Both groups may have deployed to other locations.

2.3 Data collection

The full name, sex and date of birth for persons in the MEAO veterans and comparison groups were provided to AIHW for linkage with the National Death Index and the National Cancer Statistics Clearing House. The AIHW is provided with data on vital status by all State and Territory Registrars of Births, Deaths and Marriages.

It is a legal requirement to register all deaths in Australia. Information on the underlying cause of death was available from AIHW for deaths occurring before 31 May 2010. Cause of death (where available) was provided by AIHW using the 10th revision of the International Statistical Classification of Disease codes (ICD 10). While coded cause of death was only available up to 31 May 2010, AIHW were able to provide notifications of date of death (without the cause of death)

up to 31 December 2011. For deaths that had been considered by a coroner, AIHW were able to provide the causes of death to CMVH once ethical approval had been received from the Department of Justice.

AIHW provided cancer incidence records using ICD codes for individuals who consented to linkage with the cancer registries as part of the MEAO Census Study. In addition, AIHW provided de-identified tables of cancer incidence for everyone in the MEAO veterans and comparison groups up to 31 December 2008. For most States AIHW had cancer data complete up to 2009, however, two States were only able to provide data up to 2008. Therefore the cut-off of 31 December 2008 used so the same cut-off date could be applied to all jurisdictions.

2.4 Validating the death and cancer incidence data from Australian Institute of Health and Welfare

The linking of NDI data was undertaken by AIHW in June 2012 using a probabilistic matching program. The AIHW program compares information provided by CMVH, including names, sex and date of birth, with information in the NDI. The matching process identifies some exact matches and a number of "possible" matches. A clerical review of possible matches was undertaken by two CMVH staff members independently of each other.

The clerical review used additional information from a variety of sources. A Google search (http://www.google.com.au) as well as searches on the Australian Department of Defence website (http://www.defence.gov.au) were undertaken for names in the group of "possibly dead" in an effort to confirm vital status.

A similar process was undertaken for the linkage of cancer records by AIHW staff. For the cases where there was uncertainty, AIHW contacted the State or Territory cancer registry to clarify whether the record matched the cancer record on the registry records.

2.5 Statistical methods

In the design phase, power calculations showed that a study of this size had statistical power to detect differences in all-cause mortality and all-types cancer incidence over 10 and 15 years follow-up. The results presented in this report are over a shorter follow-up period and therefore lack the statistical power required to detect overall differences. Likewise, although we present results for specific types of mortality and sites of cancer, these comparisons may also lack statistical power to detect differences in these outcomes.

For the analysis of all-cause mortality a cut-off date of 31 December 2011 was used. It can take some months for a death to appear on the NDI, so allowing a lag of approximately six months from the date of linkage, increased the likelihood of more complete coverage of deaths over the study period

For cause-specific mortality AIHW were able to provide notifications of cause of death up to 31 May 2010. Different cut-off dates were used based on whether all-cause or cause specific deaths were being studied. For cancer incidence a cut-off of 31 December 2008 was used.

For the purposes of statistical analyses, only individuals identified as matches from the NDI linkage were classified as having died. All other individuals were classified as alive. However, a sensitivity analysis was performed which included additional deaths not identified on the NDI but

were known from other sources (such as PMKeyS, Defence notifications or media reports); these could include deaths overseas or coroners' cases not yet included in the NDI.

There were two main comparisons in this analysis:

- rates of death and cancer incidence in the MEAO veterans and comparison groups
- numbers of deaths or cancers in each group, against the expected numbers of deaths or cancers based on rates for the Australian population.

2.5.1 Comparisons between groups

The first step was to determine the rate of death or cancer in each group. This rate is defined as the number of events (i.e., deaths or cancer registrations) divided by the person-years of follow-up for each group.

For each individual it was necessary to calculate the period over which they could have died or been diagnosed with cancer ('time at risk'). For the MEAO veterans group, each person's time at risk was calculated from the date of their first deployment to the Middle East (their start-date). For the comparison group time at risk was calculated from the median start date in the corresponding subgroup among the MEAO veterans group (i.e., for people of the same sex, service, service type and period of enlistment). However, if a comparison group member joined the ADF after this median date, their start date was the date they enlisted in the ADF. This substitution ensured that follow-up did not include the period before a member was recruited to the ADF.

In the mortality analysis, persons were followed up until date of death or the end of the follow-up period, whichever came first. In the cancer incidence analysis persons were followed up until date of cancer diagnosis, date of death or the end of follow-up (31 December 2008), whichever came first. In the analysis of cancer incidence, only a person's first cancer was included. If a person had more than one cancer, the subsequent diagnoses have not been included in the calculations of cancer incidence. The times at risk for all individuals in each subgroup were added together to obtain the person-years of follow-up for the subgroup.

Relative rates were calculated as the rate of an event in the MEAO veterans group divided by the rate in the comparison group. Corresponding confidence intervals were calculated. If the confidence interval does not include 1, the rates are statistically different between the two groups. Relative rates and 95% confidence intervals were calculated for subgroups (such as deaths from specific causes) where more than 20 events were observed.

Adjusted relative rates were calculated using Poisson regression. In these models, the risk of mortality or cancer incidence was allowed to vary by 10-year age band. These models also included adjustment for differences in service and sex.

2.5.2 Comparisons with the Australian population

Comparison of the ADF groups with the Australian population involves comparing the observed number of events with the number of events expected if rates of mortality or cancer incidence were the same in the ADF groups as in the general population.

The expected number of events is based on the number of people in the subgroup and national mortality and cancer incidence rates for people of the same age and sex. These rates were

obtained from AIHW General Record of Incidence of Mortality (GRIM) and Cancer incidence data cubes [1, 2]. The Australian population mortality data were available from AIHW for the years 2001-2007 and the cancer incidence data were available for 2001-2008. The expected number of events in the population was calculated by multiplying the number of person years in each 5-year age and sex group for each calendar year by the rate of mortality or cancer incidence for that age /sex group and year.

The Standardised Mortality Ratio (SMR) and Standardised Incidence Ratio (SIR) were used to compare rates in the ADF groups to Australian norms. These were defined as:

SMR = 100 × (Observed number of deaths / Expected number of deaths)

SIR = 100 × (Observed number of cancers / Expected number of cancers)

A standardised ratio equal to 100 indicates no difference between the observed and expected number of events. A standardised ratio above 100 means that the observed number of events was higher than expected, and a standardised ratio below 100 indicates that the number of events was lower than the expected number. An overall ratio (across all sex and age groups) was calculated using the direct method of standardisation [6]. Statistical p-values and confidence intervals were obtained from Poisson regression models with the observed number of events as the outcome and the expected number as the offset term in the model.

The 95% confidence intervals give a range of values around the estimated standardised ratio. For the SMR and the SIRs results, if the confidence interval does not include 100, the number of events was significantly different from that in the Australian population. We would expect a, statistically significant result to be produced by chance about 5% of the time.

For the analysis of mortality, we did not have death rates in Australian population for the years 2008-2010. Therefore, to calculate the expected number of deaths for the years 2008-2010, the Australian population mortality statistics for 2007 were used.

2.5.3 Cancer data linkage and MEAO Census Study data

As part of the MEAO Census Study participants were asked to provide consent for their study data to be linked with information held in registries (including cancer registries). In total, 12,803 respondents provided consent for linkage.

For those who consented, the details of their cancer (ICD code and date of diagnosis) were linked to their demographic record for analysis. For cancers among people who did not provide consent to linkage, or were not part of the MEAO Census Study, details of their cancers were randomly assigned to a person alive in that year of diagnosis, of the same sex, age group and deployment group (i.e., MEAO veteran or comparison), in order to most accurately estimate the person-years at risk. A marker which indicated whether a cancer occurred before the start of the study or during the follow-up period was also used in this process. This allowed us to estimate the person-years at risk for each deployment group, sex and age group.

2.5.4 Sample size

The MEAO Mortality and Cancer Incidence Study was undertaken on the full nominal roll of ADF members deployed up to January 2012 (N=33,571) to maximize statistical power. The comparison

group comprised 16,765 members randomly selected from PMKeyS and frequency matched on service (Navy, Army or Air Force), service type (Regular or Reserve, based on PMKeyS records January 2012), sex and period when they joined the ADF (before 2001, 2001-2005 and after).

In the future when sufficient numbers of cancers have occurred it will be possible to compare cancer incidence between subgroups within the ADF, including between those who did and did not report specific exposures on deployment. Currently there has not been sufficient follow-up time for enough cancers to have occurred to allow more detailed analysis to be usefully undertaken.

2.6 Ethics approvals

Ethical clearance was received from the Australian Institute of Health and Welfare Ethics Committee (protocol no EC 2011/1/2); The University of Queensland Behavioural & Social Sciences, Ethical Review Committee (protocol no 2010001163); Department of Veterans' Affairs Human Research Ethics Committee (E010/012); and the Australian Defence Human Research Ethics Committee (protocol no 2007/1076393). In addition, ethical clearance was received from each of the State and Territory cancer registries and the Department of Justice in Victoria to access causes of death for those deaths which were considered by a coroner.

3 Results

This section presents the demographic profile of those persons in the mortality and cancer incidence study and the mortality and cancer incidence rates. All-cause mortality up to 31 December 2011 is presented as well as cause-specific mortality up to 31 May 2010.

3.1 Mortality: comparison between study groups

As frequency matching was used to select the comparison group, the demographic characteristics of the MEAO veterans and the comparison group used in the analysis of all-cause mortality were similar with regard to service, service type, sex and period of enlistment (Table 3.1).

The mean age of the MEAO veterans and comparison groups at the commencement of follow-up were 30.9 (Standard Deviation (SD) 8.2) and 32.1 (SD 9.6) years respectively and the distributions of ages shown in Table 3.1 demonstrate that the comparison group was significantly older than the MEAO veterans group. Also 21% of the MEAO veterans had left the ADF by 2012 whereas over half of the comparison group were ex-serving members.

Table 3.1: Demographic characteristics of personnel in the MEAO Mortality study (with start date before 31 December 2011)

	MEAO veterans group (N=32952)[b]		Comparison group (N=16695)[b]		
Characteristic	**n**	**(%)**	**n**	**(%)**	***p*-value[a]**
Age (start of follow-up)					
17- 24	9813	(29.8)	4914	(29.4)	<0.0001
25-34	13848	(42.0)	6116	(36.6)	
35-44	6961	(21.1)	3699	(22.2)	
45-54	2124	(6.5)	1572	(9.4)	
55 and over	206	(0.6)	394	(2.4)	
Sex					
Male	29261	(88.8)	14839	(88.9)	0.78
Female	3691	(11.2)	1856	(11.1)	
Service					
Navy	7345	(22.3)	3660	(21.9)	0.34
Army	17023	(51.7)	8740	(52.4)	
Air Force	8584	(26.1)	4295	(25.7)	
Service Type (2012)[c]					
Regular	24309	(73.8)	12372	(74.1)	0.42
Reserve	8643	(26.2)	4323	(25.9)	
Period of enlistment					
Before 2001	18870	(57.3)	9460	(56.7)	0.09
2001-2005	9506	(28.8)	4795	(28.7)	
2006-2012	4576	(13.9)	2440	(14.6)	
Employee Status (2012)					
Serving	26085	(79.2)	8816	(45.5)	<0.0001
Ex-serving[d]	6867	(20.8)	9100	(54.5)	

[a] Chi-squared test
[b] 619 MEAO veterans and 70 comparisons had start dates after 31 December 2011
[c] Last known service type as of 2012
[d] Includes Inactive Reserves

There were 250 deaths identified through linkage with the NDI before the end of follow-up (31 December 2011), 105 in the MEAO veterans group and 145 in the comparison group. There were 18 additional death records identified before this cut-off date from other sources that were not picked up on the NDI linkage. The primary analyses were undertaken using only those deaths identified through the NDI linkage (n=250), as there may have been differential bias in reporting of deaths from other sources between the MEAO veterans and comparison groups.

In the analyses assessing all-cause mortality, the mean follow-up period among MEAO veterans and the comparison group was 5.1 years and 5.2 years respectively. There were 105 deaths in 169,010 person-years of follow-up in the MEAO veterans group and 145 deaths in 87,521.3 person-years of follow-up among the comparison group. The mortality rate among MEAO veterans was less than half that observed in the comparison group (0.62 and 1.66 per 1000 person-years respectively, Table 3.2).

The mortality rates were highest in males, Army personnel, and those aged 17-24 or over 45 as compared with those aged between 25 and 44. The relative rates for each subgroup ranged from 0.13 to 0.66 indicating markedly lower death rates among those deployed to the MEAO. Each of the relative rates showed that all-cause mortality was statistically significantly lower in the MEAO veterans group (except for the comparison among Navy members where the difference was not statistically significant).

Table 3.2: All-cause death rates for MEAO veterans and comparison groups by demographic characteristics (for those with start date before 31 December 2011)

	MEAO veterans group (N=32952)[f]			Comparison group (N=16695)[f]			
	Deaths	**Pyrs**	**Rate[a]**	**Deaths**	**Pyrs**	**Rate[a]**	**RR (95% CI)**
Overall	105	169010	0.62	145	87521	1.66	0.42 (0.32, 0.54) [b]
Age							
17- 24	16	20555	0.79	19	8772	2.17	0.36 (0.19, 0.71)[c]
25-34	45	77680	0.58	47	32918	1.43	0.41 (0.27, 0.62)[c]
35-44	23	51227	0.45	31	26179	1.18	0.36 (0.21, 0.63)[c]
45-54	16	17218	0.93	21	14285	1.47	0.66 (0.34, 1.27)[c]
55 and over	5	2330	2.15	27	5367	5.03	0.42 (0.16, 1.10)[c]
Sex							
Male	102	149831	0.68	133	77441	1.72	0.44 (0.34, 0.58)[d]
Female	3	19179	0.16	12	10080	1.19	0.13 (0.04, 0.46)[d]
Service							
Navy	25	48151	0.52	29	26108	1.11	0.66 (0.37, 1.17)[e]
Army	58	73626	0.79	79	36119	2.19	0.38 (0.27, 0.54)[e]
Air Force	22	47234	0.47	37	25295	1.46	0.37 (0.22, 0.64)[e]

[a] Rate per 1000 person-years (Pyrs)
[b] Adjusted for age (10 year bands), sex and Service
[c] Adjusted for sex and Service
[d] Adjusted for age (10 year bands) and Service
[e] Adjusted for age (10 year bands) and sex
[f] 619 MEAO veterans and 70 comparisons had start dates after 31 December 2011

Secondary analyses including the 18 death records not in the NDI are provided in an Annex of Supplementary Tables (Tables A-C). These extra 18 deaths comprised 13 from the MEAO veterans group and five from the comparison group. From checking other sources, we found that eight of the 13 deaths in the MEAO veterans group occurred overseas, either in the MEAO or elsewhere. The inclusion of the 18 deaths not identified on the NDI changed the estimates only marginally, and did not alter any of the conclusions presented in this report. Of the 118 deaths among MEAO

veterans identified from all sources (including the NDI), 33 (28%) persons died whilst serving in the MEAO before 31 December 2011. Of the 105 deaths in MEAO veterans identified solely through linkage with the NDI, 28 (27%) died whilst serving in the MEAO.

In the analyses assessing cause-specific mortality, the mean follow-up period was 4.3 years among both the MEAO veterans and the comparison group. The most common category of deaths in both groups was external causes, which includes suicides and transport accidents. The next most common category of death was cancers. Across each of the cause of death categories presented, the death rate was lower among the MEAO veterans group than the comparison group (Table 3.3).

Table 3.3: Cause-specific mortality for the MEAO veterans and comparison groups (for those with start date before 31 May 2010)

	MEAO veterans group (N=28279 Pyrs[e]=120517)		Comparison group (N=14470 Pyrs[e]=62225)		
	Deaths	**Rate[a]**	**Deaths**	**Rate[a]**	**RR[b] (95% CI)**
Overall	65	0.54	123	1.98	0.29 (0.22, 0.40)[c]
Infectious and parasitic diseases (A01-B99)	0		2		
Cancers (C00-C97)	12	0.10	26	0.42	0.42 (0.21, 0.86)[c]
Endocrine and metabolic diseases (E00-E90)	0		2		
Diseases of the nervous system (G00-G99)	0		2		
Diseases of the circulatory system (I00-I99)	7	0.06	18	0.29	0.40 (0.16, 1.01)[d]
Diseases of the digestive system (K00-K93)	1		4		
Ill-defined and unspecified causes (R99)	6		2		
External causes of mortality (V01-Y98)	35	0.29	66	1.06	0.23 (0.15, 0.35)[c]
Suicides (X60-X84)	9	0.07	19	0.31	0.21 (0.09, 0.47)[c]
Transport accidents (V01-V99)	12	0.10	30	0.48	0.17 (0.09, 0.34)[c]
Other accidental injury (W00-X59)	13	0.11	11	0.18	0.52 (0.23, 1.16)[c]
Unknown cause of death	4		1		

[a] Rate per 1000 person-years (Pyrs)
[b] Rate Ratio
[c] Adjusted for age (10 year bands), Sex and Service
[d] Adjusted for age (10 year bands) and Service (there were no deaths from circulatory diseases among women)
[e] Person-years

3.2 Mortality: comparison with the Australian population

The number of deaths in the MEAO veterans group was lower than the expected number calculated from rates in the general population. This was observed for all-cause deaths and for deaths from cancer, circulatory diseases and external causes (Table 3.4). In contrast, the number of deaths in the comparison group was higher than expected from the general population for all-cause mortality and external cause mortality. There was a statistically significant of deaths from transport accidents in the comparison group compared to the general population (Table 3.4). The percentage of the total number of deaths due to transport accidents was 18% in the MEAO veterans group and 24% in the comparison group. The most common transport deaths were from car accidents (3 among MEAO veterans and 12 in the comparison group) and motor cycle accidents (7 among MEAO veterans and 11 in the comparison group).

Table 3.4: Cause specific mortality for MEAO veterans and comparisons compared with death rates in the Australian population (for those with start date before 31 May 2010)

	MEAO veterans group (N=28279 Pyrs[d]=120517)			Comparison group (N=14470 Pyrs[d]=62225)		
	D[a]	E[b]	SMR[c] (95% CI)	D[a]	E[b]	SMR[c] (95% CI)
All cause	65	143.8	45.2 (35.4, 57.6)	123	101.0	121.7 (102.0, 145.3)
Cancers (C00-C97)	12	27.8	43.2 (24.5, 76.1)	26	28.0	92.7 (63.1, 136.2)
Diseases of the circulatory system (I00-I99)	7	20.3	34.4 (16.4, 72.2)	18	18.3	98.3 (61.9, 156.0)
External causes (V01-Y98)	35	65.0	53.8 (38.7, 75.0)	66	32.3	204.6 (160.7, 260.4)
Suicides (X60-X84)	9	22.9	39.3 (20.4, 75.4)	19	11.4	166.2 (106.0, 260.6)
Transport accidents (V01-V99)	12	14.8	81.3 (46.1, 143.1)	30	6.7	445.3 (311.3, 636.9)

[1] As 2008-2010 death rates from AIHW were unavailable at the time of the analysis, 2007 Population Deaths rates are used to project population death rates for 2008 -2010
[a] Observed number of deaths
[b] Expected number of deaths
[c] Standardised Mortality Ratio
[d] Person-years

3.3 Cancer incidence: comparison between study groups

There were 311 persons with cancers diagnosed before entry to the MEAO Mortality and Cancer Incidence study. These persons were excluded from the analysis of cancer incidence in the subsequent follow-up period. The rate of cancer diagnoses in the pre-study period was higher among the comparison group (n=158, 0.9 per 100 persons) than in the MEAO veterans (n=153, 0.5 per 100). The most common cancers to occur in the pre-study period were melanomas and testicular cancers (Annex, Table D).

Less complete records were available for the cancer incidence analysis than for the mortality analysis (Table 3.5). Complete cancer registry data for all states and territories were only available up to 31 December 2008. Therefore, to be eligible for inclusion, members must have deployed to the MEAO (or began follow-up in the comparison group) before the end of 2008. A higher proportion of the younger personnel in the comparison group had a start date after 2008. The comparison group used in cancer incidence analysis included a higher proportion of ex-serving personnel, and a higher proportion of those aged over 45, than the MEAO veterans group.

Using the 31 December 2008 cut-off, the mean follow-up periods among MEAO veterans and the comparison group were 3.5 years and 2.9 years respectively. There were 102 cancers in 83,040 person-years of follow-up in the MEAO veterans group and 89 cancers in 41,271 person-years of follow-up among the comparison group. The corresponding cancer incidence rates were 1.23 and 2.16 per 1000 person-years respectively. However, after adjustment for age and sex there was no statistically significant difference in the overall rates of cancer incidence between those who deployed to the MEAO and those who did not (Table 3.6).

Cancer incidence rates increased with age. Although the overall rate of cancer incidence was lower among MEAO veterans, MEAO veterans aged 35-44 had a higher rate of cancer than those of the same age in the comparison group.

Table 3.5: Demographic characteristics of personnel in the MEAO Mortality and Cancer Incidence study (with start date before 31 December 2008)

Characteristic	MEAO veterans group (N=23804) n	(%)	Comparison group (N=14207) n	(%)	*p*-value[a]
Age (at start of follow-up)					
17- 24	6785	(28.5)	3188	(22.4)	<0.001
25-34	10332	(43.4)	5618	(39.5)	
35-44	5153	(21.7)	3548	(25.0)	
45-54	1406	(5.9)	1485	(10.5)	
55 and over	128	(0.5)	368	(2.6)	
Sex					
Male	21194	(89.0)	12621	(88.8)	0.55
Female	2610	(11.0)	1586	(11.2)	
Service					
Navy	5875	(24.7)	3260	(23.0)	<0.001
Army	11472	(48.2)	7133	(50.2)	
Air Force	6457	(27.1)	3814	(26.9)	
Service Type (2012)[b]					
Regular	16166	(67.9)	10095	(71.1)	<0.001
Reserve	7638	(32.1)	4112	(28.9)	
Period of enlistment					
Before 2001	16012	(67.3)	9324	(65.6)	<0.001
2001-2005	6932	(29.1)	4774	(33.6)	
2006-2012	860	(3.6)	109	(0.8)	
Employee Status (2012)					
Serving	17437	(73.3)	5827	(41.0)	<0.001
Ex-serving[c]	6367	(26.7)	8380	(59.0)	

[a] Chi-squared test
[b] Last known service type as of 2012
[c] Includes Inactive Reserves

Table 3.6: Cancer incidence for MEAO veterans and comparison groups by demographic characteristics (for those with start date before 31 December 2008)

	MEAO veterans group (N=23804)			Comparison group (N=14207)			
	Cancers	Pyrs	Rate[a]	Cancers	Pyrs	Rate[a]	RR (95% CI)
Overall	102	83040	1.23	89	41271	2.16	1.05 (0.77, 1.43)[b]
Age							
17 - 24	7	12805	0.55	2	4132	0.48	1.15 (0.24, 5.54)[c]
25 - 34	20	39375	0.51	12	15347	0.78	0.65 (0.32, 1.33)[c]
35 - 44	41	23843	1.72	11	12950	0.85	2.12 (1.09, 4.13)[c]
45 - 54	26	6427	4.05	31	6623	4.68	0.84 (0.50, 1.42)[c]
55 and over	8	590	13.57	33	2219	14.87	0.91 (0.42, 1.98)[d]
Sex							
Male	88	73352	1.20	85	36339	2.34	0.97 (0.71, 1.34)[e]
Female	14	9688	1.45	4	4932	0.81	2.30 (0.74, 7.12)[e]

[a] Rate per 1000 person-years (Pyrs)
[b] Adjusted for age (10 year bands), and sex
[c] Adjusted for sex
[d] Unadjusted [no women aged 55 and over with cancer]
[e] Adjusted for age (10 year bands)

For most types of cancer considered there were no clear differences in incidence rates between the MEAO veterans and comparison groups. There was a higher incidence of male urogenital cancers in the MEAO veterans group than in the comparison group. The cancers of male urogenital organs were predominantly testicular and prostate cancers. The difference in incidence was not observed in the unadjusted rates, but once the confounding effects of age were accounted for, MEAO veterans had approximately twice the risk of male urogenital cancers (Table 3.7).

Table 3.7: Cancer Incidence for the MEAO veterans and comparison groups (for those with start date before 31 December 2008)

	MEAO veterans group (N=23804 Pyrs=83040)		**Comparison group** (N=14207 Pyrs=41271)		***Adjusted***
	Cancer	**Rate[a]**	**Cancer**	**Rate[a]**	**RR[b] (95% CI)**
Overall	102	1.23	89	2.16	1.05 (0.77, 1.43)
Digestive organs (C15 – C26)	10	0.12	14	0.34	0.79 (0.34, 1.87)
Bowel (C18-C20)	6	0.07	8	0.19	0.98 (0.31, 3.06)[c]
Skin (C43-C44)	23	0.28	20	0.48	0.87 (0.46, 1.63)
Melanoma (C43)	22	0.26	20	0.48	0.83 (0.44, 1.58)
Breast (C50)	6	0.07	0	-	-
Male urogenital organs (C60-C63)	34	0.46	21	0.58	1.99 (1.09, 3.64)[d]
Prostate (C61)	17	0.23	18	0.50	1.73 (0.85, 3.53)[d]
Testis (C62)	16	0.22	3	0.08	2.33 (0.67, 8.06)[d]
Lymphoid, haematopoietic and related tissue (C81-C96)	10	0.12	16	0.39	0.47 (0.20, 1.08)
Non- Hodgkin's Lymphoma(C82-C85)	8	0.10	5	0.12	1.28 (0.40, 4.08)
Other cancer types	19	0.23	18	0.44	0.86 (0.43, 1.72)

[a]Rate per 1000 person-years (Pyrs)
[b]Rate Ratio, adjusted for age (10 year bands), and Sex
[c]Rate Ratio, adjusted for age (10 year bands) [there were no bowel cancers among women]
[d]Rate Ratio; rate ratios calculated limited to males followed up, adjusted for age (10 year bands).

3.4 Cancer incidence: comparison with the Australian population

The overall number of cancers in the MEAO veterans group was similar to the expected number calculated from rates in the general population (Table 3.8). There were more prostate cancers in the MEAO veterans group than expected in the general population. There were also more testicular cancers in the MEAO veterans than in the general population (result not statistically significant). Although the SIRs were greater than 100 the percentage of people with these cancers was less than 0.1%. The number of prostate cancers in the MEAO group was 17 (0.08%), and the number of testicular cancers was 16 (0.08%) from a total of 21,194 men.

The number of cancers in the comparison group was also similar to the expected number based on population rates. In the comparison group there were no specific types of cancers with an excess incidence compared to the general population.

Table 3.8: Cause specific cancers for the MEAO veterans and comparison groups compared with cancer rates in the Australian population (for those with start date before 31 December 2008)

	MEAO veterans group (N=23804 Pyrs[e]=83040)			Comparison group (N=14207 Pyrs[e]=41271)		
	C[a]	E[b]	SIR[c] (95% CI)	C[a]	E[b]	SIR[c] (95% CI)
All cause	102	95.7	106.6 (87.8, 129.4)	89	82.7	107.6 (87.4, 132.5)
Bowel (C18-C20)	6	7.6	79.0 (35.5, 175.9)	8	8.1	99.1 (49.6, 198.2)
Melanoma (C43)	22	20.7	106.1 (69.9, 161.2)	20	14.2	141.0 (91.0, 218.6)
Prostate (C61) [d]	17	7.3	231.9 (144.1, 373.0)	18	14.5	124.4 (78.4, 197.5)
Testis (C62) [d]	16	10.0	159.6 (97.8, 260.5)	3	4.5	67.2 (21.7, 208.3)
Non-Hodgkin's lymphoma (C82-C85)	8	5.5	145.2 (72.6, 290.3)	5	4.1	121.7 (50.7, 292.5)

[a] Observed number of cancers
[b] Expected number of cancers
[c] Standardised Incidence Ratio per 100 persons
[d] SIRs calculated limited to males in the MEAO Cancer Incidence Study
[e] Person-years

4 Discussion

4.1 Mortality among MEAO veterans and other ADF members

The all-cause death rate among MEAO veterans was lower than the death rate in the comparison group of ADF personnel who did not deploy to the MEAO. This result was statistically significant. Lower deaths rates among MEAO veterans were also observed for specific causes of death, such as deaths from cancer, circulatory diseases and external causes. This was despite 28 of the 105 deaths among veterans having occurred on operations in the Middle East. The rate of mortality among MEAO veterans was approximately half that observed in the general population. This result was statistically significant and this deficit was observed for deaths from cancer, circulatory diseases and external causes.

In contrast, the mortality rate for the comparison group was higher than that in the general population. This increase was due in part to an excess of mortality from transport accidents in the period of follow-up.

Recent studies from the US military have shown an increase in the proportion of deaths due to suicide to the point where suicides accounted for more deaths of service members than transport accidents in 2010-2011 [4]. Among the MEAO veterans group, the rates of suicides and deaths from transport accidents were similar and about 50% lower than observed in the Australian population. In contrast, in the comparison group there was an excess of deaths from transport accidents.

4.2 Cancer incidence among MEAO veterans and other ADF members

One of the aims of the study was to assess whether those deployed to the MEAO had a higher incidence of cancer than those who did not. Given the short follow-up period for the cancer incidence analysis (mean 3.3 years) it is difficult to make such inferences about cancer incidence because a number of the observed cancers may have been present, but undetected, at the time of deployment to the MEAO. The analysis of cancer incidence data will be more valuable after a longer follow-up period. Repeating this analysis after 10 years has elapsed would identify more cancers which developed in the period after a person entered the study (or deployed to the MEAO).

There was no clear difference in the overall rate of cancer incidence between those deployed to the MEAO and the comparison group. After adjusting for age, there was a higher incidence of cancers of male urogenital organs in the MEAO veterans group than in the comparison group. The number of prostate cancers was greater among MEAO veterans than would be expected in the Australian population. Although this excess is apparent, the number of prostate cancers in the MEAO veterans group was 17 from a total of 21,194 men (0.08%). For prostate cancer in MEAO veterans, the mean person years at risk was 2.3 years. Given the natural history of prostate cancer [16], it is likely that some of these cancers were present but undetected before the MEAO deployment.

4.3 Mortality and cancer among ADF groups and the Australian population

Over the period of follow-up, the MEAO veterans had significantly lower all-cause death rates than the general population. However, there was no clear difference in overall cancer incidence between the MEAO group and the general population. The lower rate of mortality observed may be due to the healthy soldier effect as many conditions are likely to be screened out in the recruitment to the ADF. This phenomenon is less likely to be observed for cancer incidence because the factors that will predict the development of cancer cannot easily be detected on entry to the workforce[15].

4.4 Limitations of this study

It is important to consider potential sources of bias in this and future studies of mortality and cancer incidence in this ADF population.

Defence personnel who undertake operational deployment are required to be at the highest level of fitness. This has been termed the "Healthy Warrior effect". MEAO veterans must have been fit to deploy to the Middle East at the time of their deployment. The comparison group were not necessarily required to be fit to deploy over the same time period. ADF Medical Employment Classification was not used as a stratification variable in the generation of the comparison group because of difficulties accessing each member's medical classification history over the entire period 2001-2011. This may be a potential source of bias as the comparison group may be 'less healthy' than the group who deployed to the MEAO.

Although those who deployed to the MEAO had a lower death rate than those did not, it is unlikely that the deployment experience resulted in any protection from future mortality risk. More plausibly, the MEAO group were selected for deployment based on levels of physical and mental health above those required in the comparison group which has led to a difference in mortality rates between these groups in the early follow-up period. More than 33,000 ADF personnel deployed to the MEAO between 2001 and 2011. This deployment is a significant commitment for the ADF, which employs approximately 50,000 permanent full-time active duty personnel. Despite the comparison group being similar to the deployed group on the basis of service, service type, sex and enlistment period, the large scale of the deployment to the MEAO has made it difficult to select a truly comparable group of ADF personnel who did not deploy to the Middle East.

Those who left Defence reported worse physical and mental health outcomes in the MEAO Census study [5]. By January 2012, approximately 21% of the MEAO veterans group had discharged from the ADF, whereas the discharge rate among the comparison group was closer to 50%. The higher mortality rates in the comparison group who did not deploy may be due in part to a larger proportion of ex-serving personnel with poorer health.

It is possible that some deaths were not detected in the probabilistic matching procedures used in NDI data linkage. An additional 18 deaths were identified from alternative sources. Half of these missing deaths occurred overseas and 27% of deaths in the MEAO veterans occurred on the deployment. This possibility of differential ascertainment bias between the MEAO veterans and the comparison group was addressed by repeating each of the mortality analyses using deaths from all sources (Annex, Tables A-C). However, these supplementary tables produced very similar estimates and conclusions to the NDI linkage.

The average follow-up period was 5.2 years for all-cause mortality, 4.3 years for cause-specific mortality and 3.3 years for cancer incidence. This length of follow-up is useful to observe the death and cancer rates in the period immediately following deployment to the MEAO, however, it may be premature to interpret many of the results without resorting to speculation. Longer term follow-up will allow more informative and specific comparisons, with greater power to detect true effects.

4.5 Implications for future research

The average age at the beginning of follow-up in this analysis was 31 years. Cancer cases, cancer deaths, and circulatory disease deaths with sufficient numbers to make meaningful comparisons are not likely to be observed until much older ages. For example, the incidence of many types of cancer increases markedly above the age of 50 and may continue to increase with age. In the cancer incidence analyses, which used the cut-off date of 31 December 2008, the MEAO veterans group was followed-up for an average of 3.5 years, whereas the comparison group was observed for 2.9 years. This difference may have contributed to the higher incidence of cancers recorded among veterans. When cut-off dates later than 2008 were used in the analyses of mortality data, this difference in follow-up time between the study groups was no longer present. It is expected that this bias will decrease in subsequent analyses of cancer incidence.

The deployment to the MEAO is ongoing. The time lag between death and notification of cause of death means that MEAO veterans who deployed for the first time after May 2010 were not included in the cause-specific mortality analysis. Likewise, those who deployed for the first time after December 2008 were not included in the analyses of cancer incidence. Repeating the analyses of mortality and cancer incidence among the MEAO veterans group at 4-5 years after the cessation of Middle East deployments should enable the inclusion of all those who deployed. For future analyses it is recommended that the MEAO nominal roll be updated to include members deployed for the first time after January 2012. Likewise, the comparison group should be updated to transfer those who subsequently deployed to the MEAO into the MEAO veterans group and to add additional comparisons with similar characteristics to those who deployed after January 2012. At present there is a greater proportion of those aged 25-34 and fewer persons aged above 45 in the MEAO veterans group relative to the comparisons (Table 3.1). If this imbalance between the age groups is still present once the nominal roll has been updated, corrective sampling procedures (such as proportional sampling methods based on age group) should be considered when updating the comparison group.

The current analyses count person-years at risk from the day a MEAO veteran first deployed to the Middle East. Once Australia's deployment to the MEAO has finished and the complete MEAO deployment records for each ADF member are finalised, it may be possible to adjust the start of follow-up in this study to represent the last date of return from the Middle East. Such an adjustment would result in removing deaths that occurred in the MEAO from the primary analysis.

5 Summary, conclusions and recommendations

The MEAO veterans group has a lower rate of mortality than a frequency matched comparison group of ADF who did not deploy to the MEAO. This may be due in part to a "Healthy Warrior Effect" of healthier ADF members selected for deployment to the MEAO.

The mortality rate among the MEAO veterans group was lower than that observed in the Australian population of the same age. However, among the comparison group which included more ex-serving personnel, the death rate was higher than that of the general population.

The MEAO veterans group had a similar level of cancer incidence to the frequency matched comparison group of ADF personnel who did not deploy to the MEAO. Cancer rates were also similar for both the MEAO veteran and comparison groups and the Australian population.

The comparisons presented in this report are based on relatively short follow-up periods of between 3.3 and 5.2 years, so these results should be interpreted with caution. In the analysis of cancer incidence, longer follow-up in the MEAO group may have contributed to a higher incidence of cancers being recorded relative to the comparison group.

Further follow-up will add increased statistical power and allow more specific research questions to be addressed. This study has established a sound baseline and methodology to enable continued regular follow-up, allowing a clearer picture of the health outcomes of MEAO veterans, veterans of other conflicts, and ADF members generally, to emerge.

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